RESEARCH ARTICLE

TRANSLATIONAL AND CLINICAL RESEARCH

Martin Marinšek, et al.: Neurological outcome after out-of-hospital cardiac arrest

Neurological outcome in patients after successful resuscitation in out-of-hospital settings

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ABSTRACT

Neurological outcome is an important determinant of death in admitted survivors after out-of-hospital cardiac arrest (OHCA). Studies demonstrated several significant pre-hospital predictors of ischemic brain injury (time to resuscitation, time of resuscitation, and cause of OHCA). Our aim was to evaluate the relationship between post-resuscitation clinical parameters and neurological outcome in OHCA patients, when all recommended therapeutic strategies, including hypothermia, were on board. We retrospectively included consecutive 110 patients, admitted to medical ICU after successful resuscitation due to OHCA. Neurological outcome was defined by cerebral performance category (CPC) scale I-V. CPC categories I-II defined good neurological outcome and CPC categories III-V severe ischemic brain injury. Therapeutic measures were aimed to achieve optimal circulation and oxygenation, early percutaneous coronary interventions (PCI) in acute coronary syndromes (ACS), and therapeutic hypothermia to improve survival and neurological outcome of OHCA patients. We observed good neurological outcome in 37.2% and severe ischemic brain injury in 62.7% of patients. Severe ischemic brain injury was associated significantly with known pre-hospital data (older age, cause of OHCA, and longer resuscitations), but also with increased admission lactate, in-hospital complications (involuntary muscular contractions/seizures, heart failure, cardiogenic shock, acute kidney injury, and mortality), inotropic and vasopressor support. Good neurological outcome was associated with early PCI, dual antiplatelet therapy, and better survival. We conclude that in OHCA patients, post-resuscitation early PCI and dual antiplatelet therapy in ACS were significantly associated with good neurological outcome, but severe ischemic brain injury was associated with several in-hospital complications and the need of vasopressor and inotropic support.

KEYWORDS: Out-of-hospital cardiac arrest; OHCA; ischemic brain injury; resuscitation
INTRODUCTION

The incidence of out-of-hospital-cardiac-arrest (OHCA) in Europe is in average 84 cases/100,000 population/year with achieved return of spontaneous circulation (ROSC) in 9% - 50% of resuscitation attempt and survival to discharge of admitted patients in 6.4% - 66.9%. Majority of admitted OHCA patients are usually comatose, intubated and mechanically ventilated [1].

According to studies, 24-hour of mild therapeutic hypothermia with target temperatures of 32°-34°C, as well as temperatures up to 36°C, improved neurological outcome [2,3]. Both, ischemic brain injury and cardiogenic shock, are most significant predictors of short-term mortality [4,5]. However, neurological status alone is the major determinant of the long-term prognosis [6,7]. Neurological impairment includes cognitive impairment, restricted mobility, depression, even vegetative state or brain death in survivors of OHCA [8,9]. Post-cardiac arrest brain injury is most widely assessed by Cerebral Performance Category (CPC) scale and corresponds to quality of life and outcome [9]. CPC categories I and II represent good neurological outcome. Patients in CPC category I are conscious, alert, able to work and lead a normal life as their psychological or neurologic deficits are minor. Patients in CPC category II are conscious, but able to work part-time in sheltered environment with independent activities of daily life, moderate neurological deficits may be present [8,9]. Severe brain injury includes CPC categories III-V. Patients in CPC category III are conscious, dependent on daily support in an institution or at home with exceptional family effort with limited cognition and significant neurological deficits. Patients in CPC category IV includes a vegetative state and CPC category V includes patients with brain death or death by the traditional criteria, who never gained consciousness in the postresuscitation period [8,9].
Currently, in unconscious patients neurological prognostication is not recommended earlier than 72 h after OHCA [10-12]. In early post-resuscitation period, soon after cessation of analgesia and sedation suspicion of severe neurological dysfunction is raised by the absence of corneal and pupillary reflexes, myoclonus within the next few days, epileptic status, registered by EEG, diffuse anoxic changes on CT/MR, increased levels of brain injury markers neuron specific enolase and protein S-100 [13]. However, according to trials most significant independent predictors of neurological dysfunction after OHCA are prehospital data such as asystole / PEA as the cause of OHCA, long resuscitation time in addition to the absence of corneal and pupillary reflexes, absence of motoric response on admission, adrenalin therapy, metabolic acidosis and admission arterial pCO2 < 4.5 kPa [12,14]. Our aim was to evaluate the relationship between clinical parameters of the postresuscitation period and neurological outcome in OHCA patients, when all recommended therapeutic strategies, including hypothermia, were on board.

