

# openheart Differences in treatment and clinical outcomes in patients aged $\geq 75$ years compared with those aged $\leq 74$ years following acute coronary syndromes: a prospective multicentre study

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## ABSTRACT

**Objective** This study describes the differences in treatment and clinical outcomes in patients aged  $\geq 75$  years compared with those aged  $\leq 74$  years presenting with acute coronary syndrome (ACS) and undergoing invasive management.

**Methods** A large-scale cohort study of patients with ST-elevation/non-ST-elevation myocardial infarction (MI)/unstable angina underwent coronary angiography (January 2015–December 2019). Patients were classified as older ( $\geq 75$  years) and younger ( $\leq 74$  years). Regression analysis was used to yield adjusted risks of mortality for older versus younger patients (adjusted for history of heart failure, hypercholesterolaemia, peripheral vascular disease, chronic obstructive pulmonary disease, ischaemic heart disease, presence of ST-elevation MI on presenting ECG, female sex and cardiogenic shock at presentation).

**Results** In total, 11 763 patients were diagnosed with ACS, of which 39% were aged  $\geq 75$  years. Percutaneous coronary intervention was performed in fewer older patients than younger patients (81.2% vs 86.2%,  $p < 0.001$ ). At discharge, older patients were prescribed less secondary-prevention medications than younger patients. Median follow-up was 4.57 years. Older patients had a greater risk of in-hospital mortality than younger patients (adjusted OR (aOR) 2.12, 95% CI 1.62 to 2.78,  $p < 0.001$ ). Older patients diagnosed with ST-elevation MI had greater adjusted odds of dying in-hospital (aOR 2.47, 95% CI 1.79 to 3.41,  $p < 0.001$ ). Older age was not an independent prognostic factor of mortality at 1 year (adjusted HR (aHR) 0.95, 95% CI 0.82 to 1.09,  $p = 0.460$ ) and at longer term (aHR 0.98, 95% CI 0.87 to 1.10,  $p = 0.684$ ).

**Conclusions** Older patients are discharged with less secondary prevention. Patients aged  $\geq 75$  years are more likely to die in-hospital than younger patients.

## INTRODUCTION

Acute coronary syndrome (ACS) is a leading cause of morbidity and mortality worldwide. A global ageing population makes cardiovascular disease an even greater challenge.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Acute coronary syndrome (ACS) is a leading cause of morbidity and mortality. Observational studies have shown that older adults are more likely to suffer an ACS event; however, there are few clinical trials to support guideline-directed medical and interventional management. There is a gap in the current knowledge on the treatment and short-term/long-term outcomes of older adults suffering an ACS event.

## WHAT THIS STUDY ADDS

⇒ This study describes the medical and interventional management, short-term and long-term outcomes of patients aged over 75 years with ACS. This study shows that older patients are provided fewer medical therapeutic options than younger patients. This study also shows that older patients are more likely to die in hospital than younger patients.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There currently exists very few clinical trials, which govern guideline-directed optimal therapy in older patients. This observational study provides new insight into the importance of such trials and will undoubtedly help support future changes to current clinical guidelines.

Registry data suggest that older adults  $\geq 75$  years of age represent approximately 30% of ST-elevation myocardial infarction (STEMI) cases and 40% of non-STEMI (NSTEMI) cases in European hospitals.<sup>1 2</sup> Despite this large burden of older adults presenting with ACS to cardiac units, most of the knowledge gaps in the current literature exist in older adults age group  $\geq 75$  years<sup>3</sup> and the majority of clinical trials recruit patients aged  $< 75$  years. Thus, data to generate quality standards of healthcare for older adults with coronary

disease are insufficient. Therefore, it is not surprising that a considerable number of older patients do not receive guideline-directed medical therapy following ACS.

ACS in older adults may be complicated by the increased likelihood of concomitant comorbidities. It is well established that ACS in older patients frequently occurs in those with a greater comorbidity burden.<sup>4</sup> Older patients are at risk of being affected by geriatric syndromes, which encompasses frailty, multimorbidity, cognitive impairment, functional decline, nutritional deficiencies and polypharmacy,<sup>5–9</sup> which are in turn directly associated with cardiovascular disease and influence the multidisciplinary team decision for management of these patients.

