Predictive value of the APACHE II score in cardiogenic shock patients treated with a percutaneous left ventricular assist device

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Abstract

Background: The APACHE II score assesses patient prognosis in intensive care units. Different disease entities are predictable by using a specific factor called Diagnostic Category Weight (DCW). We aimed to validate the prognostic value of the APACHE II score in patients treated with a percutaneous left ventricular assist device because of refractory cardiogenic shock (CS).

Methods: From the Dresden Impella Registry, we analyzed 180 patients receiving an Impella CP®. The main outcome was the observed intrahospital mortality (\(\tilde{S}_{\text{hosp}}\)), which was compared to the predicted mortality estimated by the APACHE II score.

Results: The APACHE II score, which was 33.5 ± 0.6, significantly overestimated intrahospital mortality (\(\tilde{S}_{\text{hosp}}\)) 54.4 ± 3.7% vs. APACHE II 74.6 ± 1.6%; p < 0.001). Nevertheless, the APACHE II score showed an acceptable accuracy to predict intrahospital mortality (ROC AUC 0.70; 95% CI 0.62–0.78). Thus, we adapted the formula for calculation of predicted mortality by adjusting DCW. The total registry cohort was randomly divided into derivation group for calculation of adjusted DCW and validation group for testing. Intrahospital mortality was much more precisely predicted using the adjusted DCW compared to the conventional DCW (difference of predicted and observed mortality: -4.7 ± 2.4% vs. -23.2 ± 2.3%; p < 0.001). The new calculated DCW was -1.183 for the total cohort.

Conclusion: The APACHE II score has an acceptable accuracy for the prediction of intrahospital mortality but overestimates its total amount in CS patients. Adjustment of the DCW can lead to a much more precise prediction of prognosis.

1. Introduction

A precise assessment of the prognosis of patients in the intensive care unit (ICU) is of imminent interest for attending physicians. Among the various scores proposed for this purpose [1], the Acute Physiology and Chronic Health Evaluation (APACHE) II score is frequently used [2] and is applied to a broad spectrum of critically ill patients [3–5]. It assesses intrahospital mortality by using a formula (Formula I–III), which consists of a scoring system from 0 to 71 points. This value is derived from 12 acute physiologic parameters addressing organ function, resulting in the Acute Physiology Score (APS). Furthermore, patients’ ages (Age Points) and the underlying causes leading to their admission to the ICU (Chronic Health Points) e.g., non-surgical vs. surgical and urgent vs. elective surgery are considered. Depending on the underlying disease, the APACHE II score adjusts the mortality by a specific constant, the Diagnostic Category Weight (DCW), which was published by Knaus et al. [6].

Cardiogenic shock (CS) together with septic shock is one of the most ominous types of shock [7,8]. To treat CS, some landmark therapies have been added since the implementation of the APACHE II score. The

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† All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Table 1

Physiologic variables of the APACHE II score. The score considers the worst values in 12 parameters in the first 24 h, which were categorized and aggregated to create the Acute Physiology Score. The APACHE II score is obtained by adding the Age Points to the Acute Physiologic Score. APACHE, Acute Physiology and Chronic Health Evaluation; MAP, mean arterial pressure; PaO₂, partial pressure of oxygen; WBC, white blood cell; GCS, Glasgow Coma Scale.