MATERIALS AND METHODS

We retrospectively included 110 patients, successfully resuscitated in the out of hospital settings and admitted alive to the Department of medical intensive care (MICU) of the tertiary University clinical centre Maribor (Slovenia) from v 2014 - 2016 (72.7% men, mean age 65.6±13.8 years, age ≥ 65 years in 72.7%).

In the out of hospital settings, witnesses of OHCA usually activated emergency medical service (EMS) team by a telephone call to the emergency number 112 of the emergency communication center. Often, a witness started basic life support in victims of OHCA (chest compressions), until arrival of EMS team. EMS team confirmed cardiac arrest, attached the monitor and performed defibrillation in case of ventricular fibrillation (VF) or pulsless ventricular tachycardia (VT). In nonresponders and in case of asystole or pulseless electrical activity (PEA) EMS continued chest compressions and administered adrenalin. In
case of prolonged resuscitation with respiratory arrest the patients were intubated and mechanically ventilated. In case of return of spontaneous circulation (ROSC) the patients were transported to the MICU. Resuscitation time of EMS team was registered in minutes. On arrival, majority of OHCA patients were comatose, but with palpable pulse, in majority intubated and mechanically ventilated [10,11].

After arrival to the MICU all OHCA patients were monitored by continuous ECG, pulse oxymetry, continuous systemic arterial blood pressure and intermittent central venous pressure measurements. Blood samples were drawn to measure standard laboratory tests. Echocardiography was performed to measure ejection fraction (EF), left ventricular end-diastolic diameter, to evaluate valves, possible pericardial effusion or pleural pathologies [10,11].

The goal of postresuscitation care was to achieve adequate oxygenation by mechanical ventilation (MV), adequate circulation by infusion of fluids, iv. vasopressors and/or inotropes and/or mechanical circulatory support by insertion of an intraaortic balloon pump (IABP) [11]. Post-resuscitation care protocol was in agreement with the guidelines. It included oxygenation targets (SatO₂ 90-95%, arterial pO₂ 8.5-9kPa, arterial pCO₂ 5-6 kPa, normal pH), serum lactate < 2mmol/l, ventilation targets (tidal volumes 6-8ml/ideal body weight) and circulatory targets (mean arterial pressure > 70 mm Hg, heart rate 60-100/min, ScvO₂ >70%) [10,11].

We controlled involuntary muscular contractions / seizures by anticonvulsant drugs (benzodiazepins, levetiracetam, barbiturates), hyperglycemia by short-acting insulin infusion and concomitant blood glucose measurements per 2-3 hours with target blood glucose level of 6-11 mmol/l, avoiding hypoglycaemias. We controlled arrhythmias by antiarrhythmic drugs [10,11].
Acute coronary syndromes (ACS) were confirmed by standard ECG recordings, patients’ history, and troponin I measurements, followed by coronary angiography and percutaneous coronary intervention (PCI), if necessary, combined with dual antiplatelet therapy, including acetylsalicylic acid (ASA) and P2Y12 inhibitors [6,11,15].

We started targeted temperature management to prevent ischemic brain injury [2,16]. Target temperatures, measured by the urine catheter, were 32-34°C. They were achieved by a rapid infusion of 20-30 ml/kg of cold saline (4°C) over 20-30 minutes. Induction time in patients was approximately 60 minutes. The amount of infused cold saline was adjusted to worsening respiratory failure and/or pulmonary edema if present [6,10,11]. Core temperature of 32-34°C, if reached, was maintained for the next 24 hours by cooled blankets (CritiCool® device, Israel) [6]. Hypothermia was followed by gradual - 6-8 hour - rewarming till normothermia [6,10,11].

The underlying disease of OHCA, was categorized as ACS, chronic ischemic coronary heart disease without coronary occlusion or stenosis, nonischemic heart disease (valvular, cardiomyopathies, pulmonary embolism, acute heart failure) as assessed by echocardiography, troponin measurements.

Clinical and neurological assessments were performed each day by the treating intensivist. However, prognostic assessment of neurological status was started more than 72 hours after admission by an experienced neurologist, performing neurological clinical examination and additional diagnostics such as EEG, CT/MR. Neurological examination was repeated, if necessary. Most important measure to report neurological outcome was assessment of CPC categories I-V, where CPC categories I and II determined good neurological outcome and CPC categories III-V ischemic brain injury [8,9].
Survivors with good neurological outcome were candidates for preventive measures of recurrent cardiac arrest such as cardioverter-defibrillator (ICD), cardiac pacing, ectopic focus ablation, valve replacement [10,11].

