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RESEARCH ARTICLE

Impella and venoarterial extracorporeal membrane oxygenation in cardiogenic shock complicating acute myocardial infarction

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Aims This study aimed to give contemporary insight into the use of Impella and venoarterial extracorporeal membrane oxygenation (VA-ECMO) in acute myocardial infarction-related cardiogenic shock (AMICS) and into associated outcomes, adverse events, and resource demands.

Methods and results This nationwide observational cohort study describes all AMICS patients treated with Impella (ABIOMED, Danvers, MA, USA) and/or VA-ECMO in 2020–2021. Impella and/or VA-ECMO were used in 20% of all AMICS cases ($n = 4088$). Impella patients were older (34% vs. 13% >75 years, $p < 0.001$) and less frequently presented after an out-of-hospital cardiac arrest (18% vs. 40%, $p < 0.001$). In-hospital mortality was lower in the Impella versus VA-ECMO cohort (61% vs. 67%, $p = 0.001$). Adverse events occurred less frequently in Impella-supported patients: acute haemorrhagic anaemia (36% vs. 68%, $p < 0.001$), cerebrovascular accidents (4% vs. 11%, $p < 0.001$), thromboembolisms of the extremities (5% vs. 8%, $p < 0.001$), systemic inflammatory response syndrome (21% vs. 25%, $p = 0.004$), acute kidney injury (44% vs. 53%, $p < 0.001$), and acute liver failure (7% vs. 12%, $p < 0.001$). Impella patients were discharged home directly more often (20% vs. 11%, $p < 0.001$) whereas VA-ECMO patients were more often discharged to another care facility (22% vs. 19%, $p = 0.031$). Impella patients had shorter hospital stays and lower hospital costs.

Conclusion This is the largest, most recent European cohort study describing outcomes, adverse events, and resource demands based on claims data in patients with Impella and/or VA-ECMO. Overall, adverse event rates and resource consumption were high. Given the current lack of beneficial evidence, our study reinforces the need for prospectively established, high-quality evidence to guide clinical decision-making.

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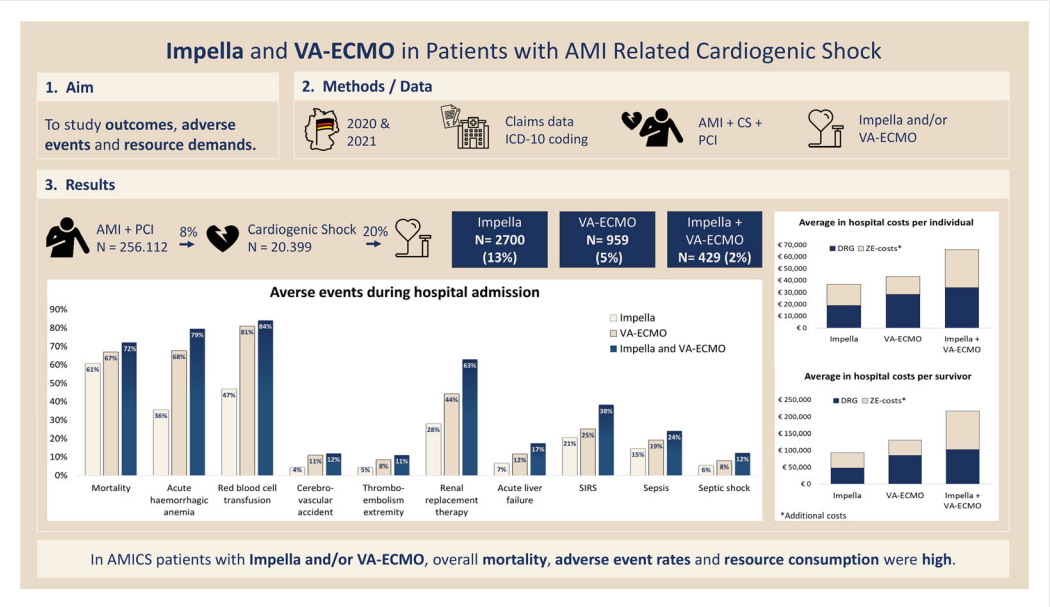
Graphical Abstract



Impella and venoarterial extracorporeal membrane oxygenation (VA-ECMO) in patients with acute myocardial infarction-related cardiogenic shock (AMICS). AMI, acute myocardial infarction; CS, cardiogenic shock; DRG, diagnosis-related group; ICD-10, International Classification of Diseases, 10th Revision; PCI, percutaneous coronary intervention; SIRS, systemic inflammatory response syndrome.