| Physiologic variables of APACHE II score | Worst value in the first 24 h | Categorized physiologic variables of APACHE II score | Worst value in the first 24 h |
|------------------------------------------|-----------------------------|------------------------------------------------|-----------------------------|
| Temperature/°C                           | 35.7 ± 0.1 (n = 179)        | Temperature                                    | 0.83 ± 1.01 (n = 180)       |
| MAP/mmHg                                 | 56.2 ± 16; (n = 180)        | MAP                                            | 2.18 ± 0.10 (n = 180)       |
| Heart rate /min                          | 110.0 ± 21; (n = 179)       | Heart rate                                     | 1.86 ± 0.09 (n = 180)       |
| Respiratory frequency / min              | 22.6 ± 0.5(180)            | Respiratory frequency                          | 0.53 ± 0.07 (n = 180)       |
| PaO₂ / kPa                               | 10.6 ± 0.4 (n = 180)       | Oxygenation                                    | 2.77 ± 0.09 (n = 180)       |
| Oxygenation/ mmHg                        | 74.4 ± 4 (180)             | pH                                             | 7.24 ± 0.012 (n = 180)      |
| Sodium / mmol/l                          | 135.9 ± 0.4 (n = 180)      | Sodium                                         | 0.22 ± 0.05 (n = 180)       |
| Potassium / mmol/l                       | 5.0 ± 0.2; (n = 180)       | Potassium                                      | 0.52 ± 0.08 (n = 180)       |
| Serum creatinine / mmol/l                | 162.5 ± 6.1; (n = 173)     | Serum creatinine                               | 1.74 ± 0.10 (n = 179)       |
| Hematocrit                               | 0.280 ± 0.006; (n = 179)   | Hematocrit                                     | 1.49 ± 0.09 (n = 179)       |
| WBC / Gpt/l                              | 18.2 ± 0.7; (n = 173)      | WBC                                            | 0.96 ± 0.07 (n = 179)       |
| GCS                                      | 6.3 ± 0.4; (n = 180)       | GCS                                            | 8.7 ± 0.4 (n = 180)         |

The current study was conducted according to the REporting of studies Conducted using Observational Routinely collected health Data statement (RECORD) guidelines.

Table 2

Physiologic variables of the APACHE II score. The score considers the worst values in 12 parameters in the first 24 h, which were categorized and aggregated to create the Acute Physiology Score. The APACHE II score is obtained by adding the Age Points to the Acute Physiologic Score. APACHE, Acute Physiology and Chronic Health Evaluation; MAP, mean arterial pressure; PaO₂, partial pressure of oxygen; WBC, white blood cell; GCS, Glasgow Coma Scale.

| Physiologic variables of APACHE II score | Worst value in the first 24 h | Categorized physiologic variables of APACHE II score | Worst value in the first 24 h |
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| Temperature/°C                           | 35.7 ± 0.1 (n = 179)        | Temperature                                    | 0.83 ± 1.01 (n = 180)       |
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| Heart rate /min                          | 110.0 ± 21; (n = 179)       | Heart rate                                     | 1.86 ± 0.09 (n = 180)       |
| Respiratory frequency / min              | 22.6 ± 0.5(180)            | Respiratory frequency                          | 0.53 ± 0.07 (n = 180)       |
| PaO₂ / kPa                               | 10.6 ± 0.4 (n = 180)       | Oxygenation                                    | 2.77 ± 0.09 (n = 180)       |
| Oxygenation/ mmHg                        | 74.4 ± 4 (180)             | pH                                             | 7.24 ± 0.012 (n = 180)      |
| Sodium / mmol/l                          | 135.9 ± 0.4 (n = 180)      | Sodium                                         | 0.22 ± 0.05 (n = 180)       |
| Potassium / mmol/l                       | 5.0 ± 0.2; (n = 180)       | Potassium                                      | 0.52 ± 0.08 (n = 180)       |
| Serum creatinine / mmol/l                | 162.5 ± 6.1; (n = 173)     | Serum creatinine                               | 1.74 ± 0.10 (n = 179)       |
| Hematocrit                               | 0.280 ± 0.006; (n = 179)   | Hematocrit                                     | 1.49 ± 0.09 (n = 179)       |
| WBC / Gpt/l                              | 18.2 ± 0.7; (n = 173)      | WBC                                            | 0.96 ± 0.07 (n = 179)       |
| GCS                                      | 6.3 ± 0.4; (n = 180)       | GCS                                            | 8.7 ± 0.4 (n = 180)         |

Patient data were extracted from the Dresden Impella Registry, which is an ongoing registry of a high-volume center, including different patients who received a pLVAD, which actively unloads the LV with a micro-axial pump. From February 2014 to May 2019, 256 patients (>18 years old) received LV unloading with a pLVAD as bridge-to-recovery strategy. After exclusion of 76 patients receiving a pLVAD during protected PCI or a percutaneous right ventricular assist device like the Impella RP®, the study included 180 patients treated with an Impella CP® due to CS.