Medical therapy of ACS frequently imposes a tablet burden on patients of all ages. Older adults are at particularly greater risk of bleeding from antiplatelet and anticoagulation therapy, falls and syncope secondary to antihypertensive therapy, as well as bradycardia and chronotropic incompetence secondary to beta-blockade.<sup>10 11</sup> Moreover, there is limited evidence to the short-term and long-term clinical outcomes for ACS patients aged  $\geq 75$  years.<sup>12</sup> This study describes the differences in treatment and clinical outcomes in patients aged  $\geq 75$  years compared with those aged  $\leq 74$  years presenting with ACS and undergoing invasive management.

## METHODS

The database, variables and methods of analysis used in this study have been presented previously by our research group.<sup>13</sup>

### Study design, setting and participants

This is a cohort study of patients between 1 January 2015 and 31 December 2019 with a presenting diagnosis of STEMI and NSTEMI and unstable angina that underwent invasive coronary angiography at a high-volume cardiac centre; the Freeman Hospital, Newcastle upon Tyne Hospitals National Health Service (NHS) Foundation Trust, UK. The Freeman Hospital receives patients referred from six district hospitals covering a population of 2 million with an annual percutaneous coronary intervention (PCI) procedure volume of  $\sim 3000$  cases (60%–65% ACS cases). Participants were classified based on their age at the point of admission, older patients were aged  $\geq 75$  years and younger patients were  $\leq 74$  years.

### Variables and data sources

Baseline data for consecutive admissions with ACS were prospectively collected in the British Cardiovascular Intervention Society database for all patients including the full procedural data. ACS diagnosis included STEMI, NSTEMI and unstable angina. Variables include age and sex; family history of coronary artery disease; medical history including history of cerebrovascular disease, heart failure, hypercholesterolaemia, hypertension, peripheral vascular disease, chronic kidney disease, diabetes mellitus, chronic obstructive pulmonary disease (COPD), angina, MI, coronary artery bypass grafting (CABG); smoking

status; baseline ECG; intervention performed in catheter laboratory. Discharge medication details were obtained from the electronic clinical record as listed at the point of discharge.

In-hospital complications were prospectively collected from the patient's electronic records, which included in-hospital mortality, emergency CABG, stroke any MI, cardiac tamponade, any arterial complication, renal failure defined as any acute kidney injury, any other complication (referral for urgent CABG, requirement for a blood transfusion, required reintervention, gastrointestinal (GI) bleed). Procedural specific complications include coronary artery perforation or dissection, arterial branch occlusion, emergency direct-current cardioversion required during procedure, stent-specific complication, cardiogenic shock, any other (no coronary artery flow, aortic dissection, heart block requiring pacing).

Long-term follow-up data were collected using the Summary Care Records (SCR), NHS Digital and tertiary centre hospital electronic patient records. SCR is an electronic record of important patient information, created from primary care physician medical records. The primary outcome was all-cause mortality censored at the point of discharge (in-hospital), 1-year postdischarge and longer-term follow-up. Secondary outcome was first emergency readmission with MI, heart failure or non-elective PCI during follow-up.

### Statistical methods

Normally distributed variables are presented as mean and SD, and proportions as count and percentage. Student's t-test was used to compare continuous variables and  $\chi^2$  or Fisher's exact test for proportions as appropriate. Mann-Whitney U test was used for non-normally distributed variables. Non-parametric data were presented as median and IQR.

Stepwise logistic regression and Cox proportional-hazards model with backwards elimination were used to analyse the association between age and mortality stratified by ACS diagnosis for in-hospital, and 1-year/long-term mortality, respectively. All variables included in the baseline descriptive statistics were included in the initial pool of variables and were eliminated based on a p value threshold of  $p < 0.05$ . Adjusted OR and HR estimates with 95% CI were reported for the final retained variables used in the regression models, which included age, female sex, family history of coronary artery disease, previous heart failure, hypercholesterolaemia, peripheral vascular disease, COPD, angina, MI, CABG, ST-elevation on baseline ECG, presence of cardiogenic shock on admission. Stepwise model coefficients were tested using  $\chi^2$  tests, goodness of fit and proportionality of hazards were checked to test the regression models used. Cumulative survival for longer-term follow-up was described for patients younger and older. The log-rank test was used to assess differences in mortality. A  $p < 0.05$  was considered statistically significant. SPSS V.27 (IBM) was used for all analyses.

