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## Special Issue

Clinical Management of Cardiogenic Shock and Cardiac Arrest

Edited by

Dr. Jaime A. Hernández-Montfort





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**Citation:** Peters, E.J.; ten Berg, S.; Bogerd, M.; Timmermans, M.J.C.; Kraaijeveld, A.O.; Bunge, J.J.H.; Teeuwen, K.; Lipsic, E.; Sjauw, K.D.; van Geuns, R.-J.M.; et al. Characteristics, Treatment Strategies and Outcome in Cardiogenic Shock Complicating Acute Myocardial Infarction: A Contemporary Dutch Cohort. *J. Clin. Med.* **2023**, *12*, 5221. <https://doi.org/10.3390/jcm12165221>

Academic Editor: Jaime A. Hernández-Montfort

Received: 30 June 2023

Revised: 3 August 2023

Accepted: 8 August 2023

Published: 10 August 2023



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**Abstract:** Cardiogenic shock (CS) complicating acute myocardial infarction (AMI) is associated with high morbidity and mortality. Our study aimed to gain insights into patient characteristics, outcomes and treatment strategies in CS patients. Patients with CS who underwent percutaneous coronary intervention (PCI) between 2017 and 2021 were identified in a nationwide registry. Data on medical history, laboratory values, angiographic features and outcomes were retrospectively assessed. A total of 2328 patients with a mean age of 66 years and of whom 73% were male, were included. Mortality at 30 days was 39% for the entire cohort. Non-survivors presented with a lower mean blood pressure and increased heart rate, blood lactate and blood glucose levels ( $p$ -value for all  $<0.001$ ). Also, an increased prevalence of diabetes, multivessel coronary artery disease and a prior coronary event were found. Of all patients, 24% received mechanical circulatory support, of which the majority was via intra-aortic balloon pumps (IABPs). Furthermore, 79% of patients were treated with at least one vasoactive agent, and multivessel PCI was performed in 28%. In conclusion, a large set of hemodynamic, biochemical and patient-related characteristics was identified to be associated with mortality. Interestingly, multivessel PCI and IABPs were frequently applied despite a lack of evidence.

**Keywords:** cardiogenic shock; acute myocardial infarction; percutaneous coronary intervention; mortality; evidence-based therapy

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## 1. Introduction

Cardiogenic shock (CS) is a clinical syndrome characterized by hypotension and end-organ hypoperfusion. Even though CS complicates only 3–13% of acute myocardial infarctions (AMI), it is the leading cause of death for patients with an acute coronary syndrome [1–3]. While overall 30-day mortality in AMI is around 6% in EU countries, mortality rates for AMI complicated by CS (AMICS) are as high as 40–50% [4–7].

In order to improve outcomes for AMICS patients, it is important to gain accurate insight into in-depth patient characteristics, current clinical management strategies and outcomes in this specific population. Data regarding these features are limited and often based on clinical trial data or diagnosis codes. In addition, only a few databases have been designed for CS to capture more in-depth variables.

The primary aim of this study was to gain insights into contemporary trends in patient characteristics, current treatment strategies and outcome for AMICS patients undergoing PCI in the Netherlands. Additional aims were to investigate differences in outcome in predefined subgroups and to explore whether the current clinical practice is consistent with available treatment guidelines.

## 2. Materials and Methods

### 2.1. Patient Selection

Baseline, procedural and outcome data from all patients undergoing PCI in the Netherlands are prospectively registered with the Netherlands Heart Registration (NHR; [www.nhr.nl](http://www.nhr.nl)) [8]. Relevant variables and their definitions as collected in the NHR are shown in Appendix A, Table A1. All patients with CS undergoing PCI for AMI between January 2017 and September 2021 were subsequently identified in the NHR database. Cardiogenic shock was defined as the presence of hypotension (systolic blood pressure  $\leq 90$  mmHg for at least 30 min or the need for supportive measures to maintain systolic blood pressure  $\geq 90$  mmHg) with signs of hypoperfusion of end-organs (cold extremities and/or oliguria  $< 30$  mL/h and/or heart rate  $\geq 60$  beats per minute). An additional set of variables was established to be collected in patients with CS. This additional data collection was executed in 14 of 30 PCI centers in the Netherlands. See Appendix B, Table A2 for the participating hospitals.

### 2.2. Variable Selection

A draft version of the set of additional variables to be collected in patients with CS was established in consultation with interventional cardiologists and intensivists from participating hospitals. After pilot testing of this draft version, the updated version was discussed in a multidisciplinary team. A few adjustments were made prior to finalizing the selection and its corresponding data dictionary. More details of the process and the final set of variables can be found in Appendix C, Figure A1.

### 2.3. Data Collection

Clinical data for all patients were retrieved from the electronic health records. Survival status was retrieved from the governmental Personal Records Database (in Dutch: *Basisregistratie Personen*) in all hospitals with a follow-up period of at least one year. Data collection was performed by trained data managers and medical doctors with supervision by an interventional cardiologist or a cardiac intensivist. To ensure quality, several automated quality controls were carried out after data submission according to the quality control system of the NHR as described elsewhere [9]. The data were pseudonymized and locked after preliminary findings were submitted to the respective hospital with the opportunity for reviewing and complementing.

### 2.4. Statistical Analysis

Statistical analysis was performed using IBM SPSS 28.0 (IBM, SPSS, Inc., Chicago, IL, USA). Normally distributed data were displayed as mean ± standard deviation (SD) and compared in survivors and non-survivors using the unpaired *t*-test. Non-normally distributed data were described as median with interquartile range (IQR) and compared with the Mann–Whitney U test. Categorical data were displayed as frequencies and percentages and compared using the chi-square test. Temporal trends were analyzed using the Mann–Kendall test. Survival curves were constructed using the Kaplan–Meier method, and comparisons between subgroups were made with the log-rank statistic. Subgroup analyses were performed for sex (male/female), out-of-hospital cardiac arrest (OHCA) (yes/no), indication of PCI (ST-elevation myocardial infarction [STEMI]/non-ST-elevation myocardial infarction [NSTEMI]) and multivessel PCI within multivessel disease (yes/no). A *p*-value < 0.05 was considered statistically significant for all analyses. Missing data were not imputed for the current analyses. Denominators were notated for categorical variables with missing data.

## 3. Results

### 3.1. Patient Characteristics

From January 2017 to September 2021, a total of 2328 patients with AMI complicated by CS and treated with PCI were identified. This was 2.4% of the total PCI population in the selected hospitals (*n* = 98,721). The mean age was 66.4 (±12.3) years, and 72.9% of patients (*n* = 1685) were male. In this cohort, the prevalence of diabetes was 20.8% (*n* = 459), mostly treated with medication only. A total of 631 patients (29.3%) experienced a prior coronary event, most commonly a prior myocardial infarction (*n* = 482, 21.4%). Patients with CS more often presented with STEMI than with NSTEMI (86.1% vs. 13.9%, *p* < 0.001), and for most patients (*n* = 1166, 58.6%), the onset of symptoms was less than 3 hours before presentation. Of all patients, 934 (40.3%) presented after an OHCA. Details on patient characteristics are displayed in Table 1. Percentages missing can be found in Tables A1 and A3 in Appendices A and D for each variable.