Keywords Acute myocardial infarction • Cardiogenic shock • Impella • Venoarterial extracorporeal membrane oxygenation • Adverse events • Resource demands

Introduction

The treatment of cardiogenic shock complicating acute myocardial infarction (AMICS) remains a challenge and mortality rates linger around 40–50%.[1,2] In the last decades, only three adequately powered and guideline-changing randomized controlled trials have been conducted in this population. In the first, immediate revascularization was demonstrated to be better than initial medical stabilization.[3] In the second trial, culprit-vessel percutaneous coronary intervention (PCI) was proven to be beneficial over multivessel PCI in patients with multivessel disease.[4] In the third trial, the IABP-SHOCK II trial, the routine use of an intra-aortic balloon pump (IABP) had no impact on survival.[5] Since the publication of the latter trial and subsequent changes in guidelines, which resulted in a decreased usage of the IABP, the use of mechanical circulatory support (MCS) with Impella (a percutaneous microaxial left ventricular assist device [pLVAD]) and/or venoarterial extracorporeal membrane oxygenation (VA-ECMO) has been increasing rapidly, notwithstanding the lack of evidence for outcome improvement.[1,2,6] The ECMO-CS trial ($n = 122$), comparing upfront VA-ECMO versus initially conservative therapy in severe or rapidly deteriorating cardiogenic shock, showed no outcome improvements in favor of immediate implementation of VA-ECMO.[7] Additionally, the INCEPTION trial ($n = 160$) and the Prague OHCA trial ($n = 256$) demonstrated that extracorporeal cardiopulmonary resuscitation (eCPR) did not significantly improve survival compared to conventional CPR in the setting of out-of-hospital cardiac arrests (OHCA).[8,9] However, both trials were relatively small-sized and likely underpowered to find a difference in survival. Likewise, the small-sized IMPRESS in Severe Shock trial showed no beneficial effect of Impella over IABP on mortality after 30 days and also after 5 years of follow-up.[10,11] Also, the very recently published ECLS-SHOCK trial ($n = 420$) showed no improvement in 30-day mortality of VA-ECMO compared to medical treatment alone.[12]

Contrary to the lack of evidence substantiating outcome improvements, it is well-known that MCS is accompanied by various adverse events and high resource demands.[13,14] The comparison of adverse event rates in AMICS patients supported by an Impella and/or VA-ECMO has been described in several small retrospective studies and only one large retrospective cohort ($n = 6290$) from the National Inpatient Sample (NIS) database from the United States of America (USA) between 2015 and 2017.[15] All previously published studies enrolled patients for over 5 years or were published more than 5 years ago. Based on these studies, three meta-analyses have been published recently. All of them report significantly lower in-hospital mortality for patients with an Impella versus VA-ECMO. However, considering the included studies and the quickly evolving MCS landscape, these meta-analyses may not resemble the most current practice.[15–18]

In addition, these meta-analyses did not report on the length of stay and healthcare costs.

This nationwide large and contemporary, retrospective study of data collected for a short period aimed to give insight into the current use of Impella and/or VA-ECMO in AMICS patients. Moreover, this study aimed to give current insight into clinical outcomes, adverse events, and resource demands allied to the use of these devices.

Methods

Data source and cohort identification

We conducted a national retrospective cohort study using publically available data from 2020 and 2021 from the Institute for the Hospital Remuneration System GmbH (Institut für das Entgeltsystem im Krankenhaus GmbH, InEK). The InEK GmbH database is an International Classification of Diseases (ICD-10) code-based database, containing all in-hospital data of Germany. Because it concerns a publically available database, individual patient data are not provided. The database does provide incidences of diseases, diagnoses, and procedures of a specifically selected population, without specific timing or dates. Cohort identification was based on the ICD-10 codes for acute myocardial infarction (AMI) (I21.0–I21.9), cardiogenic shock (R.57.0), percutaneous coronary intervention (8–839.*), Impella (8–839.46) and VA-ECMO (8–852.3*) (*Graphical Abstract*). Additional details on cohort identification can be found in the online supplementary material. After dataset extraction, the investigators only categorized diagnoses into baseline characteristics and adverse events. The investigators had no involvement in the process of diagnosing and assigning medical codes. This was done by the attending medical team at the time of admission and the coding team.

Data extraction

Baseline characteristics including age, sex, relevant comorbidities, and details regarding the AMI were extracted, as well as relevant procedures and interventions such as mechanical ventilation, transfusion of blood and blood products, dialysis, and pulmonary artery pressure monitoring. Also, data on relevant adverse events and outcomes including haemorrhage, thromboembolic events, acute kidney and liver failure, and infections as well as the length of stay and discharge destinations were noted (see online supplementary material).

Statistical analysis

To ensure unpaired groups, the incidences of baseline characteristics, procedures, and outcomes in the Impella and VA-ECMO cohorts were calculated by subtracting the incidences of the Impella + VA-ECMO cohort from either the Impella cohort or the VA-ECMO cohort (see online supplementary material). The incidences for patients without a device were calculated by subtracting the sum of incidences in the three device cohorts from the incidences in the overall AMICS cohort, these results can be found in the online supplementary *Tables S1–S3* and *Figures S1 and S2*. In-hospital mortality and discharge destinations were also calculated for the cohorts excluding the OHCA patients. Univariate comparisons for categorical variables between the Impella and VA-ECMO cohorts were performed using the Pearson Chi-square test. Odds ratios (OR) for various outcomes were calculated and the 95% confidence intervals (CI) were defined. The following cohorts were compared: Impella cohort versus VA-ECMO cohort, device cohort (sum of the Impella, VA-ECMO and VA-ECMO + Impella cohorts) versus no device cohort and the VA-ECMO + Impella cohort versus the Impella cohort and the VA-ECMO cohort (*Tables 1* and *2* and online supplementary *Tables S1 and S2*). Statistical analyses were performed using R Software including the readxl and tidyverse package (version 4.2.1, R Foundation for statistical computing, Vienna, Australia).