In all the included OHCA patients, we registered age ≥ 65 years, gender, admission lactate levels ≥ 6 mmol/L, the incidence of VF/VT or asystole/PEA as the cause of OHCA, resuscitation time ≥ 20 minutes, admission EF < 35%, ACS as the underlying disease, admission and in-hospital MV, in-hospital treatments by PCI, mild therapeutic hypothermia of 32-34°C, the need of dobutamin, noradrenalin, IABP, antibiotics. Among in hospital complications we registered in addition to CPC categories I-V the incidence of cardiogenic shock, arrhythmias, bleedings, infections, involuntary muscular contractions/seizures, and acute kidney injury (AKI) at any time of in-hospital stay, as well as in-hospital mortality. Arrhythmias were registered by continuous ECG monitoring and standard ECG recordings and were classified as atrial, ventricular or conduction disturbances. Shock was quantified clinically by the need of noradrenalin or/and inotropic support to maintain adequate circulation and systolic function [17]. Infection was defined as the presence of microorganisms in otherwise sterile milieu of the body (blood, cerebrospinal liquor, lung tissue, urinary tract) with or without clinical symptoms (fever, increased CRP, leucocytosis or leukocytopenia), or with antibiotic administration due to strong clinical suspicion of infection [18].

According to TIMI criteria, major bleeding was defined as cerebral or symptomatic bleeding in other location with haemoglobin level drop of >50 g/l or the need of ≥2 units of blood product transfusions. Minor bleeding was defined as symptomatic with a haemoglobin level drop 30-50 g/L. Minimal bleeding was defined as symptomatic with a haemoglobin level drop <30 g/l [19].

AKI was defined as an increase of serum creatinine of at least 50% within 24-48 hours [20].
In case of complications, patients were treated according to professional protocols by the discretion of the treating physician (e.g. by vasopressors, inotropic agents, MV, IABP, red blood cell transfusions, antibiotics, antiarrhythmic drugs, and pacing) [10,11].

Finally, we compared baseline characteristics, laboratory and clinical data, treatments and outcome between patients with good neurological outcome (CPC categories I and II) and patients with severe brain injury (CPC categories III-V).

**Ethical statement**

The Institutional Medical Ethics Committee (UKC-KME-02/19) approved the study. As this was a retrospective, single center observational study, the need for informed consent was waived. Personal data of all the patients were protected according to the Law on personal data protection.

**Statistical analysis**

Statistical analysis was performed using the SPSS® statistical package, version 24 (SPSS Inc., Chicago, IL, USA) for Windows®. Data were expressed as means ± standard deviations or percentages. Differences between the groups were tested by the two-sided Student’s t-test for means ± standard deviations and by the chi-square test for percentages. Kaplan-Meier survival plot was employed to show hospital survival associated with neurological status on discharge. P value <0.05 was considered statistically significant.

**RESULTS**

Baseline clinical data are presented in Table 1. Age ≥ 65 years was observed in 41.8% of all OHCA patients. Majority of admitted OHCA patients were in coma (87.3%) and mechanically ventilated (87.3%). VF/VT was the cause of OHCA in 63.6%, asystole/PEA in 35.5%. OHCA was witnessed in 73.6. Resuscitation ≥ 20 minutes by EMS was observed in 44.5%. On admission, we observed lactate levels ≥ 6 mmol/L in 30%, ejection fraction
(EF) < 35%, measured by echocardiography, in 43.6%. We diagnosed ACS on admission in 55.4% of OHCA patients, including STEMI in 43.6% and NSTEMI in 11.8%, respectively. In-hospital treatments are listed in Table 2. We reached target temperatures of 32° - 34° C by mild therapeutic hypothermia within the first few hours in 71.8% and performed PCI in 40% of cases; OHCA patients received iv. noradrenalin infusion in 75.5%, iv. inotropic support in 42.7% (dobutamin in 29.1%, levosimendan in 18.2%), IABP in 3.6%, antibiotics in 76.4% and in-hospital MV in 88.2%.

In-hospital complications are presented in Table 3. We observed bleedings in 10%, infection in 70.9%, AKI in 32.7%, involuntary muscular contractions / seizures in 27.2%, in hospital heart failure of Killip classes II-IV in 82.7%, cardiogenic shock in 75.5%, arrhythmias in 32.7%, severe ischemic brain injury (CPC categories III-V) in 62.7%, whereas good neurological outcome in 37.3% of OHCA patients and in-hospital mortality in 51.8%.

