

# Impact of hypertension on the outcome of patients admitted with acute coronary syndrome

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**Objective:** The role of hypertension and its impact on outcome in patients with acute coronary syndrome (ACS) is still debated. This study aimed to compare the outcomes of hypertensive and nonhypertensive ACS patients.

**Methods:** Using data of ACS patients enrolled in the Acute Myocardial Infarction in Switzerland Plus Registry from 1997 to 2013, characteristics at presentation and outcomes in hospital and after 1 year were analyzed. Hypertension was defined as previously diagnosed and treated by a physician. The primary endpoint was mortality. Data were analyzed using multiple logistic regressions.

**Results:** Among 41 771 ACS patients, 16 855 (40.4%) were without and 24 916 (59.6%) with preexisting hypertension. Patients with preexisting hypertension had a more favorable in-hospital outcome [odds ratio (OR) in-hospital mortality 0.82, 95% confidence interval (CI) 0.73–0.93;  $P=0.022$ ]. The independent predictors of in-hospital mortality for patients with preexisting hypertension were age, Killip class greater than 2, Charlson Comorbidity Index greater than 1, no pretreatment with statins and lower admission systemic blood pressure. Preexisting hypertension was not an independent predictor of 1-year mortality in the subgroup of patients ( $n=7801$ ) followed: OR 1.07, 95% CI 0.78–1.47;  $P=0.68$ . Independent predictors of mortality 1 year after discharge for the 4796 patients with preexisting hypertension were age, male sex and comorbidities. Angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists and statins prescribed at discharge improved the outcomes.

**Conclusion:** Outcome of ACS patients with preexisting hypertension was associated with an improved in-hospital prognosis after adjustment for their higher baseline risk. However, this effect was not long-lasting and does not necessarily mean a causal relationship exists. Short-term and long-term management of patients with hypertension admitted with ACS could be further improved.

**Keywords:** acute coronary syndrome, hypertension, therapy

**Abbreviations:** ACEI, angiotensin-converting enzyme inhibitors; ACS, acute coronary syndrome; AMI, acute myocardial infarction; AMIS, Acute Myocardial Infarction in

Switzerland; ARBs, angiotensin II receptor antagonists; BP, blood pressure; CCI, Charlson Comorbidity Index; CI, confidence interval; LBBB, left bundle branch block; MACCEs, major adverse cardiac or cardiovascular events; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; OR, odds ratio; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction

## INTRODUCTION

Hypertension is an established risk factor of atherosclerosis and its sequelae [1]. However, the impact of preexisting hypertension on prognosis in patients with acute coronary syndrome (ACS) is less clear [2,3]. Some studies suggested that preexisting hypertension and elevated blood pressure (BP) at admission contribute to a worse prognosis [4–6]. Other studies found better in-hospital outcomes in hypertensive patients with ACS than in age-matched and sex-matched normotensive individuals, perhaps because of a less severe extension of the infarction area or other unknown pathophysiologic mechanisms [7]. A previous study suggested that ACS mortality is strongly related to admission BP with a J-shaped or U-shaped curve association, with the lowest adverse event rates in the SBP range of 130–140 mmHg and DBP range of 80–90 mmHg [8]. A large study showed that elevated admission SBP in patients with ST-segment elevation myocardial infarction (STEMI) was not associated with worse outcomes [9]. We assumed that preexisting hypertension might be protective in ACS patients in the short term despite its clearly

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established role in increasing the long-term risk for coronary artery disease. Similar paradoxes have been previously described for smokers [10] as well as for patients with obesity [11].

Previous studies evaluating the role of hypertension in ACS had their own limitations. Results from randomized trials or retrospective cohorts may be subject to selection bias. Some of the studies were not powered to investigate the question in detail or did not assess important variables such as admission BP or medications. Therefore, we aimed to evaluate the impact of preexisting hypertension in ACS patients on in-hospital and 1-year outcomes using the large, comprehensive and prospective Swiss Acute Myocardial Infarction in Switzerland (AMIS) Plus Registry [12–15].

## METHODS

### The Acute Myocardial Infarction in Switzerland Plus Registry

The AMIS Plus Registry is an ongoing nationwide prospective registry of patients admitted with ACS to hospitals in Switzerland [11,16]. From 106 hospitals treating ACS in Switzerland, 82 hospitals temporarily or continuously enrolled patients in the AMIS Plus Registry since it was founded in 1997. Participating centers range from community institutions to large tertiary facilities and provide blinded data for each patient through standardized internet-based or paper-based questionnaires. Participating centers are strongly encouraged to enroll all patients fulfilling the inclusion criteria to avoid selection bias. Hospital data are provided and completed by the treating physician or a trained study nurse. All data are checked for completeness, plausibility and consistency by the AMIS Plus Data Center (Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Switzerland).

