



Risk Stratification for Patients in Cardiogenic Shock After Acute Myocardial Infarction

Janine Pöss, MD,^{a,b} Jelena Köster, MD,^{a,b} Georg Fuernau, MD,^{a,b} Ingo Eitel, MD,^{a,b} Suzanne de Waha, MD,^{a,b} Taoufik Ouarrak,^c Johan Lassus, MD, PhD,^d Veli-Pekka Harjola, MD, PhD,^e Uwe Zeymer, MD,^{c,f} Holger Thiele, MD,^{a,b} Steffen Desch, MD^{a,b}

ABSTRACT

BACKGROUND Mortality in cardiogenic shock (CS) remains high. Early risk stratification is crucial to make adequate treatment decisions.

OBJECTIVES This study sought to develop an easy-to-use, readily available risk prediction score for short-term mortality in patients with CS, derived from the IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock) trial.

METHODS The score was developed using a stepwise multivariable regression analysis.

RESULTS Six variables emerged as independent predictors for 30-day mortality and were used as score parameters: age >73 years, prior stroke, glucose at admission >10.6 mmol/l (191 mg/dl), creatinine at admission >132.6 μ mol/l (1.5 mg/dl), Thrombolysis In Myocardial Infarction flow grade <3 after percutaneous coronary intervention, and arterial blood lactate at admission >5 mmol/l. Either 1 or 2 points were attributed to each variable, leading to a score in 3 risk categories: low (0 to 2), intermediate (3 or 4), and high (5 to 9). The observed 30-day mortality rates were 23.8%, 49.2%, and 76.6%, respectively ($p < 0.0001$). Validation in the IABP-SHOCK II registry population showed good discrimination with an area under the curve of 0.79. External validation in the CardShock trial population ($n = 137$) showed short-term mortality rates of 28.0% (score 0 to 2), 42.9% (score 3 to 4), and 77.3% (score 5 to 9; $p < 0.001$) and an area under the curve of 0.73. Kaplan-Meier analysis revealed a stepwise increase in mortality between the different score categories (0 to 2 vs. 3 to 4: $p = 0.04$; 0 to 2 vs. 5 to 9: $p = 0.008$).

CONCLUSIONS The IABP-SHOCK II risk score can be easily calculated in daily clinical practice and strongly correlated with mortality in patients with infarct-related CS. It may help stratify patient risk for short-term mortality and might, thus, facilitate clinical decision making. (Intraaortic Balloon Pump in Cardiogenic Shock II [IABP-SHOCK II]; [NCT00491036](https://doi.org/10.1016/j.jacc.2017.02.027)) (J Am Coll Cardiol 2017;69:1913-20) © 2017 by the American College of Cardiology Foundation.

Cardiogenic shock (CS) is the most common cause of in-hospital death in patients with acute myocardial infarction (AMI) (1). Despite many therapeutic advances—especially early primary percutaneous intervention (PCI)—mortality

rates still approach 50% (1,2). Severity of CS and clinical outcome show broad variations. Accurate risk stratification is a critical task, which must be performed in the acute setting and often influences further treatment decisions (e.g., use of advanced



Listen to this manuscript's audio summary by JACC Editor-in-Chief Dr. Valentin Fuster.



From the ^aDepartment of Cardiology, Angiology and Intensive Care Medicine, University Heart Center Lübeck, Medical Clinic II, Lübeck, Germany; ^bGerman Center for Cardiovascular Research (DZHK), Partner Site Hamburg/Kiel/Lübeck, Lübeck, Germany; ^cInstitut für Herzinfarktforschung, Ludwigshafen, Germany; ^dCardiology, University of Helsinki, Heart and Lung Center, Helsinki University Hospital, Helsinki, Finland; ^eEmergency Medicine, University of Helsinki, Helsinki University Hospital, Helsinki, Finland; and the ^fMedizinische Klinik B, Herzzentrum Ludwigshafen, Ludwigshafen, Germany. This work was supported by grants from the German Research Foundation, the German Heart Research Foundation, the German Cardiac Society, Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte, and the University of Leipzig-Heart Center and by unrestricted grants from Maquet Cardiopulmonary and Teleflex Medical. The authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Thiele and Desch contributed equally to this work and are joint senior authors.

Manuscript received August 4, 2016; revised manuscript received January 19, 2017, accepted February 6, 2017.

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

AUC = area under the curve

CABG = coronary artery bypass grafting

CI = confidence interval

CS = cardiogenic shock

GFR = glomerular filtration rate

HR = hazard ratio

IABP = intra-aortic balloon pump

PCI = percutaneous coronary intervention

ROC = receiver-operating characteristic

therapies, such as active assist devices). Therefore, there remains an obvious need for a risk stratification tool that is simple, easily applicable in clinical practice, and readily available directly after admission at the catheterization laboratory. Furthermore, designing clinical trials in patients with CS is challenging due to the large heterogeneity and variability of outcomes in this population of critically ill patients (3). A severity scoring system might be useful to conduct trials with a more homogeneous patient population.