Severe brain injury (CPC categories III-V) in comparison to good neurological outcome (CPC categories I-II) in OHCA patients was associated significantly more likely with age ≥ 65 years, asystole/PEA as the cause of OHCA, resuscitation ≥ 20 minutes, MV on admission and during in-hospital stay, admission lactate ≥ 6 mmol/l, EF < 35% and GCS < 6 (Table 1). OHCA patients with severe brain injury (CPC categories III-V) in comparison to patients with good neurological outcome (CPC categories I-II) were significantly more likely treated in MICU by vasopressors, inotropic support by dobutamine, more likely by MV. There was no significant difference in the use of therapeutic hypothermia between patients with and without brain injury (Table 2). In elderly (≥ 65 years of age) and younger OHCA patients, hypothermia of 32-34°C was achieved in a similar rate (73.9% vs 70%).

Severe brain injury (CPC categories III-V) in comparison to good neurological outcome (CPC categories I-II) in OHCA patients was associated significantly with AKI, involuntary
muscular contractions / seizures, heart failure, in particularly shock, and hospital mortality (Table 2).

Good neurological outcome was associated significantly with VT/VF as the immediate cause of OHCA, treatment by PCI, ASA and P2Y12 inhibitors and less likely with complications and treatment by inotropic and vasopressor support (Table 1, Table 2, Table3).

Kaplan-Meier survival plot is displayed in Figure 1. At censoring, 95.1 % of OHCA patients with good neurological outcome were alive at hospital discharge compared with 20.3% of those with ischemic brain injury (log rank p < 0.0015).

DISCUSSION

In our retrospective analysis of OHCA patients, who were admitted alive to MICU, we observed severe ischemic brain injury (CPC categories III-V) in 62.7% and good neurological outcome in 37.3%. Ischemic brain injury was associated significantly with asystole /PEA as the cause of OHCA, resuscitation ≥ 20 minutes, age ≥ 65 years, admission EF < 35% and lactate ≥ 6 mmol/L, GCS < 6, involuntary muscular contractions/ seizures and with cardiogenic shock. Good neurological outcome was associated significantly with PCI treatment, the use of ASA and P2Y12 inhibitors.

According to EuReCa ONE study only approximately 5% of patients gained full neurological recovery [1]. In the last decade in our environment approximately 50% of OHCA patients, who were resuscitated, gained ROSC in the out of hospital settings [6,21]. Their overall good neurological outcome was achieved in approximately 13% between 2001 and 2004 and 17% between 2011 and 2013 [6,21]. In present retrospective analysis from 2014-2016 of our OHCA, 37.3% of those with ROSC on admission to MICU, gained patients full neurological recovery, what would represent overall good neurological outcome in 18%.
In OHCA patients, admitted alive to MICU, studies demonstrated that adequate postresuscitation care, including maintenance of adequate circulation, ventilation, oxygenation, early treatment of ACS by PCI in addition to therapeutic hypothermia, has the significant potential to decrease the incidence of ischemic brain injury [15,22]. Therefore, these measures are implemented in contemporary guidelines for postresuscitation care and were fulfilled in our patients as well [10,11].

Severe ischemic brain injury, usually categorized as CPC III-V, is major determinant of the long-term prognosis in OHCA patients. Among postresuscitation care measures therapeutic hypothermia has the potential to prevent it according to studies [2,16]. Therapeutic hypothermia, which is incorporated in postresuscitation care of OHCA patients, exerts several benefits at the cellular level. It reduces cerebral metabolism and lactate production, it reduces oxygen demand, improves cerebral energy stores and the use of glucose, decreases inflammation, production of free radicals [7].

In our OHCA patients, induction of hypothermia was started within the first few hours of in-hospital stay, most preferably within the first 1-2 hours. Hypothermia of 32-34°C was achieved in 71.8% of all OHCA patients, less in those with very early gain of consciousness and early death. Between patients with good and adverse neurological outcome we did not observe any significant differences in the achieved target temperatures 32-34°C. That finding was in agreement with a large study demonstrating, that therapeutic normothermia or temperature control at 36°C may be equally effective as hypothermia at 32-34°C on long-term regarding neurological outcomes in brain injury [3,23]. On the other hand, interaction of different variables such as age and/or other unidentified processes determine the magnitude by which hypothermia increases the activation of cold stress molecules in biological systems, which alter brain physiology during therapeutic
hypothermia. Therapeutic hypothermia is robustly influenced by age and is beneficial more in younger patients in addition to other therapeutic measures in ICU [23].

