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Hemo-metabolic impairment in patients with ST-segment elevation myocardial infarction: Data from the INTERSTELLAR registry

Min Gyu Kong et al., Hemo-metabolic impairment and mortality in STEMI

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Abstract

Background: Not only hemo-dynamic (HD) factors but also hemo-metabolic (HM) risk factors reflecting multi-organ injuries are considered as important prognostic factors in ST-segment elevation myocardial infarction (STEMI). However, studies regarding HM risk factors in STEMI patients are currently limited.

Method: Under analysis were 1,524 patients with STEMI who underwent primary percutaneous coronary intervention in the INTERSTELLAR registry. Patients were divided into HM (≥ 2 risk factors) and non-HM impairment groups. The primary outcome was in-hospital all-cause mortality, and the secondary outcome was 1-year all-cause mortality.

Results: Of 1,524 patients, 214 (14.0%) and 1,310 (86.0%) patients were in the HM and non-HM impairment groups, respectively. Patients with HM impairment had a higher incidence of in-hospital mortality than those without (24.3% vs. 2.7%, $p < 0.001$). After adjusting for

confounders, HM impairment was independently associated with in-hospital mortality (inverse probability of treatment weighting [IPTW]-adjusted odds ratio: 1.81, 95% confidence interval: 1.08–3.14). In the third door-to-balloon (DTB) time tertile (≥ 82 min), HM impairment was strongly associated with in-hospital mortality. In the first DTB time tertile (< 62 min), indicating relatively rapid revascularization, HM impairment was consistently associated with increased in-hospital mortality.

Conclusions: Hemo-metabolic impairment is significantly associated with increased risk of in-hospital and 1-year mortality in patients with STEMI. It remains a significant prognostic factor, regardless of DTB time.

Keywords: ST-segment elevation myocardial infarction, mortality, hemo-metabolic risk factors, shock, door-to-balloon time

Introduction

Improvements in clinical outcomes have been shown with the development from bare-metal stents to second-generation drug-eluting stents in patients with ST-segment elevation myocardial infarction (STEMI) [1]. Traditional recommendation for primary percutaneous coronary intervention (PCI) targeted the “door-to-balloon (DTB) time” within 90 minutes in patients with STEMI [2]. Recent European guideline recommended the “diagnosis-to-wire time” of 60 minutes or less [3]. However, despite efforts to reduce the DTB time, the mortality rate of STEMI patients remains high. Menees et al. [4] showed that although the DTB time was reduced from 83 to 67 minutes, mortality rates insignificantly changed from 4.8% to 4.7% in the United States national registry analysis. Lee et al. [5] also demonstrated improving DTB time from 101 to 54 minutes could not significantly reduce 1-year cardiovascular mortality (from 3.6% to 2.9%) over a 10-year period in Taiwan.

Hemo-dynamic (HD) factors, such as blood pressure or the DTB time, as well as hemo-metabolic (HM) risk factors, including kidney injury, liver injury, and dysglycemia, might have a significant impact on the prognosis of patients with STEMI [6]. For example, renal impairment or acute kidney injury was significantly associated with in-hospital mortality in patients with acute coronary syndrome [7, 8]. Similarly, liver injury, defined as the elevation of aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels, has also been reported as an independent predictor of in-hospital mortality and major adverse cardiovascular events in patients with STEMI [9, 10]. Moreover, previous studies have shown that dysglycemia at admission significantly affects mortality and myocardial injury, as

assessed by cardiac magnetic resonance imaging, in patients with STEMI [11, 12]. Therefore, the aim of this study was to evaluate the impact of HM risk factors such as kidney injury, liver injury, and dysglycemia on mortality in patients with STEMI.

Methods

Study population

Patients with STEMI were evaluated and enrolled in the INTERSTELLAR (Incheon-Bucheon Cohort of Patients Undergoing Primary PCI for Acute STEMI) registry (ClinicalTrial.gov identifier: NCT02804958) [13]. The INTERSTELLAR registry is a retrospective multi-center cohort study of 1,537 patients who underwent primary PCI for STEMI in four regional hospitals of Incheon and Bucheon city, South Korea between 2007 and 2014. 13 patients with no information on serum creatinine, AST, ALT, or glucose levels were excluded. Finally, 1,524 STEMI patients were analyzed with known kidney injury, liver injury, or dysglycemia.

