

Safety of early hospital discharge following admission with ST-elevation myocardial infarction treated with percutaneous coronary intervention: a nationwide cohort study

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KEYWORDS

- early discharge
- length of hospital stay PAMI-II
- STEMI

Abstract

Background: The Second Primary Angioplasty in Myocardial Infarction (PAMI-II) risk score is recommended by guidelines to identify low-risk patients with ST-elevation myocardial infarction (STEMI) for an early discharge strategy.

Aims: We aimed to assess the safety of early discharge (≤ 2 days) for low-risk STEMI patients treated with primary percutaneous coronary intervention (PCI).

Methods: Using nationwide data from the SWEDEHEART registry, we identified patients with STEMI treated with primary PCI during the period 2009-2017, of whom 8,092 (26.4%) were identified as low risk with the PAMI-II score. Low-risk patients were stratified according to their length of hospital stay (≤ 2 days vs > 2 days). The primary endpoint was major adverse cardiovascular events (MACE, including death, reinfarction treated with PCI, stroke or heart failure hospitalisation) at one year, assessed using a Cox proportional hazards model with propensity score as well as an inverse probability weighting propensity score of average treatment effect to adjust for confounders.

Results: A total of 1,449 (17.9%) patients were discharged ≤ 2 days from admission. After adjustment, the one-year MACE rate was not higher for patients discharged at > 2 days from admission than for patients discharged ≤ 2 days (4.3% vs 3.2%; adjusted HR 1.31, 95% confidence interval [CI]: 0.92-1.87, $p=0.14$), and no difference was observed regarding any of the individual components of the main outcome. Results were consistent across all subgroups with no difference in MACE between early and late discharge patients.

Conclusions: Nationwide observational data suggest that early discharge of low-risk patients with STEMI treated with PCI is not associated with an increase in one-year MACE.

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Introduction

An increasing length of hospital stay for ST-elevation myocardial infarction (STEMI) patients is associated with elevated hospital costs and increased morbidity and mortality^{1,2}. The introduction of effective mechanical reperfusion and the improvements that have been made with regard to evidence-based treatment strategies have resulted in a decrease in early mortality³ and number of bed days⁴⁻⁶.

Small randomised clinical trials⁷⁻¹⁰, as well as observational studies^{11,12}, have tried to assess the optimal length of hospital stay in patients with STEMI. The Second Primary Angioplasty in Myocardial Infarction (PAMI-II) risk score is a clinical tool that can be used to assess candidates for an early discharge strategy and is based on a clinical trial that randomised 471 low-risk STEMI patients (age <70 years, left ventricular ejection fraction [LVEF] >45%, one- or two-vessel disease undergoing successful percutaneous coronary intervention [PCI] with no persistent arrhythmias). The trial showed that early discharge is a safe alternative to traditional length of care¹. Based on these studies, early discharge within 72 hours carries a Class IIa recommendation from the European Society of Cardiology¹³. Although the PAMI-II score is based on patients with STEMI who received PCI, it was introduced in the late 1990s and has only been validated in small observational studies^{11,14}.

The objective of this study was to assess whether low-risk STEMI patients treated with PCI may be safely discharged within two days from admission in a contemporary, nationwide setting using data from the Swedish quality registry of coronary care, SWEDEHEART (Swedish Web system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies).

Methods

DATA SOURCE

All consecutive patients with symptoms suggestive of an acute coronary syndrome admitted to a coronary care unit or coronary catheterisation laboratory in Sweden are recorded prospectively in the SWEDEHEART registry¹⁵. The registry collects information on background characteristics, in-hospital examinations, coronary angiographic findings and PCI-related measures, complications, discharge medications and diagnoses. A personal identification number, unique to every Swedish citizen, allows merging with other nationwide registries. We linked the SWEDEHEART registry to the National Patient Registry and the National Population Registry to obtain data on comorbidities and date of death.

PAMI-II CALCULATION

Data concerning age, revascularisation, arrhythmias and LVEF were available in the SWEDEHEART registry. LVEF is documented as ≥50%, 40-49%, 30-39% and ≤30% in the registry, barring us from using similar LVEF cut-offs to those in the PAMI-II risk score (>45%). Therefore, we used LVEF ≥50% as a low-risk criterion whereby we probably identified fewer patients in

this group, but as a more robust low-risk feature. In the PAMI-II score, persistent arrhythmia is defined as arrhythmia that requires treatment with a pacemaker or lidocaine infusion. Today, lidocaine is not widely used as an antiarrhythmic drug. We therefore defined persistent arrhythmias as any serious arrhythmia requiring cardiopulmonary resuscitation, defibrillation, cardioversion or pacemaker. Arrhythmias treated medically with amiodarone or other antiarrhythmic drugs are not registered in SWEDEHEART. An overview of the criteria applied to define low-risk patients is shown in **Table 1**.

Table 1. Table of criteria used to define low-risk patients.

Age <70 years	One- or two-vessel disease	Left ventricular ejection fraction ≥50%	Absence of serious arrhythmias requiring defibrillation/ cardioversion or pacemaker.
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STUDY POPULATION AND DESIGN

We included all patients with STEMI between January 2009 and April 2017 (**Figure 1**). Only initial admissions during the study period were included in this report; we excluded patients presenting with cardiogenic shock or resuscitated cardiac arrest. To adhere to the PAMI-II criteria, only STEMI patients who were treated with PCI and underwent transthoracic echocardiography were included in the analysis. The PAMI-II risk score was applied, categorising 8,092 patients as low risk and this comprised the final study population. Seven patients had at least one missing variable and in these the PAMI-II risk score could not be evaluated. These patients were excluded from this study. Patients categorised as low risk according to the PAMI-II risk score were stratified according to their length of hospital stay, as ≤2 days (early discharge group; left censored at 0 days) and ≥2 days (late discharge group; right censored at y time). The Regional Ethical Review Board in Lund approved the study (approval id: 2015/297). This study adheres to the STROBE criteria (**Supplementary Appendix 1**).

OUTCOMES

The main outcome was a major adverse cardiac event (MACE) at one year defined as the first occurrence of (1) all-cause mortality, (2) PCI-treated myocardial infarction (MI), (3) hospitalisation for decompensated heart failure (HF), or (4) stroke. Using each patient's unique health record number, censorship dates and death status were ascertained by the National Board of Health and Welfare by deterministic linkage to the National Population Registry. Similar linkages were undertaken to enable estimation of rates of admission with stroke and HF from the National Patient Registry, whereas PCI-treated MI was extracted directly from the SWEDEHEART registry (without linkage) and was defined as a subsequent entry with a discharge diagnosis of MI treated with PCI. In secondary analyses, the association between early discharge and each component of the main outcome was explored. Follow-up was calculated from day of admission and all outcomes were ascertained up to April 2018 with complete follow-up of all patients.