**Table 1.** Patient characteristics for all patients, survivors at 30 days and non-survivors at 30 days.

|                                | All Patients<br>( <i>n</i> = 2328) | Alive at 30 Days<br>( <i>n</i> = 1414) | Dead at 30 Days<br>( <i>n</i> = 901) | <i>p</i> -Value |
|--------------------------------|------------------------------------|--|--------------------------------------|-----------------|
| Patient characteristics        |                                    |  |                                      |                 |
| Male                           | 1696 (72.9)                        | 1036 (73.3)                            | 649 (72.0)                           | 0.515           |
| Age—years                      | 66.4 (±12.3)                       | 64.8 (±12.1)                           | 69.0 (±12.1)                         | <0.001          |
| BMI—kg/cm <sup>2</sup>         | 26.1 (23.9–29.1)                   | 25.9 (23.7–28.8)                       | 26.2 (24.2–29.4)                     | 0.024           |
| Indication of PCI              |                                    |  |                                      | 0.005           |
| STEMI                          | 1941/2254 (86.1)                   | 1193/1359 (87.8)                       | 737/882 (83.6)                       |                 |
| NSTEMI                         | 313/2254 (13.9)                    | 166/1359 (12.2)                        | 145/882 (16.4)                       |                 |
| Out-of-hospital cardiac arrest | 934/2317 (40.3)                    | 497/1405 (35.4)                        | 432/899 (48.1)                       | <0.001          |
| In-hospital cardiac arrest     | 295 /2308 (12.8)                   | 130/1401 (9.3)                         | 165/894 (18.5)                       | <0.001          |
| Onset of AMI symptoms—hours    |                                    |  |                                      | <0.001          |
| <3                             | 1166/1991 (58.6)                   | 745/1233 (60.4)                        | 416/746 (55.8)                       |                 |
| 3–12                           | 375/1991 (18.8)                    | 245/1233 (19.9)                        | 128/746 (17.2)                       |                 |
| 12–24                          | 113/1991 (5.7)                     | 67/1233 (5.4)                          | 44/746 (5.9)                         |                 |
| >24                            | 337/1991 (16.9)                    | 176/1233 (14.3)                        | 158/746 (21.2)                       |                 |
| Intubation pre-PCI             | 1030/2307 (44.6)                   | 500/1404 (35.6)                        | 524/893 (58.7)                       | <0.001          |
| Monitoring via PA catheter     | 118/2119 (5.6)                     | 68/1287 (5.3)                          | 49/832 (5.9)                         | 0.613           |
| Medical history                |                                    |  |                                      |                 |
| Diabetes                       | 463/2219 (20.9)                    | 227/1365 (16.6)                        | 232/841 (27.6)                       | <0.001          |
| Prior coronary event           | 631/2153 (29.3)                    | 361/1310 (27.6)                        | 265/831 (31.9)                       | 0.032           |
| Prior MI                       | 482/2253 (21.4)                    | 276/1374 (20.1)                        | 202/867 (23.3)                       | 0.071           |
| Prior PCI                      | 396/2134 (18.6)                    | 239/1299 (18.4)                        | 153/822 (18.6)                       | 0.901           |
| Prior CABG                     | 139/2286 (6.1)                     | 74/1390 (5.3)                          | 65/833 (7.4)                         | 0.048           |

**Table 1.** Cont.

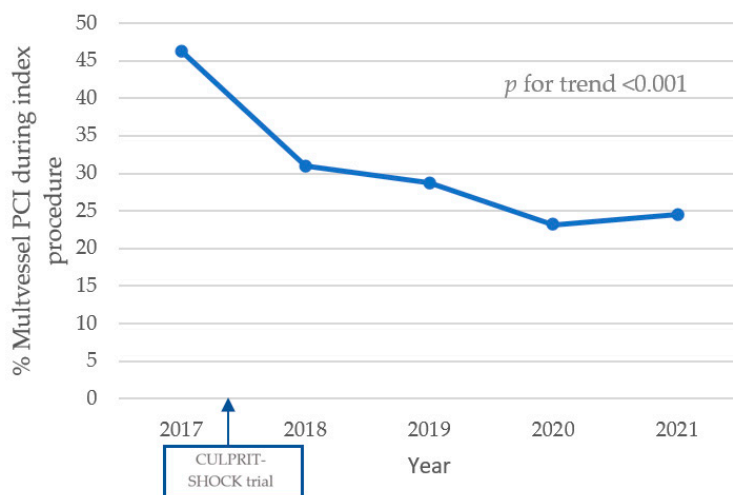
|                                      | All Patients<br>(n = 2328) | Alive at 30 Days<br>(n = 1414) | Dead at 30 Days<br>(n = 901) | p-Value |
|--------------------------------------|----------------------------|--------------------------------|------------------------------|---------|
| Hemodynamics on admission            |                            |                                |                              |         |
| Systolic blood pressure—mmHg         | 100 (80–125)               | 103 (83–127)                   | 95 (80–118)                  | <0.001  |
| Diastolic blood pressure—mmHg        | 61 (50–77)                 | 64 (50–80)                     | 60 (48–75)                   | <0.001  |
| Mean blood pressure—mmHg             | 75 (60–93)                 | 77 (63–95)                     | 72 (58–89)                   | <0.001  |
| Heart rate—bpm                       | 82 (63–101)                | 80 (60–100)                    | 89 (70–108)                  | <0.001  |
| Shock index                          | 0.76 (0.58–1.0)            | 0.72 (0.56–0.95)               | 0.86 (0.64–1.14)             | <0.001  |
| Number of vasoactive agents pre-PCI  |                            |                                |                              | <0.001  |
| None                                 | 1147/2215 (51.8)           | 833/1356 (61.4)                | 309/846 (36.5)               |         |
| 1                                    | 590/2215 (26.6)            | 320/1356 (23.6)                | 267/846 (31.6)               |         |
| 2                                    | 376/2215 (17.0)            | 171/1356 (12.6)                | 201/846 (23.8)               |         |
| ≥3                                   | 102/2215 (4.6)             | 32/1356 (2.3)                  | 69/846 (8.1)                 |         |
| Laboratory values on admission       |                            |                                |                              |         |
| Lactate—mmol/L                       | 5.5 (2.6–9.4)              | 4.2 (2.1–7.2)                  | 7.8 (3.9–11.4)               | <0.001  |
| Creatinine—μmol/L                    | 100 (82–123)               | 94 (78–113)                    | 110 (91–140)                 | <0.001  |
| eGFR—mL/min                          | 61 (48–75)                 | 65 (53–80)                     | 54 (40–67)                   | <0.001  |
| Hemoglobin—mmol/L                    | 8.3 (±1.4)                 | 8.4 (±1.3)                     | 8.1 (±1.5)                   | <0.001  |
| Glucose—mmol/L                       | 12.2 (8.8–17.1)            | 10.8 (8.3–14.9)                | 14.8 (10.4–19.9)             | <0.001  |
| Peak hs-troponin-T—ng/L <sup>a</sup> | 3534 (828–10000)           | 3292 (831–10000)               | 3954 (772–10000)             | 0.095   |
| Peak CK-MB—U/L <sup>a</sup>          | 222 (70–510)               | 203 (67–446)                   | 269 (77–600)                 | 0.013   |
| Angiographic features                |                            |                                |                              |         |
| Multivessel disease                  | 1402/2307 (60.8)           | 791 / 1399 (56.5)              | 603 / 895 (67.4)             | <0.001  |
| Number of treated vessels            |                            |                                |                              | <0.001  |
| 1                                    | 1749/2114 (82.7)           | 1115/1295 (86.1)               | 623/806 (77.3)               |         |
| ≥2                                   | 365/2114 (17.3)            | 180/1295 (13.9)                | 183/806 (22.7)               |         |
| Treated vessel                       |                            |                                |                              |         |
| Left main                            | 292/2114 (13.8)            | 142/1295 (11.0)                | 149/806 (18.5)               | <0.001  |
| Left anterior descending             | 970/2114 (45.9)            | 576/1295 (44.5)                | 388/806 (48.1)               | 0.102   |
| Circumflex artery                    | 479/2114 (22.7)            | 250/1295 (19.3)                | 226/806 (28.0)               | <0.001  |
| Right coronary artery                | 794/2114 (37.6)            | 534/1295 (41.2)                | 254/806 (31.5)               | <0.001  |
| Venous or arterial graft             | 30/2114 (1.4)              | 14/1295 (1.1)                  | 16/806 (2.0)                 | 0.103   |
| TIMI flow before PCI                 |                            |                                |                              | 0.721   |
| 0/1                                  | 1487/1943 (76.5)           | 905/1189 (76.1)                | 575/744 (77.3)               |         |
| 2                                    | 208/1943 (10.7)            | 132/1189 (11.1)                | 74/744 (9.9)                 |         |
| 3                                    | 248/1943 (12.8)            | 152/1189 (12.8)                | 95/744 (12.8)                |         |
| TIMI flow after PCI                  |                            |                                |                              | <0.001  |
| 0/1                                  | 182/1999 (9.1)             | 54/1255 (4.3)                  | 128/735 (17.4)               |         |
| 2                                    | 193/1999 (9.7)             | 111/1255 (8.8)                 | 81/735 (11.0)                |         |
| 3                                    | 1624/1999 (81.3)           | 1090/1255 (86.9)               | 526/735 (71.6)               |         |
| Arterial access                      |                            |                                |                              | <0.001  |
| Radial                               | 1013/2053 (49.3)           | 718/1242 (57.8)                | 288/798 (36.1)               |         |
| Femoral                              | 1032/2053 (50.3)           | 521/1242 (41.9)                | 505/798 (63.3)               |         |
| Other                                | 8/2040 (0.3)               | 3/1242 (0.3)                   | 5/798 (0.7)                  |         |
| Outcome                              |                            |                                |                              |         |
| Length of hospital stay—days         | 5 (1–12)                   | 10 (2–24)                      | 2 (0–6)                      | <0.001  |