**Table 1** Baseline characteristics

		Age (n=11 763)				P value
		≤74 years (n=7204)		≥75 years (n=4559)		
ACS diagnosis						
	All, n (%)	7204	(100)	4559	(100)	<0.001
	STEMI, n (%)	2931	(41)	1435	(31)	<0.001
	NSTEMI, n (%)	3461	(48)	2693	(59)	<0.001
	Unstable angina, n (%)	812	(11)	431	(9)	0.001
Patient characteristics						
Age, years	Mean (SD)	62	(8.4)	83	(5.7)	<0.001
Sex	Male, n (%)	5444	(76)	2759	(61)	<0.001
	Female, n (%)	1760	(24)	1798	(39)	<0.001
Family history CAD, n (%)		3567	(50)	1373	(30)	<0.001
Past medical history	CVD, n (%)	366	(5)	459	(10)	<0.001
	HF, n (%)	121	(2)	192	(4)	<0.001
	Hypercholesterolaemia, n (%)	3399	(47)	2258	(50)	0.013
	Hypertension, n (%)	3756	(52)	3224	(71)	<0.001
	PVD, n (%)	389	(5)	357	(8)	<0.001
	CKD, n (%)	70	(1)	30	(1)	–
	DM, n (%)	1592	(22)	1249	(27)	<0.001
	COPD, n (%)	575	(8)	607	(13)	<0.001
	Angina, n (%)	1930	(27)	1782	(39)	<0.001
	Previous MI, n (%)	1624	(23)	1450	(32)	<0.001
Smoking status	Previous CABG, n (%)	230	(3)	370	(8)	<0.001
	Non-smoker, n (%)	2170	(30)	1740	(38)	<0.001
	Current smoker, n (%)	2501	(35)	377	(8)	<0.001
Baseline ECG	STEMI, n (%)	2827	(39)	1359	(30)	<0.001
	NSTEMI, n (%)	4377	(61)	3200	(70)	<0.001
Procedural characteristics						
Intervention	Angiogram only, n (%)	991	(13.8)	855	(18.8)	<0.001
	PCI performed, n (%)	6213	(86.2)	3704	(81.2)	<0.001
Arterial access	RRA, n (%)	6237	(87)	3655	(80)	<0.001
	RFA, n (%)	630	(9)	617	(14)	<0.001
	Other, n (%)	327	(5)	278	(6)	<0.001
PCI findings	Left main disease, n (%)	590	(9)	747	(20)	<0.001
	RCA disease, n (%)	3899	(63)	2787	(75)	0.021
	Single vessel disease, n (%)	3944	(63)	2174	(58)	<0.001
	Multivessel disease, n (%)	2289	(37)	1547	(42)	<0.001

'–' represents inability to test for significant differences due to one or more variables containing zero count.

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; DM, diabetes mellitus; HF, heart failure; MI, myocardial infarction; NSTEMI, non-STEMI; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery; RFA, right femoral artery; RRA, right radial artery; STEMI, ST-elevation myocardial infarction.

## RESULTS

### Baseline characteristics

In total, 11 763 patients were admitted with ACS during the study period, of which 39% of patients were aged

≥75 years (mean age 83 years) (table 1). Older patients were less likely than younger patients to be diagnosed with STEMI (30% vs 39%,  $p<0.001$ ), but more likely to be diagnosed with NSTEMI (70% vs 61%,  $p<0.001$ ). There

**Table 2** Complications by age

	≤74 years		≥75 years		P value
	(n=7204)		(n=4559)		
<b>In-hospital complications</b>					
All complications, n (%)	243	(3.4)	277	(6.1)	<0.001
In-hospital mortality, n (%)	124	(1.7)	160	(3.5)	<0.001
Emergency CABG, n (%)	11	(0.2)	8	(0.2)	–
Stroke, n (%)	4	(0.1)	17	(0.4)	<0.001
MI, n (%)	7	(0.1)	2	(0.0)	<0.001
Renal failure, n (%)	1	(0.0)	4	(0.1)	–
Any other, n (%)	96	(1.3)	86	(1.9)	0.033
<b>Procedural complications</b>					
All-complications, n (%)	214	(3.0)	170	(3.8)	<0.001
Perforation/dissection, n (%)	99	(1.4)	83	(1.8)	0.095
Side branch occlusion, n (%)	18	(0.2)	18	(0.4)	–
DCCV required, n (%)	12	(0.2)	7	(0.2)	–
Stent complication, n (%)	8	(0.1)	3	(0.1)	–
Tamponade, n (%)	3	(0.0)	7	(0.2)	0.042
Arterial complication, n (%)	2	(0.0)	3	(0.1)	–
Shock, n (%)	2	(0.0)	1	(0.0)	–
Any other, n (%)	70	(1.0)	48	(1.1)	0.01

'–' represents inability to test for significant differences due to one or more variables containing zero count. CABG, coronary artery bypass grafting; DCCV, direct current cardioversion; MI, myocardial infarction.

was male predominance in both age categories (76% of younger patients, 61% of older patients), but significantly more women were ≥75 years (39% vs 24%,  $p<0.001$ ) (table 1).