Patients were divided into HM and non-HM impairment groups. The HM impairment was defined as the presence of two or more HM risk factors such as kidney injury, liver injury, and dysglycemia, based on initial laboratory findings. HM risk factors were defined as follows: estimated glomerular filtration rate < 45 mL/min/1.73 m^2 was defined as kidney injury; a 2-fold increase in the serum AST or ALT level above the upper normal limit (AST > 80 U/L or ALT > 80 U/L) was defined as liver injury; and hypoglycemia (serum glucose < 70 mg/dL) or hyperglycemia (serum glucose > 200 mg/dL) was defined as dysglycemia. The study protocol was approved by the Institutional Review Board of Soonchunhyang University Bucheon Hospital (approval number: 2020-06-039). The need for informed consent by the participants was waived by IRB approval.

Data collection and outcome definition

Data were collected at each hospital through electronic medical record reviews and standardized telephone interviews in cases of follow-up failure. The primary outcome was in-hospital all-cause mortality. The secondary outcome was all-cause mortality within 1 year, including in-hospital mortality.

Statistical analysis

Baseline characteristics regarding HM impairment status were compared using the χ^2

test for categorical variables and the unpaired Student t-test for continuous variables. The cumulative incidence of all-cause death was estimated using the Kaplan–Meier method, and the curves were compared using the log-rank test. To identify the independent impact of HM impairment and other mortality predictors, weighted the Cox proportional hazard model analysis with inverse probability of treatment weighting (IPTW) was performed using covariates, including age, sex, systolic blood pressure, heart rate, body mass index (BMI), Killip class, smoking status, diabetes, hypertension, DTB time, left ventricular ejection fraction (LVEF), and multi-vessel disease (MVD). All analyses were performed using SPSS software (version 20.0; IBM Corp., Armonk, NY, USA). All p-values were two-sided, and a value of $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Of the 1,524 patients, 214 (14.0%) belonged to the HM impairment group (≥ 2 risk factors) and 1,310 (86.0%) belonged to the non-HM impairment group (< 2 risk factors). The patients' baseline characteristics are shown in Table 1. Patients with HM impairment were older and had a higher prevalence of diabetes, hypertension, proximal culprit vessel disease, and MVD. In contrast, the non-HM impairment group had a higher BMI, LVEF, prevalence of male sex, and current smoking status. There were no significant differences in the DTB time or use of antiplatelet agents between the two groups.

In-hospital and 1-year mortality according to the HM impairment

There were 87 (5.7%) deaths during the index hospitalization and 107 (7.0%) within 1 year. Patients with HM impairment had a higher incidence of in-hospital mortality than those without HM impairment (24.3% vs. 2.7%, $p < 0.001$; Fig. 1). After adjusting for potential confounding factors, including age, systolic blood pressure, heart rate, Killip class, DTB time, infarct-related artery, and MVD, HM impairment was independently associated with in-hospital mortality (IPTW-adjusted odds ratio [OR]: 1.81, 95% confidence interval [CI]: 1.08–3.14; $p < 0.030$).

Kaplan–Meier analysis showed worse secondary outcome results in the HM impairment group (Fig. 2). The cumulative incidence of all-cause mortality was higher in patients with HM impairment than in those without (27.1% vs. 3.7%, log-rank $p < 0.001$). The HM impairment group also showed a strong association with 1-year mortality (IPTW-adjusted hazard ratio [HR]: 2.44, 95% CI: 1.76–3.39, $p < 0.001$; Table 2).

Clinical outcomes according to the number of HM risks

Figure 3 shows strong associations between clinical outcomes and the number of HM risks. The more HM risk factors, the higher the in-hospital mortality (0-to-3 risks: 1.4% vs. 4.5% vs. 20.7% vs. 46.7%, p for trend < 0.001) and 1-year mortality (0-to-3 risks: 2.3% vs. 5.8% vs. 23.4% vs. 50.0%, p for trend < 0.001).

Independent predictors of in-hospital mortality

Table 3 shows the results of the multivariate logistic regression analysis for in-hospital mortality. The HM impairment was independently associated with increased in-hospital mortality (adjusted OR: 4.42, 95% CI: 2.35–8.36, p < 0.001). Other variables, such as older age, lower systolic blood pressure, higher HR, higher Killip class (II–IV), current smoking, diabetes, lower LVEF, left anterior descending culprit lesion, and MVD, also independently predicted higher in-hospital mortality. However, the DTB time was not independently associated with higher in-hospital mortality.