The data center queries the treating physicians or study nurses in case of incomplete, implausible or inconsistent data. To control and assure data quality, for the last 5 years external auditing has been additionally performed regularly in randomly selected hospitals with randomly selected patients. The auditing objective in AMIS Plus participating hospitals was to review the selected data items per source data verification in order to assess the level of compliance with the protocol and guidelines. The grading of findings was performed according to the ‘procedure for reporting of good-clinical-practice compliance inspections’ requested by the European Medicines Agency. The AMIS Plus Registry was approved by the Swiss Supra-Regional Ethics Committee for Clinical Studies, the Swiss Board for Data Security and the Cantonal Ethics Commissions. The AMIS Plus project is supported by the Swiss Societies of Cardiology, Internal Medicine and Intensive Care Medicine.

### Patient selection

The present analysis included all ACS patients enrolled in AMIS Plus between January 1997 and December 2013. The ACS definition included patients with acute myocardial infarction (AMI) and patients with unstable angina. AMI was defined according to the universal definition of myocardial infarction (MI) by characteristic symptoms and ECG changes and cardiac marker elevation (either creatine

kinase Muscle-Brain fraction at least twice the upper limit of normal or troponin I or T above individual hospital cutoff levels for MI) [17]. Patients included in this analysis were categorized as having STEMI or non-STEMI (NSTEMI) based on the initial ECG findings. Classification of STEMI included evidence of AMI as above and ST-segment elevation and new left bundle branch block (LBBB) on the initial ECG. NSTEMI included patients with ischemic symptoms, ST-segment depression or T-wave abnormalities in the absence of ST elevation on the initial ECG [18]. Unstable angina was diagnosed if symptoms or ECG changes were compatible with ACS and cardiac marker levels remained lower than cutoff or normal levels.

### Baseline evaluation at hospital admission

All patients were extensively evaluated at hospital admission. The usual evaluation included taking the patient’s history of preexisting comorbidities, assessing the medications, measuring BP with usual devices, measuring cardiac markers as well as recording an ECG. In the context of this study, preexisting hypertension was assumed if history of hypertension was known and previously treated according to the guidelines [19–21]. To measure the extent of comorbidities, we used the weighted Charlson Comorbidity Index (CCI) [22,23]. Patients were considered obese if the BMI was at least 30 kg/m<sup>2</sup> and as smokers if the patient was a current smoker at the time of hospital admission.

### Follow-up and endpoints

The AMIS Plus Registry assesses in-hospital outcomes in all patients, including mortality and the occurrence of major adverse cardiac or cardiovascular events (MACCEs). Since 2006, the registry also assesses the outcomes 12 months after hospital discharge. For the present analysis, the primary endpoint was in-hospital and 1-year mortality. The secondary composite endpoint MACCE was analyzed and included re-infarction, stroke and death in hospital.

### Statistical analysis

First, baseline characteristics were descriptively analyzed according to the hypertension status and then in-hospital and 1-year outcomes. As hypertension may be associated with age, sex, comorbidities and other circumstances, we performed the multiple logistic regression models using in-hospital and 1-year mortality as the dependent variable. This first model, which included all ACS patients, was adjusted for the following independent variables: preexisting hypertension, age, sex, Killip class greater than 2, CCI greater than 1 and presence of a STEMI. To control the impact of ACS type on in-hospital mortality, this model was repeated separately for patients with STEMI and patients with NSTEMI or unstable angina. To control the impact of immediate therapy on in-hospital mortality of all ACS patients, the model was repeated to additionally include guideline recommended therapy, such as one of the P2Y<sub>12</sub> blockers (clopidogrel, prasugrel or ticagrelor), beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor antagonists (ARBs) and statins.