Brain tissue is particularly vulnerable not only to ischemia during OHCA, but also to secondary injury occurring in postresuscitation period due to imbalance in postresuscitation cerebral oxygen delivery and microcirculatory reperfusion injury, endothelial dysfunction, free radical formation, intracellular calcium accumulation [7]. Ischemic brain injury is a multifactorial complication in OHCA patients, admitted to MICU alive. Studies demonstrated that strong predictor of good neurological outcome and survival were VF/VT as the immediate cause of OHCA in addition to cardiac etiology of VF/VT and resuscitation < 20 minutes [14]. In our patients coronary artery disease was most frequent etiology, in particular acute coronary syndromes in patients with good neurological outcome.

Another study demonstrated that unfavorable vs. favorable neurological outcomes were associated with multiorgan failure syndrome on admission and during in-hospital stay, but independent predictors of unfavorable neurological outcome were MV on admission, high admission SAPS II score, and neurological dysfunction on admission [24]. In our OHCA patients with ischemic brain injury we observed significant more likely the use of noradrenalin, dobutamin and MV, reflecting respiratory and cardiovascular failure in these patients. In addition, admission EF < 35% was significantly associated with ischemic brain injury, reflecting acute systolic myocardial dysfunction in these subset of OHCA patients. Involuntary muscular contractions/seizures were associated with ischemic brain injury as well. If present, EEG was recorded. In case of epileptogenic EEG activity, antiepileptic drugs were added (levetiracetam iv., benzodiazepins iv., barbiturates iv.) till cessation to prevent secondary brain injury [10,11,13]. In addition, CT scans were performed to exclude
or confirm morphological changes such as brain edema, bleedings, localized or generalized brain hypoperfusion.

According to studies, good neurological outcome is more likely in early EEG reactivity, adequate EEG responses to auditory stimuli and absence of abnormalities on CT/MRI within 1 week of ROSC [10,11,13]. Several studies stressed the importance of underlying cardiac disease. In more than 50% of our OHCA patients ACS was the underlying disease. ACS were more likely, though nonsignificantly, observed in patients with a good neurological outcome in comparison to those with ischemic brain injury. However, good neurological outcome was more likely when PCI and dual antiplatelet therapy was used.

In addition, EF < 35%, which was associated with ischemic brain injury, was the consequence of possible prior chronic cardiac disease, but also acute systolic dysfunction or cardiogenic shock due to global myocardial hypoperfusion during OHCA, but also by ACS, and reperfusion injury in the postresuscitation period.

Among significant limitations of our study is its retrospective nature. However, the data originate from the real life. We also observed that hypothermia of 32-34°C was not achieved in nearly 30% of OHCA patients – mainly due to early death, or early improvement of neurological status. However, therapeutic hypothermia was performed on top of other recommended therapeutic strategies, aimed to optimize oxygenation, circulation, cardiac function, early treatment of ACS. Our data confirmed the significant role of neurological outcome for survival of OHCA patients.

CONCLUSION

We conclude that early and optimal postresuscitation care is important in improving neurological outcome of OHCA patients and should include 24-hour of target temperature management – at least target temperatures < 36°C. Our results did not confirm the
significant role of hypothermia between 32-34°C for neurological outcome, but the role of other therapeutic strategies such as the early treatment of ACS by PCI and dual antiplatelet therapy. We also confirmed the role of older age, the cause of OHCA, cardiac dysfunction, involuntary muscular contractions/seizures during in-hospital stay. Further studies are needed to elucidate the role of age in therapeutic hypothermia in OHCA patients.

