Multimorbidity and Readmissions in Older People with Acute Coronary Syndromes

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Keywords

Acute coronary syndromes · Over 70 years of age · Multimorbidity · Readmissions

Abstract

Aims: This study aimed to examine the multimorbidity as well as the 30-day and 1-year readmission rates in a large, unselected cohort of elderly patients with acute coronary syndrome (ACS). **Methods and Results:** All patients ≥ 70 years hospitalized due to ACS during January 1, 2006, to December 31, 2013, and registered in the SWEDEHEART registry were included. In-hospital multimorbidity and disease burden were determined. Outcomes included 30-day and 1-year all-cause mortality, any readmission, and readmissions due to ACS, heart failure, ischaemic stroke or transient ischaemic attack (TIA), and bleeding events. Out of 80,176 patients, 25.6% had ST-elevation myocardial infarction (STEMI) and 74.4% non-ST-segment elevation ACS (NSTEMI). The mean age was 79.8 (± 6.4 standard deviation) and 43.4%

were women. Multimorbidity, or two chronic diseases, was present in 67.7%, thereof in 53.0% of STEMI patients and 72.7% of NSTEMI patients. In-hospital mortality was 7.0%. Of the 74,577 patients who survived to discharge, 24.6% were readmitted within 30 days and 59.5% were readmitted during the following year. Multimorbid patients had a higher risk of readmissions than those without multimorbidity. Multimorbid STEMI patients were admitted the following year in 56.2% of cases compared to 44.5% of STEMI patients without multimorbidity, adjusted odds ratio (OR) 1.35 (95% confidence interval: 1.26–1.45). Multimorbid patients with NSTEMI were readmitted in 63.4% of cases the following year compared with 49.1% of those without multimorbidity, adjusted OR 1.42 (1.35–1.50). More than half of the readmissions were due to cardiovascular causes (ACS, stroke, TIA, or heart failure) or bleeding events. **Conclusions:** Older people with ACS have a high multimorbidity burden and a high readmission rate both within 30 days and 1 year. Half of the readmissions were due to a cardiovascular event or a bleeding event. The presence of multimorbidity increases the risk

of readmissions for patients with ACS. As hospital admissions are costly for the health care system and can include risks, especially for older patients, there may be opportunities in better risk stratifying this group at discharge for subsequent decrease in readmission rates.

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Introduction

Worldwide, the population is ageing, and in a few decades, older patients will be an even more predominant group in health care [1]. Already around 60% of hospitalizations due to acute coronary syndromes (ACS) are in people 65 years or older [2]. The average age of patients having a myocardial infarction is approximately 76 years for women and 70 years for men in Sweden [3]. With increasing age, more ACS patients will have multimorbidity, defined as at least two chronic diseases. From previous studies, we know that multimorbidity leads to increased risk of readmissions [4, 5]. Both the European Society of Cardiology and the American Heart Association have recently published consensus guidelines on multimorbidity and other geriatric syndromes in patients with ACS [6, 7].

The readmission rate of older people with ACS varies. Previous studies have shown a 30-day readmission rate of 11–35% [8–10] and a 1-year readmission rate of 40–60% [8, 10, 11]. The prevalence of multimorbidity varies in different ACS populations and increases with age [12]. In Sweden, all coronary care units register their ACS patients in the national quality registry SWEDEHEART (The Swedish Web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies). Furthermore, Sweden has a nationwide database for all hospital admissions/readmissions. This gives us a unique chance to examine multimorbidity and readmission rates after all admissions to coronary care units.

The purpose of this article was to determine the multimorbidity and disease burden in an unselected large cohort of older ACS patients, as well as to examine outcome including 30-day and 1-year readmission rates. Readmission could be due to cardiovascular causes and bleeding events, as well as other causes. Since multimorbid as well as older people often are excluded from clinical trials, we think this study, in an unselected and nationwide population, is important to illustrate a major problem – high readmission rates in older multimorbid patients with ACS.

Materials and Methods

We included all patients who were 70 years or older and hospitalized due to ACS during January 1, 2006, to December 31, 2013, and registered in the SWEDEHEART registry. Only index admissions were included. This age cutoff was chosen because the average age in Sweden for the first myocardial infarction has been approximately 70 years in men and 76 for women, respectively. In previous studies, 70 years of age has been chosen as a cutoff for older people because of mortality inclining after that age [13]. The study was performed with the approval of the Swedish Ethical Review Authority and in accordance with the Declaration of Helsinki.