Older patients less frequently had a family history of coronary artery disease (30% vs 50%,  $p<0.001$ ) and were more likely to be non-smokers (than younger patients 38% vs 30%,  $p<0.001$ ), table 1. In comparison to younger patients, older patients more frequently had history of cerebrovascular disease (10% vs 5%,  $p<0.001$ ), heart failure (4% vs 2%,  $p<0.001$ ), hypercholesterolaemia (50% vs 47%,  $p=0.013$ ), peripheral vascular disease (8% vs 5%,  $p<0.001$ ), diabetes mellitus (27% vs 22%,  $p<0.001$ ), COPD (13% vs 8%,  $p<0.001$ ) and evidence of ischaemic heart disease such as angina (39% vs 27%,  $p<0.001$ ), previous MI (32% vs 23%,  $p<0.001$ ) and previous CABG (8% vs 3%,  $p<0.001$ ) (table 1).

### Angiography and PCI

Angiographic and procedural data are shown in table 1. Older patients experienced greater in hospital complications than younger patients (6.1% vs 3.4%,  $p<0.001$ ) (table 2). Older patients, in comparison to younger patients, were more likely to die in-hospital (3.5% vs 1.7%,  $p<0.001$ ), as well as experience stroke or other complications such as cardiac tamponade, GI bleeding, symptomatic anaemia requiring blood transfusion and repeat coronary intervention. Older patients more

frequently experienced complications secondary to angiographic procedures than younger patients (3.8% vs 3.0%,  $p<0.001$ ).

### Secondary prevention therapy

Older patients were prescribed secondary prevention medication less frequently than younger patients (table 3). This included aspirin (87% vs 94%,  $p<0.001$ ), beta-blocker (81% vs 87%,  $p<0.001$ ), ACE inhibitor or angiotensin receptor blockers (ARB (81% vs 89%,  $p<0.001$ ) and statin 86% vs 92%,  $p<0.001$ ). Older patients were prescribed a second antiplatelet such as clopidogrel or prasugrel less frequently than younger patients (45% vs 53%,  $p<0.001$ ). However, there was no difference in the frequency of prescription of ticagrelor. Aldosterone antagonists were prescribed in less than 10% of patients admitted with ACS.

### Follow-up

Median follow-up for younger and older patients was 4.57 years and 5.01 years, respectively. For all patients diagnosed with ACS, older patients were more likely than younger patients to have an emergency hospital readmission within the follow-up period (22.7% vs 17.3%,  $p<0.001$ ). Older patients diagnosed with STEMI were less likely to be readmitted than younger patients (4.7% vs 5.8%,  $p=0.043$ ), and more likely to be readmitted following NSTEMI (17.7% vs 11.2%,  $p<0.001$ ).

**Table 3** Discharge medication by age

	≤74 years (n=7204)		≥75 years (n=4559)		P value
ACEi/ARB, n (%)	6423	(89)	3689	(81)	<0.001
Aldosterone antagonist, n (%)	498	(7)	284	(6)	–
Aspirin, n (%)	6761	(94)	3965	(87)	<0.001
Beta-blocker, n (%)	6288	(87)	3686	(81)	<0.001
Clopidogrel/Prasugrel, n (%)	3809	(53)	2064	(45)	<0.001
Statin, n (%)	6636	(92)	3928	(86)	<0.001
Ticagrelor, n (%)	2850	(40)	1874	(41)	–

‘–’ represents inability to test for significant differences due to one or more variables containing zero count.  
ARB, angiotensin receptor blockers.

Readmission was most commonly secondary to MI, which was overall more prevalent in older patients compared with younger (13.1% vs 12.4%,  $p<0.001$ ). There was no difference in the time to first emergency hospital readmission between older and younger patients (mean (SD)) 1.65 (1.4) vs 1.68 (1.4) years.