Length of stay evaluation

The public InEK GmbH database reports the index-hospital length of stay using the mean and standard deviation. The pooled mean and standard deviation over 2020 and 2021 were calculated using weighted averages. The mean and standard deviation of the Impella and VA-ECMO cohort were derived from the mean and standard deviation of all Impella and VA-ECMO patients (including overlap) and the overlapping cohort (Impella + VA-ECMO). Similarly, the mean and standard deviation of the no device cohort derived from the mean and standard deviation of the total AMICS cohort and the device cohorts (online supplementary *Table S3*). A statistically significant difference between the index-hospital length of stay between the Impella and VA-ECMO cohorts was tested using a two-tailed *t*-test tool for summary statistics.

Cost calculation

In Germany, each patient is assigned a diagnosis-related group (DRG), with corresponding costs. On top of costings, some specific procedures are attributed with an additional fee. The total costs per cohort were calculated by summing the overall DRG costs and the overall additional charges. The overall in-hospital costs for the Impella and VA-ECMO cohorts were calculated by subtracting the overall in-hospital costs of the Impella + VA-ECMO cohort from both the Impella and VA-ECMO cohort, resulting in three separate cohorts. Average costs per patient and survivor were calculated by dividing the total in-hospital costs of a cohort by the number of patients or survivors in that cohort. All cost calculations were calculated in Excel 2016. As it concerns a publicly available database, the sporadic DRGs and procedures are not reported due to privacy concerns and could therefore not be included in the analysis. Hence, the costs are at least slightly underestimated (see online supplementary material for a more elaborate description of the costs and cost calculation).

Results

General

In 2020–2021, 256 112 cases of AMI in combination with a PCI have been registered in the German DRG system. Of these, 8% were complicated by cardiogenic shock ($n = 20\,399$). Of all AMICS cases, 20% received Impella and/or VA-ECMO support ($n = 4088$). Impella was used most often, namely in 13% ($n = 2700$) of all AMICS patients, VA-ECMO was used in 5% ($n = 959$) and 2% ($n = 429$) received haemodynamic support using both devices (*Figure 1*, *Graphical Abstract*).

Baseline and cardiogenic shock characteristics

The baseline characteristics of the patients are depicted in *Table 1*. Concerning sex, comorbidities, myocardial infarction type, and findings from coronary angiography, Impella

Table 1 Baseline characteristics of patients who received mechanical circulatory support with Impella and/or venoarterial extracorporeal membrane oxygenation for acute myocardial infarction-related cardiogenic shock

	Impella ($n = 2700$)	VA-ECMO ($n = 959$)	VA-ECMO + Impella ($n = 429$)	p-value[a,b]
Demographics, *n* (%)				
Age category, years				
<55	353 (13)	235 (25)	122 (28)	<0.001
55–64	629 (23)	322 (34)	159 (37)	<0.001
65–74	788 (29)	277 (29)	113 (26)	0.860
>75	930 (34)	125 (13)	35 (8)	<0.001
Male sex	2020 (75)	761 (79)	344 (80)	0.005
Comorbidities, *n* (%)				
Hypertension	1014 (38)	295 (31)	151 (35)	<0.001
Hypercholesterolaemia	843 (31)	264 (28)	120 (28)	0.032
Diabetes mellitus	838 (31)	232 (24)	75 (17)	<0.001
Peripheral arterial disease	296 (11)	126 (13)	16 (4)	0.070
Prior myocardial infarction	176 (7)	52 (5)	23 (5)	0.228
Chronic renal failure[c]	399 (15)	76 (8)	30 (7)	<0.001
Chronic lung disease[d]	126 (5)	32 (3)	8 (2)	0.082
At admission, *n* (%)				
OHCA	476 (18)	384 (40)	165 (38)	<0.001
Acidosis	1078 (40)	431 (45)	213 (50)	0.007
Acute respiratory failure	2258 (84)	790 (82)	399 (93)	0.372
Myocardial infarct type				
Non-STEMI	845 (31)	206 (21)	80 (19)	<0.001
STEMI anterior	1181 (44)	435 (45)	233 (54)	0.386
STEMI inferior	492 (18)	242 (25)	73 (17)	<0.001
STEMI not specified	163 (6)	70 (7)	39 (9)	0.169
MI not specified	19 (1)	6 (1)	4 (1)	0.801
Coronary angiography, *n* (%)				
Single vessel CAD	336 (12)	173 (18)	63 (15)	<0.001
Two-vessel CAD	570 (21)	200 (21)	95 (22)	0.867
Three-vessel CAD	1613 (60)	510 (53)	238 (55)	<0.001
Left main stenosis	670 (25)	208 (22)	95 (22)	0.052
Bypass graft stenosis	51 (2)	23 (2)	NA	0.336
Stent stenosis	166 (6)	69 (7)	36 (8)	0.256

CAD, coronary artery disease; MI, myocardial infarction; OHCA, out-of-hospital cardiac arrest; STEMI, ST-elevation myocardial infarction; VA-ECMO, venoarterial extracorporeal membrane oxygenation.
[a]Comparison Impella versus VA-ECMO.
[b]*P*-values corresponding with Impella versus VA-ECMO + Impella and VA-ECMO versus VA-ECMO + Impella can be found in online supplementary *Table S1*.
[c]Stage 3–5 (estimated glomerular filtration rate <60 ml/min/1.73 m^2).
[d]Chronic obstructive pulmonary disease stage I–IV.

and VA-ECMO patients were quite comparable. However, Impella-supported patients were older (34% vs. 13% >75 years, $p < 0.001$) and presented with an OHCA less often compared to VA-ECMO-supported patients (18% vs. 40%, $p < 0.001$).