CS was defined as the presence of cardiac disease (myocardial infarction, cardiomyopathy, or valvular heart disease), systolic blood pressure <90 mmHg for >15 min or requirement of catecholamines to maintain systolic blood pressure above 90 mmHg, and clinical signs of impaired end-organ perfusion as indicated by serum lactate levels above 4 mmol/L. Implantation of the pLVAD was always performed in a cardiac catheterization laboratory by an experienced interventional cardiologist (>20 implantations per annum). The study was approved by the Ethics Committee at TU Dresden (EK 457-122-014).

We compared the predicted mortality estimated by the APACHE II score with the real-world mortality of patients with CS in the Dresden Impella Registry.

The main outcome was the inhospital mortality of the registry patients. The APACHE II score and the predicted mortality were calculated for each patient according to Knaus et al.’s methods [6]. The Chronic Health Points were always scored as five, because of the existing CS with NYHA function class IV. DCW was differentiated into “post cardiac arrest,” “cardiogenic shock,” and “heart valve surgery.”

Furthermore, baseline characteristics and other clinical parameters, which are not included in the APACHE II score, such as pre-existing diseases, cause of CS, status of cardiopulmonary resuscitation (CPR), serum lactate, use of catecholamines, and length of ICU stay were analyzed.

The total study population was divided into different subgroups depending on their sex, status of CPR, age, serum lactate, and pre-existence of coronary artery disease (CAD). Inhospital mortality and predicted mortality were determined separately for each cohort. Finally, CS patients with AMI were separated from the total study population and analyzed similarly. Subgroup analyses which depended on the status of AMI, type of CAD, and culprit lesion were additionally performed.

2.4. Statistical analysis

Cumulative mortality was characterized with the use of Kaplan-Meier plots. Inhospital mortality was conservatively determined by the Kaplan-Meier estimator at survivors’ mean hospital stay lengths (S(thaop)). The log-rank test was performed to compare the inhospital
mortality between the subgroups. A two-tailed $\chi^2$ test was performed to compare the predicted mortality and registry mortality. If the expected frequency was less than six, Fisher’s exact test was used instead of the $\chi^2$ test. A receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was estimated to determine the predictive value of the APACHE II score for inhospital mortality of the total study population as well as the CS patients with AMI. If the difference between the predicted mortality and registry mortality reached significance, we calculated an adjusted DCW by using the survival data from the Dresden Impella Registry in the formula created by Knaus et al. [6]. The total cohort was randomly divided into a derivation group and a validation group of the same sample size. In the derivation group, $\hat{S}(t_{\text{obs}})$ was determined and the adjusted DCW was calculated. Predicted mortality of the validation group was then computed using the newly calculated DCW of the derivation group and compared with $\hat{S}(t_{\text{obs}})$. The validity of the adjusted DCW was tested using two approaches for analyzing goodness-of-fit and effect size. First, predictive performance was assessed by the Hosmer-Lemeshow test, a goodness-of-fit statistic, combined with a bootstrapping method based on 1000 replications. A p-value < 0.05 indicated poor congruence between the observed and predicted deaths within each decile of the cohort’s expected risk of death. Second, differences between $\hat{S}(t_{\text{obs}})$ and the predicted mortality of each patient in the validation group were analyzed using the Wilcoxon test. Finally, an adjusted DCW was calculated for the total registry cohort, including all subgroups. Data were analyzed using SPSS (version 27.0, Statistical Package for the Social Sciences, International Business Machines, Inc., Armonk, New York, USA). The global type I error level was set at 0.05. Metric parameters are reported as means ± the standard error of the mean. Mortality data are given as the Kaplan-Meier estimator ± the standard error. Statistical consultation was given by Institute for Medical Informatics and Biometry (IMB) of Technische Universität Dresden.