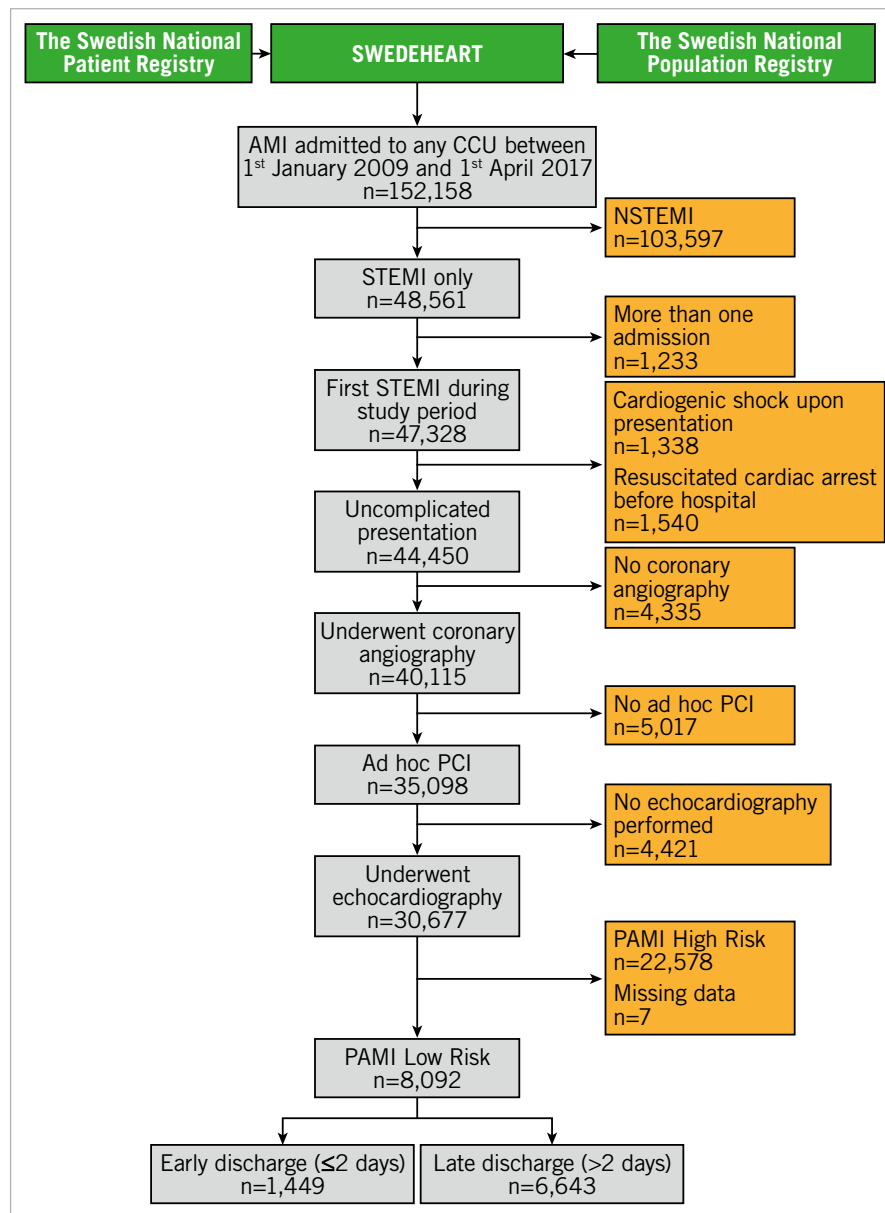


Figure 1. Study flow chart. Patients with ST-segment elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention (PCI) were included in this study. All patients had to undergo echocardiography during hospitalisation. The PAMI-II risk score was used to identify low-risk patients as candidates for early discharge. Low-risk patients were subsequently stratified according to length of hospital stay as early discharge within 2 days from admission or late discharge with a hospital stay exceeding 2 days. Shown are the numbers of patients remaining after each step of the inclusion and exclusion criteria.

SUBGROUP ANALYSES

We explored the rates of the main endpoint in men versus women, age ≥ 60 versus < 60 years, weights equal to and above versus below the cohort median of 84 kg, and the presence of known diabetes mellitus, hypertension, history of MI and number of diseased coronary arteries versus the absence of these factors. Two landmark analyses were conducted to test the robustness of the results: first, a landmark analysis assessing one-year MACE rates from discharge, and second, a 30-day landmark analysis from discharge to assess one-year MACE rates in patients discharged within two days compared to later discharge.

STATISTICAL ANALYSES

Baseline characteristics are presented as medians with interquartile range for continuous variables, counts with percentages for categorical variables. Differences between groups were calculated with the Mann-Whitney U test and the chi-squared test. The incidence of MACE together with the other outcome measures was calculated using Kaplan-Meier estimates. The association between early and late discharge and the hazards of MACE and the individual components of MACE was estimated using propensity score-adjusted Cox proportional hazards models with bootstrap resampling and are presented as hazard ratios (HR) with

95% CI. As the length of hospital stay was not randomly decided, we used two different methods to account for confounding and indication bias. The first method was a propensity score-adjusted Cox regression model. Propensity scores were computed from a logistic regression model predicting length of hospital stay. The covariates that were entered into this model were age, sex, creatinine, calendar year, diabetes, history of coronary artery disease (including any history of MI, PCI or coronary artery bypass grafting [CABG]) and in-hospital use of intravenous diuretics; the latter was added to the model due to differences observed between groups. All models had to pass the proportional hazards assumptions of Cox regression by assessment of Schoenfeld's residuals. The second method was an inverse probability weighting propensity score analysis. This method estimates the average treatment effects (ATE) and the average treatment effect on the treated (ATET) by calculating the propensity score for hospital stay (using the same covariates as in model 1) and derives the inverse probabilities used to balance the covariate distribution. The only variable with missing values was creatinine, which had 245 (3.1%) missing values; due to the low missingness rate, no imputation was undertaken. Given the potential for type I error due to multiple testing, secondary analyses and subgroup analyses should be interpreted as exploratory and hypothesis-generating. All statistical analyses were performed using Stata version 14.1 for Mac (StataCorp). A two-sided p-value <0.05 was considered statistically significant.