Hospital stay

In addition to haemodynamic support, patients also received various other forms of organ support. Renal replacement therapy was required in 28% of the Impella-supported patients, compared with 44% of the VA-ECMO-supported patients (OR 2.04, 95% CI 1.75–2.38; $p < 0.001$). In patients who received a combination of Impella and VA-ECMO, this percentage was even higher, namely 63%. Red blood cell transfusions were given to 47% of the Impella-supported patients and 81% of the VA-ECMO-supported patients (OR 4.84, 95% CI 4.05–5.78; $p < 0.001$). Impella patients were also given platelet transfusions and fresh frozen plasma less often compared to VA-ECMO-supported patients (4% vs. 28%; OR 8.63, 95% CI 6.83–10.91, $p < 0.001$; and 14% vs. 46%, OR 5.49, 95% CI 4.64–6.50, $p < 0.001$, respectively) (*Table 2*). The adverse event rates in these cohorts are depicted in *Figure 2*, showing that both haemorrhagic and thromboembolic events occurred less often in patients who received Impella support compared to patients who received VA-ECMO support. Infections, systemic inflammatory response syndrome, and septic shock were also observed less often in the Impella than in the VA-ECMO population. Haemodynamic support with both devices was associated with even higher rates of adverse events compared with

Table 2 Clinical course details on interventions, adverse events and outcomes

	Impella ($n = 2700$)	VA-ECMO ($n = 959$)	VA-ECMO + Impella ($n = 429$)	OR (95% CI)[a]	*p*-value[b]
Diagnostic procedures, *n* (%)					
Pulmonary artery pressure monitoring	301 (11)	105 (11)	61 (14)	0.98 (0.77–1.24)	0.866
Organ support, *n* (%)					
Cardiopulmonary resuscitation	1388 (51)	620 (65)	310 (72)	1.73 (1.49–2.01)	<0.001
Mechanical ventilation[c]	2234 (83)	706 (74)	374 (87)	0.58 (0.49–0.69)	<0.001
Renal replacement therapy[d]	757 (28)	425 (44)	270 (63)	2.04 (1.75–2.38)	<0.001
Transfusions, *n* (%)					
Packed red blood cells	1265 (47)	777 (81)	361 (84)	4.84 (4.05–5.78)	<0.001
Platelets[e]	115 (4)	266 (28)	166 (39)	8.63 (6.83–10.91)	<0.001
Fresh frozen plasma	365 (14)	443 (46)	278 (65)	5.49 (4.64–6.50)	<0.001
Adverse events, *n* (%)					
Cerebrovascular accident	120 (4)	105 (11)	51 (12)	2.64 (2.01–3.47)	<0.001
Ischaemic	91 (3)	75 (8)	49 (11)	2.43 (1.77–3.33)	<0.001
Haemorrhagic	29 (1)	30 (3)	2 (0)	2.97 (1.77–4.97)	<0.001
Thromboembolism extremity	122 (5)	80 (8)	47 (11)	1.92 (1.43–2.57)	<0.001
Upper airway bleeding[f]	254 (9)	173 (18)	121 (28)	2.12 (1.72–2.61)	<0.001
Gastro-intestinal bleeding	160 (6)	72 (8)	40 (9)	1.29 (0.97–1.72)	0.084
Bleeding after surgical intervention	567 (21)	243 (25)	146 (34)	1.28 (1.08–1.52)	0.005
Acute haemorrhagic anaemia	964 (36)	649 (68)	341 (79)	3.77 (3.22–4.41)	<0.001
Acute kidney failure	1183 (44)	510 (53)	282 (66)	1.46 (1.26–1.69)	<0.001
(Sub)acute liver failure	178 (7)	111 (12)	75 (17)	1.85 (1.44–2.37)	<0.001
Infections					
SIRS	557 (21)	241 (25)	164 (38)	1.29 (1.08–1.53)	0.004
Sepsis	394 (15)	184 (19)	103 (24)	1.39 (1.15–1.69)	0.001
Septic shock	149 (6)	76 (8)	52 (12)	1.47 (1.10–1.96)	0.008
Delirium	429 (16)	130 (14)	54 (13)	0.83 (0.67–1.03)	0.085
Outcomes, mean ± SD/*n* (%)					
Length of stay	11.4 ± 16.4	13.8 ± 19.2	17.6 ± 21.6	NA	<0.001
Hospital mortality	1640 (61)	642 (67)	309 (72)	1.31 (1.12–1.53)	0.001
Discharged to other care facility	507 (19)	211 (22)	85 (20)	1.22 (1.02–1.46)	0.031
Discharged home	553 (20)	106 (11)	35 (8)	0.48 (0.38–0.60)	<0.001

CI, confidence interval; OR, odds ratio; SD, standard deviation; SIRS, systemic inflammatory response syndrome; VA-ECMO, venoarterial extracorporeal membrane oxygenation.
[a]Odds for Impella versus VA-ECMO.
[b]Comparison Impella versus VA-ECMO. The OR for Impella versus VA-ECMO + Impella and VA-ECMO versus VA-ECMO + Impella can be found in online supplementary *Table S2*.
[c]Sum of endotracheal intubation, mask ventilation, and high-flow nasal canula.
[d]Continuous venovenous haemofiltration, continuous venovenous haemodialysis and continuous venovenous haemodiafiltration.
[e]Apheresis-retrieved platelets not included.
[f]Nose, throat, or airway bleed.