Clinical outcomes according to the HM impairment in DTB time tertiles

In the third DTB time tertile (≥ 82 min), the HM impairment showed a strong association with in-hospital (adjusted OR: 6.03, 95% CI: 2.31–16.36, p < 0.001) and 1-year (adjusted HR: 3.02, 95% CI: 1.46–6.25, p = 0.003) mortality (Table 4). In the first DTB time tertile (< 62 min), which represents relatively rapid revascularization, the HM impairment was consistently associated with increased in-hospital (adjusted OR: 13.23, 95% CI: 2.40–87.57, p = 0.004) and 1-year (adjusted HR: 5.56, 95% CI: 1.76–17.51, p = 0.003) mortality.

HD shock and HM impairment

The in-hospital mortality was compared between four subgroups classified according to their HD shock and HM impairment status (Fig. 4): Group 1, HD shock (–)/HM impairment (–); Group 2, HD shock (+)/HM impairment (–); Group 3, HD shock (–)/HM impairment (+); and Group 4, HD shock (+)/HM impairment (+). Initial systolic blood pressure < 90 mmHg was defined as HD shock.

Group 4 had the highest in-hospital mortality among the four subgroups (50.0%). The HM impairment without HD shock group (Group 3) showed higher in-hospital mortality than the HD shock without HM impairment group (Group 2; 16.0% vs. 3.9%, p = 0.007).

Discussion

The main findings of the present study are as follows: (1) patients with HM impairment had a higher incidence of in-hospital and 1-year mortality than patients without HM impairment; (2) HM impairment was significantly associated with higher in-hospital mortality even after adjusting for potential confounding factors including age, systolic blood

pressure, heart rate, Killip class, DTB time, infarct-related artery, and MVD; (3) regardless of rapid revascularization, the HM impairment was consistently associated with increased in-hospital mortality; and (4) the HM impairment without HD shock group had higher in-hospital mortality than the HD shock without HM impairment group.

Early revascularization is recommended in patients with acute myocardial infarction (AMI) and cardiogenic shock, including STEMI, because it promotes the recovery of normal macrovascular hemodynamics such as cardiac index [14, 15]. However, Menees et al. [4] showed that despite improvements in national DTB times according to the guideline recommendations for STEMI, in-hospital and short-term mortality rates remained unaffected. Vallabhajosyula et al. [16] also demonstrated that, despite the current strategy of early and aggressive revascularization in patients with cardiogenic shock due to AMI, in-hospital mortality remains high. The current study demonstrated that rapid revascularization did not impact in-hospital mortality, while the HM impairment did significantly impact in-hospital mortality in the logistic regression analysis for in-hospital mortality (Table 3). The subgroup analysis according to DTB time showed that the HM impairment is consistently associated with increased in-hospital mortality (Table 4). This means that the HM impairment is still a significant prognostic factor, even when rapid revascularization occurs.

In a large-scale cohort, multi-organ failure was associated with an increase in the adjusted odds of in-hospital mortality compared to patients without organ failure. Theoretically, low cardiac output due to cardiac dysfunction is associated with end-organ hypoperfusion and hypoxia [17, 18]. Acute organ failure is thought to be due to systemic inflammation and impaired microcirculation, in addition to low cardiac output in AMI [19, 20]. Recently, Esposito et al. [6] proposed in the “hemo-metabolic” problem model that the initial HD insult subsequently evolves into a metabolic insult, resulting in persistent hypoperfusion and multi-organ failure in patients with cardiogenic shock. Furthermore, recent studies showed that HM shock related to hypoperfusion and organ injury is associated with the short-term mortality [21, 22].

Figure 4 showed that HD shock patients with HM impairment had the worst prognosis in the present study. Even with HD shock, patients without HM impairment had better clinical outcomes than those with HM impairment. The HM impairment in this study reflected a progressed and complex stage of HD problems. It has previously been shown that HD problem persistence, reduced tissue perfusion, and elevated filling pressures lead to a “hemo-metabolic impairment” reflecting multi-organ ischemia, hepatic and venous congestion, and worsening multi-organ failure [17].