We were ultimately interested in factors potentially explaining the association of preexisting hypertension with mortality. Therefore, the second multiple logistic regression

**TABLE 1. Baseline characteristics and immediate drug therapy of acute coronary syndrome patients according to hypertension history (n = 41 771)**

	Patients with preexisting hypertension (n = 24 916)	Patients without preexisting hypertension (n = 16 855)	P
Female (%)	31.3	21.2	<0.001
Age in years [mean (SD)]	69.3 (12.2)	61.6 (13.2)	<0.001
STEMI (%)	51.7	62.7	<0.001
Resuscitation prior admission (%)	979/24488 (4.0)	815/16643 (4.9)	<0.001
Delay h:min (symptom to admission) median (IQR)	4:05 (2:00, 11:40)	3:30 (1:45, 10:00)	<0.001
Admission SBP (mmHg), mean (SD)	141 (29)	131 (25)	<0.001
Admission DBP (mmHg), mean (SD)	81 (18)	79 (16)	<0.001
Heart rate (beats/min), mean (SD)	80 (21)	77 (20)	<0.001
Killip class >2 (%)	1906/24472 (7.8)	876/16620 (5.3)	<0.001
Diabetes mellitus (%)	6499/24210 (26.8)	1801/16698 (10.8)	<0.001
Dyslipidemia (%)	14372/22388 (64.2)	7257/15757 (46.1)	<0.001
Current smoker (%)	6875/22671 (30.3)	7778/16058 (48.4)	<0.001
Obese (BMI >30) (%)	5087/20576 (24.7)	1916/13884 (13.8)	<0.001
Charlson Comorbidity Index >1 (CCI >1) (%)	6170/19497 (31.6)	1509/12128 (12.4)	<0.001
<b>Immediate therapy</b>			
Percutaneous coronary intervention (%)	15472/21684 (71.4)	11292/14024 (80.5)	<0.001
P2Y <sub>12</sub> blocker (%)	15897/24499 (64.9)	10967/16718 (65.6)	0.14
Beta-blocker (%)	16247/24097 (67.4)	10695/16389 (65.3)	<0.001
ACEI/ARB antagonist (%)	13373/24023 (55.7)	6750/16294 (41.4)	<0.001
Statin (%)	14608/19927 (73.3)	9640/12439 (77.5)	<0.001

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; P2Y<sub>12</sub> blockers, clopidogrel, prasugrel or ticagrelor; STEMI, ST-segment elevation myocardial infarction.

model was performed including only the subgroup of patients with hypertension again using in-hospital and 1-year mortality as the dependent variable. The following independent variables were included in the model: age, sex, Killip class greater than 2, CCI greater than 1, presence of a STEMI, admission SBP, and drugs used regularly prior to the current event as a monotherapy or combined with diuretics (i.e., ACEI, ARB, beta-blockers, and Ca-channel blockers) and statins. To analyze the data according to BP at admission and 1-year mortality, additional logistic regressions were performed using BP values of 140, 150 and 160 mmHg as dichotomous variables adjusted for age, sex, Killip class greater than 2, CCI greater than 1 and added the maximum creatine kinase value as a measurement of the infarct burden. The results are presented as percentages for categorical variables and analyzed using the nonparametric Pearson  $\chi^2$  test or Fisher's exact test as appropriate. Continuous normally distributed variables are expressed as means  $\pm$  one standard deviation (SD) and compared using the Student's two-tailed unpaired *t*-test. Continuous non-normally distributed variables are expressed as medians and interquartile ranges, and analyzed using the Mann-Whitney U test. Results of logistic regression are reported as odds ratios (ORs) with 95% confidence interval (CI). A probability value of *P* less than 0.05 was considered significant. All analyses were performed using IBM SPSS Statistics (version 22; SPSS Inc, Chicago, Illinois, USA).

## RESULTS

### Study population

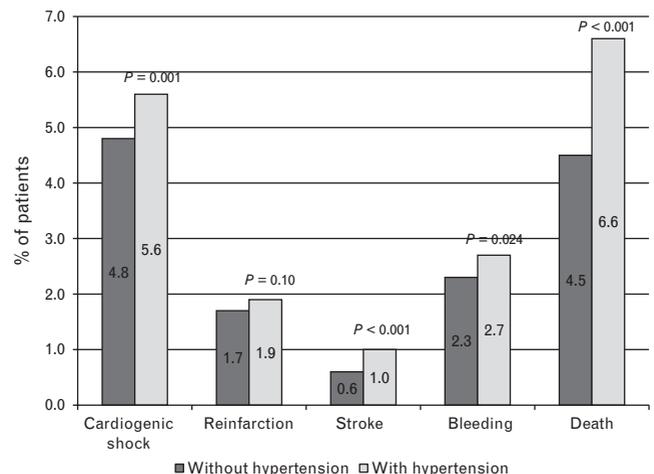
Between January 1997 and December 2013, 43 912 patients with ACS from 82 Swiss hospitals were enrolled in the AMIS Plus Registry. There was no documentation of history of hypertension for 2141 (4.9%) patients; therefore, these patients were excluded from the analysis. Of the 41 771

included patients, 16 855 (40.4%) had no preexisting hypertension, whereas 24 916 (59.6%) had previous hypertension. The baseline details of patients are described in Table 1.