Primary outcomes were 30-day and 1-year readmissions due to any cause. Secondary outcomes were in-hospital mortality as well as 30-day and 1-year all-cause mortality and readmissions due to ACS, heart failure, ischaemic stroke or TIA, or bleeding events. Results are presented for all ACS patients and for two subgroups: ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarctions (NSTEMI-ACS).

Patient characteristics and disease burden were identified from the SWEDEHEART registry and the Swedish National Patient Registry, which collects information about diagnoses at discharge from all hospital stays in Sweden, as well as diagnoses from outpatient hospital specialist care [14]. Outcomes after discharge came from the Swedish National Patient Registry, but episodes of new ACS were also identified from the SWEDEHEART registry. The International Classification of Diseases, 10th Revision (ICD-10), codes for both patient characteristics and outcomes can be found in online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000522016).

The SWEDEHEART registry is a national quality registry in Sweden collecting nationwide data for patients with myocardial infarction admitted to coronary care units. All hospitals providing acute coronary care in Sweden participate in SWEDEHEART, and the registry annually includes 18,000 myocardial infarctions. The registry includes over 100 variables, for example, patients' medical history, strategy before admission, clinical conditions, management during hospital stay, treatment at discharge, and diagnosis. The registry also contains angiographic data, procedural data, and treatment decisions for all patients who are investigated with coronary angiography (CA) and/or revascularized with percutaneous coronary interventions (PCI) at every Swedish centre performing these procedures. To ensure validity of data, 20 randomly selected hospitals are monitored each year and data entered into the SWEDEHEART registry for 40 randomly selected patients compared to patient records [15].

In Sweden, the standard treatment for STEMI is reperfusion therapy with primary PCI. Thrombolysis is only used in the most rural areas (in less than 5% of STEMI). The standard treatment for NSTEMI-ACS, in accordance with the guidelines of the European Society of Cardiology, is diagnostic CA with revascularization when appropriate. Both STEMI and NSTEMI-ACS are treated with acetylsalicylic acid and a P2Y₁₂ receptor antagonist (together those two are called dual antiplatelet therapy, DAPT) and statins. Most patients have a follow-up after discharge from a specialist nurse or a cardiologist in a cardiology outpatient unit after 6–8 weeks with a second visit after 12–14 months. Many hospitals additionally provide a visit within 2 weeks to a specialist nurse [3].