This study has several important implications. First, the present analysis of a large-scale multi-center cohort by comparing the characteristics and clinical outcomes of patients with STEMI. Second, a novel concept was proposed that the “hemo-metabolic impairment” reflected the state of multiple metabolic risks and multi-organ dysfunction. The present study also demonstrated that the HM impairment is an independent risk factor for in-hospital mortality in patients with STEMI. Third, it was shown, herein, that an HM impairment might be a more important risk factor for in-hospital mortality than the DTB time. Based on the current results, it was suggested that the management of the patient’s metabolic state might be an important initial treatment strategy for patients with STEMI. Furthermore, it is herein suggested, to consider the early use of acute mechanical circulatory support devices and decongestion therapy in HD shock patients with HM impairment to improve circulatory dysfunction and multi-organ hypoperfusion.

Limitations of the study

The present study has several limitations. First, this was a retrospective, observational study. To evaluate the impact of the HM impairment, this study had intrinsic limitations of non-randomized comparisons, such as the different distributions of other clinical risk factors and the possibility of unmeasured confounding factors, although Cox regression analysis with IPTW was used to overcome this intrinsic limitation. Second, data on lactate levels were not collected, which is a good marker of systemic hypoperfusion that would have reflected the patient’s HM status. However, the patient’s HM status was sufficiently analyzed by adding the “dysglycemia” factor and suggesting a new concept of “hemo-metabolic impairment”. Third, the endpoint was only all-cause mortality. Various clinical outcomes such as cardiovascular death, in-hospital reinfarction, in-hospital stroke, and bleeding events may further elucidate the impact of HM impairment in STEMI.

Conclusions

The HM impairment is significantly associated with an increased risk of in-hospital and 1-year mortality in STEMI patients who underwent primary PCI. The HM impairment remains a significant prognostic factor regardless of the DTB time.

Acknowledgments

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Conflict of interest: None declared

References

1. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Clinical outcomes with drug-eluting and bare-metal stents in patients with ST-segment elevation myocardial infarction: evidence from a comprehensive network meta-analysis. J Am Coll Cardiol. 2013; 62(6): 496–504, doi: 10.1016/j.jacc.2013.05.022, indexed in Pubmed: 23747778.

2. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients With Acute Myocardial Infarction). Circulation. 2004; 110(5): 588–636, doi: 10.1161/01.CIR.0000134791.68010.FA, indexed in Pubmed: 15289388.

3. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018; 39(2): 119–177, doi: 10.1093/eurheartj/ehx393, indexed in Pubmed: 28886621.

4. Menees DS, Peterson ED, Wang Y, et al. Door-to-balloon time and mortality among patients undergoing primary PCI. N Engl J Med. 2013; 369(10): 901–909, doi: 10.1056/NEJMoa1208200, indexed in Pubmed: 24004117.

5. Lee WC, Fang HY, Chen HC, et al. Effect of improved door-to-balloon time on clinical outcomes in patients with ST segment elevation myocardial infarction. Int J Cardiol. 2017; 240: 66–71, doi: 10.1016/j.ijcard.2017.02.156, indexed in Pubmed: 28390745.

6. Esposito ML, Kapur NK. Acute mechanical circulatory support for cardiogenic shock: the "door to support" time. F1000Res. 2017; 6: 737, doi: 10.12688/f1000research.11150.1, indexed in Pubmed: 28580136.

7. Vavalle JP, van Diepen S, Clare RM, et al. Renal failure in patients with ST-segment elevation acute myocardial infarction treated with primary percutaneous coronary intervention: Predictors, clinical and angiographic features, and outcomes. Am Heart J. 2016; 173: 57–66, doi: 10.1016/j.ahj.2015.12.001, indexed in Pubmed: 26920597.

8. De Rosa R, Morici N, De Servi S, et al. Impact of renal dysfunction and acute kidney injury on outcome in elderly patients with acute coronary syndrome undergoing percutaneous coronary intervention. Eur Heart J Acute Cardiovasc Care. 2020 [Epub ahead of print]: 2048872620920475, doi: 10.1177/2048872620920475, indexed in Pubmed: 32374175.

9. Oh PC, Eom YS, Moon J, et al. Prognostic impact of the combination of serum transaminase and alkaline phosphatase determined in the emergency room in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. PLoS One. 2020; 15(5): e0233286, doi: 10.1371/journal.pone.0233286, indexed in Pubmed: 32442225.

10. Huseynov A, Baumann S, Becher T, et al. Liver and cholestatic parameters as prognostic biomarkers of in-hospital MACE in patients with STEMI. Eur J Clin Invest. 2016; 46(8): 721–729, doi: 10.1111/eci.12655, indexed in Pubmed: 27369447.