Until now, few studies of risk stratification in CS have been performed. Most of these, such as a post hoc analysis from the TRIUMPH (Tilarginine Acetate Injection in a Randomized International Study in Unstable MI Patients With Cardiogenic Shock) trial, only identified and described predictors for worse outcome, without proposing a risk-scoring model (4-6). Although several scores have been developed based on patient registry data and randomized clinical trials (7-10), almost all of them share certain limitations: 1) they were not validated; 2) they were derived from small studies; 3) the etiology of CS often was not restricted to AMI; and 4) the parameters used cannot be easily assessed directly in the catheterization lab. Furthermore, some of the underlying studies were performed decades ago and included AMI patients without coronary revascularization. Consequently, potentially relevant variables relating to the revascularization procedure, such as procedural success as assessed by Thrombolysis In Myocardial Infarction flow grade were not included in these analyses and scores.

SEE PAGE 1921

The aim of this study was to develop a simple, easy-to-use, readily available, fully validated risk score for short-term mortality prediction in the catheterization laboratory in patients with AMI-related CS undergoing PCI enrolled in the largest randomized CS trial to date.

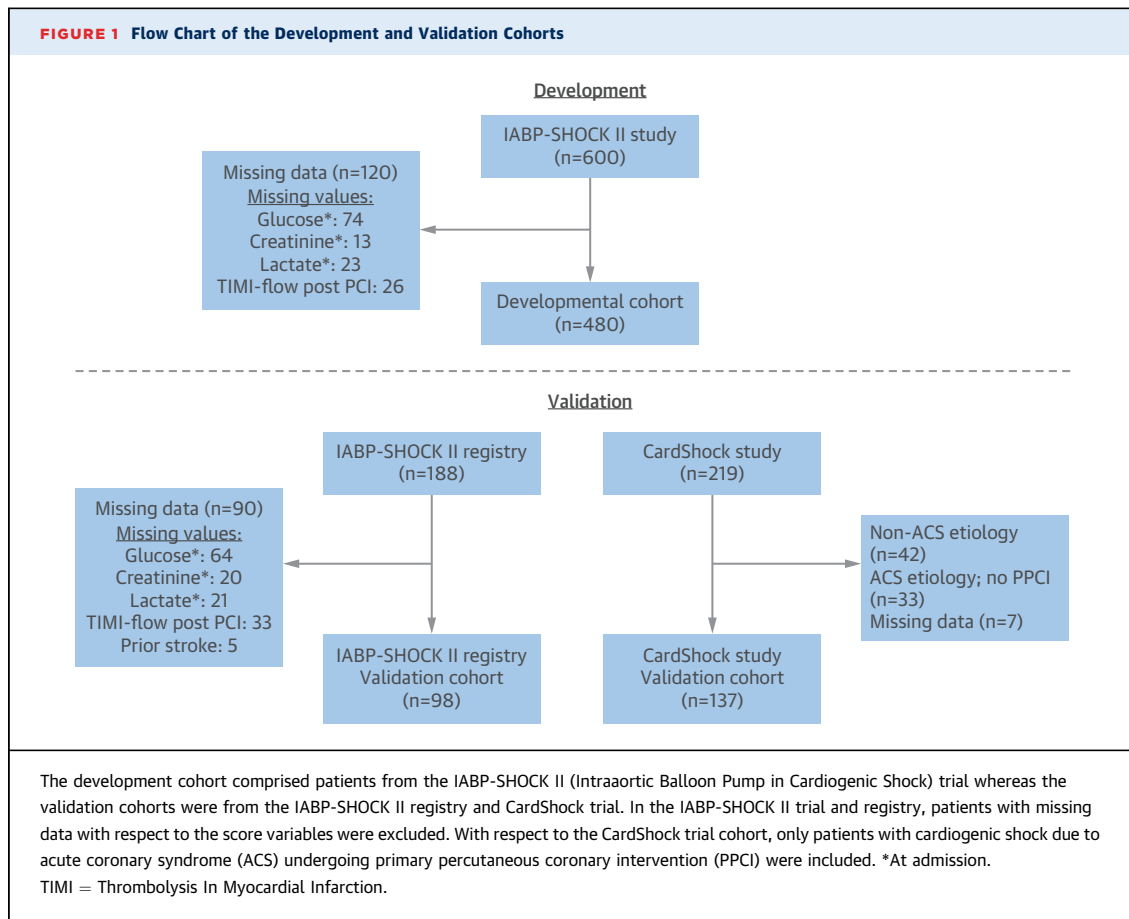
METHODS

The present analysis is a substudy of the randomized IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) trial. In this trial, intra-aortic balloon pump (IABP) support was compared with no IABP support in patients with AMI-related CS. There were no significant differences between the 2 treatment groups with respect to short- and long-term outcomes. The design of the trial and its main results

have been published previously (11-13). Briefly, 600 patients were enrolled in 37 centers in Germany and randomly allocated to either IABP support or to a control group in a 1:1 fashion. CS was defined as hypotension, pulmonary congestion, and signs of end-organ hypoperfusion. Exclusion criteria were duration of CS >12 h, cardiopulmonary resuscitation >30 min, severe cerebral deficit, mechanical causes of CS, age >90 years, absolute contraindications against IABP insertion, shock of other cause, or severe concomitant disease with life expectancy <6 months. All patients underwent cardiac catheterization immediately after hospital admission. The primary endpoint was 30-day all-cause mortality. Patients with AMI complicated by CS who met any exclusion criterion of the IABP-SHOCK II trial were enrolled into an associated registry (n = 188). The study, which was conducted according to the Declaration of Helsinki, was approved by the local ethics committees and all patients or their legal representatives gave written informed consent.