Table 1. Patient characteristics

	All ACS (N = 80,176) (%)	STEMI (N = 20,540) (%)	NSTE-ACS (N = 59,636) (%)	Not multimorbid STEMI (N = 9,603) (%)	Not multimorbid NSTE-ACS (N = 16,223) (%)	p value	Multimorbid STEMI (N = 10,843) (%)	Multimorbid NSTE-ACS (N = 43,273) (%)	p value
Age, mean (±SD)	79.8 (6.4)	79.6 (6.4)	79.9 (6.4)	78.6 (6.1)	78.7 (6.3)		80.5 (6.5)	80.3 (6.4)	
70–<80 years	50.2	51.6	49.6	58.7	57.7		45.3	46.7	
80–<90 years	42.3	41.2	42.7	36.5	36.5	0.062	45.5	45.0	0.0077
90–<100 years	7.5	7.1	7.6	4.7	5.8		9.1	8.2	
100 years old or more	0.1	0.1	0.1	0.0	0.0		0.1	0.1	
Women	43.4	43.6	43.4	42.1	43.2	0.0051	45.0	43.4	0.0008
Weight, mean (±SD), kg	74.5 (14.5)	73.9 (14.2)	74.8 (14.6)	73.4 (13.4)	74.0 (13.47)	0.0022	74.3 (14.9)	75.1 (15.0)	0.0043
Missing weight	n = 6,593	n = 1,778	n = 4,815	n = 1,295	n = 606		n = 1,292	n = 4,193	<0.0001
BMI, mean (±SD), kg/m ²	26.1 (5.9)	25.8 (7.9)	26.2 (4.9)	25.5 (8.2)	25.7 (5.1)	0.026	26.1 (7.7)	26.3 (4.9)	0.0046
Missing BMI	n = 19,253	n = 468	n = 44,994	n = 1,892	n = 3,536		n = 2,670	n = 11,054	
Active smokers	10.5	13.2	9.6	14.7	11.3	<0.0001	11.8	8.9	<0.0001
Missing smoking status	n = 9,410	n = 2,334	n = 7,076	n = 749	n = 1,378		n = 1,532	n = 5,642	
Hypertension	64.2	57.5	66.5	35.3	37.2	0.0021	77.8	77.6	0.66
Previous stroke	12.3	10.0	13.1	1.7	1.8	1.00	18.0	17.4	0.05
Diabetes	26.0	21.3	27.5	4.9	4.6	0.21	36.0	36.3	0.73
COPD	6.9	4.9	7.6	1.0	1.0	1.00	8.5	10.1	<0.0001
PVD	5.0	3.1	5.7	0.2	0.3	0.38	5.7	7.7	<0.0001
Tumour	7.3	6.5	7.6	1.8	1.5	0.090	10.6	9.9	0.021
Heart failure	17.4	10.0	19.9	0.2	0.6	<0.0001	18.8	27.2	<0.0001
Anaemia	9.9	7.3	10.8	0.8	1.1	0.0083	13.2	14.4	0.0011
Atrial fibrillation	16.2	11.4	17.9	1.1	1.5	0.0076	20.6	24.0	<0.0001
Previous MI	28.5	17.8	32.1	0.5	0.8	0.0045	33.3	44.0	<0.0001
Previous PCI	12.0	7.3	13.6	0.2	0.1	0.16	13.8	18.7	<0.0001
eGFR, mean (±SD), mL/min	59.1 (24.3)	59.6 (24.1)	58.9 (24.4)	64.0 (22.7)	64.8 (22.4)		55.7 (24.7)	56.6 (24.7)	
≥90	10.2	10.3	10.1	11.8	12.5		8.9	9.2	
60≤ eGFR <90	35.1	35.7	34.9	42.5	43.6	0.0046	29.6	31.5	0.0018
30≤ eGFR <60	44.3	44.5	44.3	40.9	39.3		47.7	46.2	
eGFR <30	10.4	9.5	10.7	4.8	4.6	0.0060	13.7	13.1	0.0010
Missing eGFR	n = 8,651	n = 2,430	n = 6,221	n = 991	n = 1,270		n = 1,400	n = 4,014	
Chronic diseases, n									
<2	32.3	47.0	27.3	100	100		0	0	
≥2	67.7	53.0	72.7	0	0		100	100	
Missing number of chronic diseases	234	94	140						
CAD-specific index									
Low burden	28.2	32.6	26.8	49.9	51.7		17.4	17.4	
Moderate burden	8.9	7.5	9.4	3.1	3.2		11.3	11.8	
High burden	62.8	59.9	63.8	47.0	45.1	0.0064	71.3	70.8	0.65
Missing CAD-specific index	n = 8,873	n = 2,599	n = 6,274	n = 1,218	n = 1,681		n = 1,336	n = 4,548	

Table 1 (continued)

	All ACS (N = 80,176) (%)	STEMI (N = 20,540) (%)	NSTE-ACS (N = 59,636) (%)	Not multimorbid STEMI (N = 9,603) (%)	Not multimorbid NSTEMI-ACS (N = 16,223) (%)	p value	Multimorbid STEMI (N = 10,843) (%)	Multimorbid NSTEMI-ACS (N = 43,273) (%)	p value
Medications at admission									
ACE inhibitors	24.7	18.3	26.9	8.6	12.0	<0.0001	27.0	32.6	<0.0001
Angiotensin II antagonists	15.7	12.7	16.7	7.3	8.7	<0.0001	17.6	19.7	<0.0001
Calcium antagonists	22.5	19.4	23.3	12.1	13.3	0.0066	25.9	27.2	0.010
β-Blockers	46.7	35.5	50.5	17.5	24.6	<0.0001	51.6	60.3	<0.0001
Statins	32.1	21.0	35.8	7.4	12.5	<0.0001	33.3	44.6	<0.0001
Acetylsalicylic acid	49.3	34.3	54.2	14.1	25.8	<0.0001	53.6	64.9	<0.0001
P2Y ₁₂ receptor antagonist	7.2	4.2	8.3	1.2	1.9	<0.0001	6.9	10.7	<0.0001
Oral anticoagulants	7.9	5.1	8.8	1.8	2.7	<0.0001	8.2	11.1	<0.0001
Digitalis	4.1	3.0	4.4	0.8	1.2	0.0019	5.0	5.7	0.0071
Long-acting nitroglycerin	19.0	9.0	22.4	1.8	6.1	<0.0001	15.5	28.5	<0.0001