Values are n (%) or median (25th to 75th percentile). BMI = body mass index; PCI = percutaneous coronary intervention; (N)STEMI = (non-)ST-elevation myocardial infarction; (A)MI = (acute) myocardial infarction; PA catheter = pulmonary artery catheter; CABG = coronary artery bypass grafting; Shock Index was calculated as heart rate/systolic blood pressure; eGFR = estimated glomerular filtration rate; CK-MB = creatine phosphokinase-MB; Vasoactive agents pre-PCI = number of drugs that were administered before PCI (from noradrenaline, adrenaline, dopamine, dobutamine and enoximone/milrinone); TIMI = thrombolysis in myocardial infarction; Length of hospital stay is in days. <sup>a</sup> Peak values within 3 days after PCI.

### 3.2. Angiographic Features

The most frequently treated vessel was the left anterior descending artery (n = 970, 45.9%), followed by the right coronary artery (n = 794, 37.6%) and the circumflex artery (n = 479, 22.7%). Thrombolysis in myocardial infarction (TIMI)-flow < 3 was present in 87.2% (n = 1695) of patients before PCI and in 18.8% (n = 375) of patients after PCI. Of all patients with multivessel disease, multivessel PCI was performed in 28% (n = 359). A decreasing trend over the years was observed in multivessel PCIs performed in patients

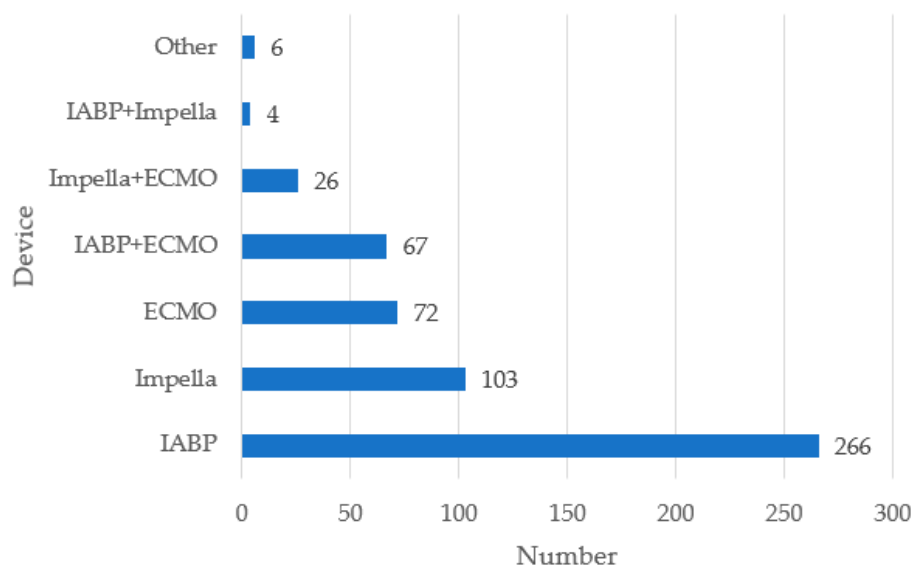
with multivessel disease (See Figure 1). Vascular access was achieved through the radial artery in 49.3% and the femoral artery in 50.2% of patients. A temporal trend toward less femoral access was seen over the years (60.7%, 55.6%, 52.6%, 47.8% and 48.5% from 2017 to 2021;  $p$ -value for trend = 0.019). Overall, unadjusted mortality was significantly higher in the femoral access group (63.3% vs. 36.1%,  $p < 0.001$ ).



**Figure 1.** Percentage of multivessel PCIs during index procedure within patients with multivessel disease.

### 3.3. Mechanical and Pharmacological Support

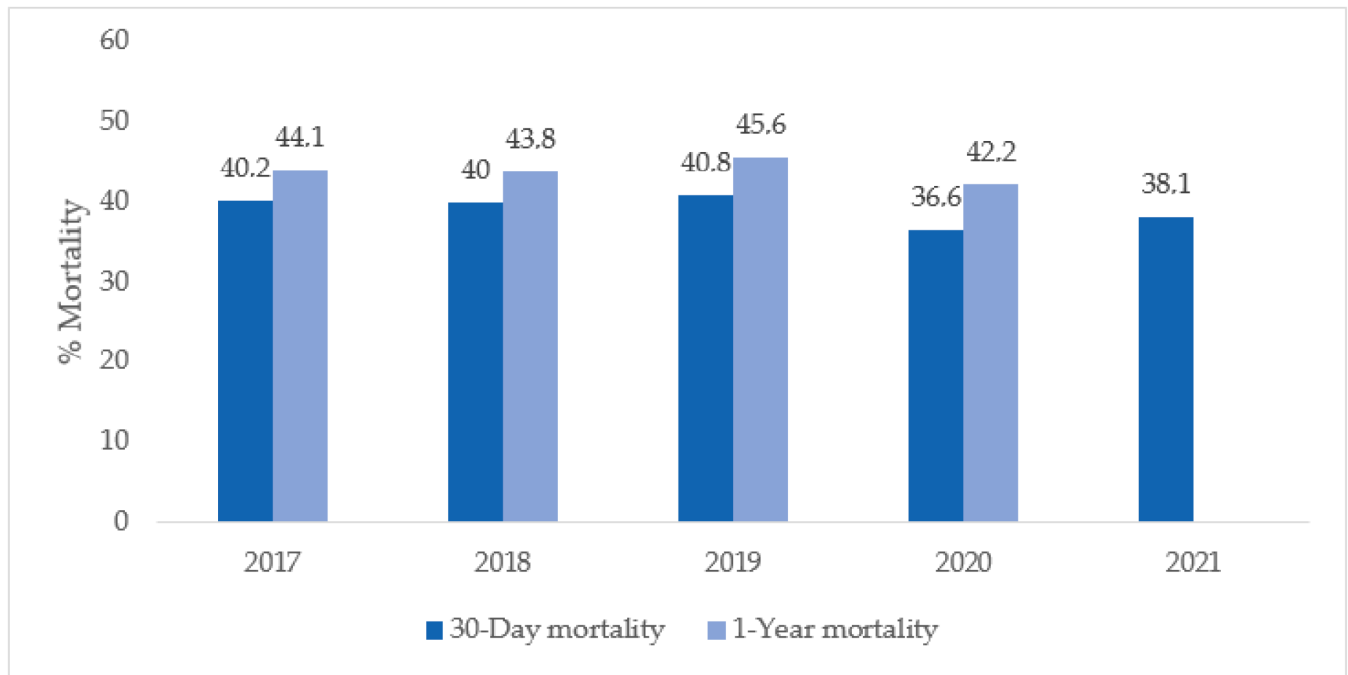
The majority of patients (79.1%,  $n = 1842$ ) received at least one inotropic/vasopressor drug during admission. A total of 710 patients (32.4%) were treated with two vasoactive agents, and  $\geq 3$  agents were administered to 494 patients (22.5%). Norepinephrine was the drug most frequently used (70.9%,  $n = 1613$ ) either in combination or not with other drugs, followed by dobutamine (30.9%,  $n = 699$ ) and enoximone/milrinone (20.2%,  $n = 458$ ). Mechanical circulatory support was initiated in 544 patients (23.6%). As demonstrated in Figure 2, this amount was mainly driven by intra-aortic balloon pumps (IABPs).