STATISTICAL ANALYSIS. The model was developed on the randomized population of the IABP-SHOCK II trial (n = 600) using a stepwise multivariable Cox proportional hazards regression analysis with the forward selection technique. Unselected extensive univariable testing was performed including all database variables potentially associated with mortality. Variables significantly related to mortality in univariable testing (p < 0.10) were further examined in multivariable analysis. Herein, 6 variables remained statistically significant associated with mortality. These variables constitute the score parameters. Only patients with complete datasets for these 6 score candidate variables were considered for further testing. Patients treated conservatively (19 of 600; 3.2%), as well as patients undergoing immediate coronary artery bypass grafting (CABG) (6 of 600; 1%), were excluded from the present analysis. In 17 of 600 (2.8%) patients, CABG was performed after PCI. Of these, 4 patients had to be excluded due to missing parameters. The remaining 13 patients were included in the analysis.

Continuous variables were dichotomized. The optimal cutoff points were defined using the Youden index. The scoring system was determined by rounding the respective parameter estimates, attributing either 1 or 2 points to each variable, based on the observed hazard ratio (HR). Parameters with a rounded HR of 2 or more were assigned 2 points; those with a rounded HR below 2 were assigned 1 point. According to the score, the population was classified into 3 risk categories: low (0 to 2), intermediate (3 or 4), and high (5 to 9). Comparison of



30-day mortality rates was done by chi-square testing and by Kaplan-Meier analysis with pairwise log-rank testing. Receiver-operating characteristic (ROC) analysis was performed to assess discriminative power. Calibration of the score was assessed in the 2 validation cohorts by dividing the sample into 5 equal groups based on the predicted probability, then plotting the mean probability of each quintile against the observed frequency of 30-day mortality for that group.

Patients included in the IABP-SHOCK II registry served as an internal validation cohort. External validation was performed in the subset of patients with infarction-related CS who underwent PCI enrolled in a European multicenter study (CardShock [NCT01374867] trial) (10). Comparison of 30-day mortality rates in the 2 validation cohorts, according to the different score categories, was done by chi-square testing as well as by Kaplan-Meier analysis with pairwise log-rank testing. Furthermore, ROC analysis was performed to assess the discriminative power of the score. All statistical analyses were performed using SAS for Windows version 9.3 (SAS Institute, Cary, North Carolina) by an independent

statistician at the Institut für Herzinfarktforschung, Ludwigshafen, Germany.

RESULTS

Of the 600 patients enrolled in the trial, only 480 patients with complete datasets for the selected 6 variables were included as the final cohort (Figure 1). Thirty-day mortality rates did not differ between the cohorts of included and excluded patients (40.4% and 42.0%, respectively; $p = 0.75$). Per the baseline characteristics of these patients (Table 1), 69% were men and mean age was 70 years. All patients had infarct-related CS with the classical cardiovascular risk factors; for example, nearly three-quarters had arterial hypertension and >42% had dyslipidemia. In addition, they were characterized by several comorbidities, such as peripheral arterial disease or renal insufficiency. Of the 480 patients, 194 (40.6%) died within 30 days.

VARIABLE IDENTIFICATION AND SCORE CREATION. After multivariable testing, the following 6 variables remained statistically significant predictors and were included in the model: age, history of stroke, glucose