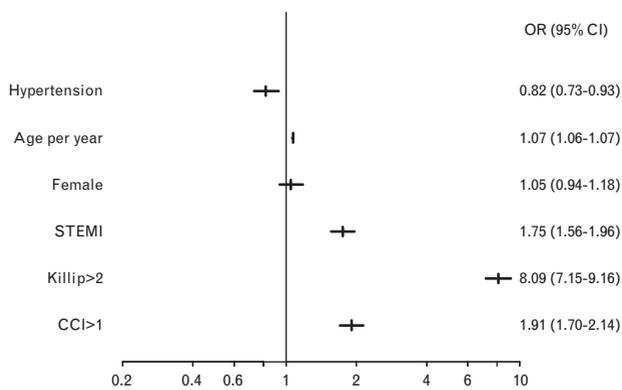
Patients with preexisting hypertension were somewhat older and less often experienced a STEMI compared with patients without preexisting hypertension. The classical cardiovascular risk factors and other comorbidities were more frequent in patients with preexisting hypertension. These patients were also less likely to be chosen for immediate mechanical revascularization.

### In-hospital outcome

Overall complication rates and crude in-hospital mortality were higher in hypertensive patients (Fig. 1).



**FIGURE 1** Complications and crude in-hospital mortality of acute coronary syndrome patients according to hypertension history (n = 41 771).



**FIGURE 2** Independent predictors of in-hospital mortality. 95% CI, 95% confidence interval; CCI >1, Charlson Comorbidity Index greater than 1; OR, odds ratio; STEMI, ST-segment elevation myocardial infarction.

However, after adjustment for covariates, patients with preexisting hypertension had better in-hospital mortality (OR 0.82, 95% CI 0.73–0.93;  $P=0.002$ ; Fig. 2). ACS patients with preexisting hypertension also had better outcomes regarding the composite endpoint of MACCEs (OR 0.85, 95% CI 0.76–0.96;  $P=0.006$ ).

Even after adjustment for immediate antiplatelet therapy and percutaneous coronary intervention (PCI), a history of hypertension remained significant (OR 0.86, 95% CI 0.76–0.97;  $P=0.022$ ). Logistic models performed separately for patients with NSTEMI/unstable angina and those with STEMI showed that NSTEMI/unstable angina patients with preexisting hypertension had significantly improved in-hospital mortality (OR 0.67, 95% CI 0.55–0.83;  $P<0.001$ ), whereas no significant improvement was seen in STEMI patients (OR 0.91, 95% CI 0.78–1.07;  $P=0.26$ ).

The relation between admission SBP and prognosis followed a J-shaped curve associated with increased mortality below the range of 130–140 mmHg for ACS patients with preexisting hypertension ( $P=0.002$ ) and below the range of 120–130 mmHg for patients without previous hypertension ( $P=0.004$ ; Fig. 3). Adjusted OR of 1-year mortality for BP above 140 mmHg at admission for hypertensive patients was 0.57 (95% CI 0.42–0.77;  $P<0.001$ ), for BP above 150 mmHg 0.62 (95% CI 0.45–0.86;  $P<0.001$ ) and for BP above 170 mmHg, the OR was 0.61 (95% CI 0.49–0.96;  $P=0.042$ ).

In the subgroup of patients with preexisting hypertension, the following baseline characteristics were

independent predictors of increased in-hospital mortality: higher age, presence of a STEMI, higher Killip class, increasing numbers of comorbidities, no pretreatment with statins and lower admission SBP. Pretreatment with ACEI, ARB and beta-blockers or calcium-channel blockers showed no effect on in-hospital mortality (Table 2). Similar predictors were found for patients without preexisting hypertension, but the presence of a STEMI was no longer significantly associated with the endpoint (Table 2).

### Outcome 1 year after discharge

We carried out a follow-up of 7801 patients 12 months after hospitalization. Patients with preexisting hypertension had worse unadjusted outcomes (Fig. 4). The percentage of ACS patients who underwent any re-intervention was not significantly different between the patients with and those without preexisting hypertension ( $P=0.078$ ), but stroke ( $P=0.020$ ), reinfarction ( $P<0.001$ ) and crude mortality were higher in patients with hypertension ( $P<0.001$ ) during the follow-up period of 1 year (Fig. 4).