11. Eitel I, Hintze S, de Waha S, et al. Prognostic impact of hyperglycemia in nondiabetic and diabetic patients with ST-elevation myocardial infarction: insights from contrast-enhanced magnetic resonance imaging. Circ Cardiovasc Imaging. 2012; 5(6): 708–718, doi: 10.1161/CIRCIMAGING.112.974998, indexed in Pubmed: 23051889.

12. Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. Int J Cardiol. 2013; 167(6): 2572–2579, doi: 10.1016/j.ijcard.2012.06.054, indexed in Pubmed: 22795245.

13. Moon J, Suh J, Oh PC, et al. Relation of stature to outcomes in Korean patients undergoing primary percutaneous coronary intervention for acute ST-elevation myocardial infarction (from the INTERSTELLAR registry). Am J Cardiol. 2016; 118(2): 177–182, doi: 10.1016/j.amjcard.2016.04.046, indexed in Pubmed: 27236252.

14. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med. 1999; 341(9): 625–634, doi: 10.1056/NEJM199908263410901, indexed in Pubmed: 10460813.

15. Lim N, Dubois MJ, De Backer D, et al. Do all nonsurvivors of cardiogenic shock die with a low cardiac index? Chest. 2003; 124(5): 1885–1891, doi: 10.1378/chest.124.5.1885, indexed in Pubmed: 14605064.

16. Vallabhajosyula S, Dunlay S, Prasad A, et al. Acute noncardiac organ failure in acute myocardial infarction with cardiogenic shock. J Am Coll Cardiol. 2019; 73(14): 1781–1791, doi: 10.1016/j.jacc.2019.01.053, indexed in Pubmed: 30975295.

17. Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. Circulation. 2008; 117(5): 686–697, doi: 10.1161/CIRCULATIONAHA.106.613596, indexed in Pubmed: 18250279.

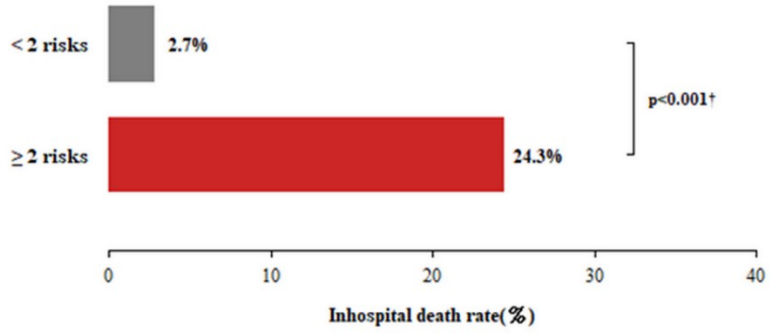
18. Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med. 2012; 367(14): 1287–1296, doi: 10.1056/NEJMoa1208410, indexed in Pubmed: 22920912.

19. Fang L, Moore XL, Dart AM, et al. Systemic inflammatory response following acute myocardial infarction. J Geriatr Cardiol. 2015; 12(3): 305–312, doi: 10.11909/j.issn.1671-5411.2015.03.020, indexed in Pubmed: 26089856.

20. den Uil CA, Lagrand WK, van der Ent M, et al. Impaired microcirculation predicts poor outcome of patients with acute myocardial infarction complicated by cardiogenic shock. Eur Heart J. 2010; 31(24): 3032–3039, doi: 10.1093/eurheartj/ehq324, indexed in Pubmed: 20829210.

21. Zweck E, Thayer KL, Helgestad OKL, et al. Phenotyping cardiogenic shock. J Am Heart Assoc. 2021; 10(14): e020085, doi: 10.1161/JAHA.120.020085, indexed in Pubmed: 34227396.

22. Jentzer JC, Schrage B, Patel PC, et al. Association between the acidemia, lactic acidosis, and shock severity with outcomes in patients with cardiogenic shock. J Am Heart Assoc. 2022; 11(9): e024932, doi: 10.1161/JAHA.121.024932, indexed in Pubmed: 35491996.