Results





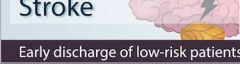
PATIENT CHARACTERISTICS

Among the 30,677 patients with uncomplicated STEMI treated with primary PCI and undergoing transthoracic echocardiography during hospital stay, the PAMI-II risk score identified 8,092 (26.4%) patients as low risk. Reasons for not being considered as having a low risk according to the PAMI-II score were age ≥ 70 years (58.3%), LVEF <50% (67.4%), persistent arrhythmia (7.6%), multivessel disease (26.8%), and successful PCI not achieved (<1%). Patients not considered low risk had a significantly higher risk of MACE within one year, 4,956 (22.0%) compared to 329 (4.1%) for individuals identified as low risk (unadjusted HR 6.00, 95% CI: 5.36-6.70, $p < 0.001$) (**Supplementary Figure 1**).

In total, 1,449 (17.9%) patients considered as low risk with the PAMI-II score were discharged within two days from admission (early discharge group) and 6,643 (82.1%) had a longer hospital stay (late discharge group). Differences in patient characteristics are shown in **Table 2**. Early discharge was more frequent during the last three years of the study period. Patients in the early discharge group were of similar age. Comorbidities and medications at presentation were also similar in the early and late discharge groups (**Table 2**). A radial vascular approach was more common in the early discharge group (83.9% vs 72.4%, $p < 0.001$). Significant differences in length of hospital stay were observed among different centres (**Supplementary Figure 2**).

COMPARISON OF EARLY DISCHARGE AND LATE DISCHARGE

The two groups were well balanced in their baseline characteristics before propensity score weighting. After adjustment, the one-year MACE rate was not higher for patients discharged at >2 days from admission than for patients discharged ≤ 2 days from admission (4.3% vs 3.2%; adjusted HR 1.31, 95% CI: 0.92-1.87, $p = 0.14$) (**Figure 2, Central illustration**). The one-year rate of all-cause mortality was not higher for patients discharged >2 days from admission than for patients discharged ≤ 2 days of admission (1.0% vs 1.0%; adjusted HR 1.12, 95% CI: 0.56-2.24, $p = 0.75$), PCI-treated reinfarction (1.2% vs 1.6%; adjusted HR 1.23, 95% CI: 0.71-2.13, $p = 0.46$), hospitalisation due to HF (1.5% vs 0.7%; adjusted HR 1.98, 95% CI: 0.98-4.02, $p = 0.06$), or stroke (0.3% vs 0.6%), for which proportional hazard assumptions were not fulfilled (**Table 3**). Similar results were observed for unadjusted analyses as well as for short-term outcomes (**Supplementary Table 1**). After inverse probability weighting and adjustment, there were no outcome differences between patients with short hospital stay compared to longer stay regarding any outcome measure for both 30-day and one-year outcomes (**Table 3**).

One-year outcome	Early discharge	Late discharge
MACE 	46 (3.2%)	283 (4.3%)
	HR (95% CI): 1.31 (0.92-1.87), $p = 0.14$	
Death 	14 (1.0%)	68 (1.0%)
	HR (95% CI): 1.12 (0.56-2.24), $p = 0.75$	
HF admission 	10 (0.7%)	99 (1.5%)
	HR (95% CI): 1.98 (0.98-4.02), $p = 0.06$	
Reinfarction 	18 (1.2%)	105 (1.6%)
	HR (95% CI): 1.23 (0.71-2.13), $p = 0.46$	
Stroke 	5 (0.3%)	42 (0.6%)

Early discharge of low-risk patients with STEMI treated with PCI appears to be considered safe.

Central illustration. Early discharge of low-risk patients with STEMI treated with PCI appears to be safe.

SUBGROUP, SENSITIVITY AND LANDMARK ANALYSES

Results of the primary endpoint, MACE within 365 days, were consistent across all subgroups with no difference in MACE between early and late discharge patients (**Figure 3**). Early discharge was not associated with a higher incidence of one-year MACE in the landmark analyses at discharge or after 30 days from admission (**Figure 2, Supplementary Figure 3**). There were no differences in MACE rates in a separate sensitivity analysis stratified according to admission year into ≤ 2010 , 2011-2014 and ≥ 2015 .

Discussion

In this nationwide observational study of patients with STEMI treated with PCI, the PAMI-II risk score identified 1/4 of patients as low risk in whom early discharge was not associated with short- or long-term adverse outcome.