3. Results

3.1. Baseline characteristics

Between February 2014 and May 2019, 180 patients received an Impella CP® due to refractory CS in the Dresden Impella Registry. At the time of admission, patients were 66.8 ± 1.0 years old and predominantly male (70.0%). They showed a typical distribution of cardiovascular risk factors found in developed countries. CPR before insertion of the pLVAD was performed in 49.4% of patients ($n = 89$), for a mean duration of 28.3 ± 3.1 min. Cardiac arrest occurred in 29.4% in-hospital ($n = 53$) and in 20.0% out-of-hospital ($n = 36$). In 120 of 180 patients, the CS was caused by myocardial infarction, whereas decompenated cardiomyopathy and decompensated valvular heart disease occurred less frequent. ST-elevation was present in 66.7% of the myocardial infarctions ($n = 80$). The culprit lesion was mostly detected in the left main stem (30.8%, $n = 37$) and left anterior descending artery (40.0%, $n = 48$). Revascularization was performed by PCI in 95.0% of cases ($n = 114$) and coronary artery bypass graft was performed in 1.7% ($n = 2$). In 3.3% of cases, the PCI failed (n = 4). The maximum level of creatine kinase was 83.1 ± 12.4 μkat/l (Tables 1 and 2 in Data in Brief [45]).

3.2. Calculation of APACHE II score

According to Knaus et al. [6], the worst values of the 12 physiologic variables comprising the APACHE II score in the first 24 h were ascertainment and categorized for each patient; these are shown in Table 1. The Glasgow Coma Scale, partial pressure of oxygen, pH value, and mean arterial pressure showed the highest point score values. The sum of the means of all physiologic parameters, the APS, was 24.2 ± 0.6 ($n = 180$). The Age Points, calculated as described by Knaus et al. [61], had a score of 4.3 ± 0.1 ($n = 180$). The APACHE II score was obtained by adding the APS, Age Points, and Chronic Health Points. Finally, the APACHE II score of the Dresden Impella Registry averaged 33.5 ± 0.6 ($n = 180$).

3.3. Comparison of predicted and observed mortality

The predicted mortality calculated by the APACHE II score was overestimated compared to the observed mortality of CS patients by the Dresden Impella Registry (APACHE II 74.6 ± 1.6% vs. registry 54.4 ± 3.7%; $n = 180$; $p < 0.001$). A conservative model was used for comparison, which determined the registry’s calculated mortality at survivors’ mean hospital stay using the Kaplan-Meier estimator (Fig. 1A). Kaplan-Meier curves had no censoring in the first 30 days. Patients with CS-complicating AMI showed a mortality of 54.2 ± 4.5% ($n = 120$) at survivors’ mean length of hospital stay (22.3 ± 1.9 d, $n = 47$). The predicted mortality was significantly higher (76.3 ± 1.9%; $n = 120$; $p < 0.001$; Fig. 1B). The APACHE II score overestimated mortality in nearly all subgroups, except in patients who were younger than 50 years, and in patients with an initial serum lactate level between 5 and 10 mmol/l. Among patients with CS caused by myocardial infarction, similar results were obtained, as displayed in Table 2. The difference between the observed and predicted mortality was especially high in patients who had received CPR and patients with a serum lactate level between 4.0 and 4.9 mmol/l.

The ROC AUC of APACHE II score showed a valid prediction of inhospital mortality, measuring 0.70 (95% CI 0.62–0.78; $p < 0.001$) in the total cohort and 0.70 (95% CI 0.60–0.80; $p < 0.001$) in the subgroup of patients with AMI (Fig. 2A).