ACKNOWLEDGMENTS

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### TABLE 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics (%)</th>
<th>Good neurological outcome (n = 41)</th>
<th>Brain injury (n = 69)</th>
<th>All (n = 110)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 65 years</td>
<td>26.8</td>
<td>50.7</td>
<td>41.8</td>
<td>0.017</td>
</tr>
<tr>
<td>Men</td>
<td>75.6</td>
<td>71</td>
<td>72.7</td>
<td>0.668</td>
</tr>
<tr>
<td>Witnessed OHCA</td>
<td>80.5</td>
<td>69.6</td>
<td>73.6</td>
<td>0.120</td>
</tr>
<tr>
<td>VT/VF</td>
<td>85.4</td>
<td>50.7</td>
<td>63.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Asystole / PEA</td>
<td>14.6</td>
<td>49.3</td>
<td>36.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Resuscitation ≥ 20 minutes</td>
<td>21.9</td>
<td>57.9</td>
<td>44.5</td>
<td>0.001</td>
</tr>
<tr>
<td>GCS on admission &lt; 6</td>
<td>68.3</td>
<td>98.3</td>
<td>87.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>68.3</td>
<td>98.6</td>
<td>87.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lactate ≥ 6 mmol/l</td>
<td>7.3</td>
<td>43.4</td>
<td>30</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>EF &lt; 35%</td>
<td>24.4</td>
<td>55</td>
<td>43.6</td>
<td>0.001</td>
</tr>
<tr>
<td>ACS</td>
<td>68.3</td>
<td>47.8</td>
<td>55.4</td>
<td>0.148</td>
</tr>
<tr>
<td>STEMI</td>
<td>53.7</td>
<td>37.7</td>
<td>43.6</td>
<td>0.309</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>14.6</td>
<td>10.1</td>
<td>11.8</td>
<td>0.763</td>
</tr>
</tbody>
</table>

Legend: OHCA, out-of-hospital cardiac arrest; VT, ventricular tachycardia; VF, ventricular fibrillation; PEA, pulsless electrical activity; GCS, Glasgow coma scale; EF, ejection fraction; ACS, acute coronary syndromes; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction
### TABLE 2. In-hospital treatments

<table>
<thead>
<tr>
<th>Treatments (%)</th>
<th>Good neurological outcome (n = 41)</th>
<th>Brain injury (n = 69)</th>
<th>All (n = 110)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia &lt; 34°C</td>
<td>63.4</td>
<td>76.8</td>
<td>71.8</td>
<td>0.077</td>
</tr>
<tr>
<td>PCI</td>
<td>53.7</td>
<td>31.9</td>
<td>40</td>
<td>0.043</td>
</tr>
<tr>
<td>Noradrenalin</td>
<td>56.1</td>
<td>87</td>
<td>75.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inotropic support</td>
<td>22</td>
<td>55.1</td>
<td>42.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Dobutamin</td>
<td>7.3</td>
<td>42</td>
<td>29.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Levosimendan</td>
<td>17.1</td>
<td>18.8</td>
<td>18.2</td>
<td>1.000</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>2.4</td>
<td>4.3</td>
<td>3.6</td>
<td>1.000</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>70.7</td>
<td>98.6</td>
<td>88.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA</td>
<td>80.5</td>
<td>56.5</td>
<td>65.5</td>
<td>0.013</td>
</tr>
<tr>
<td>P2Y12 inhibitors</td>
<td>68.3</td>
<td>26.1</td>
<td>41.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>70.7</td>
<td>79.7</td>
<td>76.4</td>
<td>0.354</td>
</tr>
</tbody>
</table>

Legend: PCI; percutaneous coronary intervention, ASA; acetylsalicylic acid
### TABLE 3. In-hospital complications

<table>
<thead>
<tr>
<th>Complications (%)</th>
<th>Good neurological outcome (n = 41)</th>
<th>Brain injury (n = 69)</th>
<th>All (n = 110)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleedings</td>
<td>2.4</td>
<td>14.5</td>
<td>10.1</td>
<td>0.053</td>
</tr>
<tr>
<td>Infection</td>
<td>73.2</td>
<td>69.6</td>
<td>70.9</td>
<td>0.829</td>
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<tr>
<td>Acute kidney injury</td>
<td>9.7</td>
<td>46.3</td>
<td>32.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>39</td>
<td>29</td>
<td>32.7</td>
<td>0.300</td>
</tr>
<tr>
<td>Involuntary muscular contractions / seizures</td>
<td>9.7</td>
<td>37.7</td>
<td>27.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure (Killip classes ≥ II)</td>
<td>56.1</td>
<td>98.6</td>
<td>82.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>56.1</td>
<td>87.0</td>
<td>75.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>4.9</td>
<td>79.7</td>
<td>51.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
FIGURE 1. Kaplan-Meier survival curves in patients with ischemic brain injury and good neurological outcome after OHCA. Kaplan-Meier survival plot in green represents survival with ischemic brain injury and in blue survival with good neurological outcome. At censoring, 95.1% of OHCA patients with good neurological outcome were alive at hospital discharge compared with 20.3% of those with ischemic brain injury (log-rank p < 0.0015).