Results in this table are shown as percentages except age, weight, BMI, and estimated glomerular filtration rate that are shown as mean $\pm$ standard deviation (SD). ACS, acute coronary syndromes; STEMI, ST-elevation myocardial infarction; NSTEMI-ACS, non-ST-elevation acute coronary syndromes; kg, kilograms; BMI, body mass index; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate, calculated with the Cockcroft-Gault formula; CAD, coronary artery disease; ACE, angiotensin-converting enzyme; P2Y₁₂ receptor, adenosine diphosphate receptor on platelets. Missing values are shown as numbers and are not included in the denominator, if missing values are less than 3%, no value is shown. CAD-specific index: coronary artery disease-specific index, see online supplementary material.

Definitions

The definition of myocardial infarction used in this article is the same as that used in SWEDEHEART and in all Swedish hospitals; it adheres to the standards of the European Society of Cardiology for definition of myocardial infarctions and ACS [16]. The treating physician makes the final diagnosis. STEMI is defined as the presence of ST-elevation on electrocardiogram (ECG) or new left bundle-branch block on ECG in addition to suspicion of ongoing ischaemia [17]. Renal function was calculated with the Cockcroft-Gault formula and presented as estimated glomerular filtration rate (eGFR). Multimorbidity was defined as two chronic diseases: hypertension, history of stroke or transient ischaemic attacks, previous myocardial infarction, heart failure, atrial fibrillation, peripheral vascular diseases, diabetes, kidney disease, cancer, anaemia, and chronic obstructive pulmonary disease. Multimorbidity burden was measured by the Coronary Artery Disease (CAD)-specific index, allocating patients to low, medium, or high burden giving scores for different comorbidities, as well as smoking status and renal function [18], a description can be found in online supplementary material. Bleeding events were defined as all hospitalizations with a diagnosis of haemorrhage without regard to type or anatomical location, as well as fatal bleeds with the bleeding diagnosis as a first or a second cause of death. ICD-10 codes for bleeding events can be found in online supplementary material, and these codes have previously been used with high sensitivity to identify bleeding events in patients with atrial fibrillation [19].

Statistical Analysis

Descriptive statistics were employed for the whole group as well as subgroups of STEMI and NSTEMI-ACS patients with and without multimorbidity; categorical variables were reported as frequency values and proportions, continuous variables with a near-symmetrical as mean $\pm$ standard deviation (SD), and continuous variables without appropriately near-symmetrical distributions as medians (range). For comparison between groups, Fisher's exact test (lowest 1-sided *p* value multiplied by) was used for dichotomous variables. The Mantel-Haenszel χ^2 test was used for ordered categorical variables. The χ^2 test was used for non-ordered categorical variables, and the *t* test was used for continuous variables.

To examine the effects of multimorbidity on outcomes, the outcomes for STEMI patients with multimorbidity were compared to those without multimorbidity using multivariate logistic regression adjusting for age, gender, renal disease (eGFR ≥ 90 mL/min, $60 \leq$ eGFR < 90 mL/min, $30 \leq$ eGFR < 60 mL/min, and eGFR < 30 mL/min), heart failure, CAD-specific index, standard risk reduction treatment (treated with acetylsalicylic acid, P2Y₁₂ receptor antagonists, and statins), and the use of CA (with or without following intervention with PCI or coronary artery bypass grafting [CABG]). Covariates for the multivariate analyses were chosen as they are known predictors of mortality and negative outcomes (5, 9–11). Missing values were handled as an own category in the adjustment. Same calculations were performed for NSTEMI-ACS patients. Missing variables are shown as numbers in tables if they exceed 3%.