For all those diagnosed with ACS, mortality was greater in older patients than younger patients, which was consistent throughout follow-up (in-hospital: 3.7% vs 1.8%,  $p<0.001$ ; 1 year 12.8% vs 4.2%,  $p<0.001$ ; long term 21% vs 6.4%,  $p<0.001$ ) (table 4). Older patients had a greater chance of mortality during follow-up regardless of the presenting diagnosis (STEMI or NSTEMI), cumulative survival is shown in figure 1. Older patients had a steeper increase in mortality within the first-year postdischarge, followed by a plateau in mortality for the duration of follow-up, which was similar to younger patients.

The unadjusted OR of dying in hospital was significantly greater for older patients compared with younger patients (OR 2.13, 95% CI (1.69 to 2.69)  $p<0.001$ ) (table 5). When adjusted for confounders there remained an increased chance of dying in hospital for older patients (adjusted OR 2.12, 95% CI 1.62 to 2.78,  $p<0.001$ ), particularly those diagnosed with STEMI (adjusted OR 2.47, 95% CI 1.79 to 3.41,  $p<0.001$ ). There was no difference between older and younger patients in the adjusted risk of dying during follow-up at 1 year (adjusted HR 0.95, 95% CI 0.82 to 1.09,  $p=0.460$ ) and longer term (adjusted HR 0.98, 95% CI 0.87 to 1.10,  $p=0.684$ ).

The independent factors for mortality in our population stratified by ACS diagnoses at 1-year and long-term follow-up are presented in online supplemental table 1. At 1-year and long-term follow-up, mortality in older patients was significantly associated with previous heart failure, hypercholesterolaemia, a history of angina or CABG, ST-elevation on baseline ECG and cardiogenic shock on admission. Online supplemental table 2 shows the independent risk factors for mortality in older patients only. Similar to the total population, mortality in older patients at 1 year and long-term follow-up was significantly associated with previous heart failure, hypercholesterolaemia, a history of angina, ST-elevation on baseline ECG and cardiogenic shock on admission.

## DISCUSSION

This large-scale observational study of 11 763 patients admitted with ACS represents a 4-year sample period of patients presenting to a large cardiac intervention centre in the Northeast of England. We have shown that approximately 40% of patients presenting with ACS were aged ≥75 years.

The important findings of this study are that older patients versus younger patients with ACS:

1. Have a greater comorbidity burden.
2. Are less frequently prescribed secondary prevention medication.
3. Experience greater in-hospital and procedural complications.
4. Are more likely to have an emergency hospital readmission.
5. Have greater adjusted odds of dying in-hospital but have the same adjusted risk of mortality at 1 year and during long-term follow-up.

This study showed that patients (figure 2) aged over 75 years were more likely to be diagnosed with NSTEMI and younger patients more likely to be diagnosed with STEMI. This difference likely represents the differing age-related mechanisms by which ACS manifests. Physiological ageing results in specific cellular and extracellular matrix changes. Older patients thus have stiffer ventricular walls resulting in ventricular hypertrophy and resulting increased metabolic demand, which when coupled with impaired diastolic coronary perfusion pressures and endothelial dysfunction results in a metabolic supply-demand imbalance.<sup>14 15</sup> Such physiological changes secondary to ageing demonstrate that coronary perfusion autoregulation is more likely to be impaired in an aged myocardium, which therefore increases the risk of NSTEMI in older patients. In our study, 70% of older patients presented with baseline ECG changes consistent with NSTEMI, which may be explained by the above physiological processes. However, it is well described that older adults in the clinical setting have demonstrable abnormalities on their ECG regardless of an acute presentation, which may complicate interpretation in suspected ACS.<sup>16</sup>