Impella or VA-ECMO alone (*Figure 2*, *Graphical Abstract*, and online supplementary *Table S2*).

Mortality and discharge destination

In this AMI cohort ($n = 256\,112$), in-hospital mortality was 7%. An almost seven-fold increase to 52% is seen in AMICS patients ($n = 20\,399$). For the Impella and VA-ECMO cohorts, in-hospital mortality was even higher (61% and 67%, respectively; $p = 0.001$). The in-hospital mortality in the VA-ECMO + Impella cohort was 72%. Whereas 85% of the AMI patients were directly discharged home after their primary hospitalization, this was only 31% in AMICS patients. In the Impella cohort, 20% were discharged home directly, in the VA-ECMO cohort this was only 11% ($p < 0.001$). Admission to another care facility after the initial treatment was needed in 19% of the patients from the Impella cohort and 22% of the patients from the VA-ECMO cohort ($p = 0.031$).

In the AMICS cohort excluding OHCA patients, in-hospital mortality was 51%. For the Impella cohort, the VA-ECMO cohort, and the cohort of patients supported by both devices, in-hospital mortality was 59%, 67%, and 70%, respectively, when excluding OHCA patients (*Figure 3*).

Length of stay

The average hospital length of stay in the AMI cohort was 6.7 ± 6.8 days, while for the AMICS cohort, this was

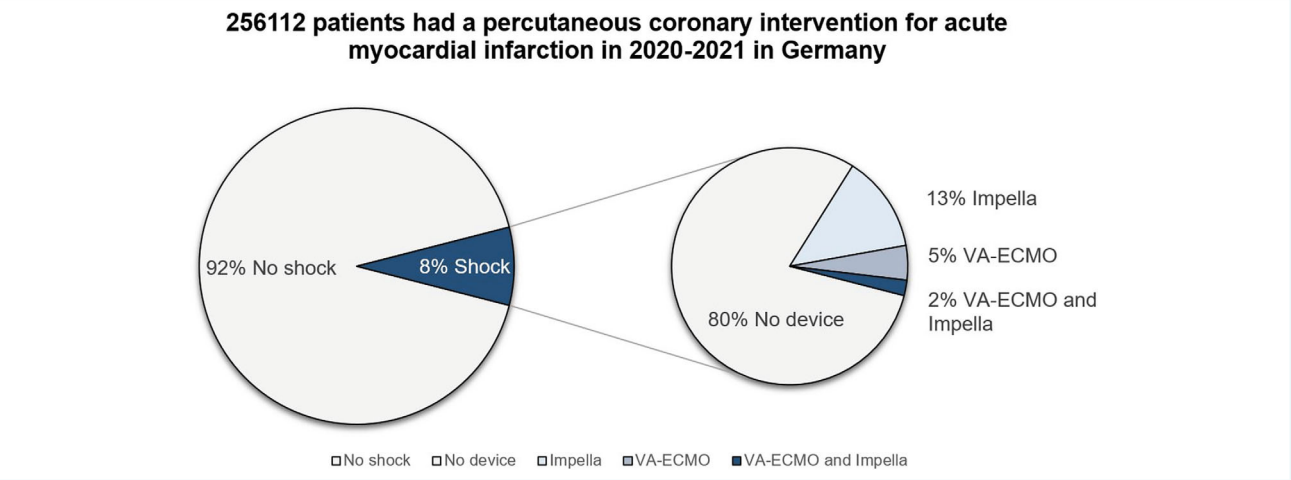


Figure 1 Incidence and prevalence of acute myocardial infarction-related cardiogenic shock and the use of Impella and/or venoarterial extracorporeal membrane oxygenation (VA-ECMO) in the study population.