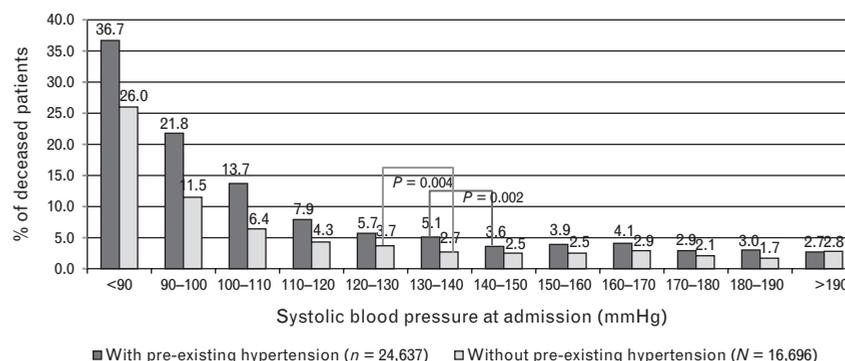
However, after adjustment for covariates, history of hypertension was not an independent predictor of mortality after 1 year (OR 1.07, 95% CI 0.78–1.47;  $P=0.68$ ; Fig. 5). The most decisive factors of mortality were comorbidities (OR 4.44, 95% CI 3.36–5.88;  $P<0.001$ ) and patient age (OR for each additional year 1.08, 95% CI 1.06–1.09;  $P<0.001$ ).

For 4796 ACS patients with preexisting hypertension, age, comorbidities and male sex were associated with worse outcomes 1 year after discharge. In 3005 patients without preexisting hypertension, independent predictors of follow-up mortality were similar (Table 3).

With regard to prescribed antihypertensive drugs at discharge as monotherapy or only combined with diuretics, patients who received ACEI/ARB had lower mortality (OR 0.45, 95% CI 0.30–0.78;  $P=0.004$ ). Other antihypertensives had no effect on mortality. However, statins prescribed at discharge improved 1-year outcome (OR 0.48, 95% CI 0.32–0.71;  $P=0.001$ ).

### DISCUSSION

To examine the impact of preexisting hypertension on outcome in patients admitted for ACS, we analyzed the data from the large prospective national AMIS Plus Registry. Unadjusted in-hospital mortality was higher in hypertensive patients. After correction for age, sex, Killip class and



**FIGURE 3** In-hospital mortality of acute coronary syndrome patients according to preexisting hypertension and admission SBP.

**TABLE 2. Independent predictors of in-hospital mortality**

	Patients with preexisting hypertension			Patients without preexisting hypertension		
	OR	95% CI	P	OR	95% CI	P
Age per additional year	1.07	1.06–1.08	<0.001	1.08	1.06–1.09	<0.001
Female sex	1.16	0.96–1.41	0.13	1.20	0.93–1.55	0.17
STEMI	1.45	1.19–1.75	<0.001	1.09	0.85–1.40	0.49
Killip class >2	4.62	3.69–5.78	<0.001	7.73	5.85–10.2	<0.001
Charlson Comorbidity Index >1	2.09	1.72–2.53	<0.001	1.71	1.29–2.26	<0.001
Admission SBP (per mmHg)	0.977	0.974–0.980	<0.001	0.973	0.968–0.977	<0.001
Pretreatment drugs as monotherapy or in combination with diuretics						
ACE/ARB antagonist mono or with diuretics	0.85	0.68–1.08	0.19	1.14	0.68–1.91	0.62
Beta-blocker mono or with diuretics	1.04	0.80–1.34	0.79	0.72	0.46–1.14	0.17
Calcium-channel blocker mono or with diuretics	1.16	0.83–1.62	0.38	0.99	0.36–2.74	0.98
Statin	0.73	0.58–0.91	0.006	0.77	0.53–1.12	0.17

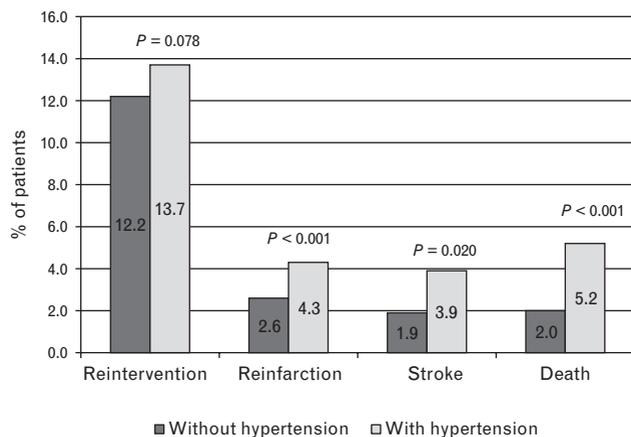
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor antagonist; CCI >1, Charlson Comorbidity Index.