The observed mortality was significantly higher in patients who received CPR before implantation of the pLVAD compared to patients who did not receive CPR (CPR 62.9 ± 5.1%; $n = 89$ vs. No CPR 46.2% ± 5.2%; $n = 91$; $p = 0.004$; Fig. 1C). Furthermore, an increased initial serum lactate was associated with elevated mortality (4–4.9 mmol/l: 30.0 ± 5.9%; $n = 60$; 5–10 mmol/l: 60.5 ± 7.5%; $n = 43$; vs. > 10 mmol/l: 70.6 ± 5.5%; $n = 68$; $p < 0.001$; Fig. 1D). Similar results were observed in the myocardial infarction subgroup.

3.4. Adjustment of diagnostic category weight

The adjusted DCW was calculated in the randomly formed derivation group by inserting the determined APACHE II score (33.7 ± 0.8; $n = 90$) and the observed mortality at survivors’ mean hospital stay (57.8 ± 5.2%; $n = 90$) into the formula by Knaus et al. (Formula II & III) [6]. The adjusted DCW was determined to be −1.089 ($n = 90$) for the total derivation cohort. The predicted mortality in the randomly assigned validation group, which was calculated using the adjusted DCW, was 55.8 ± 2.4% ($n = 90$). The observed mortality at survivors’ mean hospital stay was 51.1 ± 5.3% ($n = 90$) in this group (Table 3). The differences between $\hat{S}(t_{\text{obs}})$ and the predicted mortality calculated by the conventional DCW and the adjusted DCW for each patient were used for the validation. Thereby, the adjusted DCW showed a more accurate prediction of inhospital mortality as compared to the conventional DCW ($Δ = −4.7 ± 2.4%$ vs. $Δ = −23.2 ± 2.3%$; $p < 0.001$; Fig. 2B). Furthermore, the Hosmer-Lemeshow statistic indicated an improved goodness-of-fit for adjusted DCW (7.579; $p = 0.371$ vs. 10.64; $p = 0.155$).

Finally, the DCW was recalculated in all subgroups showing significant differences between the observed and predicted mortality. The adjusted DCW of the total cohort was −1.183, which is concomitant with a 59.8% reduced predicted mortality compared to the original DCW for CS. A marked difference showed the estimated DCW in patients who received CPR compared to the original DCW for post-cardiac arrest. In this subgroup, the newly calculated DCW decreased the inhospital mortality predicted by the APACHE II score by 81.4%. The adjusted DCW values of all subgroups are given in Table 2.
Table 2
Comparison of observed and predicted mortality. Predicted mortality estimated by the APACHE II score was overestimated compared to the observed mortality determined by the Kaplan-Meier estimator at survivors’ mean hospital stay. Results are given for the total cohort as well as for patients with CS-complicating acute myocardial infarction. Furthermore, subgroup analyses for both cohorts are displayed. An adjusted Diagnostic Category Weight was calculated by using survival data from the Dresden Impella Registry and the formula created by Knaus et al. [6] if the difference between the observed and predicted mortality achieved significance.