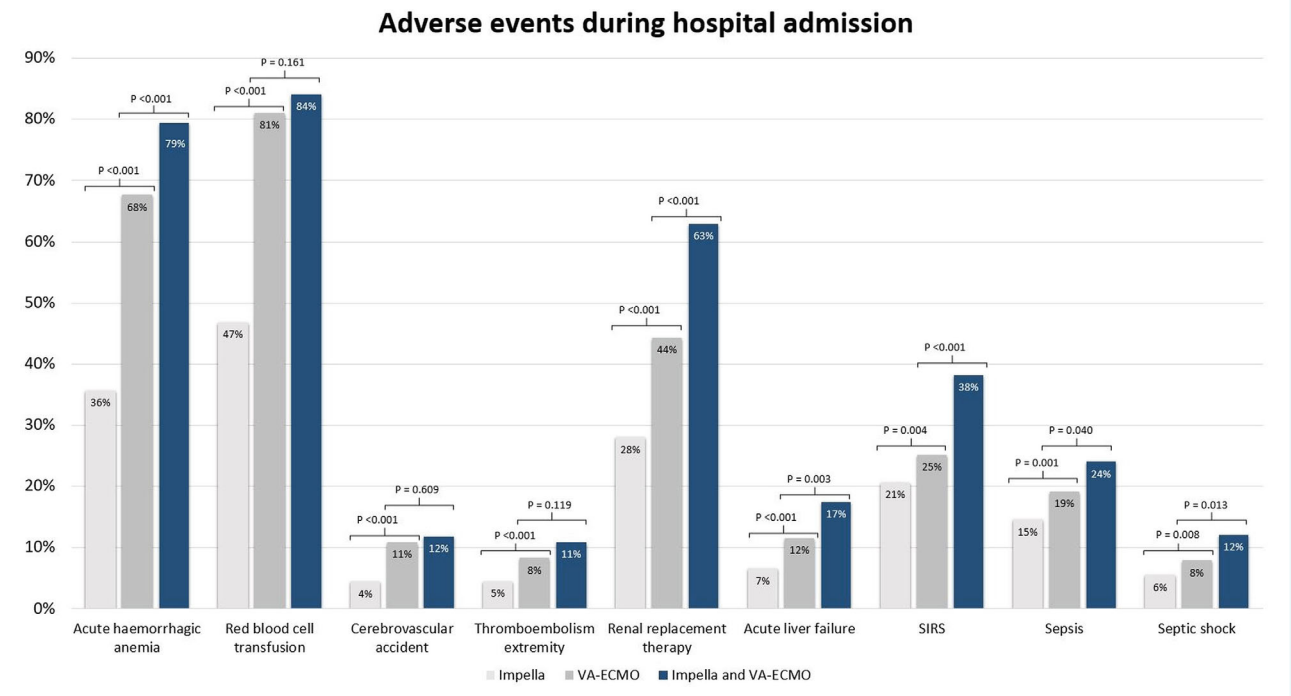


Figure 2 In-hospital adverse events in patients supported by Impella, venoarterial extracorporeal membrane oxygenation (VA-ECMO), or Impella + VA-ECMO. For each adverse event, the three bars represent (from left to right): the Impella cohort, the VA-ECMO cohort, and the Impella + VA-ECMO cohort. SIRS, systemic inflammatory response syndrome.

10.5 ± 13.5 days (online supplementary *Table S3*). The average index hospital length of stay of Impella-supported patients was shorter than that of VA-ECMO-supported patients (11.4 ± 16.4 days vs. 13.8 ± 19.2 days; $p < 0.001$). The index hospital length of stay of patients receiving both devices was 17.6 ± 21.6 days. The significant differences in length of stay between the Impella and VA-ECMO groups persisted when analysing only the surviving and discharged patients (online supplementary *Table S3*).

Costs

The average index in-hospital costs for an Impella-supported patient were €36 655.18, whereas the average index in-hospital