comorbidities, however, in-hospital mortality in previously known hypertensive ACS patients was lower. The higher BP on admission was prognostically favorable for both hypertensive and nonhypertensive patient groups, which is in accordance with the results from the 'PROVE-IT-TIMI' 22 trial [8]. The relation between admission SBP and prognosis in this study followed the J-shaped curve associated with increased mortality below the range of 130–140 mmHg for ACS patients with preexisting hypertension and below the range of 120–130 mmHg for patients without previous hypertension. From the additional analysis of BP at admission and 1-year outcome, we could conclude that the initial BP measurement does not seem to have an effect on nonhypertensive patients. However, patients with preexisting hypertension did profit from a SBP above 140 and up to 170 mmHg. Thus, our data suggest that the goal of initial BP management in patients with prehypertension admitted with ACS should not be to lower BP below 160–170 mmHg. However, these results were based on a single measurement of BP at admission in all ACS patients regardless of delay, transfer, measurement utilities, medication, comorbidities or start of therapy. We do see the need to include follow-up BP recordings and we did not consider DBP measurements which are difficult to measure in the emergency room.

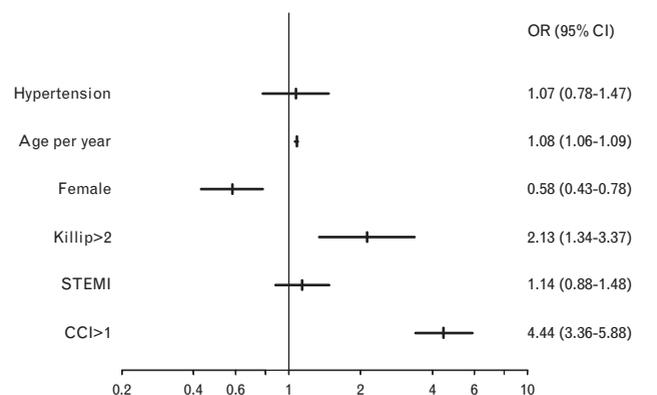
The prehospital and hospital delays may have a great impact on the outcome of patients hospitalized for STEMI as well as NSTEMI. NSTEMI patients with preexisting hypertension had a somewhat shorter delay between symptom onset and admission compared with those with STEMI. However, these patients underwent PCI with longer delays than patients without preexisting hypertension (data not shown). This excess delay, which may adversely affect prognosis, can be explained by higher age, comorbidity and female sex as observed in former analyses [14,22,24]. Regarding cardiovascular risk factors in hypertensive patients such as hypercholesterolemia, smoking and overweight, the results of our study are similar to the results from the large cohort survey from Italy [25], except for diabetes mellitus, which in our hypertensive patient group was double the incidence than their population of hypertensive patients.

Patient's age, the extent of reduced left ventricular function as documented by Killip classes, comorbidities, STEMI and lower admission BP were associated with worse in-hospital outcomes of patients with hypertension hospitalized for ACS.

The 'protective' effect of hypertension in ACS patients is difficult to explain. Pretreatment with potentially cardioprotective antihypertensive drugs had no apparent effect



**FIGURE 4** Outcome 1 year after the discharge of acute coronary syndrome patients according to preexisting hypertension (n = 7801).



**FIGURE 5** Independent predictors of mortality 1 year after discharge. OR, odds ratio; 95% CI, 95% confidence interval; CCI >1, Charlson Comorbidity Index greater than 1; STEMI, ST-segment elevation myocardial infarction.

**TABLE 3. Independent predictors of mortality 1 year after discharge in acute coronary syndrome patients with or without preexisting hypertension**

	Patients with preexisting hypertension			Patients without preexisting hypertension		
	OR	95% CI	P	OR	95% CI	P
Age per additional year	1.08	1.06–1.09	0.001	1.08	1.05–1.10	<0.001
Female sex	0.61	0.44–0.85	0.003	0.47	0.22–0.98	0.044
STEMI	1.06	0.86–2.66	0.71	1.51	0.86–2.66	0.15
CCI >1	4.73	3.42–6.53	<0.001	3.79	2.13–6.75	<0.001

ACS, acute coronary syndrome; CCI, Charlson Comorbidity Index; CI, confidence interval; OR, odds ratio; STEMI, ST-segment elevation myocardial infarction.