**Table 4** Outcomes by age

		≤74 years (n=7204)		≥75 years (n=4559)		P value
Emergency hospital readmission						
ACS	All-cause, n (%)	1249	(17.3)	1033	(22.7)	<0.001
	MI, n (%)	890	(12.4)	598	(13.1)	<0.001
	HF, n (%)	346	(4.8)	428	(9.4)	<0.001
	PCI, n (%)	13	(0.2)	6	(0.1)	–
STEMI	All-cause, n (%)	417	(5.8)	213	(4.7)	0.043
	MI, n (%)	296	(4.1)	128	(2.8)	0.007
	HF, n (%)	119	(1.7)	83	(1.8)	0.011
	PCI, n (%)	2	(0.0)	2	(0.0)	0.391
NSTEMI	All-cause, n (%)	809	(11.2)	807	(17.7)	<0.001
	MI, n (%)	587	(8.1)	468	(10.3)	<0.001
	HF, n (%)	214	(3.0)	335	(7.3)	<0.001
	PCI, n (%)	8	(0.1)	4	(0.1)	0.444
Time to emergency readmission						
ACS	Mean, years (SD)	1.68	(1.4)	1.65	(1.5)	0.696
STEMI	Mean, years (SD)	1.67	(1.4)	1.61	(1.4)	0.697
NSTEMI	Mean, years (SD)	1.69	(1.4)	1.67	(1.5)	0.738
Mortality						
ACS	In-hospital, n (%)	127	(1.8)	168	(3.7)	<0.001
	1 year, n (%)	306	(4.2)	585	(12.8)	<0.001
	Long term, n (%)	461	(6.4)	959	(21.0)	<0.001
STEMI	In-hospital, n (%)	95	(1.3)	126	(2.8)	<0.001
	1 year, n (%)	164	(2.3)	273	(6.0)	<0.001
	Long term, n (%)	202	(2.8)	358	(7.9)	<0.001
NSTEMI	In-hospital, n (%)	32	(0.4)	39	(0.9)	0.031
	1 year, n (%)	135	(1.9)	308	(6.8)	<0.001
	Long term, n (%)	247	(3.4)	592	(13.0)	<0.001

'–' represents inability to test for significant differences due to one or more variables containing zero count.

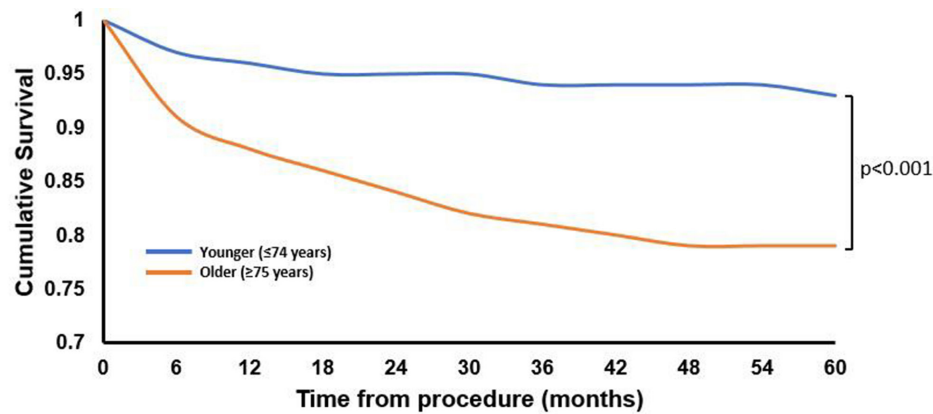
ACS, acute coronary syndrome; HF, heart failure; NSTEMI, non-STEMI; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

Older patients had a greater frequency of comorbidities for all variables studied. This includes greater frequency of past medical conditions such as stroke, heart failure and ischaemic heart disease (angina, MI), as well as conditions that increase cardiovascular risk including hypertension, hypercholesterolaemia and diabetes. Multimorbidity is defined as the presence of two or more chronic conditions, a characteristic ubiquitous in older adults with cardiovascular disease.<sup>17</sup> Of concern, almost 50% of patients presenting with ischaemic heart disease had greater than 5 comorbidities.<sup>18</sup> ACS in older adults frequently occurs in the context of multiple comorbidities, which in turn is associated with a greater risk of geriatric syndrome prevalence. Together these likely contribute to poorer outcomes for these patients.<sup>19</sup>

Older patients were less frequently prescribed secondary prevention medication in comparison to

younger patients. Current guidelines for medical therapy of ACS do not stipulate age-specific treatment strategies, thus medical therapy should be ubiquitous to all adults. Due to the lack of clinical trials focused specifically on older patients, prescribing in older adults becomes even more focused on risk–benefit balance and the potential impact of polypharmacy on the person. Polypharmacy is defined as the concomitant use of ≥5 chronically prescribed medications and has implications on patients both socially (eg, increasing risk of falls and reduced mobility) as well as medically (eg, increased prevalence of drug–drug and drug–disease interactions).<sup>20</sup>

Antiplatelet agents (aspirin, clopidogrel and prasugrel) were prescribed less frequently in older patients. There were no differences in the prescription of ticagrelor, which was prescribed with much less frequency. This trend may represent caution by clinicians due to the