| Parameter | Sub-category | APACHE II score mean + SEM; (n) | Survivors’ length of hospital stay (th hosp) / d mean + SEM; (n) | Mortality at survivors’ mean hospital stay /% $\hat{S}(\text{thosp}) \pm \text{SE}(\text{thosp}); (n)$ | Predicted Mortality by APACHE II score /% mean + SEM; (n) | p-Wert Adjusted Diagnostic Category Weight |
|-----------|-------------|---------------------------------|---------------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|---------------------------------------------|
| All patients | All patients | 33.5 ± 0.6; (180) | 22.9 ± 1.6; (71) | 54.4 ± 3.7; (180) | 74.6 ± 1.6; (180) | <0.001 | -1.183 |
| | CPR | No CPR | 30.2 ± 0.8; (91) | 23.7 ± 2.0; (44) | 46.2 ± 5.2; (91) | 61.9 ± 2.3; (91) | 0.037 | -1.044 |
| | CPR | 36.8 ± 0.7; (89) | 21.6 ± 2.6; (27) | 62.9 ± 5.1; (89) | 87.5 ± 1.3; (89) | <0.001 | -1.328 |
| | Serum lactate | 4–4.9 mmol/l | 29.2 ± 1.0; (60) | 21.8 ± 2.2; (38) | 30.0 ± 5.9; (60) | 61.5 ± 3.0; (60) | <0.001 | -1.593 |
| | | 5–10 mmol/l | 33.6 ± 1.1; (43) | 22.3 ± 3.6; (14) | 60.5 ± 7.5; (43) | 75.8 ± 3.2; (43) | 0.104 | -0.962 |
| | | >10 mmol/l | 37.3 ± 0.7; (68) | 27.3 ± 2.4; (16) | 70.6 ± 5.5; (68) | 85.8 ± 1.7; (68) | 0.039 | -1.053 |
| Only acute myocardial infarction patients (n = 120) | All patients | 33.9 ± 0.7; (120) | 22.3 ± 1.9; (47) | 54.2 ± 4.5; (120) | 76.3 ± 1.9; (120) | <0.001 | -1.264 |
| | CPR | No CPR | 30.4 ± 1.0; (53) | 22.5 ± 2.4; (26) | 45.3 ± 6.8; (53) | 62.8 ± 2.9; (53) | 0.080 | 1 |
| | CPR | 36.6 ± 0.8; (67) | 22.1 ± 3.0; (21) | 61.2 ± 6.0; (67) | 86.9 ± 1.7; (67) | <0.001 | -1.371 |
| | Serum lactate | 4–4.9 mmol/l | 29.5 ± 1.2; (37) | 19.7 ± 2.6; (23) | 29.7 ± 7.5; (37) | 62.7 ± 3.7; (37) | 0.005 | -1.652 |
| | | 5–10 mmol/l | 33.6 ± 1.4; (28) | 22.2 ± 4.2; (11) | 53.6 ± 9.4; (28) | 76.9 ± 4.0; (28) | 0.048 | -1.244 |
| | | >10 mmol/l | 37.4 ± 0.8; (49) | 27.9 ± 3.3; (11) | 71.4 ± 6.5; (49) | 86.6 ± 1.9; (49) | 0.085 | -1.029 |
3.5. Clinical parameters not included in the APACHE II score

The highest serum lactate level in the first 24 h was 9.1 ± 0.4 mM in the CS cohort of the Dresden Impella Registry (n = 180). Norepinephrine was required in 91.8% of patients for vasopressor support (n = 156). The highest norepinephrine dosage in the first 24 h averaged between all patients was 0.83 ± 0.08 µg/kg/min (n = 151). Dobutamine was used in 51.1% of patients; 7.8 ± 0.6 µg/kg/min was the highest dosage in the first 24 h (n = 92). The left ventricular ejection fraction measured 26.2 ± 1.1% before implantation of the pLVAD (n = 146), and LV assistance was performed for 53.5 ± 5.3 h in average (n = 179). A total of 85.4% of the cases were on mechanical ventilation with a mean duration of 194.1 ± 22.1 h (n = 140). Patients who survived and were discharged had a mean ICU stay length of 19.2 ± 1.6 d (n = 71; Table 3 in Data in Brief [45]). A ROC analysis was performed to test accuracy of serum lactate to predict intrahospital mortality at different times (0, 2, 4, 8, 12 and 24 h after insertion of pLVAD). The ROC AUC of serum lactate was always below the ROC AUC of the APACHE II score. Significance level was only reached 24 h after insertion of percutaneous left ventricular assist device (AUC 0.650; 95% CI 0.512–0.787; p = 0.040).