Table 2. Treatment and outcomes during admission

	All ACS (N = 80,176) (%)	STEMI (N = 20,540) (%)	NSTE-ACS (N = 59,636) (%)	p value	Not multimorbid STEMI (N = 9,603) (%)	Not multimorbid NSTEMI-ACS (N = 16,223) (%)	p value	Multimorbid STEMI (N = 10,843) (%)	Multimorbid NSTEMI-ACS (N = 43,273) (%)	p value
Medications at discharge										
ACE inhibitors	52.3	59.9	49.7	<0.001	66.6	53.0	<0.0001	54.1	48.5	<0.0001
Angiotensin II receptor blockers	16.2	12.8	17.4	<0.001	8.4	10.1	<0.0001	16.8	20.2	<0.0001
Calcium antagonists	19.4	11.5	22.1	<0.001	6.8	13.3	<0.0001	15.7	25	<0.0001
β-Blockers	83.2	82.5	83.4	0.0028	84.9	84.1	0.11	80.6	83.2	<0.0001
Statins	74.3	77.1	73.4	<0.001	84.1	79.2	<0.0001	71.1	71.2	0.75
Acetylsalicylic acid	86.9	87.4	86.7	0.010	91.2	92.1	0.018	84.1	84.7	0.061
P2Y ₁₂ receptor antagonist	67.5	78.4	63.7	<0.001	85.1	70.5	<0.0001	72.6	61.2	<0.0001
Oral anticoagulants	9.5	7.6	10.1	<0.001	5.9	5.3	0.035	9.2	12.0	<0.0001
Digitalis	4.3	3.5	4.6	<0.001	2.0	2.0	0.99	4.9	5.5	0.015
Long-acting nitroglycerin	24.7	11.8	29.1	<0.001	5.4	13.4	<0.0001	17.4	35.1	<0.0001
Diuretics	42.6	36.0	44.8	<0.001	25.2	26.5	0.029	45.7	51.7	<0.0001
Acetylsalicylic acid, P2Y ₁₂ receptor antagonist and statins at discharge	54.4	65.7	50.5	<0.001	75.5	59.9	<0.0001	57.4	47	<0.0001
Angiography/coronary intervention										
Angiography	10.8	5.6	12.6		4.8	13.1		6.3	12.4	
Angiography + PCI	44.0	70.0	35.1		79.2	45.9		62.1	31.0	
Angiography + CABG	6.2	2.2	7.6	<0.001	2.5	11.1	<0.0001	2.0	6.3	<0.0001
No examination/intervention	38.9	22.2	44.7		13.5	29.9		29.6	50.3	<0.0001
NSTEMI	N/A	N/A	86.5		N/A	87.6		N/A	86.1	
UAP	N/A	N/A	13.5			12.4			13.9	
Days in hospital, mean (±SD) and median (range)	7.4 (7.1)	7.2 (6.5)	7.5 (7.3)	<0.001	6.90 (6.19)	7.24 (6.48)	<0.0001	7.43 (6.83)	7.63 (7.58)	0.0084
In-hospital mortality	6.0 (4.0; 8.0)	5.0 (4.0; 8.0)	6.0 (4.0; 9.0)		5 (1; 254)	6 (1; 372)		6 (1; 307)	6 (1; 374)	
	7.0	12.2	5.2	<0.001	8.3	3.4	<0.0001	15.3	5.8	<0.0001

Results in this table are shown as percentages except days in hospital that are shown as mean (±standard deviation) and median (range). Missing values are not included in the denominator and are less than 3% for all outcomes. ACS, acute coronary syndromes; N/A stands for not applicable; STEMI, ST-elevation myocardial infarction; NSTEMI-ACS, non-ST-elevation acute coronary syndromes; ACE, angiotensin-converting enzyme; P2Y₁₂, adenosine diphosphate receptor on platelets; PCI, percutaneous coronary interventions; CABG, coronary artery bypass grafting; NSTEMI, non-ST-elevation myocardial infarction; UAP, unstable angina pectoris.

Fig. 1. a, b Treatment with dual antiplatelet therapy together with statins and coronary angiography during 9 years in elderly patients with and without multimorbidity. STEMI, ST-elevation myocardial infarction; NSTEMI-ACS, non-ST-elevation acute coronary syndromes.

Table 3. Outcomes after discharge

Outcomes after discharge		All ACS (N = 74,577) (%)	STEMI (N = 18,040) (%)	NSTE-ACS (N = 56,537) (%)	p value
30 days	Total mortality	3.3	3.5	3.3	<0.0001
	All-cause readmissions	25.6	21.4	25.7	<0.0001
	Readmission due to ACS	6.4	4.8	7.0	<0.0001
	Readmission due to stroke or TIA	0.8	0.9	0.7	<0.0001
	Readmission due to heart failure	2.9	3.5	2.7	<0.0001
	Readmission due to a bleeding event ^a	1.9	1.8	1.9	<0.0001
	Readmission due to other causes	13.6	10.4	13.4	<0.0001
One year	Total mortality	14.6	12.1	15.4	<0.0001
	All-cause readmissions	59.5	53.1	61.5	<0.0001
	Readmission due to ACS	15.8	11.1	17.3	<0.0001
	Readmission due to stroke or TIA	3.4	3.3	3.4	<0.0001
	Readmission due to heart failure	9.4	8.6	9.6	<0.0001
	Readmission due to a bleeding event	6.6	6.2	6.8	<0.0001
	Readmission due to other causes	24.3	23.9	24.4	<0.0001