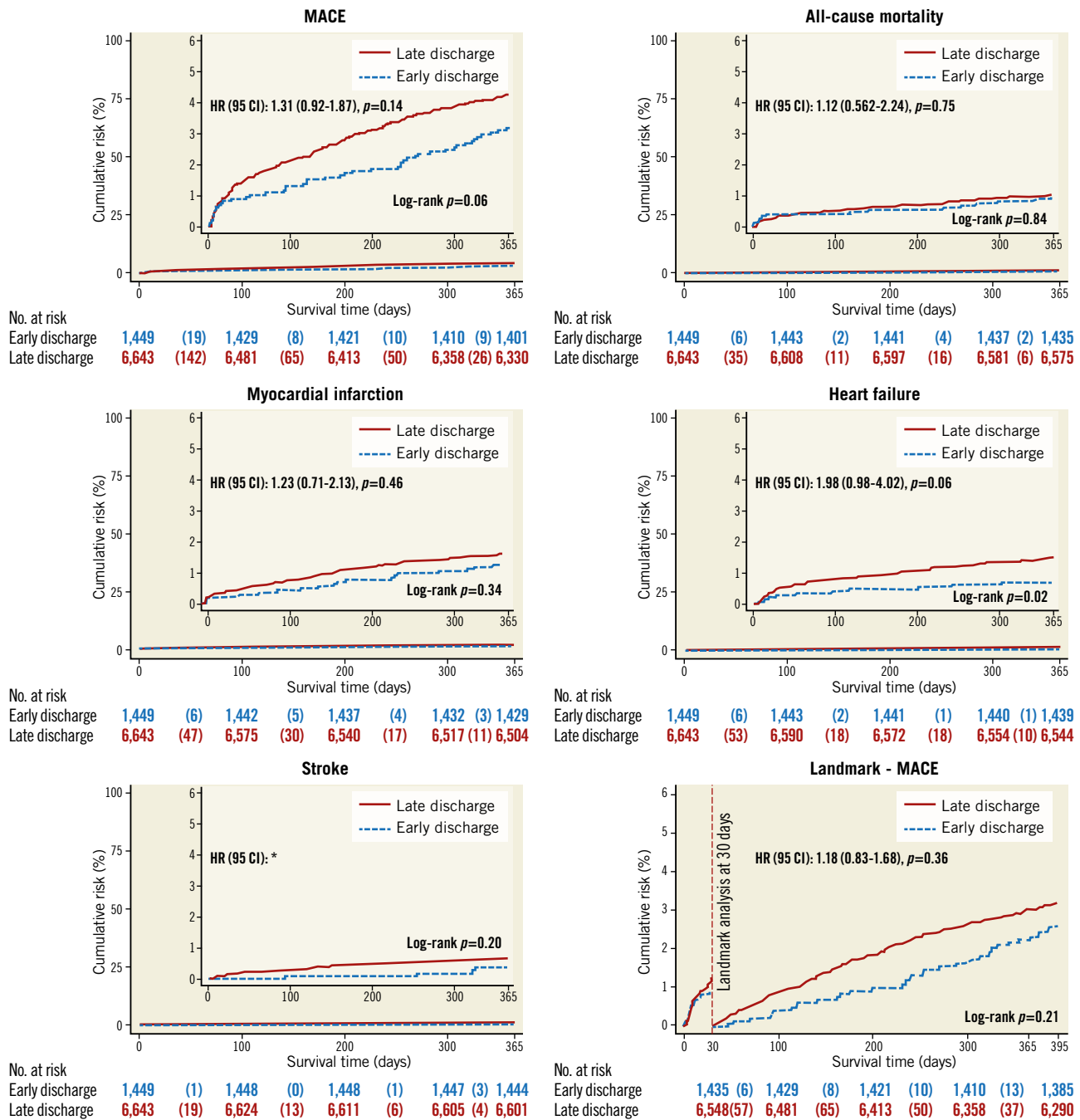


Figure 2. Kaplan-Meier failure estimate graphs for the primary endpoint, secondary endpoints and landmark analysis. A) Cumulative incidence and propensity score-adjusted hazard ratio of the composite primary endpoint of major adverse cardiovascular events (MACE) consisting of first event of death, reinfarction treated with PCI, stroke or hospitalisation due to heart failure in low-risk patients categorised according to length of hospital stay. No differences were observed between the early discharge and longer hospital stay groups. B-E) The cumulative incidence and propensity score-adjusted hazard ratio of each component of the primary endpoint in low-risk patients categorised according to length of hospital stay. F) The cumulative incidence and propensity score-adjusted hazard ratio of MACE after the landmark at 30 days from discharge for low-risk patients categorised according to length of hospital stay. * Proportional hazard assumptions were not fulfilled.

Our results serve as a real-world validation of the PAMI-II risk score¹. To the best of our knowledge, this is the largest study assessing the safety of early discharge in low-risk STEMI patients. It supports the findings of smaller observational

studies^{11,12}, as well as small randomised clinical trials⁷⁻¹⁰, that early discharge of low-risk STEMI patients is safe. In our study, patients categorised as low risk had very low rates of death, reinfarction requiring PCI treatment, stroke or HF hospitalisation

Table 2. Baseline characteristics.