**Figure 2.** Use of mechanical circulatory support.

### 3.4. Survival

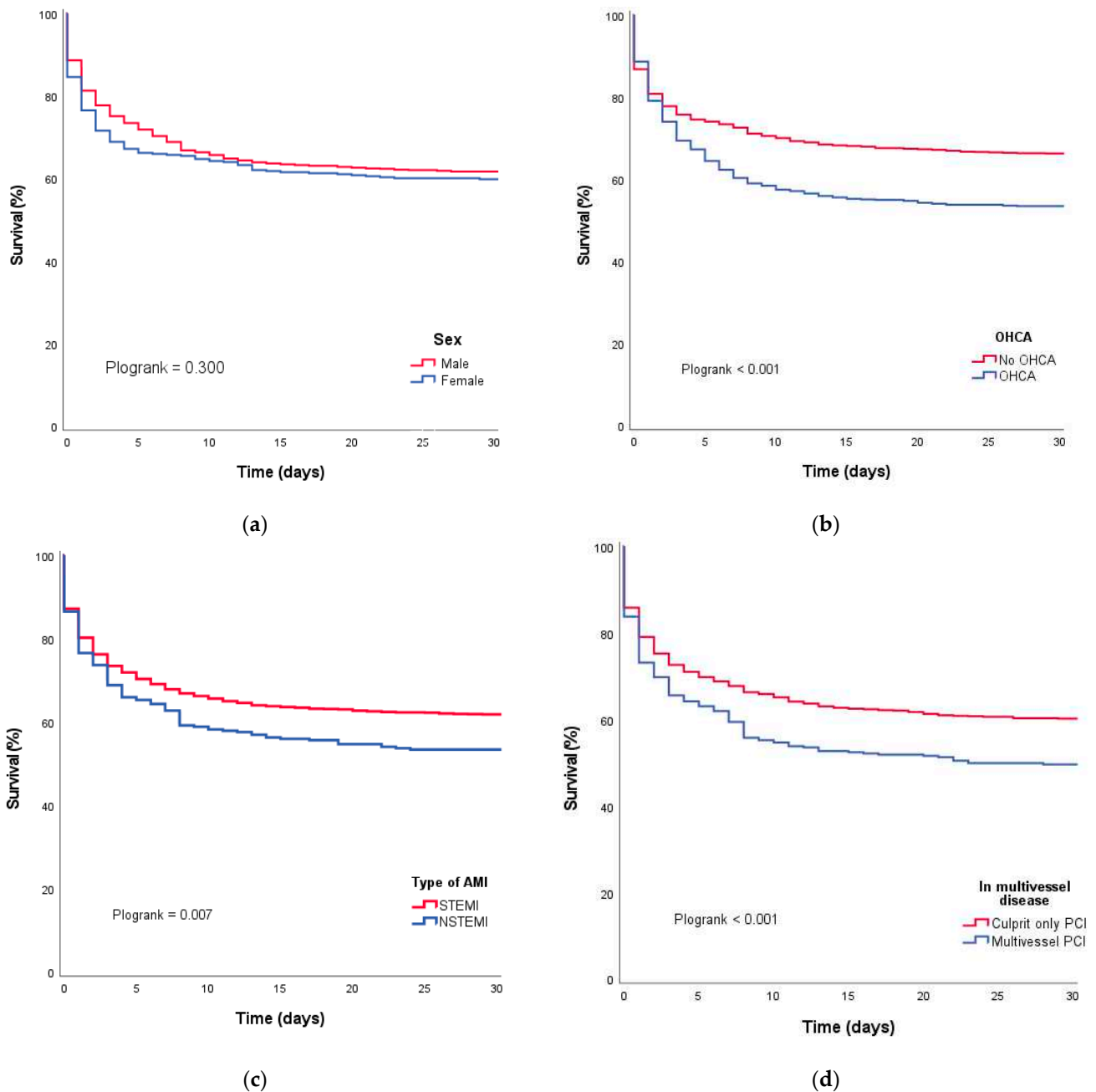
The overall 30-day mortality was 38.7% ( $n = 901$ ), and this percentage was stable over the observation period of four years (details are shown in Figure 3). Survival curves for subgroups are shown in Figure 4. The survival rate was higher in patients presenting with STEMI in comparison to NSTEMI (61.8% vs. 53.4%,  $p = 0.005$ ). On average, those presenting with STEMI were younger (67 vs. 69 years,  $p < 0.001$ ) and had lower rates of diabetes (19.1% vs. 31.2%,  $p < 0.001$ ) and prior coronary events (24.2% vs. 51.5%,  $p < 0.001$ ) than those presenting with NSTEMI. In addition to that, the left ventricular ejection fraction at baseline was lower in NSTEMI patients (35% vs 40%,  $p = 0.009$ ), who also presented with multivessel disease more often (76.5% vs. 57.9%,  $p < 0.001$ ). A higher mortality rate was also seen in patients presenting after an OHCA compared to patients who did not experience an OHCA (48.1% vs. 35.4%,  $p < 0.001$ ). The increase in mortality was even higher for cardiac arrests occurring in-hospital (18.5% vs. 9.3%,  $p < 0.001$ ). Mortality at 30 days was higher when revascularization was unsuccessful (TIMI-flow 0 or 1 post-PCI). In patients with multivessel disease, undergoing multivessel PCI was associated with increased mortality. The overall mortality rate at one year was 44.0% (732/1665) with rates ranging from 42.2% to 45.6% for the individual years of index procedures.



|   |         |         |         |         |                 |
|---|---------|---------|---------|---------|-----------------|
| ■ | 143/356 | 161/403 | 197/483 | 217/593 | 183/480         |
| ■ | 157/356 | 176/403 | 219/480 | 180/427 | NA <sup>a</sup> |
|   | 2017    | 2018    | 2019    | 2020    | 2021            |

<sup>a</sup> 1-Year follow-up was not completed at the time of submission.