Missing values are not included in the denominator and are less than 3% for all outcomes; for categorical variables, % is presented. ACS, acute coronary syndromes; STEMI, ST-elevation myocardial infarction; NSTE-ACS, non-ST-elevation acute coronary syndromes; TIA, transient ischaemic attack. ^aBleeding events were defined as all hospitalizations with diagnoses of haemorrhage without regard to type or anatomical location, as well as fatal bleeds with the bleeding diagnosis as a first or a second cause of death. ICD-10 codes for bleeding events can be found in online supplementary material.

Results

Baseline Variables and Morbidity

During 2006–2013, 80,176 patients, 70–103 years old, were admitted due to ACS and registered in SWEDE-HEART. Of these, 20,540 (25.6%) had an STEMI and 59,636 had NSTE-ACS (74.4%). The mean age for all ACS patients was 79.8 (± 6.4 SD [standard deviation]) and 43.4% were women. Of the whole group (80,176 patients), 26.0% had diabetes, 17.4% had heart failure, and 54.7% had eGFR under 60 mL/min/1.73 m². Multimorbidity was present in 67.7%, and the multimorbidity burden according to the CAD-specific index was high in 62.8% of the patients (Table 1). In the patient group with STEMI, 53.0% had multimorbidity and 59.9% had high multimorbidity burden, while of those with NSTE-ACS, 72.7% had multimorbidity and 63.8% high multimorbidity burden. In patients without multimorbidity, the multimorbidity burden was considered high for 47.0% of STEMI patients and 45.1% of NSTE-ACS patients (Table 1).

Treatments and Investigations

At discharge, 86.9% of all ACS patients 70 years and older were treated with acetylsalicylic acid, 67.5% received a P2Y₁₂ receptor antagonist, and 74.3% were on

statin therapy. The proportion of older patients receiving both DAPT and statins at discharge was 54.4%. CA with or without a coronary intervention was performed in 61.1% of the ACS patients, in 77.9% of STEMI patients and 55.3% of those with NSTE-ACS (Table 2). In both patients with STEMI and NSTE-ACS, treatment with DAPT together with statins was more common in patients without multimorbidity than those with multimorbidity. In STEMI patients without multimorbidity, 75.5% were treated with DAPT and statins compared to 57.1% in the multimorbid group. The corresponding figures for NSTE-ACS patients without multimorbidity treated with DAPT and statins were 59.9% compared to 47.0% in those with multimorbidity. CA was performed in most STEMI patients both with and without multimorbidity, 86.5% and 71.1% (Table 2). The use of DAPT together with statins as well as diagnostic CA increased in all patient categories during the 9 years the study was performed (shown in Fig. 1).

Mortality and Readmissions

In-hospital mortality was 7.0% for all ACS patients, 12.2% for those with STEMI and 5.2% for those with NSTE-ACS. Of the 74,577 patients who survived to discharge, 24.6% were readmitted within 30 days, whereof

Missing values are not included in the denominator and are less than 3% for all outcomes; for categorical variables, % is presented. STEMI, ST-elevation myocardial infarction; CI, confidence interval; NSTEMI-ACS, non-ST-elevation acute coronary syndromes; TIA, transient ischaemic attack. ^aLogistic regression adjusting for age, gender, renal disease (9.0% missing), heart failure, Coronary Artery Disease-specific index (10.3% missing), statins and double antiplatelet drugs, and the use of coronary angiography (with or without following intervention with either percutaneous coronary intervention or coronary artery bypass graft). Missing values handled as an own category in the adjustment. ^bBleeding events were defined as all hospitalizations with diagnoses of haemorrhage without regard to type or anatomical location, as well as fatal bleeds with the bleeding diagnosis as a first or a second cause of death. ICD-10 codes for bleeding events can be found in online supplementary material.