Fig. 1. Comparison of observed and predicted mortality. Observed outcomes are illustrated by 30-day Kaplan-Meier curves. The solid line indicates the predicted outcome calculated by the APACHE II score. The dashed line shows survivors’ mean length of hospital stay. The APACHE II score overestimates mortality compared to observed mortality in CS patients of the Dresden Impella Registry. (A) Results of the total cohort [n = 180]. (B) Results of patients with CS-complicating acute myocardial infarction [n = 120]. (C) Significantly higher mortality observed in CS patients who received CPR before pLVAD implantation (green [n = 89]) compared to patients that did not (blue [n = 91]). Observed mortality was overestimated in both groups. (D) 30-day Kaplan-Meier curves of patients with initial serum lactate of 4.0–4.9 mmol/l (blue [n = 60]), 5.0–10.0 mmol/l (green [n = 43]), and > 10 mmol/l (ocher [n = 68]). Increased initial serum lactate was associated with higher mortality. APACHE, Acute Physiology and Chronic Health Evaluation; CS, cardiogenic shock; CPR, cardiopulmonary resuscitation; pLVAD, percutaneous left ventricular assist devices. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
In this study, the prognostic value of the APACHE II score was evaluated in a large real-world registry including CS patients who received LV unloading with a micro-axial heart pump. There were three main conclusions. First, the predicted mortality calculated by the APACHE II score is overestimated in modern guideline-based treated CS patients with micro-axial heart pump. Nevertheless, the APACHE II score has an acceptable accuracy for prediction of inhospital mortality, which can be more precisely estimated by using an adjusted DCW (DCW in total cohort: \(-1.183\)). To our knowledge, this is the first study that adjusted DCW to reflect recent treatment of CS since the implementation of the APACHE II score three decades ago.

We assumed that the observed differences between predicted and observed mortality were caused by innovations in treatment. The mortality of CS, especially in patients with AMI, has declined in the last 20 years [29]. PCI, which is now widely used, is certainly the most responsible innovation for improved outcomes in patients with CS-complicating AMI [9,30]. However, the difference between predicted mortality and observed mortality was consistent in all CS cohorts, including patients without AMI. Changes in intensive care medicine might have contributed to this effect. Medical treatment is more differentiated due to a broader spectrum of inotropic drugs as well as growing evidence of its use [12,31,32]. Furthermore, mechanical circulatory support (MCS) devices have shown rapid development in the last two decades, with the aim of improving the hemodynamic situation in CS, such as maintaining perfusion pressure or reducing the requirement for catecholamines [33]. One of the most used MCS devices, the intra-aortic balloon pump (IABP), showed no beneficial effect on the outcomes of patients with CS-complicating AMI in the IABP-Shock II trial nor in its 6-year follow-up [14,34]. Due to these results, the clinical use of IABP declined, whereas other MCS devices, such as the currently used Impella CP®, received a broad clinical implementation [35]. Until now, micro-axial heart pumps cannot show improved outcome in patients with CS. However, the data have several limitations [20,36]. Finally, the DANGER trial (NCT01633502) will hopefully be able to clarify the effect of the micro-axial heart pump on outcome in patients with CS-complicating AMI [37]. Refractory CS often causes multiorgan dysfunction syndrome due to peripheral hypoperfusion with microcirculatory dysfunction, which can be aggravated by systemic inflammatory response syndrome [33]. Developments in renal replacement therapy or lung-protective ventilation might also be responsible for the differences between predicted and observed mortality [38,39].

However, mortality of our cohort was high compared to other studies (30-day mortality [interventional arm]: SHOCK trial 46.7%; IABP-Shock II trial 39.7%) [9,40]. This might be explained by the more severe disease burden of Dresden Impella Registry patients with higher initial serum lactate and more frequent CPR with longer durations.