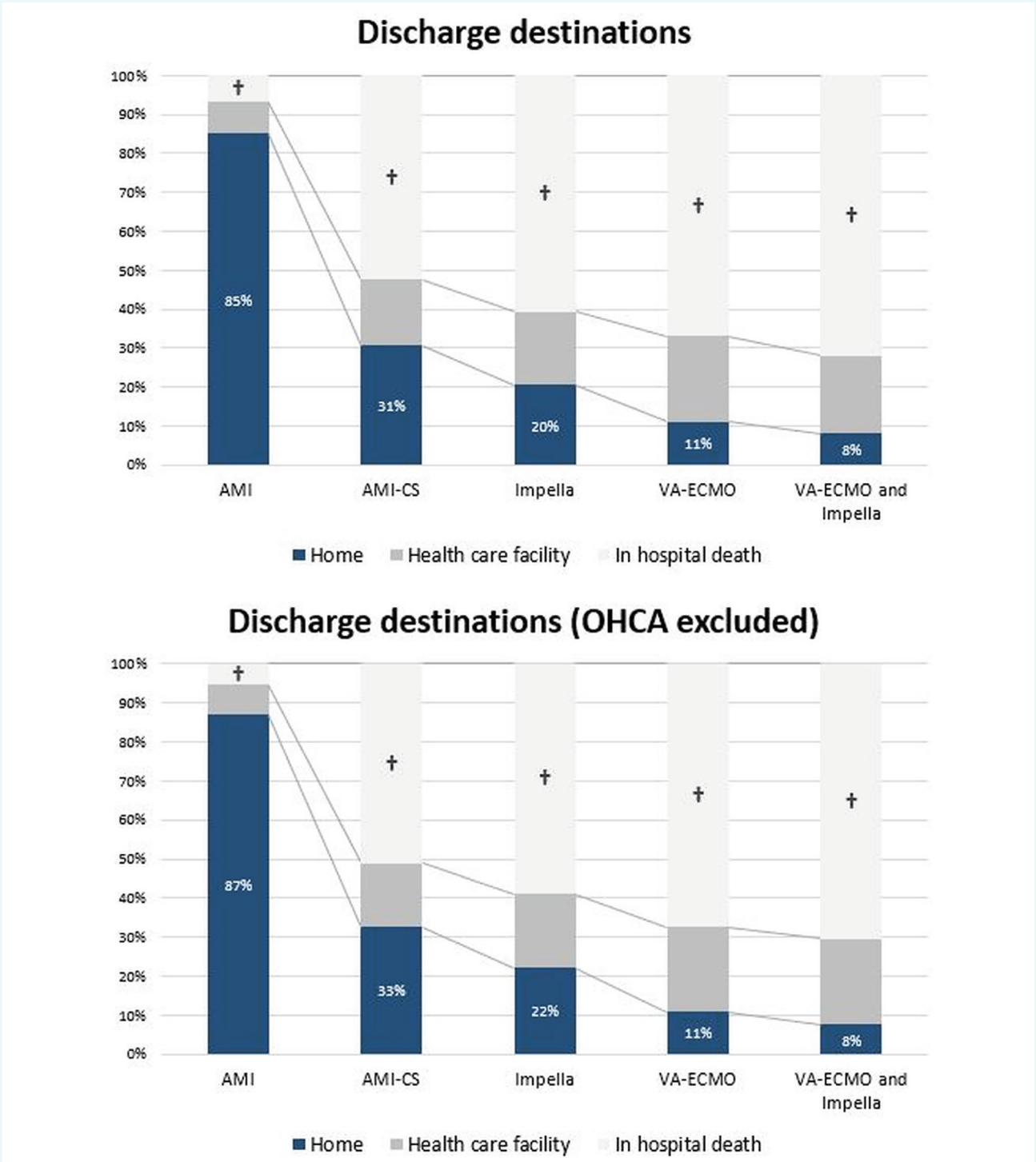


Figure 3 Discharge destinations per patient population. This figure illustrates the distribution of discharge destinations for five patient cohorts (from left to right): patients with acute myocardial infarction (AMI), patients with acute myocardial infarction-related cardiogenic shock (AMICS), patients with AMICS who received Impella support, patients with AMICS who received venoarterial extracorporeal membrane oxygenation (VA-ECMO) support, and patients with AMICS who received Impella + VA-ECMO support. The top figure represents all patients, while the one below excludes patients who experienced an out-of-hospital cardiac arrest (OHCA). The columns indicate the percentage of patients who were discharged home, transferred to a health care facility, or who died before discharge, arranged from bottom to top.