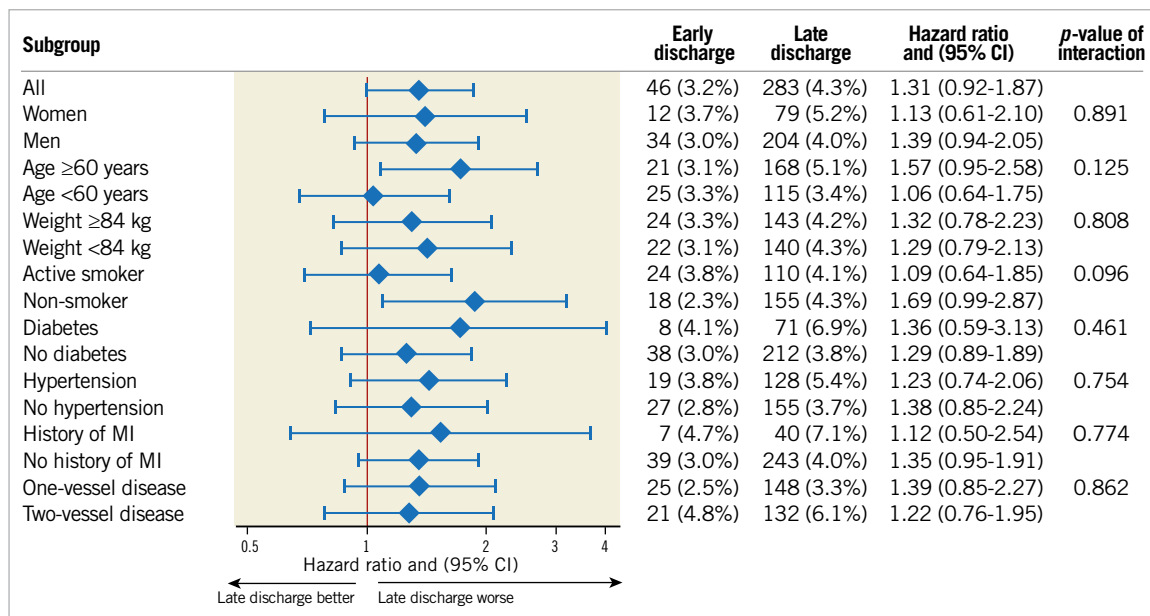
		Total 8,092 (100.0%)	Early discharge 1,449 (17.9%)	Late discharge 6,643 (82.1%)	p-value
Variable	Age, years	59.0 (53.0-65.0)	59.0 (53.0-65.0)	59.0 (53.0-65.0)	0.69
	Body mass index	27.1 (24.7-30.0)	27.1 (24.7-29.9)	27.2 (24.7-30.1)	0.54
	Men	6,254 (77.3%)	1,129 (77.9%)	5,125 (77.1%)	0.53
	Women	1,838 (22.7%)	320 (22.1%)	1,518 (22.9%)	0.53
Smoking status	Never smoked	2,313 (30.0%)	401 (28.6%)	1,912 (30.3%)	0.32
	Ex-smoker	2,068 (26.8%)	370 (26.4%)	1,698 (26.9%)	0.32
	Current smoker	3,339 (43.3%)	630 (45.0%)	2,709 (42.9%)	0.32
Inclusion period*	≤2010	1,870 (100%)	260 (13.9%)	1,610 (86.1%)	<0.001
	2011-2014	4,006 (100%)	677 (16.9%)	3,329 (83.1%)	<0.001
	≥2015	2,216 (100%)	512 (23.1%)	1,704 (76.9%)	<0.001
Past medical history	Diabetes	1,223 (15.1%)	194 (13.4%)	1,029 (15.5%)	0.04
	Hypertension	2,893 (35.8%)	500 (34.5%)	2,393 (36.0%)	0.28
	Hyperlipidaemia	1,494 (18.8%)	269 (18.8%)	1,225 (18.8%)	0.99
	History of CAD	806 (10.0%)	166 (11.5%)	640 (9.6%)	0.04
	History of MI	709 (8.8%)	148 (10.2%)	561 (8.4%)	0.03
	History of PCI	538 (6.6%)	112 (7.7%)	426 (6.4%)	0.07
	History of CABG	48 (0.6%)	14 (1.0%)	34 (0.5%)	0.04
	CHF	92 (1.1%)	12 (0.8%)	80 (1.2%)	0.22
	Stroke	231 (2.9%)	37 (2.6%)	194 (2.9%)	0.44
	Renal failure	83 (1.0%)	16 (1.1%)	67 (1.0%)	0.74
Past medications	ACE inhibitors	917 (11.5%)	160 (11.2%)	757 (11.5%)	0.72
	Angiotensin receptor blockers	831 (10.4%)	147 (10.3%)	684 (10.4%)	0.89
	Beta-blockers	1,315 (16.4%)	226 (15.8%)	1,089 (16.6%)	0.47
	Aspirin	1,009 (12.6%)	184 (12.8%)	825 (12.5%)	0.75
	Statins	1,286 (16.0%)	229 (16.0%)	1,057 (16.0%)	0.94
	Diuretics	527 (6.6%)	77 (5.4%)	450 (6.8%)	0.04
	Oral anticoagulants	87 (1.1%)	10 (0.7%)	77 (1.2%)	0.12
In-hospital characteristics	Heart rate, bpm	72 (61-84)	71 (62-84)	72 (61-84)	0.98
	SBP, mmHg	144 (126-163)	145 (127-165)	143 (126-163)	0.17
	Serum creatinine, µmol/L	75 (65-87)	75 (66-87)	75 (65-87)	0.91
	eGFR-CK Depi, mL/min/1.73 m ²	93 (80-101)	93 (80-101)	93 (80-100)	0.43
	Haemoglobin, g/L	144 (134-153)	143 (135-153)	144 (134-153)	0.70
Admission ECG	AF/AFL	117 (1.4%)	13 (0.9%)	104 (1.6%)	0.053
Office/duty hours	Planned - office hours	55 (0.7%)	5 (0.4%)	50 (0.8%)	0.14
	Acute - office hours	2,465 (31.3%)	451 (31.7%)	2,014 (31.2%)	0.14
	Acute - duty hours	4,885 (62.1%)	897 (63.0%)	3,988 (61.8%)	0.14
	Subacute - office hours	383 (4.9%)	55 (3.9%)	328 (5.1%)	0.14
	Subacute - duty hours	84 (1.1%)	16 (1.1%)	68 (1.1%)	0.14
	Symptoms to PCI, min	177.0 (116.0-330.0)	180.0 (120.0-339.0)	176.0 (115.0-329.0)	0.34
FMC to PCI, min	70.0 (49.0-108.0)	70.0 (50.0-110.0)	70.0 (48.0-107.0)	0.34	
Vascular approach	Femoral artery	1,786 (22.1%)	186 (12.8%)	1,600 (24.1%)	<0.001
	Radial artery	6,025 (74.5%)	1,216 (83.9%)	4,809 (72.4%)	<0.001
	Combined/other	281 (3.5%)	47 (3.2%)	234 (3.5%)	<0.001
Angiographic findings	1-vessel disease not LM	5,465 (67.5%)	1,010 (69.7%)	4,455 (67.1%)	0.22
	2-vessel disease not LM	2,597 (32.1%)	435 (30.0%)	2,162 (32.5%)	0.22
Culprit vessel PCI	LM	13 (0.2%)	3 (0.2%)	10 (0.2%)	0.33
	LAD	2,374 (29.3%)	424 (29.3%)	1,950 (29.4%)	0.33
	LCx	745 (9.2%)	142 (9.8%)	603 (9.1%)	0.33
	RCA	3,534 (43.7%)	604 (41.7%)	2,930 (44.1%)	0.33
	Branches	1,425 (17.6%)	276 (19.0%)	1,149 (17.3%)	0.33
	Procedure with stent implanted	7,805 (96.5%)	1,408 (97.2%)	6,397 (96.3%)	0.10
Other in-hospital treatments	CPAP	48 (0.6%)	10 (0.7%)	38 (0.6%)	0.60
	IV inotropes	77 (1.0%)	19 (1.3%)	58 (0.9%)	0.12
	IV nitroglycerine	598 (7.4%)	83 (5.7%)	515 (7.8%)	0.008
	IV diuretics	295 (3.6%)	34 (2.3%)	261 (3.9%)	0.004
	Complication in lab or ward	297 (3.7%)	48 (3.3%)	249 (3.7%)	0.42

Percentages are calculated on complete case data. *Percentage in rows. CABG: coronary artery bypass graft; CHF: chronic heart failure; CPAP: continuous positive airway pressure; LAD: left anterior descending artery; LCx: left circumflex artery; LM: left main artery; MI: myocardial infarction; PAD: peripheral artery disease; RCA: right coronary artery

Table 3. Effect of early discharge on outcome: results from propensity score-adjusted and inverse probability weighting propensity score analyses.

One-year outcome	Early discharge	Late discharge	Unadjusted HR (95% CI), p-value	PS-adjusted HR (95% CI), p-value	ATE coefficient (95% CI), p-value	ATET coefficient (95%CI), p-value
MACE	46 (3.2%)	283 (4.3%)	1.35 (0.99-1.86), p=0.06	1.31 (0.92-1.87), p=0.14	0.008 (-0.004-0.020), p=0.22	0.007 (-0.005-0.018), p=0.27
All-cause mortality	14 (1.0%)	68 (1.0%)	1.06 (0.60-1.89), p=0.84	1.12 (0.56-2.24), p=0.75	-0.001 (-0.007-0.006), p=0.91	-0.001 (-0.007-0.006), p=0.80
HF admission	10 (0.7%)	99 (1.5%)	2.17 (1.03-4.53), p=0.04	1.98 (0.98-4.02), p=0.06	0.006 (0.001-0.013), p=0.07	0.006 (-0.001-0.013), p=0.093
Reinfarction	18 (1.2%)	105 (1.6%)	1.28 (0.74-2.22), p=0.38	1.23 (0.71-2.13), p=0.46	0.003 (-0.004-0.01), p=0.44	0.003 (-0.005-0.01), p=0.45
Stroke	5 (0.3%)	42 (0.6%)	-	-	0.002 (-0.002-0.006), p=0.24	0.002 (-0.002-0.006), p=0.26

The average treatment effect (ATE) and average treatment effect on the treated (ATET) shows the effect of length of stay on outcome for the entire population and patients with longer hospital stay, respectively, after propensity score weighting. The ATE and ATET can be multiplied by 100 to be interpreted as the difference in percent points. Analyses marked with a hyphen did not fulfil proportional hazard assumptions. HF: heart failure; MACE: major adverse cardiovascular events; PS: propensity score

**Figure 3. Forest plot visualising hazard ratios of MACE stratified by length of hospital stay. Subgroup analysis for the primary endpoint major adverse cardiovascular events (MACE) showing Kaplan-Meier event rates and propensity score-adjusted hazard ratio with interaction test performed for age, sex, weight, smoking status, diabetes, hypertension, history of myocardial infarction (MI) and number of diseased vessels. There were no significant interactions indicating a risk with early discharge in any subgroup.**

within the first year of admission, with no significant differences found between patients with short hospital stay compared to longer in any investigated outcome measure. Importantly, the low mortality rate of 1% (which did not differ between groups) is supportive of the safety of early discharge. To account for confounders and indication bias (i.e., sicker patients who need longer hospital stay will have a longer stay), we used propensity score analyses and inverse probability weighting propensity scores. The two landmark analyses that were undertaken were not associated with adverse outcome, suggesting a low rate of residual confounding.