2.9% were readmitted within 7 days. In total, 59.5% of all ACS patients 70 years or older were readmitted within a year from discharge. More than half of those readmissions were due to cardiovascular causes or bleeding events (Table 3). Readmissions rates were higher in the NSTEMI-ACS group, 61.5% versus 53.1% within 1 year ($p < 0.0001$).

Mortality and readmissions 1 year after discharge were higher in multimorbid patients than in those without multimorbidity. In STEMI patients, the 1-year mortality was 14.2% versus 6.3%, adjusted odds ratio (OR) 1.37 (95% confidence interval [CI] 1.19–1.59), and 1-year readmissions were 56.2% versus 44.5%, adjusted OR 1.35 (1.26–1.45), in those with and without multimorbidity, respectively. In patients with NSTEMI-ACS, the 1-year mortality after discharge was 16.5% versus 7.7%, adjusted OR 1.30 (1.18–1.43), and readmissions were 63.4% versus 49.1%, adjusted OR 1.42 (1.35–1.50), in those with multimorbidity and those without, respectively (Table 4).

Discussion/Conclusion

Most people over 70 years old with ACS have multimorbidity and high multimorbidity burden. This is especially prevalent in those with NSTEMI-ACS where 73% have multimorbidity and 64% a high multimorbidity burden. More than half of the patients that survived to discharge were readmitted during the following year, where of almost half of the readmissions were due to cardiovascular causes or bleeding events. Multimorbidity increased the risk of readmissions in patients with STEMI as well as NSTEMI-ACS. The disease burden in older people is reflected in their treatment as 46% of all ACS patients did not receive standard therapy with both statins and DAPT, and 22% of STEMI patients did not undergo CA, while the CA rates in Swedish STEMI patients under 70 years old during the last 15 years has been between 90 and 99%.

The high proportion of patients with multimorbidity in this older ACS population reflects the high prevalence of multimorbidity in the general older population, as up to 70% of community-dwelling people over 65 years old have multimorbidity [12, 20]. The rate of diabetes in older people with ACS has been reported to vary from 15 to 35%, hypertension from 45 to 79%, and anaemia 10–43% [21–23], in concordance with our results. The prevalence of diabetes in the general population of Swedish 70 year olds in 2005 was 16%, and the prevalence for hypertension was 73% [24]. Multimorbidity burden was considered high in a considerable proportion of patients without multimorbidity according to the CAD-specific index,

as this index takes into consideration renal function and smoking status [18]. The presence of comorbidities can influence the benefit/risk balance of ACS treatment, either through increasing the risk of new ACS or the risk of bleeding events, renal failure, or other complications. Therefore, when treating older people with ACS, all comorbidities must be considered.

The low proportion of older patients receiving standard therapy with DAPT and statins as well as a rather large percentage with STEMI not undergoing CA may have many different causes. Most importantly, the study included patients treated from 2006 to 2013, and during this period, and since, the use of all these therapies has increased. For example, CA in STEMI patients over 80 years old in Swedish Coronary Care units during 1994–2014 increased from less than 60% to around 74–82% (women vs. men) and for those who were 65–79 years old from 50–60% to over 80–90% [25] and the use of DAPT in all myocardial infarction patients from 65% to over 80% [3]. Half of the patients in this study were over 80 years old. There was an increase in the use of these therapies in Sweden in this age group as well during the study period, for example, statin use from less than 50% to 80% in men. Also, concerns about adverse events of these treatments, especially bleeding events, partly explain these results. The annual risk for a major bleeding event in those who are over 85 years old receiving ASA alone is over 4% [26]. A study in multimorbid older patients in Sweden with ACS showed a readmission rate of 10% due to bleeding events for 1 year [27]. Aside from the high age of patients in that study, 10% had anaemia at admission and 55% had eGFR under 60 mL/min, all of these are factors that increase the risk of bleeding events [28, 29]. Complications after statin use are also more common in elderly patients, especially those with multimorbidity and polypharmacy [30].