TABLE 1 Baseline Characteristics

	IABP-SHOCK II Trial Development Cohort (n = 480)	IABP-SHOCK II Registry Validation Cohort (n = 98)	CardShock Trial Validation Cohort (n = 137)
Demographic data			
Age, yrs	70 (58-77)	71 (59-76)	68 (61-76)
Male	331/480 (69)	75/98 (73.5)	106/137 (77.4)
Height, cm	174 (167-180)	175 (168-180)	171 (165-176)
Weight, kg	80 (73-90)	85 (75-94)	78 (70-85)
BMI, kg/m ²	27.3 (24.7-30.0)	27.2 (24.8-31.1)	26.8 (24.2-26.5)
Systolic blood pressure, mm Hg	90 (80-109)	105 (81-121)	85 (74-96)
Diastolic blood pressure, mm Hg	58 (48-68)	60 (47.5-76)	51 (43-60)
Mechanical ventilation	270/480 (56.3)	52/98 (53.1)	81/137 (59.1)
Cardiopulmonary resuscitation	209/480 (43.5)	49/98 (50)	39/137 (28.5)
Cardiovascular risk factors/cardiovascular diseases			
Smoking	165/475 (34.7)	33/95 (34.7)	58/137 (42.3)
Arterial hypertension	341/477 (71.5)	66/96 (68.8)	81/137 (59.1)
Dyslipidemia	201/476 (42.2)	27/96 (28.1)	64/137 (46.7)
Diabetes mellitus	162/478 (33.9)	40/96 (41.7)	39/137 (28.5)
History of myocardial infarction	109/480 (22.7)	15/98 (15.3)	31/137 (22.6)
History of stroke	39/480 (8.1)	5/98 (5.1)	12/137 (8.8)
Known peripheral artery disease	62/480 (12.9)	18/98 (18.4)	14/137 (10.2)
Prior PCI	99/479 (20.7)	14/98 (14.3)	20/137 (14.6)
Prior CABG	26/480 (5.4)	10/98 (10.2)	6/137 (4.4)
Laboratory results			
Baseline serum creatinine			
μmol/l	114.0 (92.5-146.0)	129.1 (95.5-171.0)	119.7 (78.5-101.0)
mg/dl	1.3 (1.1-1.7)	1.5 (1.1-1.9)	1.4 (0.9-1.1)
Baseline glucose			
mmol/l	11.6 (8.1-16.8)	10.9 (8.0-17.6)	13.6 (8.3-18.1)
mg/dl	209 (146-303)	196 (144-317)	245 (150-326)
Baseline arterial lactate, mmol/l	3.7 (2.1-7.3)	3.8 (1.7-7.7)	4.3 (1.8-5.2)
Catheterization lab data			
Primary PCI	480/480 (100)	98/98 (100)	137/137 (100)
TIMI flow grade 3 after PCI	395/480 (82.3)	80/98 (81.6)	98/137 (71.5)

Values are mean (interquartile range) or n/N (%).
BMI = body mass index; CABG = coronary artery bypass grafting; IABP-SHOCK = Intraaortic Balloon Pump in Cardiogenic Shock; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

TABLE 2 Results of Multivariable Cox Regression Analysis

	Hazard Ratio (95% CI)	Parameter Estimate	p Value
Age >73 yrs	1.54 (1.16-2.05)	0.43	0.003
History of stroke	2.09 (1.39-3.15)	0.73	0.0004
Glucose >10.6 mmol/l (191 mg/dl)*	1.48 (1.10-2.01)	0.39	0.01
Creatinine >132.6 μmol/l (1.5 mg/dl)*	1.57 (1.17-2.11)	0.44	0.003
Arterial lactate >5 mmol/l*	1.98 (1.47-2.66)	0.68	<0.0001
TIMI flow grade <3 after PCI	2.73 (1.11-6.73)	0.72	0.03

*At admission.
CI = confidence interval; other abbreviations as in Table 1.

at admission, creatinine at admission, arterial blood lactate at admission, and TIMI flow grade <3 after PCI. The results of the regression analysis are shown in Table 2. The cutoff points were determined by the Youden index as follows: age >73 years, glucose at admission >10.6 mmol/l (191 mg/dl), creatinine at admission >132.6 μmol/l (1.5 mg/dl), and arterial lactate at admission >5 mmol/l. Subsequently, the IABP-SHOCK II score was created attributing either 1 or 2 points to the variables (Central Illustration). The score has a minimum of 0 and a maximum of 9 points. Using the score, the population was classified into 3 risk categories: low (0 to 2), intermediate (3 or 4), and high (5 to 9), as shown in the Central Illustration. Of 480 patients, 235 (49.0%) were at low risk, 181 (37.7%) were at intermediate risk, and 64 (13.3%) were at high risk.

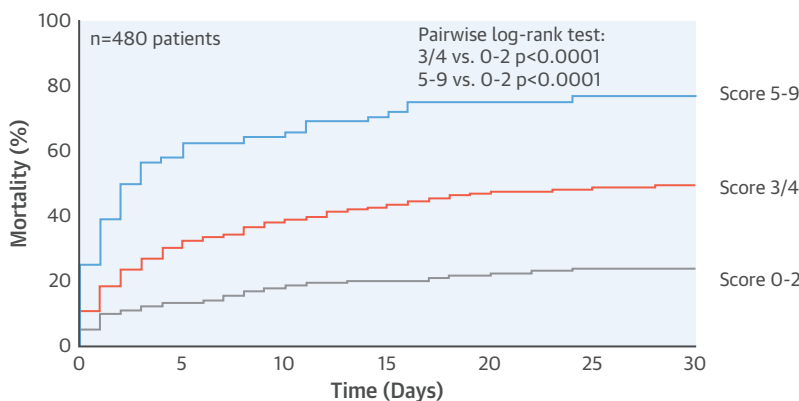
We repeated the analysis by entering the laboratory results (lactate, creatinine, and glucose) as well as age as continuous variables. In this analysis, there was no difference compared to the analysis with dichotomized variables. The parameters remaining significant after multivariable testing were the same as in the first analysis. Expectedly, the HRs were slightly lower when variables were entered as continuous variables. Notably, the attribution of 1 or 2 points according to the rounded HR (i.e., 2 points for parameters with a rounded HR of ≥2 and 1 point for parameters with an HR <2) for determination of the scoring system also remained unchanged.