Patients with longer hospital stay were more frequently treated with intravenous diuretics and discharged with diuretic prescriptions, probably signalling early symptomatic HF. In line with this finding, we observed a trend towards more frequent hospitalisations due to HF in this group. Although this trend was not statistically significant in any analyses except unadjusted analyses, a subgroup of low-risk patients, e.g., patients needing intravenous diuretics, heart rate regulation due to atrial fibrillation/flutter or patients in whom radial artery access was not possible, may naturally require a longer hospital stay. However, this relates to a small proportion of all patients identified as low-risk patients and does

not explain the significant interhospital differences in length of hospital stay observed in Sweden (**Supplementary Figure 1**). We believe this to be a much larger variation than expected and is more reflective of local hospital traditions rather than different proportions of high-risk patients. The interhospital difference in hospital stay among low-risk patients inherently contributes to an uneven distribution in hospital cost for STEMI patients in Swedish hospitals. Adherence to guideline recommendations on the use of the PAMI-II risk score could reduce hospital costs. According to our findings, about 1,000 STEMI patients each year may be identified as candidates for early discharge in Sweden (10 million population), of whom $\approx 18\%$ were discharged from the coronary care unit (CCU) within two days. Adherence to early discharge of low-risk STEMI patients would result in the saving of $\approx 1,700$ care days per year (calculated as total care days among low-risk patients with >2 days minus care days if they were discharged within 2 days). Assuming that only patients with a length of stay of 3-5 days are candidates for early discharge would result in $\approx 1,200$ care days saved per year. In countries with large populations, a higher incidence of STEMI, and with the increased proportion of patients treated with PCI, a more efficient use of hospital and CCU beds could result in substantial cost reduction and increased availability of cardiac health care to those in need. A major concern with early discharge is that patient education and information comprehension might be compromised.

However, when early follow-up by coronary care staff is available, this is of lesser concern, and information on medication and lifestyle changes might even be better understood outside of the acute care setting.

There is a need for a more standardised hospitalisation strategy while continuing to secure patient safety. Ongoing small randomised clinical trials assessing the safety of early discharge, e.g., the EDAMI study⁷ (N=1,558, www.clinicaltrials.gov identifier: NCT01868256) will hopefully support the concept of a standardised hospitalisation strategy for low-risk patients. A large randomised clinical trial addressing this topic in the modern era is warranted to ascertain the safety of early discharge. However, a major difficulty with such a study is that it would require a large number of patients as outcome is infrequent in low-risk patients. For example, investigating the superiority of a prolonged hospital stay with a baseline mortality of 1% and an absolute risk reduction of 0.5% would require roughly 10,000 patients.

Limitations and strengths

Our definition of low-risk features differed somewhat from the original PAMI publication. This was due to the constraints of the available data. However, we believe that the definitions used in this study are more reflective of a low-risk patient in a contemporary clinical setting. We acknowledge the risk of residual confounding and indication bias inherent to observational studies. Although baseline differences were minor and unadjusted analyses were consistent with adjusted analyses, indicating low rates of confounding, residual confounding and indication bias cannot

be ruled out completely. A proportion of patients identified as low risk may have needed a longer hospital stay, as indicated by the more frequent use of intravenous diuretics. Our study benefits from a number of strengths as well. It is a nationwide study using a validated high-quality registry including more than 8,000 low-risk patients with STEMI admitted over eight years and treated according to current guidelines¹⁵.

Conclusions

In a nationwide population of STEMI patients, the PAMI-II risk score adequately identified patients with a very low risk of short- and long-term adverse outcome in whom early discharge within two days may be considered safe.

Impact on daily practice

The safety of early discharge following ST-elevation myocardial infarction (STEMI) has been examined in observational studies and randomised clinical trials that are either small or were conducted prior to the widespread use of mechanical reperfusion with percutaneous coronary intervention. Using contemporary data from nationwide population-based registries, we show that early discharge within two days of admission is safe in low-risk patients with STEMI. A more standardised hospitalisation strategy for low-risk STEMI patients, that secures patient safety and reduces the length of hospital stay, may result in a more efficient use of coronary care unit beds and substantial cost reduction, and increase the availability of cardiac health care to those in need.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. STROBE Statement—Checklist of items that should be included in reports of cohort studies.

Supplementary Table 1. Effect of early discharge on short-term outcome: results from propensity score-adjusted and inverse probability weighting propensity score analyses.

Supplementary Figure 1. Kaplan-Meier failure estimates for the primary composite endpoint (MACE).

Supplementary Figure 2. Length of hospital stay by centre.

Supplementary Figure 3. Landmark analyses at discharge.

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Supplementary data

Supplementary Appendix 1. STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	10 and Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (e.g., average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10-11

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorised (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10-11 and table 2
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