**Figure 3.** Yearly trend in 30-day and 1-year mortality.



**Figure 4.** Survival curves for (a) males and females; (b) OHCA yes or no; (c) STEMI and NSTEMI; (d) multivessel and single-vessel PCI.

#### 4. Discussion

We described a real-time reflection of patients with CS who underwent percutaneous revascularization in the Netherlands with national registry data. A total of 2328 shock patients were identified with a mean age of 66.4 years and of whom 72.9% were male. An overall 30-day mortality rate of 38.7% was found. Mortality was higher in patients presenting with NSTEMI compared to patients with STEMI. Higher mortality rates were also seen in patients presenting after an OHCA and in patients who underwent multivessel PCI. Mortality was similar for male and female patients.



A substantial proportion of the observed results paralleled those reported in previous studies, such as the mean age of almost 70 years and the fact that only a small proportion of patients were female. Mean age and gender distribution were as expected based on the existing literature [10,11]. Also, the more generally available baseline values for blood pressure and heart rate were very similar to those found in other CS populations, as well as admission levels of lactate and blood glucose [12,13]. Blood levels of glucose, lactate and hemoglobin have been adopted into several risk-scoring systems for mortality in cardiogenic shock [14,15]. We also found that higher admission levels of glucose and lactate and lower admission levels of hemoglobin were associated with higher mortality. As infarct size is directly correlated to LV function and mortality, it was not surprising to find higher levels of high-sensitive troponin-T and creatine kinase-MB in non-survivors.

Some remarkable findings were also observed. The reported mortality rate was relatively low compared to general AMICS cohorts that reported mortality rates around 50% [4]. This could partly be attributable to the fact that in this NHR CS cohort, per the definition, all patients underwent PCI, whereas in other cohorts, revascularization rates of around 90% were described [2,4,16]. In addition to revascularization being the only proven effective therapy for AMICS, this could also have led to a more favorable selection of patients who reached the hospital and were in sufficient condition to undergo revascularization [17].

Another interesting observation was that mortality was higher in patients presenting with NSTEMI than in patients presenting with STEMI. Previous research on this topic is inconclusive, and survival benefit has been described for both NSTEMI and STEMI etiology of shock [2,4,18]. In this Dutch cohort, demographic features differed between these groups. In general, NSTEMI patients had more severe clinical risk factors, as they were older and had more comorbidities and worse cardiac function at baseline, which could explain the higher mortality rate [19,20]. In our study, we also found that the mortality rate in patients presenting after an OHCA was higher than for non-OHCA patients, which is in line with findings by Ostensfeld et al. but in contrast with other results from Denmark [4,13]. This could again be due to lower revascularization rates in the two latter Danish cohorts than in the current Dutch cohort. As described in the results, in-hospital cardiac arrests (IHCAs) affected mortality more than OHCA. This phenomenon is not uncommon, and we hypothesized that a higher rate of comorbidities in IHCA patients causes this difference, as this has been described previously [21].

Even though the evidence with regard to therapeutic strategies is limited, a few statements have been adopted into the guidelines for the treatment of AMICS. In 2017, multivessel PCI for the index procedure was shown to be associated with a worse outcome than single-vessel PCI in patients with multivessel disease [12]. Although the recommendations from the CULPRIT-SHOCK trial were not clearly seen in the first years after publication, it is evident that in the subsequent years, multivessel PCI during the index procedure was performed less and less in patients with multivessel disease. This could be interpreted as a real-world implementation of new evidence in routine clinical practice. The authors hypothesized that despite the results of the CULPRIT-SHOCK trial, physicians may still feel the need to perform immediate multivessel PCI in case of a lack of hemodynamic improvement after initial treatment of the culprit lesion.

In the current cohort, the most frequently used vasoactive agent was norepinephrine, which was administered to 71% of patients. This strategy was consistent with both the American and the European recommendation on medical therapy in CS, as norepinephrine is suggested as the first-choice vasopressor [19,20].

Finally, the role of mechanical circulatory support (MCS) in the treatment of AMICS patients remains unclear. Even though a survival benefit for patients treated with MCS has yet to be established, almost one quarter of patients in this cohort were supported with at least one MCS device. After the results of the IABP-SHOCK II trial were published in 2012, the routine use of IABP was no longer recommended by the guidelines [22]. Despite these results, 14.6% ( $n = 337$ ) of patients were treated with an IABP either in combination

or not with another device. Randomized evidence from large trials concerning Impella or veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is not readily available, as trials are still recruiting. Treating physicians may at times feel the need to deploy MCS despite the current lack of evidence for their usage. Even though the incidence of MCS use in the Netherlands seems high, rates of MCS use in other contemporary cohorts are similar, ranging from 19% to 35% [23,24]. The distribution between Impella and VA-ECMO, with Impella being used more often, is comparable with other reports.

To the best of our knowledge, this is the largest cohort of patients with CS who underwent PCI with data available on clinical, biochemical and angiographic parameters. It provides a real-world insight covering 49% of all CS patients nationwide in the selected timeframe. Data collection was performed with great care, and high standards of quality control as set by the NHR, were applied. In addition to that, patient survival status was retrieved from the governmental Personal Records Database, guaranteeing reliable documentation. Finally, the amount of variables with high percentages of missing data were limited, especially for those variables that are routinely collected in all patients undergoing PCI.

However, this registry had some limitations as well. Firstly, some selection bias may have been introduced by the partly retrospective aspect of the study. Patients who were initially classified as being in shock but had no source documents confirming the diagnosis of shock other than being labeled as such in the electronic health record, were excluded from the analysis. Nevertheless, this would only strengthen the data on true CS patients. Unfortunately, we did not incorporate the Society for Cardiovascular Angiography and Interventions (SCAI) class definition in our comprehensive CS registry. Regrettably, we did not capture data on bleeding either, which may be of interest, especially in patients treated with mechanical circulatory support.

Furthermore, in some of the additionally collected shock variables, the percentage of missing data exceeded 40%. This was only the case in 5 of these 49 variables, and this was dealt with by providing details on percentages and denominators.

Lastly, despite applying strict criteria and only including AMICS patients who underwent PCI, some heterogeneity in the population was inevitable. Only AMI-related CS in patients who underwent PCI was included, but associations between risk factors and outcome could vary for different sub-etiologies; e.g., high lactate on admission might be more indicative of a bad prognosis in non-resuscitated patients than in patients presenting after an OHCA. Nevertheless, we believe that the present variety is in fact a strength because it reflects a real-world population.

## 5. Conclusions

This contemporary Dutch cohort describes characteristics and outcomes of 2328 patients with AMICS undergoing PCI. The all-cause mortality at 30 days was 38.7%. Considerable differences were seen in patient, hemodynamic and biochemical characteristics between survivors and non-survivors. Interestingly, multivessel PCI and IABPs were frequently applied despite currently available evidence.

**Author Contributions:** Conceptualization, E.J.P., A.O.K., J.J.H.B., K.T., E.L., R.-J.M.v.G., K.D.S., A.D., E.A.D., A.E.E., L.C.O., A.P.J.V. and J.P.S.H.; methodology, E.J.P. and M.J.C.T.; formal analysis, E.J.P. and M.J.C.T.; writing—original draft preparation, E.J.P.; writing—review and editing, S.t.B., M.B., M.J.C.T., A.O.K., J.J.H.B., K.T., E.L., K.D.S., R.-J.M.v.G., A.D., E.A.D., M.M., P.D., N.J.W.V., G.B., J.M.M.C., I.A.F., A.E.E., W.K.L., L.C.O., A.P.J.V., J.P.S.H. and Participating Centers of the PCI Registration Committee of the Netherlands Heart Registration. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This was an observational study. The Medical Research Ethics Committees United (MEC-U) confirmed that no ethical approval was required under the Medical Research Involving Human Subjects Act (WMO).