Number at risk												
Months		0	6	12	18	24	30	36	42	48	54	60
Younger (≤74 years)		7204	6969	6907	6865	6844	6340	5356	4540	3852	3169	1425
Older (≥75 years)		4559	4127	3996	3922	3833	3574	3080	2640	2287	1945	891

**Figure 1** Cumulative survival older versus younger patients

increased bleeding risk in older adults. Clopidogrel has been shown to have the same cardiovascular outcome benefit as prasugrel and ticagrelor with less bleeding risk in older patients.<sup>21 22</sup> A limitation of this study is that the extracted data are coded as ‘clopidogrel/prasugrel’ and do not distinguish between the two, thus we are unable to extract specific prescription frequencies. The frequency of prasugrel prescription in older patients is significantly lower due to the cautions around serious bleeding risks in those aged over 75 years.<sup>10</sup> Statin prescription was lower in older patients, despite these patients have a greater frequency of hypercholesterolaemia. Evidence suggests that statins are safe and effective in reducing

adverse cardiovascular outcome in older patients with ACS, similar to younger patients.<sup>23</sup> Statins are often used to reduce cardiovascular risk over a 10-year period, thus clinicians may consider the prescription in older patients futile, however, it remains important to find the right balance of risk-benefit when prescribing for older patients.

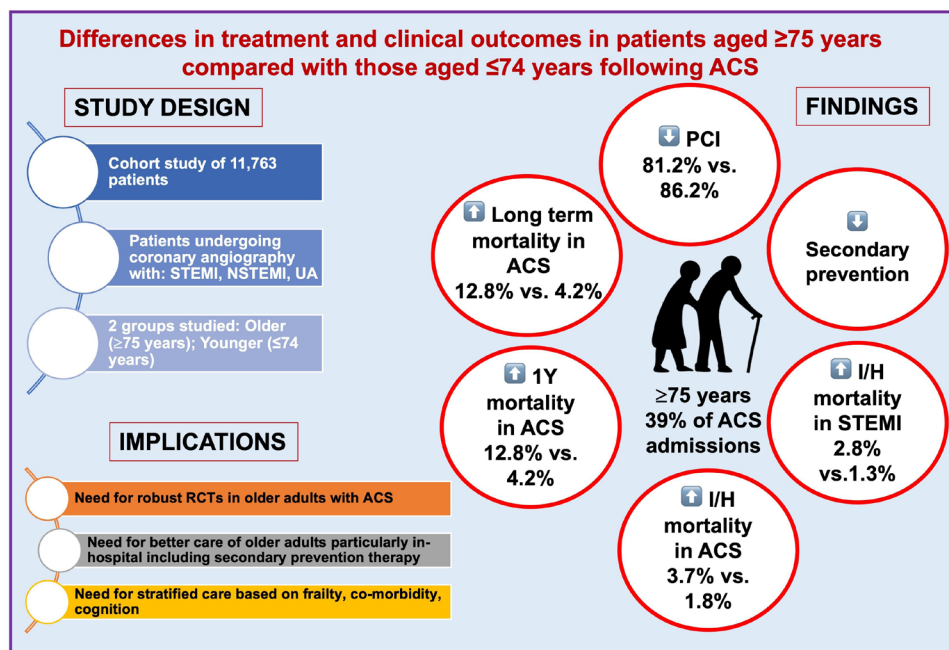
ACE inhibitors and ARB prescribed post-ACS are known to improve long-term outcomes and reduce ventricular dysfunction<sup>24</sup>; however, as seen in this study, they are frequently underprescribed in older patients due to their negative effects on renal function and blood pressure (BP). Similarly, beta-blockers are well known to

**Table 5** Mortality in older patients (≥75) compared with younger (≤74, reference group), stratified by diagnosis

		Unadjusted OR				Adjusted* OR			
		OR	95% CI		P value	OR	95% CI		P value
			Upper	Lower			Upper	Lower	
In-hospital	ACS	2.13	1.69	2.69	<0.001	2.12	1.62	2.78	<0.001
	STEMI	2.87	2.18	3.78	<0.001	2.47	1.79	3.41	<0.001
	NSTEMI	1.67	1.04	2.66	0.033	1.29	0.77	2.15	0.329
		Unadjusted HR				Adjusted* HR			
		HR	95% CI		P value	HR	95% CI		P value
			Upper	Lower			Upper	Lower	
1 year	ACS	0.85	0.74	0.98	0.023	0.95	0.82	1.09	0.460
	STEMI	0.85	0.70	1.04	0.109	0.95	0.77	1.17	0.658
	NSTEMI	0.92	0.75	1.13	0.445	0.89	0.72	1.09	0.274
Long term	ACS	0.92	0.82	1.02	0.138	0.98	0.87	1.10	0.684
	STEMI	0.92	0.77	1.09	0.335	0.98	0.82	1.18	0.838
	NSTEMI	0.98	0.84	1.14	0.786	0.95	0.82	1.11	0.537