Group	Category	OR (95% CI)	p-value
<2 risks	Reference	1	
≥2 risks	Crude OR	11.69 (7.42-18.63)	<0.001
	Adjusted OR*	4.42 (2.35-8.36)	<0.001
	IPTW OR**	1.81 (1.08-3.14)	0.03

Figure 1. In-hospital mortality in accordance with the hemo-metabolic (HM) impairment (≥ 2 risks); † P-value was calculated by the chi-square test; *Adjusted for age, systolic blood pressure (SBP), hazard ratio (HR), Killip class, door-to-balloon (DTB) time, infarct-related artery (IRA) culprit, and multi-vessel disease (MVD); **Propensity score was calculated using the following factors: age, sex, diastolic blood pressure, SBP, HR, body mass index (BMI), Killip class, smoking status, diabetes, HTN, DTB time, ejection fraction (EF), IRA culprit, proximal culprit, and MVD. Inverse probability of treatment weighting-odds ratio (IPTW-OR) was calculated with adjustment for age, sex, SBP, heart rate, BMI, Killip class, smoking status, diabetes, HTN, atrial fibrillation, EF, and MVD after IPTW; CI — confidence interval; OR — odds ratio.

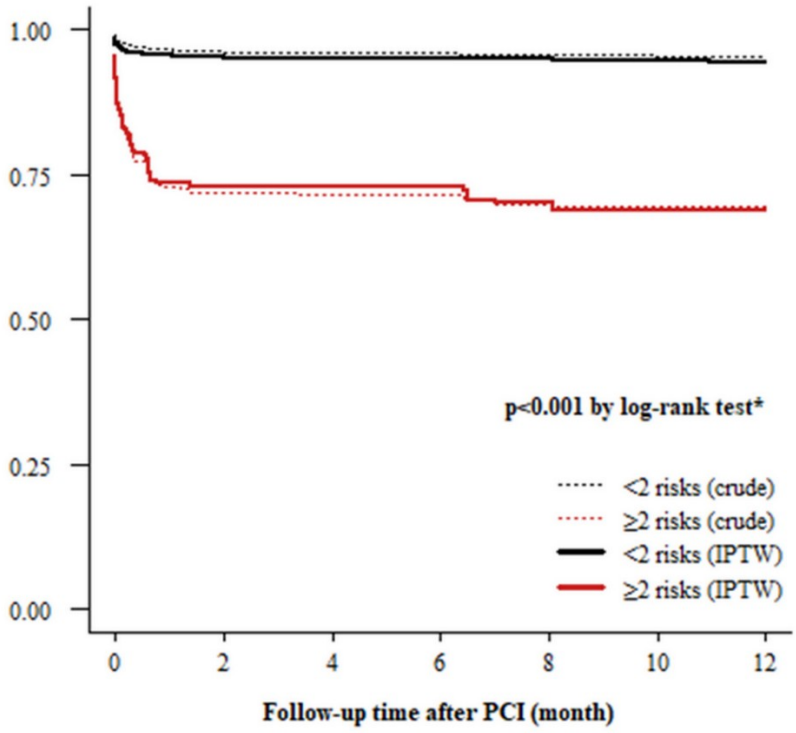


Figure 2. Kaplan–Meier curves for all-cause mortality within 1-year; *Log-rank test was applied for the inverse probability of treatment weighting (IPTW)-adjusted survival curve; PCI — percutaneous coronary intervention.

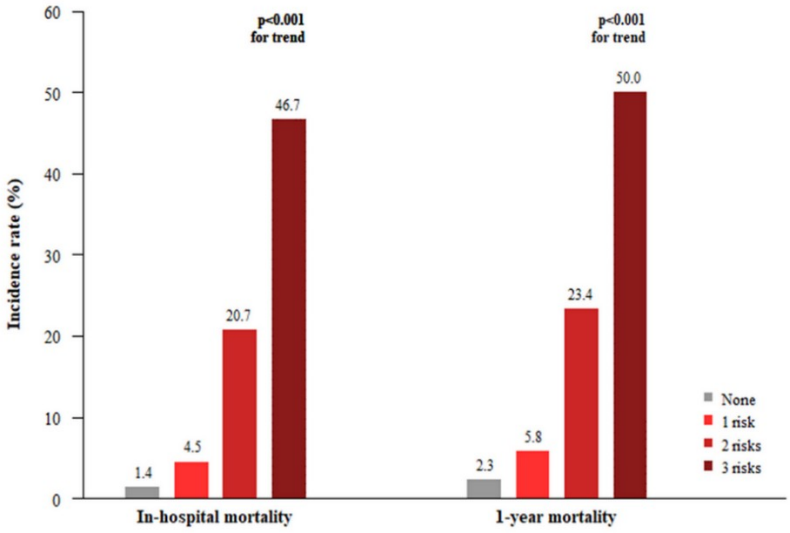


Figure 3. Clinical outcomes according to the number of hemo-metabolic risks.