**Informed Consent Statement:** Patient consent was waived due to the nature of the study.

**Data Availability Statement:** The data presented in this study were obtained from the Netherlands Heart Registration and are not openly available. Data may be provided upon request.

**Conflicts of Interest:** The authors declare no conflict of interest.

## Appendix A

**Table A1.** Variables collected for all patients who underwent PCI in the Netherlands. The Dutch version can be found at: [www.nhr.nl](http://www.nhr.nl).

| Variable  | Outcome  | Missing No. (%) |
|---|--|-----------------|
| <b>Age</b><br><i>Difference between date of birth and date of intervention.</i>   | Continuous   | 0 (0)           |
| <b>Sex</b>  | Male<br>Female   | 0 (0)           |
| <b>Creatinine—<math>\mu\text{mol/L}</math></b><br><i>Last measured concentration of creatinine (measured no longer than 3 months prior to the intervention or on the day of the intervention).</i>  | Continuous (1–2000)  | 191 (8.2)       |
| <b>Diabetes mellitus</b><br><i>Indicate the most intensive therapy that was used to treat diabetes</i>  | None<br>Diabetes, treatment unknown<br>Diabetes, no treatment<br>Diabetes, diet<br>Diabetes, oral medication<br>Diabetes, insulin<br>Diabetes, other | 109 (4.7)       |
| <b>LVEF—%</b><br><i>Fraction of blood ejected from the left ventricle with each contraction (expressed as percentage; registered no more than 6 months prior to the intervention).</i>  | Continuous (1–99)  | 1627 (69.9)     |
| <b>Dialysis</b><br><i>Chronic hemodialysis or peritoneal dialysis due to renal failure at the time of the current admission.</i>  | No<br>Yes  | 318 (13.7)      |
| <b>Multivessel disease</b><br><i>Presence of multivessel disease during the current intervention. For first interventions: stenosis of <math>\geq 70\%</math> in <math>\geq 2</math> native vessels with a diameter of at least 1.5 mm. In patients with a prior coronary intervention: <math>\geq 70\%</math> stenosis in <math>\geq 1</math> native coronary arteries that have not yet been treated and/or multivessel disease during previous intervention.</i> | No<br>Yes  | 21 (0.9)        |
| <b>Prior MI</b><br><i>Patient had at least one documented prior myocardial infarction (excluding infarctions occurring during the same admission that were the reason for the current intervention).</i>  | No<br>Yes  | 75 (3.2)        |

Table A1. Cont.

| Variable  | Outcome  | Missing No. (%) |
|---|--|-----------------|
| <b>Indication of PCI</b><br><i>Status of the patient during the current intervention:</i><br>NSTEMI: presence of acute chest pain in the absence of ST elevation (including stable angina);<br>STEMI: presence of acute chest pain and (>20 mm) ST elevation.   | NSTEMI<br>STEMI  | 24 (1.1)        |
| <b>Cardiogenic shock</b><br><i>The presence of hypotension (systolic blood pressure (SBP) <math>\leq</math> 90 mmHg for <math>\geq</math> 30 min or support to maintain SBP <math>\geq</math> 90 mmHg) and end-organ hypoperfusion (cold extremities and/or oliguria &lt; 30 mL/hour and/or tachycardia <math>\geq</math> 60 beats per minute (bpm)).</i> | No<br>Yes  | 0 (0)           |
| <b>OHCA</b><br><i>Patients who were defibrillated (and received chest compressions) outside the hospital (prior to and related to the reason for the current intervention).</i>   | No<br>Yes, treatment unknown<br>Yes, defibrillation only<br>Yes, defibrillation and compressions | 11 (0.5)        |
| <b>Prior PCI</b><br><i>Patient underwent PCI prior to current intervention.</i>   | No<br>Yes  | 194 (8.3)       |
| <b>Prior CABG</b><br><i>Patient underwent coronary artery bypass graft surgery prior to current intervention.</i>   | No<br>Yes  | 42 (1.8)        |
| <b>PCI vascular access site</b><br><i>Vascular access site used for current intervention.</i>   | Radial<br>Femoral<br>Brachial<br>Ulnar<br>Other  | 275 (11.8)      |
| <b>PCI-treated vessel</b><br><i>Name of dilated coronary artery:</i><br>LM: left main<br>LAD: left coronary artery<br>RCX: circumflex artery<br>AL/IM: anterolateral / intermediate branch<br>RCA: right coronary artery<br>Venous graft<br>Arterial graft  | LM<br>LAD<br>RCX<br>AL/IM<br>RCA<br>Venous graft<br>Arterial graft                               | 214 (9.2)       |
| <b>Survival status</b><br><i>Survival status (as determined after verification of the personal records database or date of last contact).</i>   | Alive<br>Deceased  | 7 (0.3)         |
| <b>Date of survival status</b><br><i>Days between PCI and either verification of survival status (alive patients) or date of death (deceased patients).</i>   | Continuous   | 6 (0.3)         |

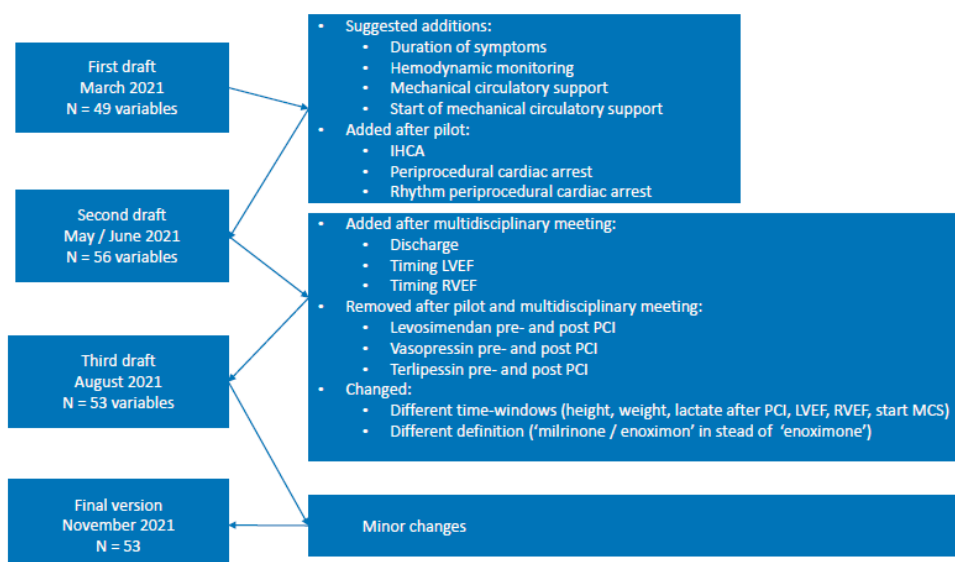
## Appendix B

**Table A2.** Participating centers and PCI registration committee members.

| Hospital                                    | Physician                |
|---|--------------------------|
| Amphia Ziekenhuis                           | Dr. M. Meuwissen         |
| Amsterdam Universitair Medische Centra, AMC | Prof. Dr. J.P. Henriques |
| Amsterdam Universitair Medische Centra, VU  | Dr. K.M.J. Marques       |
| Catharina Ziekenhuis                        | Dr. K. Teeuwen           |
| Erasmus Medisch Centrum                     | Dr. J. Daemen            |
| HagaZiekenhuis                              | Dhr. C.E. Schotborgh     |
| Isala (ziekenhuis)                          | Dr. V. Roolvink          |
| Leids Universitair Medisch Centrum          | Dr. R. Scherptong        |
| Medisch Centrum Leeuwarden                  | Dhr. J. Brouwer          |
| Noordwest Ziekenhuisgroep                   | Dr. A. Dedic             |
| Radboud Universitair Medisch Centrum        | Dhr. C. Camaro           |
| Rijnstate Ziekenhuis                        | Dr. P.W. Danse           |
| Universitair Medisch Centrum Groningen      | Dr. E. Lipšic            |
| Universitair Medisch Centrum Utrecht        | Dr. A.O. Kraaijeveld     |