The high readmission rate shown in this study is in concordance with some studies in unselected cohorts of older people with ACS which show the 1-year readmission rate to be up to 60% and the 30-day readmission rate to be around 20–35% [8, 9, 11]. An American study in unselected ACS population found 1-year admissions to be 62%, and half of those were not cardiovascular, results that are almost identical to those we found [10]. The factors that are most associated with readmissions after ACS are age, diabetes, length of stay of 7 days or more, pulmonary disease, peripheral artery disease, renal disease, and heart failure [10, 31]. Multimorbidity is also associated with higher readmission risk and other outcomes as was shown in this study [32]. In addition to being costly, hos-

pital admissions often cause a loss of function and increased dependency in older people [33]. Therefore, finding ways to reduce readmissions is important. In an ACS population, an early follow-up visit to a nurse 14 days after discharge reduced readmissions [34] supporting that this high readmission rate can be reduced with different methods.

Older patients are a very heterogeneous group regarding how heavy the multimorbidity burden is, how frail or fit they are, the prevalence of cognitive impairment, and polypharmacy, as well as different levels of dependency. As patients become more multimorbid, frail, and dependent, the goal of treatment shifts from prolonging life to increasing the quality of life and eventually to palliative care. The multimorbidity and its accompanying polypharmacy becomes problematic as it increases the risk for medication-related side effects of evidence-based treatments for ACS such as statins and ACE inhibitors and antiplatelet drugs. These prescription decisions and clinical decisions are ethically challenging as it can be near impossible to judge the tipping point for more risks than benefits associated with ACS treatments. The 2020 ESC guidelines do state that older patients should receive the same diagnostic as well as revascularization treatments, but the evidence level is category B [35], indicating that not many randomized studies are behind the recommendations. Personalizing care in cooperation with the patients' wishes is important. To improve the quality of care of older people with ACS and reduce readmission rates, it is essential to take multimorbidity and other geriatric syndromes into account when tailoring individual follow-up routines. In the elderly, it is also important to do an accurate risk-benefit analysis of different kinds of treatment. Both the AHA and ESC now recommend this [6, 7, 35]. The risk associated with antiplatelet drugs is partially time related, so the use of bleeding prediction models such as the PRECISE-DAPT score [29] might aid in shortening the length of DAPT treatment in those with the highest bleeding risk. To recognize ACS patients with frailty already in the coronary care unit is also important. With geriatric consultant teams and subacute care at geriatric rehabilitation wards, the frail patients could get important support [6]. After discharge, the frailest and most multimorbid ACS patients might benefit from earlier follow-up than usual, i.e., within 7 days of discharge to decrease readmissions [36].

Strengths and Limitations

This study provides insights into a large, nationwide, real-life cohort of multimorbid older people with ACS

who are often excluded from randomized trials. As the SWEDEHEART Registry is used in all coronary care units in Sweden and the Swedish Patient Registry includes all admissions, this study focuses on the complex aftermath after ACS in older people rather than only the cardiovascular outcomes. The all-inclusive nature of SWEDEHEART minimizes selection bias, and this nationwide insight into the quality of care for older people with ACS may help to further improve both treatment and follow-up and may potentially save resources.

The older patients who were not admitted to coronary care units are not included in this study, and among those patients might be the most frail and complex older patients. When using hospital diagnoses to look at the multimorbidity burden, the registries underdiagnose diseases that often do not lead to admission, an example is chronic obstructive pulmonary disease and peripheral vascular disease. The multimorbidity burden of these ACS patients might therefore be even higher than is described.

The most important limitation of this study is that it includes data from more than 7 years ago. However, these are the data we as of now have available to publish. During this time, the implementation of both medical therapy and interventions with CA, PCI, and CABG has changed. However, the readmission rates have not declined from 2013 to 2019 [3], so we believe the data remain both important and relevant. A further unfortunate limitation is that we did not register peptic ulcer disease in the year before admission in this study which is an important factor in the risk for bleeding events.

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Statement of Ethics

The study was performed with the approval of the Swedish Ethical Review Authority, Reference No. Dnr 2015/272, and its content complies with the Declaration of Helsinki. As data in the SWEDEHEART registry are collected as part of health care quality improvement, informed consent from participants is not required by the Swedish law, but patients are made aware of the registry and its use and can decline participation.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Gudny Stella Gudnadottir is responsible for the idea behind the paper, she is the main contributor to the design of the work, the acquisition, and interpretation of data, and assisted in the analyses for the work. She is also responsible for drafting the manuscript. Thorarinn contributed substantially to the design of the work as

well as acquisition and interpretation. Katarina Wilhelmson contributed with drafting of the work as well as interpretation. Annica Ravn-Fischer contributed with the acquisition as well as interpretation of the work. All authors contributed to revising the actual content and have approved the final version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data Availability Statement

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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