on mortality in our study. Analysis of pretreatment with beta-blockers, calcium antagonists, ACEI, ARB or diuretics in monotherapy or combination therapy showed no effects on in-hospital mortality. We previously saw that pretreatment of beta-blockers and particularly immediate treatment after admission in patients with ACS had a slight protective effect on in-hospital outcome [26], regardless of the history of hypertension. In the subgroup of patients who consented, we found no difference for adjusted 1-year mortality in hypertensive versus nonhypertensive patients. The long-term adverse effects of hypertension may therefore be responsible for the vanishing short-term advantages in hypertensive ACS patients. Not surprisingly, prescription of an ACEI or ARB at discharge resulted in lower 1-year mortality in these patients. A similar favorable effect was demonstrated in the prescription of statins. These observations underline the utmost importance of consequent secondary prevention after ACS especially in hypertensive patients, who to some extent are undertreated as shown in our analysis. This is in accordance with the large studies from Italy. The study from Lombardia with an extremely large number of hypertensive patients on real-world drug utilization patterns showed that the discontinuation of the initial single antihypertensive drug treatment is common, but this is less the case with ARB medication, whereas switching to another monotherapy or to combination treatment occurred at much lower rates [27]. Another large cohort survey that included over 52 000 patients showed that there is poor persistence of BP control: only 22% of hypertensive patients had optimal to high-normal BP [25]. Both these large population studies along with our study of hypertensive patients hospitalized for ACS support the need for more effective and comprehensive management of patients with hypertension.

### Limitations

Our study should be interpreted in the context of the following limitations. First, the weakness of AMIS Plus is common to all registries, the study is observational in nature and participation is voluntary depending on the staff availability and motivation. However, the number of hospitals in this study is extremely high and reflects the treatment strategy in Switzerland. The quality of data is checked by external audits. Quality control and benchmarking is the task of every hospital, but this is not reflected in the provision of resources, staff or financial support and no group is fighting to close this gap. For this reason, the registry is dependent on the financial support of sponsors and donors, who do not play any role in data acquisition, analysis or interpretation of the results.

Furthermore, we are aware that the treating physician is using the current guidelines for the documentation of elevated BP which changes regularly, and it was unknown how long the history of hypertension existed. The BP value used for this study is admission BP and the BP trends during hospitalization were not documented. Furthermore, we performed analyses based on SBP only. Although regular medication is documented, there were no data on the duration or compliance to treatment before the acute event. However, the huge number of patients included enabled assessment of the different aspects of hypertension on ACS outcomes and evaluation of which factors were associated with worse outcomes in hypertensive ACS patients.

### Conclusion

ACS patients with hypertension are older, sicker and present with more cardiovascular risk factors and comorbidities compared with those without hypertension. Despite a higher risk profile, hypertensive patients paradoxically underwent less frequently invasive revascularization. History of hypertension itself was nevertheless associated with a more favorable in-hospital prognosis. This effect vanished within 1 year after discharge.

Prescription of ACEI and ARB as well as statins improved long-term outcome. Short-term and long-term management of patients with hypertension admitted with ACS can be further improved.

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### AMIS plus participants 1997–2014

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### Conflicts of interest

The authors declare that there are no conflicts of interest related to this study.