\*Adjusted for: female sex, family history of coronary artery disease, previous heart failure, hypercholesterolaemia, peripheral vascular disease, COPD, angina, MI, CABG, ST-elevation on baseline ECG, presence of cardiogenic shock on admission.

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; NSTEMI, non-STEMI; STEMI, ST-elevation myocardial infarction.



**Figure 2** Central illustration. ACS, acute coronary syndrome; NSTEMI, non-STEMI; PCI, percutaneous coronary intervention; RCT, randomised controlled trial; STEMI, ST-elevation myocardial infarction UA, unstable angina.

improve long-term outcomes in ACS patients due to their anti-ischæmic and antiarrhythmic properties. However, side effects such as bradycardia and chronotropic incompetence frequently impede their longevity of prescription in older patients. Interestingly, a recent observational study in patients aged  $\geq 65$  years demonstrated that beta-blockers may provide no additional benefit to long-term cardiovascular outcomes to patients after 3 years post-ACS.<sup>25</sup> More work is needed to understand the short-term and long-term impact of such medical management in the older person.

This study has shown that older patients are more likely than younger patients to be readmitted with MI or heart failure post-ACS. Large-scale observational studies and subsequent meta-analyses have studied invasive management for ACS in older patients, which has revealed a reduced risk of hospitalisation but does not affect overall mortality.<sup>26</sup>

This study shows older patients are more likely to die than younger patients. This study has shown that when we adjusted for such confounders then older age was not independently associated with the risk of 1-year and long-term mortality. Other factors such as previous heart failure, hypercholesterolaemia, a history of angina or CABG, ST-elevation on baseline ECG and cardiogenic shock on admission were associated with the risk of 1-year and long-term mortality.

Older patients, by definition, are at greater risk of mortality than younger patients, which may be compounded by factors such as premorbid functional, frailty status and comorbidities beyond age alone.<sup>6,27</sup> There remain very few clinical trials or observational studies investigating long-term outcomes post-ACS in older people, and therefore, it is challenging to discuss

this finding in a wider context. The SENIOR-RITA trial randomised adults aged  $\geq 75$  years with NSTEMI to invasive or conservative management. This trial will more reliably inform practice in older patients with NSTEMI and provide important information on the effect of geriatric syndromes in this context.<sup>28</sup>

### STRENGTHS AND LIMITATIONS

This study describes important shortcomings in the management and clinical outcomes of a large cohort of older patients following ACS. Other strengths include the robust and extensive reporting of demographic, procedural and outcome data from this large sample of patients with long-term follow-up. However, we acknowledge potential limitations of our work. A limitation of this study is that we do not have access to coding for the full scope of geriatric syndromes such as frailty data, baseline functional status or cognitive function, which would lend greater power to the effect of comorbidity on this patient cohort. We describe differences in the prescription of secondary prevention in older patients versus younger patients following ACS, however, due to the limitations of using coded data we were unable to assess whether there may be valid clinical reasons for not prescribing in certain circumstances for example, less ACEi or beta-blocker used in the presence of low BP or postural hypotension. Unfortunately, due to restrictions with data coding, we are unable to provide an extended analysis of cardiovascular mortality or the extent to the underlying diagnoses for emergency hospital readmissions. Regardless of these limitations, we present important findings, which will influence the direction of future management of older patients with ACS.



## CONCLUSION

This large-scale cohort study showed that 39% of ACS patients were aged  $\geq 75$  years, significantly more comorbid and received differential management to younger patients. Furthermore, older patients were more likely to suffer in hospital complications and had higher in-hospital, 1-year and long-term mortality than younger patients. However, older age was not an independent factor of 1-year and long-term mortality. Currently, there is no definitive evidence from randomised clinical trials for the optimal management of ACS in older patients. Thus, clinical decision-making should be person-centred and considered on a case-by-case basis involving the multi-disciplinary team, pharmacy, patient, family/caregiving staff in order to provide the best quality management for this vulnerable patient group.

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