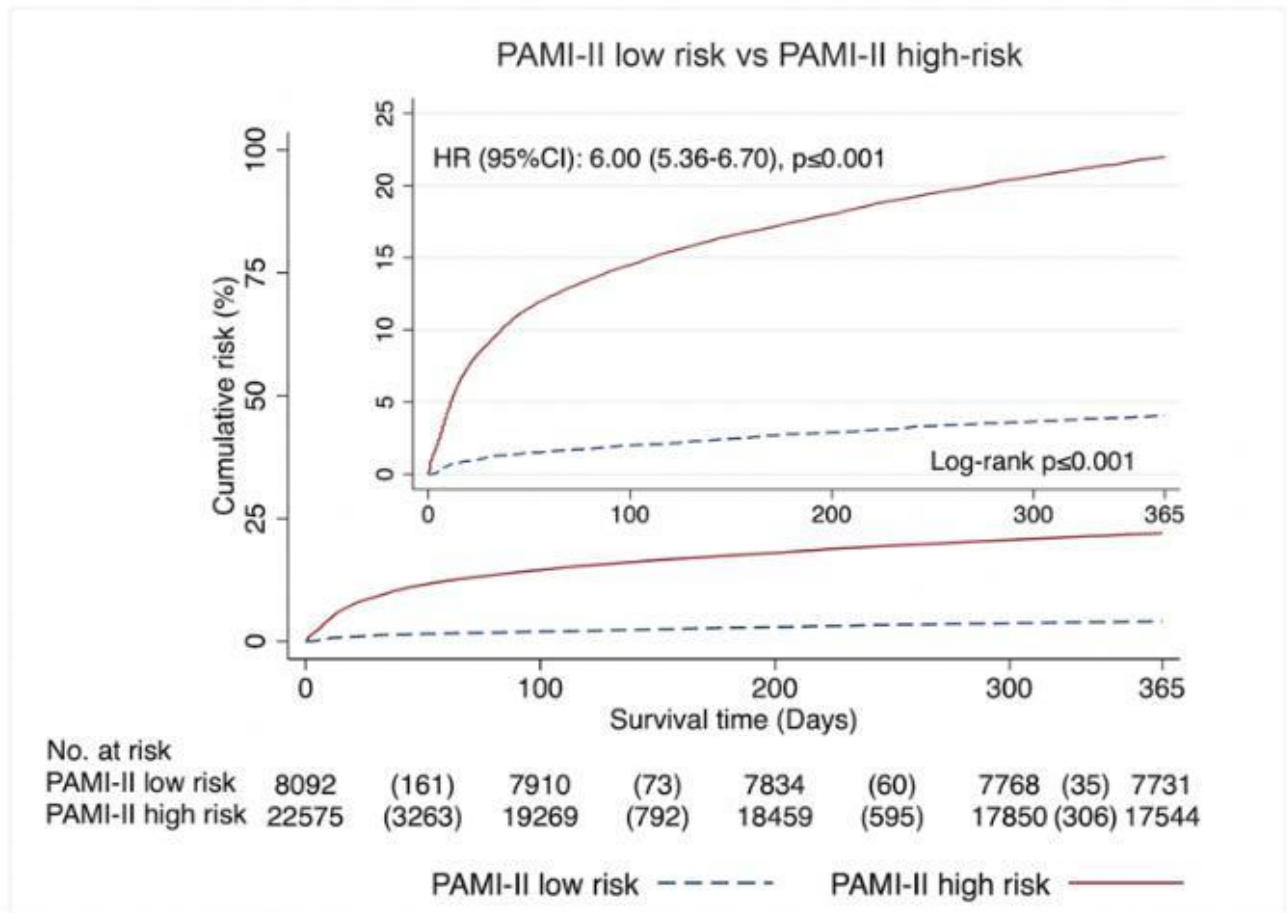
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Supplementary Table 1. Effect of early discharge on short-term outcome: results from propensity score-adjusted and inverse probability weighting propensity score analyses.

	Early discharge	Late discharge	Unadjusted HR (95% CI), <i>p</i> -value	PS-adjusted HR (95% CI), <i>p</i> -value	ATE coefficient (95% CI), <i>p</i> -value	ATET coefficient (95% CI), <i>p</i> -value
30-day outcomes						
MACE	13 (0.9%)	85 (1.3%)	1.43 (0.80–2.56), <i>p</i> =0.23	–	0.003 (-0.003–0.01), <i>p</i> =0.29	0.003 (-0.003–0.01), <i>p</i> =0.33
All-cause mortality	6 (0.4%)	20 (0.3%)	–	–	-0.001 (-0.005–0.003), <i>p</i> =0.53	-0.001 (-0.006–0.003), <i>p</i> =0.50
HF admission	4 (0.3%)	34 (0.5%)	1.86 (0.58-5.98), <i>p</i> =0.30	–	0.002 (-0.002–0.006), <i>p</i> =0.28	0.002 (-0.002–0.006), <i>p</i> =0.31
Reinfarction	3 (0.2%)	27 (0.4%)	–	–	0.002 (-0.001–0.005), <i>p</i> =0.17	0.002 (-0.001–0.005), <i>p</i> =0.15
Stroke	0 (0%)	11 (0.2%)	–	–	–	–

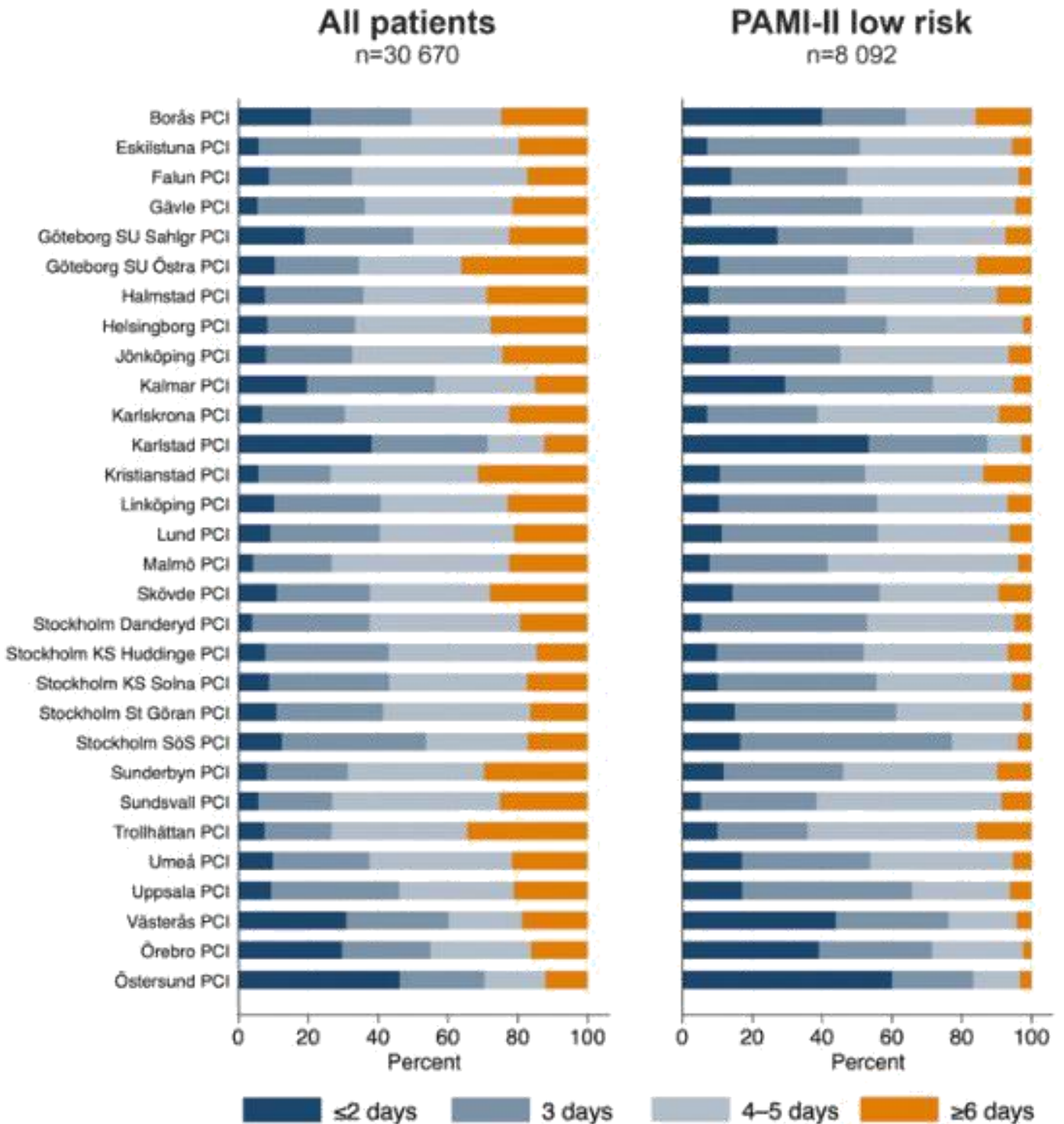
The average treatment effect (ATE) and average treatment effect on the treated (ATET) shows the effect of length of stay on outcome for the entire population and patients with longer hospital stay, respectively, after propensity score weighting. The ATE and ATET can be multiplied by 100 to be interpreted as the difference in percent points. Analyses marked with a hyphen did not fulfil assumptions of proportional hazard or the ATE and ATET were not possible to calculate.