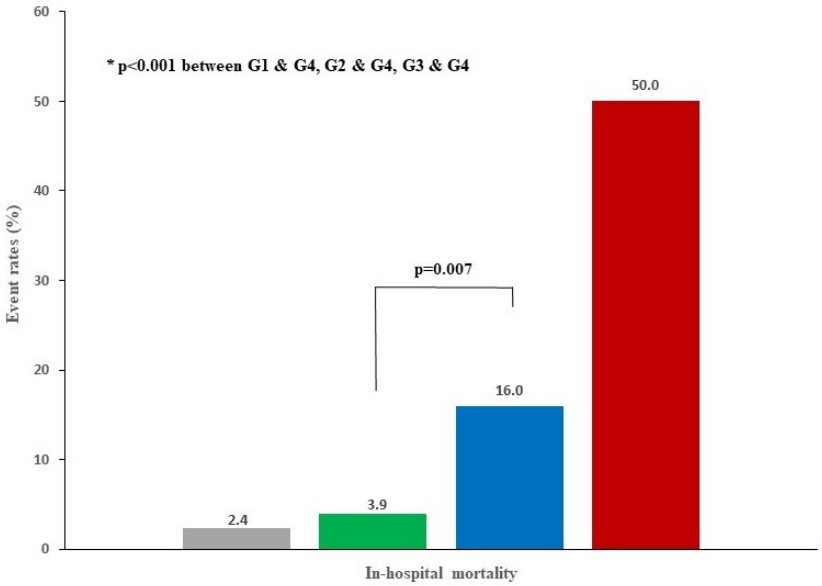


Figure 4. In-hospital mortality in accordance with the four subgroups; *Group 1 (gray): HD shock (–)/HM impairment (–); Group 2 (green): HD shock (+)/HM impairment (–); Group 3 (blue): HD shock (–)/HM impairment (+); Group 4 (red): HD shock (+)/HM impairment (+); HD — hemo-dynamic; HM — hemo-metabolic.

Table 1. Baseline characteristics in accordance with the hemo-metabolic (HM) impairment.

Variable	Non-HM impairment	HM impairment	P
	< 2 risks (n = 1310)	≥ 2 risks (n = 214)	
Age [years]	59.2 ± 12.8	68.4 ± 12.6	< 0.001
Male	1074 (82.0%)	134 (62.6%)	< 0.001
SBP [mmHg]	125.7 ± 28.7	114.9 ± 34.5	< 0.001
DBP [mmHg]	77.0 ± 18.1	69.9 ± 22.7	< 0.001
Heart rate [bpm]	76.6 ± 19.7	85.5 ± 28.4	< 0.001
BMI [kg/m^2]	24.2 ± 3.2	23.4 ± 3.6	0.002
Killip class II–IV	228 (17.5%)	104 (48.8%)	< 0.001
Cardiogenic shock	77 (5.9%)	42 (19.6%)	< 0.001
Current smoking status	733 (56.0%)	76 (35.7%)	< 0.001
Diabetes mellitus	305 (23.3%)	106 (49.5%)	< 0.001
Dyslipidemia	254 (19.4%)	48 (22.4%)	0.301
Hypertension	611 (46.6%)	128 (59.8%)	< 0.001
Atrial fibrillation	69 (6.8%)	18 (10.5%)	0.086
Creatinine [mg/dL]	1.1 ± 1.1	1.6 ± 1.1	< 0.001
Glucose [mg/dL]	161.8 ± 65.7	266.5 ± 133.7	< 0.001
AST [U/L]	56.0 ± 116.8	161.4 ± 189.1	< 0.001
ALT [U/L]	33.0 ± 36.1	76.6 ± 115.8	< 0.001
DTB time [min]	129.7 ± 425.7	167.9 ± 665.6	0.494
LVEF [%]	48.8 ± 12.4	41.1 ± 15.9	< 0.001
IRA culprit:			0.022
LAD	660 (51.0%)	107 (51.2%)	
LCX	138 (10.7%)	21 (10.0%)	
LM	11 (0.9%)	7 (3.3%)	
RCA	484 (37.4%)	74 (35.4%)	
Proximal culprit	571 (44.2%)	114 (54.5%)	0.005
MVD	758 (58.7%)	145 (69.4%)	0.003
ASA	1145 (88.1%)	188 (89.1%)	0.689
Clopidogrel	1235 (95.1%)	196 (92.9%)	0.187
Ticagrelor	46 (4.1%)	9 (4.9%)	0.642
Prasugrel	9 (0.8%)	1 (0.5%)	0.701

Data are represented as the mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables; SBP — systolic blood pressure; DBP — diastolic blood pressure; BMI — body mass index; AST — aspartate aminotransferase; ALT — alanine aminotransferase; DTB — door-to-balloon; LVEF —

Table 2. Clinical outcomes in accordance with the hemo-metabolic (HM) impairment.