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### REFERENCES

- Levy D, Wilson PW, Anderson KM, Castelli WP. Stratifying the patient at risk from coronary disease: new insights from the Framingham Heart Study. *Am Heart J* 1990; 119:712–717.
- Picariello C, Lazerri C, Attana P, Chiostrini M, Gensini GF, Valente S. The impact of hypertension on patients with acute coronary syndromes. *Int J Hypertens* 2011; 2011:563657.
- Radovanovic D, Urban P, Simon R, Schmidli M, Maggiorini M, Rickli H, et al. Outcome of patients with acute coronary syndrome in hospitals of different sizes. A report from the AMIS Plus Registry. *Swiss Med Wkly* 2010; 140:314–322.
- Aylward PE, Wilcox RG, Horgan JH, White HD, Granger CB, Califf RM, Topol EJ. Relation of increased arterial blood pressure to mortality and stroke in the context of contemporary thrombolytic therapy for acute myocardial infarction. A randomized trial. GUSTO-I investigators. *Ann Intern Med* 1996; 125:891–900.
- Fresco C, Avanzini F, Bosi S, Franzosi MG, Maggioni AP, Santoro L, Bellanti G. Prognostic value of a history of hypertension in 11,483 patients with acute myocardial infarction treated with thrombolysis. GISSI-2 Investigators. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. *J Hypertens* 1996; 14:743–750.
- Kang DG, Jeong MH, Ahn Y, Chae SC, Hur SH, Hong TJ, et al. Clinical effects of hypertension on the mortality of patients with acute myocardial infarction. *J Korean Med Sci* 2009; 24:800–806.
- Abrignani MG, Dominguez IJ, Biondo G, Di Girolamo A, Novo G, Barbagallo M, et al. In-hospital complications of acute myocardial infarction in hypertensive subjects. *Am J Hypertens* 2005; 18:165–170.
- Bangalore S, Qin J, Sloan S, Murphy SA, Cannon CP. What is the optimal blood pressure in patients after acute coronary syndromes? Relationship of blood pressure and cardiovascular events in the pravastatin or atorvastatin evaluation and infection therapy-thrombolysis in myocardial infarction (PROVE IT-TIMI) 22 trial. *Circulation* 2010; 122:2142–2151.
- Huang B, Yang Y, Zhu J, Liang Y, Tan H. Clinical characteristics and short-term outcomes in patients with elevated admission systolic blood pressure after acute ST-elevation myocardial infarction: a population-based study. *BMJ Open* 2014; 4:e005097.
- Katayama T, Iwasaki Y, Sakoda N, Yoshioka M. The etiology of 'smoker's paradox' in acute myocardial infarction with special emphasis on the association with inflammation. *Int Heart J* 2008; 49:13–24.
- Witassek F, Schwenkglenks M, Erne P, Radovanovic D. Impact of body mass index on mortality in Swiss hospital patients with ST-elevation myocardial infarction: does an obesity paradox exist? *Swiss Med Wkly* 2014; 144:w13986.
- Jeger RV, Radovanovic D, Hunziker PR, Pfisterer ME, Stauffer JC, Erne P, Urban P. Ten-year trends in the incidence and treatment of cardiogenic shock. *Ann Intern Med* 2008; 149:618–626.
- Radovanovic D, Nallamothu BK, Seifert B, Bertel O, Eberli F, Urban P, et al. Temporal trends in treatment of ST-elevation myocardial infarction among men and women in Switzerland between 1997 and 2011. *Eur Heart J Acute Cardiovasc Care* 2012; 1:183–191.
- Schoenenberger AW, Radovanovic D, Stauffer JC, Windecker S, Urban P, Eberli FR, et al. Age-related differences in the use of guideline-

- recommended medical and interventional therapies for acute coronary syndromes: a cohort study. *J Am Geriatr Soc* 2008; 56:510–516.
15. Schoenenberger AW, Radovanovic D, Stauffer JC, Windecker S, Urban P, Niedermaier G, *et al.* Acute coronary syndromes in young patients: presentation, treatment and outcome. *Int J Cardiol* 2011; 148:300–304.
  16. Radovanovic D, Erne P. Amis plus: Swiss registry of acute coronary syndrome. *Heart* 2010; 96:917–921.
  17. Thygesen K, Alpert JP, White HD, on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J* 2007; 28:2525–2538.
  18. Urban P, Radovanovic D, Erne P, Stauffer JC, Pedrazzini G, Windecker S, Bertel O. Impact of changing definitions for myocardial infarction: a report from the AMIS Registry. *Am J Med* 2008; 121:1065–1071.
  19. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, *et al.* 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; 28:1462–1536.
  20. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, *et al.* 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (esh) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34:2159–2219.
  21. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, *et al.* Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS iv. *J Hum Hypertens* 2004; 18:139–185.
  22. Radovanovic D, Seifert B, Urban P, Eberli FR, Rickli H, Bertel O, *et al.* Validity of Charlson Comorbidity Index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS Plus Registry 2002–2012. *Heart* 2014; 100:288–294.
  23. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40:373–383.
  24. Radovanovic D, Erne P, Urban P, Bertel O, Rickli H, Gaspoz JM. Gender differences in management and outcomes in patients with acute coronary syndromes: results on 20,290 patients from the AMIS Plus Registry. *Heart* 2007; 93:1369–1375.
  25. Volpe M, Tocci G, Trimarco B, Rosei EA, Borghi C, Ambrosioni E, *et al.* Blood pressure control in Italy: results of recent surveys on hypertension. *J Hypertens* 2007; 25:1491–1498.
  26. Cuculi F, Radovanovic D, Pedrazzini G, Regli M, Urban P, Stauffer J-C, Erne P, on behalf of the AMIS Plus Investigators. Is pretreatment with  $\beta$ -blockers beneficial in patients with acute coronary syndrome? *Cardiology* 2010; 115:91–97.
  27. Corrao G, Zambon A, Parodi A, Poluzzi E, Baldi I, Merlino L, *et al.* Discontinuation of and changes in drug therapy for hypertension among newly-treated patients: a population-based study in Italy. *J Hypertens* 2008; 26:819–824.