Per the score risk categories of low, intermediate, and high, the observed mortality rates assessed by chi-square testing were 23.8%, 49.2%, and 76.6%, respectively (p < 0.0001). The Central Illustration depicts the Kaplan-Meier curves for 30-day mortality according to the 3 score categories. In c-statistics, the predictive value of the score with respect to 30-day mortality was good with an area under the curve (AUC) of 0.74 (95% confidence interval [CI]: 0.69 to 0.78).

INTERNAL AND EXTERNAL VALIDATION. Of the 188 patients included in the registry, complete data were available for 98 patients, who served as the first validation cohort. Of these patients, 45 (45.9%) were low risk, 39 (39.8%) were intermediate risk, and 14 (14.3%) were high risk. Once again, event rates of the excluded patients were comparable to the included patients (54.8% vs. 53.6%, respectively; p = 0.88). Overall 30-day mortality was 53.1%. In addition, the data of 137 patients with infarction-related CS who underwent primary PCI included in the multicenter, observational CardShock trial were used for external validation. Of these patients 81 (59%) were low risk, 35 (26%) were intermediate risk, and 21 (15%) were high risk. Of the 137 patients, 55 (40.1%) died.

CENTRAL ILLUSTRATION Cardiogenic Shock Complicating Acute Myocardial Infarction: IABP-SHOCK II Risk Score

Score		Risk categories	
Variable	Points	Category	Points
Age >73 years	1	Low	0-2
History of stroke	2	Intermediate	3/4
Glucose >10.6 mmol/l (191 mg/dl)*	1	High	5-9
Creatinine >132.6 μmol/l (1.5 mg/dl)*	1		
Arterial lactate >5 mmol/l*	2		
TIMI flow grade <3 after PCI	2		
Maximum	9		



Pöss, J. et al. *J Am Coll Cardiol.* 2017;69(15):1913-20.

Using a stepwise multivariable regression analysis, we sought to create a risk score for mortality in patients with cardiogenic shock complicating acute myocardial infarction. The scoring system was determined by rounding the respective parameter estimates, attributing either 1 or 2 points to each variable, based on the observed hazard ratio, and the total score separated by risk category: low: 0 to 2 points; intermediate: 3 or 4 points; and high: 5 to 9 points. In total, 480 patients included in the development population were classified according to the IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock) risk score into the low-risk (n = 235; 49.0%), intermediate-risk (n = 181; 37.7%), or high-risk (n = 64; 13.3%) categories. The Kaplan-Meier analysis for 30-day mortality showed a highly significant, stepwise increase in mortality. *At admission. PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

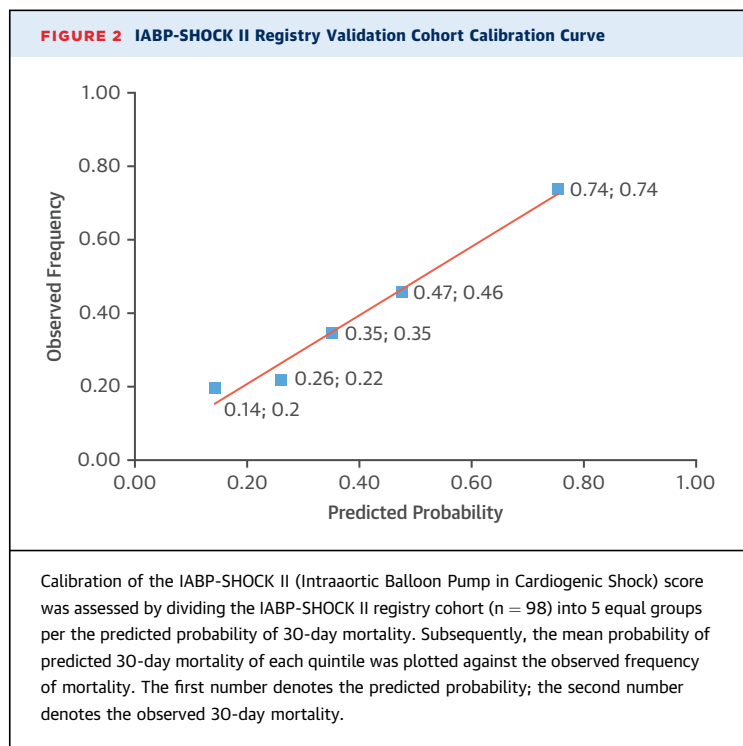
In the validation analysis performed in the IABP-SHOCK II registry patients, c-statistics showed good discrimination, with an AUC of 0.79 (95% CI: 0.70 to 0.88). Comparison of the predicted probabilities with the observed frequencies of 30-day mortality according either to score quintiles or to the 3 categories demonstrated good calibration of the score (Figure 2). The observed mortality rates (low vs. intermediate vs. high) in chi-square testing were 31.1%, 63.2%, and 100%, respectively (p < 0.0001) (Figure 3A).

External validation in the CardShock cohort showed similar results with 30-day mortality rates of 28.0% (low), 42.9% (intermediate), and 77.3% (high; p < 0.001) and an AUC of 0.73 (95% CI: 0.64 to 0.81). Figure 3B depicts the Kaplan-Meier curves with pairwise comparisons by log-rank test (score 0 to 2 vs. score 3 or 4; p = 0.04; score 0 to 2 vs. score 5 to 9; p = 0.008).