Variable	Non-HM impairment (n = 1310)	HM impairment (n = 214)	Unadjusted		Covariate-adjusted*		IPTW†	
			OR/HR (95% CI)	P	OR/HR (95% CI)	P	OR/HR (95% CI)	P
In-hospital mortality	35 (2.7%)	52 (24.3%)	11.69 (7.42–18.63)	< 0.001	4.42 (2.35–8.36)	< 0.001	1.81 (1.08–-3.14)	0.03
1-year mortality	49 (3.7%)	58 (27.1%)	8.41 (5.74–12.30)	< 0.001	3.05 (1.88–4.94)	< 0.001	2.44 (1.11–5.35)	0.026

*Adjusted for age, systolic blood pressure, HR, Killip class, door-to-balloon time, infarct-related artery culprit, and multi-vessel disease; †Propensity score was calculated using the following factors: age, sex, systolic blood pressure, diastolic blood pressure, HR, body mass index, Killip class, smoking status, diabetes, HTN, door-to-balloon time, ejection fraction, infarct-related artery culprit, proximal culprit and multi-vessel disease; IPTW-HR was calculated with adjustment for age, sex, systolic blood pressure,

Table 3. Logistic regression analysis for in-hospital mortality.

Variable	Multivariable	
	OR (95% CI)	**P**
Number of HM risk factors:		
< 2 risks	1 (Reference)	
≥ 2 risks	4.42 (2.35–8.36)	< 0.001
Age [years]	1.05 (1.03–1.08)	< 0.001
Male	0.24 (0.17–0.33)	< 0.001
SBP [mmHg]	0.98 (0.97–0.99)	< 0.001
Heart rate [bpm]	1.02 (1.01–1.03)	0.003
Killip class II–IV	3.34 (1.78–6.32)	< 0.001
Current smoking status	2.51 (1.81–3.51)	< 0.001
Diabetes mellitus	2.67 (1.95–3.68)	< 0.001
DTB time [min]	1.00 (1.00–1.00)	0.537
LVEF	0.91 (0.90–0.93)	< 0.001
IRA culprit:		
RCA	1 (Reference)	
LAD	2.37 (1.15–5.16)	0.024
LCX	1.52 (0.40–5.01)	0.514
LM	4.98 (0.91–29.29)	0.065
Multi-vessel disease	2.39 (1.17–5.20)	0.021

OR — odds ratio; CI — confidence interval; HM — hemo-metabolic; SBP — systolic blood pressure; DTB — door-to-balloon; LVEF — left ventricular ejection fraction; IRA — infarct-related artery; RCA — right coronary artery; LAD — left anterior descending; LCX — left circumflex artery; LM — left main coronary artery

Table 4. Risk for clinical outcomes according to the hemo-metabolic impairment in tertiles of the door-to-balloon time.

Variable	DTB time category	Unadjusted		Covariate-adjusted*	
		OR/HR (95% CI)	P	OR/HR (95% CI)	P
In-hospital mortality	1st tertile (<62 min)	17.67 (5.77–60.47)	< 0.001	13.23 (2.40–87.57)	0.004
	2nd tertile (62–81 min)	8.14 (2.96–22.78)	< 0.001	2.71 (0.80–9.14)	0.104
	3rd tertile (≥82 min)	12.58 (5.74–28.65)	< 0.001	6.03 (2.31–16.36)	< 0.001
All-cause mortality	1st tertile (< 62 min)	9.39 (3.90–22.59)	< 0.001	5.56 (1.76–17.51)	0.003
	2nd tertile (62–81 min)	10.64 (4.60–24.60)	< 0.001	3.09 (1.21–7.87)	0.018
	3rd tertile (≥ 82 min)	6.53 (3.48–12.25)	< 0.001	3.02 (1.46–6.25)	0.003

*Adjusted for age, systolic blood pressure, HR, Killip class, DTB time, infarct-related artery culprit, and multi-vessel disease; OR — odds ratio; HR — hazard ratio; CI — confidence interval; DTB — door-to-balloon