## Appendix C Detailed Description of Variable Selection Process

Initially, a draft version of the set of variables to be collected in patients with CS was constructed by members of the PCI registration committee of the Netherlands Heart Registration. This preliminary set was reviewed and updated by the NHR PCI registration committee. In the meantime, the draft version was tested for feasibility and completeness in three hospitals by a physician. The second draft version, which resulted from this pilot testing and the external input, was subsequently discussed in a multidisciplinary meeting in which variables and definitions were reviewed by clinicians, data managers and other involved parties. The third draft version of the set of variables along with its corresponding data dictionary were then again presented to the involved parties for approval. A few more adjustments were made prior to finalizing the selection. See Figure A1 for the process flow.



**Figure A1.** Final variable selection. A total of 53 variables were selected for the final registry, that can be found in Tables A1 and A3 together with its corresponding data dictionary. Percentages of missing data are shown per variable and were higher in in the additionally collected shock variables than in the standard PCI variables.

## Appendix D

Table A3. Additional shock variables.

| Variable  | Outcome  | Missing No. (%) |
|---|--|-----------------|
| <b>Start of cardiogenic shock</b><br><i>Timing of cardiogenic shock:</i><br><i>Pre-PCI: up to and including the first pressure registration;</i><br><i>During or post-PCI: after first pressure registration but before leaving the cath lab;</i><br><i>After leaving cath lab: could be identified by linkage of index admission to catecholamine use.</i>   | Pre-PCI<br>During or post-PCI<br>After leaving cathlab               | 57 (2.4)        |
| <b>Duration of symptoms</b><br><i>Amount of time between start of symptoms and hospital presentation.</i>   | >24 h<br>>12 h, ≤24 h<br>>6 h, ≤12 h<br>>3 h, ≤6 h<br>≤3 h           | 337 (14.5)      |
| <b>Systolic blood pressure—mmHg</b><br><i>Systolic blood pressure according to first in-hospital measurement pre-PCI. In case of absence of an in-hospital measurement, a measurement by the emergency medical team can be used.</i>  | Continuous (0–300)   | 279 (12.0)      |
| <b>Diastolic blood pressure—mmHg</b><br><i>Diastolic blood pressure according to first in-hospital measurement pre-PCI. In case of absence of an in-hospital measurement, a measurement by the emergency medical team can be used.</i>  | Continuous (0–300)   | 309 (13.3)      |
| <b>Heart rate—bpm</b><br><i>Heart rate according to first in-hospital measurement pre-PCI. In case of absence of an in-hospital measurement, a measurement by the emergency medical team can be used.</i>   | Continuous (0–300)   | 329 (14.1)      |
| <b>OHCA witnessed</b><br><i>Ambulance witnessed: emergency medical team witnessed collapse and acted accordingly;</i><br><i>Layperson witnessed: someone (other than emergency medical team) saw or heard collapse and acted accordingly;</i><br><i>Unwitnessed: no one saw or heard collapse;</i><br><i>No OHCA: patient was not defibrillated (nor received chest compressions) prior outside the hospital, prior to and related to the reason for the current intervention;</i><br><i>Unknown; unknown whether collapse was witnessed.</i> | Ambulance witnessed<br>Layperson witnessed<br>Unwitnessed<br>No OHCA | 48 (2.1)        |
| <b>OHCA duration</b><br><i>Time to return of spontaneous circulation.</i>   | ≥30 min<br><30 min<br>No OHCA  | 106 (4.6)       |
| <b>IHCA</b><br><i>Patient was defibrillated (and received chest compressions) in the hospital before entering the cath lab.</i>   | No<br>Yes  | 22 (1.0)        |
| <b>Height—kg</b><br><i>Most recently reported height (measured during index admission). When height is not measured during index admission, the most recently reported height (up to one year old) can be used.</i>   | Continuous (20–270)  | 398 (17.1)      |
| <b>Weight—cm</b><br><i>Most recently reported weight (measured during index admission). When weight is not measured during index admission, the most recently reported weight (up to one year old) can be used.</i>   | Continuous (0.3–250)   | 320 (13.7)      |

Table A3. Cont.

| Variable  | Outcome  | Missing No. (%) |
|---|--|-----------------|
| <b>Lactate on admission—mmol/L</b><br><i>First measured blood lactate level on admission (<math>\pm 1</math> h around PCI).</i>   | Continuous (0.0–40.0)  | 802 (34.5)      |
| <b>Hemoglobin on admission—mmol/L</b><br><i>First measured hemoglobin level on admission (<math>\pm 1</math> h around PCI).</i>   | Continuous (0.0–15.0)  | 139 (6.0)       |
| <b>Glucose on admission— mmol/L</b><br><i>First measured glucose level on admission (<math>\pm 1</math> h around PCI).</i>  | Continuous (1.0–40.0)  | 283 (12.2)      |
| <b>Creatinine on admission—<math>\mu</math>mol/L</b><br><i>First measured creatinine level on admission (<math>\pm 1</math> h around PCI).</i>  | Continuous (1.0–2000.0)  | 233 (10.0)      |
| <b>CK-MB max—U/L</b><br><i>Highest creatinine kinase-MB level during index admission (up to 3 days after PCI).</i>  | Continuous (0–10,000)  | 1196 (51.4)     |
| <b>hs-Troponin-T—<math>\mu</math>g/L</b><br><i>Highest high-sensitive troponin-T level during index admission (up to 3 days after PCI).</i>   | Continuous (0–150,000)   | 412 (17.7)      |
| <b>Left ventricular ejection fraction (LVEF)—%</b><br><i>Fraction of blood ejected from the left ventricle with each contraction (expressed as percentage; measured during shock). The most recent measure is to be used (up to 2 h before and 24 h after intervention). If more than one ejection fraction is available, the lowest registered value should be registered.</i>   | Continuous (1–99)  | 1102 (47.3)     |
| <b>Timing LVEF</b><br><i>Timing of echo that measured left ejection fraction. If more than one ejection fraction is available, the timing of the lowest registered ejection fraction should be registered.</i>  | 2 h prior to PCI until leaving cathlab<br>$\leq 3$ h after leaving cathlab<br>$>3$ and $\leq 6$ h after leaving cathlab<br>$>6$ and $\leq 12$ h after leaving cathlab<br>$>12$ and $\leq 24$ h after leaving cathlab | 193 (8.3)       |
| <b>Right ventricular ejection fraction (RVEF)—%</b><br><i>Fraction of blood ejected from the right ventricle with each contraction (expressed as percentage; measured during shock). The most recent measure is to be used (up to 2 h before and 24 h after intervention). If more than one ejection fraction is available, the lowest registered value should be registered.</i> | Continuous (1–99)  | 1523 (65.4)     |
| <b>Timing RVEF</b><br><i>Timing of echo that measured right ejection fraction. If more than one ejection fraction is available, the timing of the lowest registered ejection fraction should be registered.</i>   | 2 h prior to PCI until leaving cathlab<br>$\leq 3$ h after leaving cathlab<br>$>3$ and $\leq 6$ h after leaving cathlab<br>$>6$ and $\leq 12$ h after leaving cathlab<br>$>12$ and $\leq 24$ h after leaving cathlab | 236 (10.1)      |
| <b>Admission</b><br><i>Days between date of admission and date PCI was performed.</i>   | Continuous   | 19 (0.8)        |
| <b>Intubation before PCI</b><br><i>Patient was intubated prior to PCI (up to first pressure registration).</i>  | No<br>Yes  | 21 (0.9)        |