DISCUSSION

There are 4 major strengths of the proposed IABP-SHOCK II score. First, the large, homogeneous population of patients with AMI-related CS undergoing early revascularization was from the largest, contemporary randomized clinical trial in this setting. Second, it was based on simple, dichotomized variables and thus can be rapidly and easily calculated in clinical routine. Third, it included variables that are readily available directly in the catheterization laboratory after hospital admission and does not require elaborate assessment of variables. Fourth, it has been validated in the IABP-SHOCK II registry as well as in an external CS cohort.

As CS is known to have unacceptably high and variable mortality rates, early risk stratification of the



patients is a crucial clinical task, which remains challenging in the acute setting (14). Many studies aimed to identify predictors for adverse outcome, but only a few studies have proposed a risk score. In a monocentric trial including 74 patients with ST-segment elevation myocardial infarction and CS, age >75 years, left main coronary artery occlusion, left ventricular ejection fraction <25%, and post-procedural TIMI flow grade <3 were significantly associated with dismal prognosis (15). A score based on these 4 variables predicted 1-year survival. Other scores were developed based on data of patients included in registries and clinical trials, such as the ACC-NCDR (American College of Cardiology-National Cardiovascular Data Registry) registry (7), GUSTO-I (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trial (8), and the SHOCK (Should we emergently revascularize Occluded Coronaries for cardiogenic shock) trial and registry (9). Harjola et al. (10) developed a risk score based on patients with CS in the CardShock study. This model included age >75 years, confusion at presentation, previous AMI or CABG, acute coronary syndrome etiology, reduced left ventricular ejection fraction, arterial blood lactate, and estimated glomerular filtration rate (GFR).

However, these available scoring systems have several limitations. Some of them, such as the score proposed by Garcia-Alvarez et al. (15), are based on

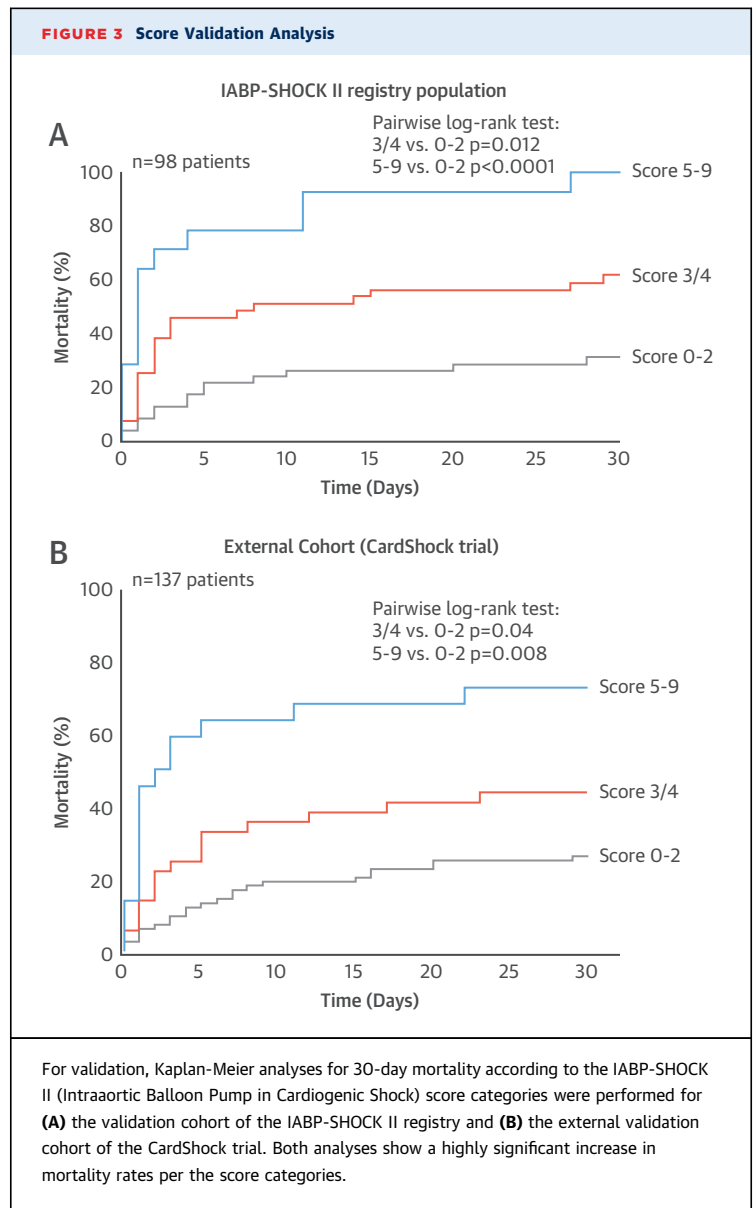
very small trials. Another major point of criticism: some scores were developed based on clinical trials performed in the pre-PCI era, thus including patients either undergoing fibrinolysis or no early revascularization at all, including the aforementioned GUSTO-I and SHOCK trial scores (7,9). As performance of early revascularization is known to be the most important measure to reduce mortality in CS, the use of pre-PCI trials might induce a certain bias. Furthermore, variables of the revascularization procedure, which have been shown to be independently associated with clinical outcome, such as TIMI flow grade, could not be taken into account. Other scores are complex and impracticable in clinical routine, especially in an acute setting. Notably, most of the scores are not validated. However, to demonstrate that a proposed prognostic model is valuable, it is insufficient to prove that it predicts outcome in the initial development cohort. Rather, evidence is needed showing that the model performs well in other patient cohorts too.