MACE: major adverse cardiovascular events



Supplementary Figure 1. Kaplan-Meier failure estimates for the primary composite endpoint (MACE).

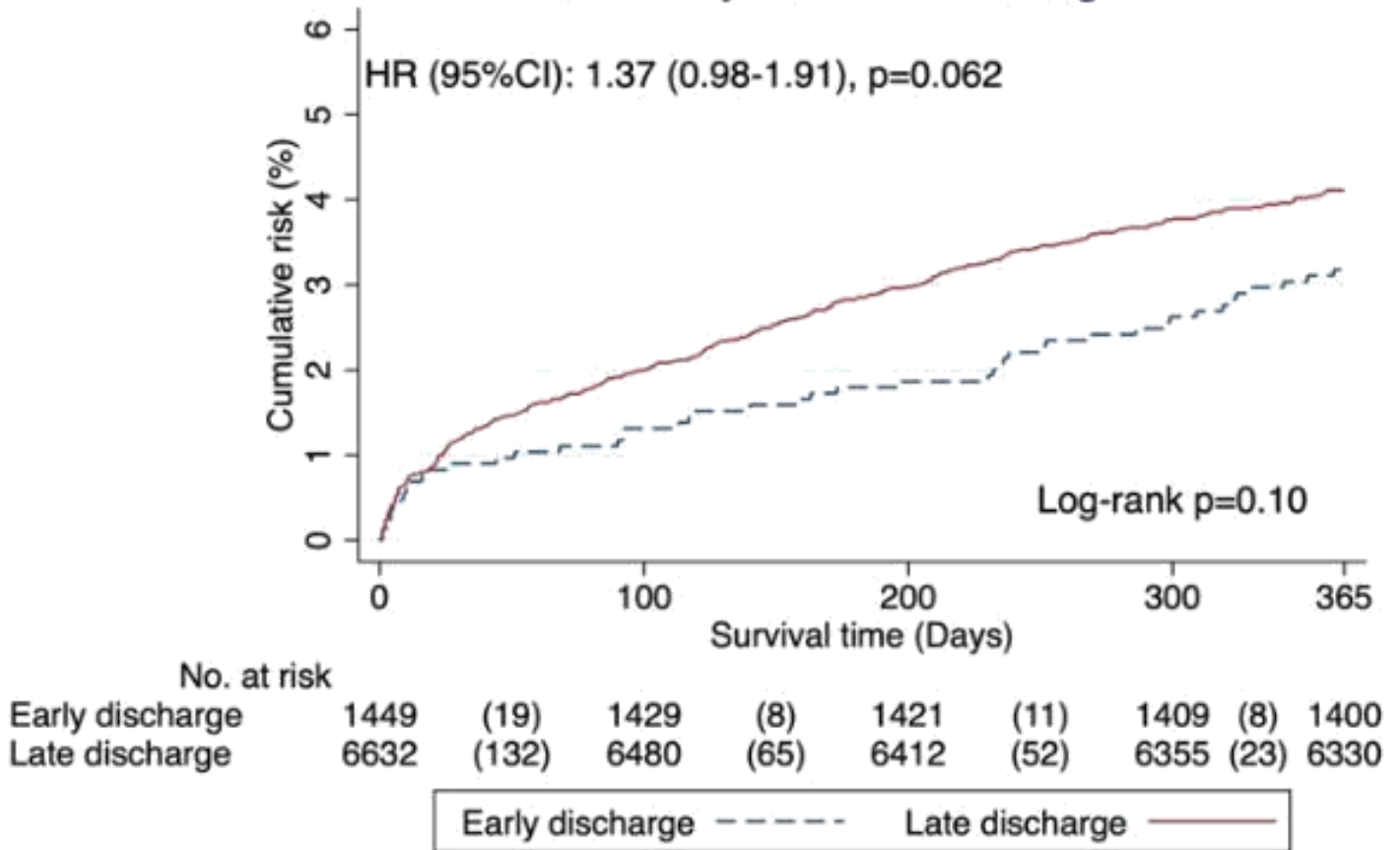
Cumulative incidence and crude hazard ratio of the composite primary endpoint major adverse cardiovascular events (MACE), consisting of first event of death, reinfarction treated with PCI, stroke or hospitalisation due to heart failure in patients with ST-elevation myocardial infarction as categorised by the PAMI-II risk score as low versus high risk.



Supplementary Figure 2. Length of hospital stay by centre.

The left panel shows the proportion of patients discharged within 2 days, 3 days, 4-5 days and ≥ 6 days for all patients by different PCI centres in Sweden. The right panel shows the proportion of length of hospital stay for patients identified as candidates for early discharge using the PAMI-II risk score showing a significant discrepancy in length of stay between PCI centres.

Landmark analysis from discharge – MACE



Supplementary Figure 3. Landmark analyses at discharge.

Cumulative incidence and propensity score-adjusted hazard ratio of the composite primary endpoint major adverse cardiovascular events (MACE), consisting of first event of death, reinfarction treated with PCI, stroke or hospitalisation due to heart failure after the landmark at discharge for low-risk patients categorised according to length of hospital stay. Solid line represents patients with longer hospital stay and dashed line represents patients discharged within two days.