Table A3. Cont.

| Variable  | Outcome   | Missing No. (%) |
|---|---|-----------------|
| <b>Intubated when leaving HCK</b><br><i>Patient was intubated when leaving the cathlab.</i>   | No<br>Yes   | 26 (1.1)        |
| <b>Mechanical circulatory support</b><br><i>Type of mechanical circulatory support that was initiated during index admission.</i>                       | None<br>IABP<br>Impella<br>ECMO<br>IABP + ECMO<br>Impella + ECMO<br>IABP + Impella<br>Other   | 24 (1.0)        |
| <b>Start of mechanical circulatory support</b><br><i>Moment that mechanical circulatory support was initiated.</i>                                      | None<br>Prior to HCK<br>In HCK (before first i.c. measurement)<br>After first measurement<br>After leaving HCK, <24 h<br>After leaving HCK > 24 h | 69 (3.0)        |
| <b>Hemodynamical monitoring</b><br><i>Whether or not patient was hemodynamically monitored with Swan-Ganz or PiCCO catheter during index admission.</i> | None<br>Swann-Ganz<br>PiCCO   | 196 (8.4)       |
| <b>Periprocedural cardiac arrest</b><br><i>Whether or not a cardiac arrest occurred during stay in the cathlab.</i>                                     | No<br>Yes, prior to first measurement<br>Yes, after first measurement   | 22 (0.9)        |
| <b>Rhythm periprocedural cardiac arrest</b><br><i>Initial rhythm of periprocedural cardiac arrest.</i>  | None<br>VF/VT<br>PEA/asystole   | 74 (3.2)        |
| <b>TIMI flow grade pre-PCI</b><br><i>TIMI flow measured pre-PCI.</i>  | 0<br>1<br>2<br>3  | 385 (16.5)      |
| <b>TIMI flow grade post-PCI</b><br><i>TIMI flow measured post-PCI.</i>  | 0<br>1<br>2<br>3  | 329 (14.1)      |
| <b>Norepinephrine prior to PCI</b><br><i>Whether or not a patient received norepinephrine pre-PCI (up to first pressure registration).</i>              | No<br>Yes   | 49 (2.1)        |
| <b>Norepinephrine after PCI</b><br><i>Norepinephrine use in the first 24 h after PCI.</i>   | No<br>Yes, continued<br>Yes, initiated in HCK<br>Yes, initiated <24 h after leaving HCK   | 55 (2.4)        |
| <b>Dobutamine prior to PCI</b><br><i>Whether or not a patient received dobutamine pre-PCI (up to first pressure registration).</i>                      | No<br>Yes   | 42 (1.8)        |



Table A3. Cont.

| Variable  | Outcome   | Missing No. (%) |
|---|---|-----------------|
| <b>Dobutamine after PCI</b><br><i>Dobutamine use in the first 24 h after PCI.</i>   | No<br>Yes, continued<br>Yes, initiated in HCK<br>Yes, initiated <24 h after leaving HCK | 65 (2.8)        |
| <b>Enoximone or milrinone prior to PCI</b><br><i>Whether or not a patient received enoximone/milrinone pre-PCI (up to first pressure registration).</i>                       | No<br>Yes   | 35 (1.5)        |
| <b>Enoximone or milrinone after PCI</b><br><i>Enoximone/milrinone use in the first 24 h after PCI.</i>  | No<br>Yes, continued<br>Yes, initiated in HCK<br>Yes, initiated <24 h after leaving HCK | 52 (2.2)        |
| <b>Adrenaline prior to PCI</b><br><i>Whether or not a patient received adrenaline pre-PCI (up to first pressure registration).</i>  | No<br>Yes   | 80 (3.4)        |
| <b>Adrenaline after PCI</b><br><i>Adrenaline use in the first 24 h after PCI.</i>   | No<br>Yes, continued<br>Yes, initiated in HCK<br>Yes, initiated <24 h after leaving HCK | 75 (3.2)        |
| <b>Dopamine prior to PCI</b><br><i>Whether or not a patient received dopamine pre-PCI (up to first pressure registration).</i>  | Yes<br>No   | 34 (1.5)        |
| <b>Dopamine after PCI</b><br><i>Dopamine use in the first 24 h after PCI.</i>   | No<br>Yes, continued<br>Yes, initiated in HCK<br>Yes, initiated <24 h after leaving HCK | 54 (2.3)        |
| <b>Lactate after PCI—mmol/L</b><br><i>Blood lactate level measured 6–24 h after PCI. When more than one measurement is available, the highest value should be registered.</i> | Continuous (0.0–40.0)   | 866 (37.2)      |
| <b>SOFA score on admission</b><br><i>Sequential organ failure assessment score on ICU admission.</i>  | Continuous (6–24)   | 1888 (81.1)     |
| <b>SOFA score after 24 h</b><br><i>Sequential organ failure assessment score 24 h after ICU admission.</i>  | Continuous (6–24)   | 1954 (83.9)     |
| <b>Discharge</b><br><i>Days between admission date and discharge date.</i>  | Continuous  | 542 (23.3)      |
| <b>Heart transplant</b><br><i>Patient received a heart transplant or a heart–lung transplant.</i>   | No<br>Yes   | 0 (0)           |
| <b>Days after PCI</b><br><i>Days between PCI and heart transplant/heart–lung transplant.</i>  | Continuous  | 2 (0.1)         |
| <b>VAD</b><br><i>Patient received a permanent ventricular assist device.</i>  | No<br>Yes   | 0 (0)           |
| <b>Days after PCI</b><br><i>Days between PCI and implantation of permanent ventricular assist device.</i>   | Continuous  | 4 (0.2)         |

Table A3. Cont.

| Variable   | Outcome   | Missing No. (%) |
|--|---|-----------------|
| <b>Cause of death (ARC-2) [25]</b>   |   |                 |
| <i>Cardiovascular death: death resulting from cardiovascular causes. The following categories may be collected:</i>                                |   |                 |
| 1. Death caused by acute MI;   |   |                 |
| 2. Death caused by sudden cardiac (including unwitnessed) death;   |   |                 |
| 3. Death resulting from heart failure;   |   |                 |
| 4. Death caused by stroke;   |   |                 |
| 5. Death caused by cardiovascular procedures;  |   |                 |
| 6. Death resulting from cardiovascular hemorrhage;   |   |                 |
| 7. Death resulting from other cardiovascular cause.  | Unknown<br>Cardiovascular death<br>Non-cardiovascular death | 96 (4.1)        |
| <i>Non-cardiovascular death: death that is not thought to be the results of a cardiovascular cause. The following categories may be collected:</i> |   |                 |
| 1. Death resulting from malignancy;  |   |                 |
| 2. Death resulting from pulmonary causes;  |   |                 |
| 3. Death caused by infection (includes sepsis);  |   |                 |
| 4. Death resulting from gastrointestinal causes;   |   |                 |
| 5. Death resulting from accident/trauma;   |   |                 |
| 6. Death caused by other non-cardiovascular organ failure;   |   |                 |
| 7. Death resulting from other non-cardiovascular cause.  |   |                 |

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