The recently published score proposed by Harjola et al. (10), was developed in the whole CardShock study population, an unselected cohort of CS patients with a broad spectrum of etiologies (i.e., not only AMI related). We developed our score only for patients with AMI-related CS undergoing PCI, and included data on TIMI flow after PCI. AMI is by far the leading cause of CS and is independently associated with mortality compared to CS without AMI (10). The CardShock study was chosen for validation of our score because it is a large, recently published European prospective observational multicenter study on CS. For validation, however, we selected only patients with AMI-related CS undergoing primary PCI. Most of the variables included in our score are well-known risk factors for worse clinical outcomes of CS patients. Age, a major independent risk factor, was consequently included in almost all other proposed scoring systems for CS (6-10,15). Similarly, renal insufficiency was incorporated in many other scores (4,7-9). Because GFR might not provide a correct measure of renal function in the setting of acute renal failure and because it has been shown that creatinine has a better predictive value for 1-year mortality compared to GFR assessed by different equations in a subanalysis of the IABP-SHOCK II trial (16), we decided to use creatinine as the measure of renal function. Given that in most patients (including our cohort) renal function before the onset of CS was not recorded, it remains unclear whether it arises from acute renal failure or whether it is due to a pre-existing chronic renal insufficiency. Most likely, it is a combination of these 2 situations, which are both related to an adverse clinical outcome. Lactate

concentrations are also known to be strongly and independently associated with mortality in CS. This underlined the importance of impaired tissue hypoperfusion for clinical outcome.

The association between reduced TIMI flow after PCI and adverse outcomes is pathophysiologically plausible and was an independent predictor for mortality in the study from Garcia-Alvarez et al. as well as in the large German ALKK (Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte) registry (6,15). Serum glucose levels have been shown to be an independent predictor of mortality in AMI and AMI-related CS, especially in patients without diabetes mellitus (17,18). However, interestingly, none of the previously mentioned existing scores included serum glucose levels. Also, history of stroke was not included in the previous scores. In contrast to other studies, previous AMI or CABG as signs for more severe ischemic heart disease were not predictive in our analysis. This might be due to the low prevalence of these conditions in our patients.

The results of our analyses show a stepwise increase in mortality according to the different score categories, both in the IABP-SHOCK II trial as well as in the 2 validation cohorts. Furthermore, the score showed a good performance for prediction of the risk for short-term mortality in all investigated cohorts and is well calibrated. CS is known to be characterized by highly variable mortality rates and clinical trials on CS are difficult to interpret due to the highly heterogeneous patient cohorts (3). This might be 1 explanation for the lack of evidence-based therapeutic approaches in CS. Categorization of the patients according to the proposed IABP-SHOCK II score might help prospectively create homogenous collectives for future observational and randomized clinical trials. Beyond this, and more importantly, the score might serve as a tool for early clinical risk stratification of CS patients, which can be performed directly after PCI in the catheterization laboratory. All variables can easily be assessed and are readily available by point-of-care testing or immediate blood gas analysis, such as glucose or blood lactate. We believe that it might also be helpful for clinical decision making with respect to the selection of management strategies (e.g., deciding whether to implant a mechanical support device). Of course, calculation of a single score will never be the only variable determining such a far-reaching decision, which must take into account many other individual aspects, such as the patient's comorbidities and neurological situation. However, the score might provide valuable assistance for the clinician.



STUDY LIMITATIONS. The main limitation of this study was that with 480 patients in the development cohort and 137 and 98 patients in the validation cohorts, the populations were still rather small. However, it should be emphasized that the IABP-SHOCK II trial is the largest recent randomized, controlled clinical trial in the setting of infarct-related CS and the CardShock study is a large European prospectively enrolled cohort of patients with CS. Another limitation was that a certain number of patients needed to be excluded from the analyses due to missing data regarding the score variables. However, event rates were comparable in the included and excluded sample of patients—both in the developmental and registry validation cohorts.

This finding precluded a relevant bias of our analysis. Furthermore, both in IABP-SHOCK II and in Card-Shock, TIMI flow after PCI was not assessed by a core laboratory. Available data showed that TIMI flow was usually classified higher if it was investigator reported compared to core-lab assessment (19). This might produce a certain bias with respect to the true predictive value of a “correctly” assessed TIMI flow. However, the score will be applied in clinical routine, where TIMI flow will be assessed by the treating physician. Therefore, the fact that TIMI flow was investigator reported is rather an advantage, as it is closer to the real-life setting.