The APACHE II score is based on parameters that predict the inhospital mortality of patients with CS, as proven by ROC analysis. Other studies showed similar results, but the predictive value of the APACHE II score decreased over the years [41,42]. The measured AUC in the ROC analysis was comparable to other scoring systems of CS (Sepsis-related Organ Failure Assessment [SOFA] score 0.64 [95% CI 0.55–0.73], or Simplified Acute Physiology Score [SAPS] II score 0.67

### Table 3

**Derivation and validation of the adjusted Diagnostic Category Weight.** The total study cohort was randomly divided into a derivation group and a validation group with identical sample sizes. The first one was used to calculate the adjusted Diagnostic Category Weight and the second one was used for its validation using two different approaches. APACHE, Acute Physiology and Chronic Health Evaluation.

| Parameter          | Apache II score mean + SEM; (n) | Survivors’ length of hospital stay \[t_{\text{hosp}}/d\] mean + SEM; (n) | Mortality at survivors’ mean hospital stay / % \[S_{\text{hosp}}\pm SE_{\text{hosp}}\]; (n) | Predicted Mortality by Apache II score / % mean + SEM; (n) | Adjusted Diagnostic Category Weight |
|--------------------|---------------------------------|--------------------------------------------------|--------------------------------------------|------------------------------------------------|----------------------------------|
| Derivation         | 33.7 ± 0.8; (90)                | 22.6 ± 2.6; (34)                                   | 57.8 ± 5.2; (90)                          | 74.8 ± 2.3; (90)                                   | −1.089                           |
| Validation         | 33.3 ± 0.8; (90)                | 23.2 ± 2.2; (37)                                   | 51.1 ± 5.3; (90)                          | 55.8 ± 2.4; (90)                                   |                                   |

### 4. Discussion

Fig. 2. (A) Receiver operating characteristic curves of the APACHE II score predicting for inhospital death illustrated for the total cohort (black) and patients with cardiogenic shock-complicating acute myocardial infarction (blue). The area under the curve with the corresponding 95% confidence interval is given at the bottom of the diagram. APACHE, Acute Physiology and Chronic Health Evaluation. (B) Difference between the Kaplan-Meier estimator at survivors’ mean hospital stay \(\hat{S}(t_{\text{hosp}})\) and the predicted mortality estimated by the APACHE II score using the conventional DCW and the adjusted DCW in the validation group. The adjusted DCW leads to a more precise prediction of inhospital mortality. APACHE, Acute Physiology and Chronic Health Evaluation; DCW, Diagnostic Category Weight. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
5. Limitations

Our study had several limitations. First, the Dresden Impella Registry is a prospective single-center registry, which consecutively enrolled patients with CS who received a micro-axial heart pump. The study was not randomized and was guided by local experience. The adjusted DCW showed a more precise estimation of mortality in a randomly assigned validation group. A more accurate prediction of patient prognosis might be of substantial value for attending physicians in the ICU, but before this, external validation is needed.

6. Conclusions

The APACHE II score has an acceptable accuracy for predicting the outcomes of CS patients receiving LV unloading with a micro-axial heart pump but overestimates the total amount of inhospital mortality. An adjustment of the DCW with a value of about –1.2 could lead to a more precise prognosis being calculated by the APACHE II score.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: FW reports personal fees from Abiomed, Abbott, Biotronik, Boston Scientific, Corvia, MSD, NeoVasc, outside the submitted work. NM reports personal fees from Abiomed, Edwards LifeScience, Medtronic, Biotronik, Novartis, Sanofi Genzyme, Bayer, Pfizer, and AstraZeneca, outside the submitted work. AL reports grants from Novartis, personal fees from Medtronic, Abbott, Edwards Lifesciences, Boston Scientific, Astra Zeneca, Novartis, Pfizer, Abiomed, Bayer, Boehringer, and other from Picardia, Transverse Medical, Claret Medical, outside the submitted work. The other authors have disclosed that they do not have any potential conflicts of interest.

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