CONCLUSIONS

The IABP-SHOCK II risk score is a simple tool that can be rapidly calculated in the catheterization laboratory setting and applied in clinical routine. It might therefore serve for identifying patients for future clinical trials and, more importantly, it might help stratify patients according to their risk for short-term mortality and thus facilitate clinical decision making.

ADDRESS FOR CORRESPONDENCE: Dr. Janine Pöss, Medical Clinic II, University Heart Center Lübeck, University Hospital Schleswig-Holstein, Ratzeburger Allee 160, 23538 Lübeck, Germany. E-mail: janine.poess@uksh.de.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The IABP-SHOCK II score, which incorporates age, prior stroke, admission blood glucose, creatinine and lactate levels, and impaired post-PCI coronary flow, can effectively stratify patients with infarct-related CS for 30-day risk of mortality.

TRANSLATIONAL OUTLOOK: Future studies should evaluate the utility of this risk score to guide selection of patients with infarct-related CS for advanced mechanical circulatory support modalities.

REFERENCES

- Goldberg RJ, Spencer FA, Gore JM, Lessard D, Yarzebski J. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation* 2009;119:1211–9.
- Aissaoui N, Puymirat E, Tabone X, et al. Improved outcome of cardiogenic shock at the acute stage of myocardial infarction: a report from the USIK 1995, USIC 2000, and FAST-MI French Nationwide Registries. *Eur Heart J* 2012;33:2535–43.
- Thiele H, Allam B, Chatellier G, Schuler G, Lafont A. Shock in acute myocardial infarction: the Cape Horn for trials? *Eur Heart J* 2010;31:1828–35.
- Katz JN, Stebbins AL, Alexander JH, et al. Predictors of 30-day mortality in patients with refractory cardiogenic shock following acute myocardial infarction despite a patent infarct artery. *Am Heart J* 2009;158:680–7.
- Sutton AG, Finn P, Hall JA, Harcombe AA, Wright RA, de Belder MA. Predictors of outcome after percutaneous treatment for cardiogenic shock. *Heart* 2005;91:339–44.
- Zeymer U, Vogt A, Zahn R, et al. Predictors of in-hospital mortality in 1333 patients with acute myocardial infarction complicated by cardiogenic shock treated with primary percutaneous coronary intervention (PCI). *Eur Heart J* 2004;25:322–8.
- Klein LW, Shaw RE, Krone RJ, et al. Mortality after emergent percutaneous coronary intervention in cardiogenic shock secondary to acute myocardial infarction and usefulness of a mortality prediction model. *Am J Cardiol* 2005;96:35–41.
- Hasdai D, Holmes DR Jr., Califf RM, et al. Cardiogenic shock complicating acute myocardial infarction: predictors of death. *Am Heart J* 1999;138:21–31.
- Sleeper LA, Reynolds HR, White HD, Webb JG, Dzavik V, Hochman JS. A severity scoring system for risk assessment of patients with cardiogenic shock: a report from the SHOCK Trial and Registry. *Am Heart J* 2010;160:443–50.
- Harjola VP, Lassus J, Sionis A, et al. Clinical picture and risk prediction of short-term mortality in cardiogenic shock. *Eur J Heart Fail* 2015;17:501–9.
- Thiele H, Schuler G, Neumann FJ, et al. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock: Design and rationale of the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial. *Am Heart J* 2012;163:938–45.
- Thiele H, Zeymer U, Neumann FJ, et al. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock. Final 12-month results of the randomised Intra-aortic Balloon Pump in cardiogenic shock II (IABP-SHOCK II) trial. *Lancet* 2013;382:1638–45.
- Thiele H, Zeymer U, Neumann FJ, et al. Intra-aortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med* 2012;367:1287–96.
- Pöss J, Desch S, Thiele H. Shock management in acute myocardial infarction. *EuroIntervention* 2014;10:T74–82.
- Garcia-Alvarez A, Arzamendi D, Loma-Osorio P, et al. Early risk stratification of patients with cardiogenic shock complicating acute myocardial infarction who undergo percutaneous coronary intervention. *Am J Cardiol* 2009;103:1073–7.
- Fuerna G, Poenisch C, Eitel I, et al. Prognostic impact of established and novel renal function biomarkers in myocardial infarction with cardiogenic shock: A biomarker substudy of the IABP-SHOCK II-trial. *Int J Cardiol* 2015;191:159–66.
- Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. *Lancet* 2000;355:773–8.
- Yang JH, Song PS, Song YB, et al. Prognostic value of admission blood glucose level in patients with and without diabetes mellitus who sustain ST segment elevation myocardial infarction complicated by cardiogenic shock. *Crit Care* 2013;17:R218.
- Alhadramy O, Westerhout CM, Brener SJ, Granger CB, Armstrong PW, APEX AMI Investigators. Is visual interpretation of coronary epicardial flow reliable in patients with ST-elevation myocardial infarction undergoing primary angioplasty? Insights from the angiographic substudy of the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial. *Am Heart J* 2010;159:899–904.

KEY WORDS acute coronary syndrome, mortality, percutaneous coronary intervention, prognosis, risk score, TIMI flow grade