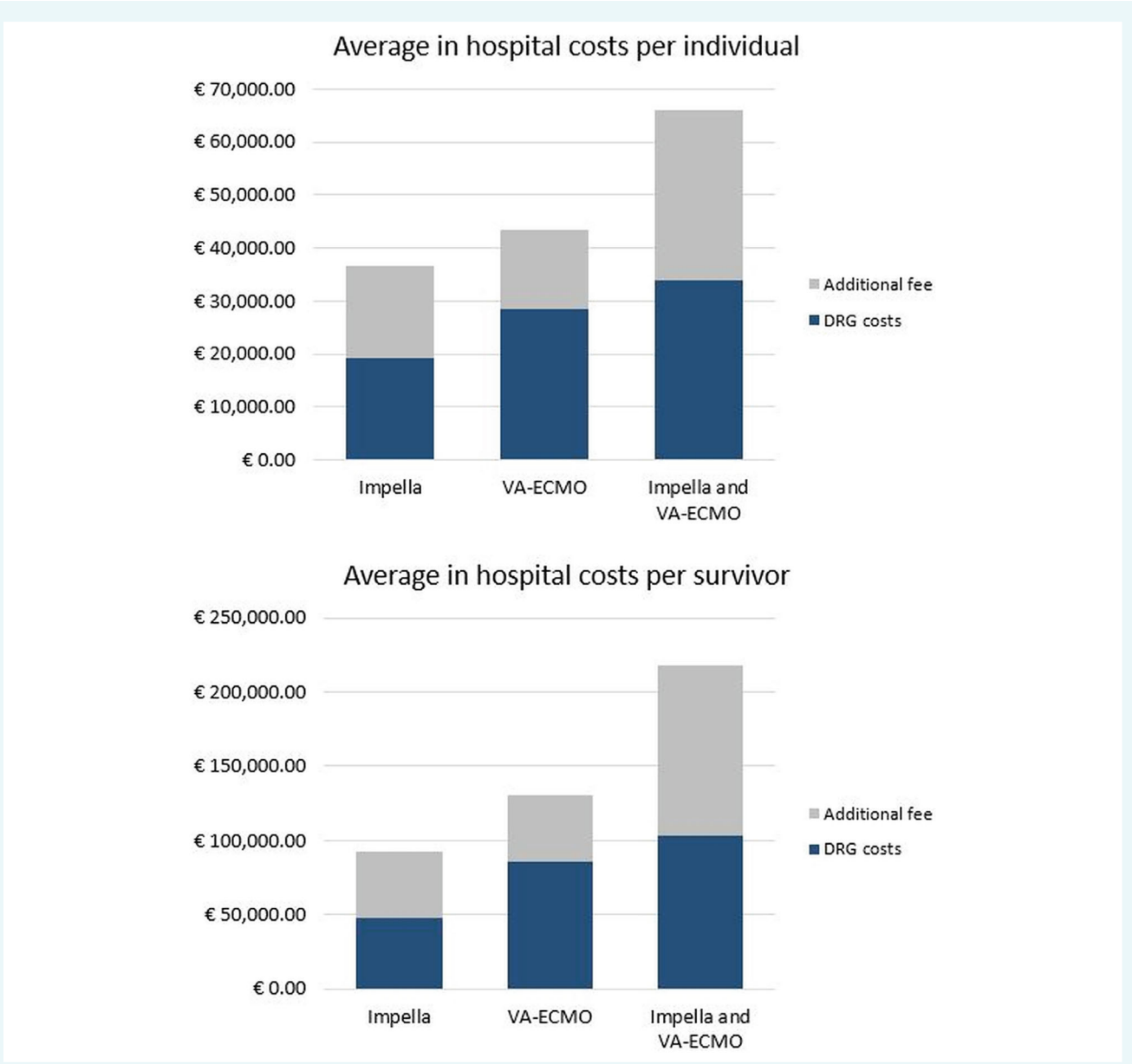


Figure 4 Average costs of the index admission. This figure shows the average in-hospital costs per individual (top) and per survivor (bottom) of three cohorts (from left to right): patients who received Impella support, patients who received venoarterial extracorporeal membrane oxygenation (VA-ECMO) support, and patients who received Impella + VA-ECMO support. Each column represents the diagnosis-related group (DRG) costs plus the additional fees for that cohort.

costs for a VA-ECMO-supported patient were €43 322.53. The index in-hospital costs for a patient supported by both devices were €66 150.86 on average. The average index in-hospital costs per AMICS survivor supported by an Impella, VA-ECMO, or a combination of devices were €93 060.85, €130 703.27, and €218 061.87, respectively (*Figure 4*, *Graphical Abstract*).

Discussion

Our study included 4088 consecutive cardiogenic shock patients and is the largest European and second largest worldwide cohort of patients supported by Impella and/or VA-ECMO. Additionally, by describing data from 2020 and 2021 only, this study provides a unique present-day insight into the rapidly evolving MCS landscape.

In this study, mortality in AMI patients was 7%. An almost seven-fold increase to 52% was seen in patients suffering from AMICS (*Figure 3*). Impella and/or VA-ECMO were deployed in 20% of all AMICS cases. In-hospital mortality in these cohorts was even higher (61% and 67% for the Impella and VA-ECMO cohort, respectively). In-hospital mortality rates are slightly higher compared to previous studies. This might be due to the unselected, real-world, national, registry-based character of this study.[17] Like

our study, higher in-hospital mortality in VA-ECMO patients compared to Impella patients has been reported previously.[16–18] However, as underscored by the recent publication of Almarzooq *et al.*,[19] the differences in clinical outcomes between Impella and VA-ECMO in this observational data analysis must be interpreted in the setting of possible unmeasured and unadjusted confounders in patient and institutional characteristics. For instance due to physicians' preferences and device availability, but also depending on cardiogenic shock severity (according to the SCAI classification), risk modifiers, and cardiogenic shock phenotype.[8,19–21] Nevertheless, the Impella and VA-ECMO patients in our study were quite comparable with regard to comorbidities and cardiogenic shock aetiology, though Impella patients were older and presented less frequently after an OHCA. In contrast to previous literature,[21–23] in-hospital mortality rates in our cohort were comparable when OHCA patients were excluded from the analysis (*Figure 3*). Although contra-intuitive, this finding is underscored by some previous studies.[12,24,25] Helgestad *et al.*[26] even reported lower in-hospital mortality in AMICS patients with OHCA than in those without OHCA. Possibly, the absence of difference in mortality in patients with and without an OHCA can be explained by a possible very high shock severity (SCAI E) in our population.[27] Also, our study population differs from the general AMICS population by exclusion bias. Supposedly, patients with severe neurological damage after OHCA did not receive Impella or VA-ECMO support. Another possible explicatory confounder could be the symptom-to-balloon time, which might have been shorter in the OHCA patients.[9,28] Nonetheless, the high mortality rates and the significant proportion of patients experiencing OHCA or undergoing CPR, raise the question whether identification of patients that might benefit from Impella and/or VA-ECMO could be improved.

Compared to VA-ECMO-supported patients, Impella-supported patients experienced fewer ischaemic and haemorrhagic adverse events, such as acute haemorrhagic anaemia, cerebrovascular accidents, and thromboembolisms of the extremities. Also, acute kidney injury, acute or subacute liver failure, and systemic inflammatory response syndromes were less frequent in the Impella versus the VA-ECMO cohort. Consequently, Impella patients less often received renal replacement therapy and transfusions than VA-ECMO-supported patients. These findings are in accordance with previous literature, such as the meta-analysis from Ahmad *et al.*, reporting significantly lower incidences of stroke, access-site bleeding, major bleeding, and limb ischaemia in Impella patients.[15,16] The findings are of importance as the literature shows that in addition to patient characteristics, adverse events are also associated with the device characteristics, such as the required arteriotomy size. Moreover, vascular complications are associated with higher mortality rates and in-hospital costs.[29]

In our study, Impella patients were directly discharged home more often and had a shorter length of stay compared to VA-ECMO patients. These findings have also been reported previously.[14,15,30,31] Additionally, the associated in-hospital costs were on average lower for Impella patients compared to VA-ECMO patients, which is also in accordance with previous literature.[14,31,32] These high costs are partly attributable to the high adverse event rates; for instance, blood and blood product transfusions and renal replacement therapy are additionally charged. However, the cost differences might also be (partly) explained by differences between the groups in the underlying patient characteristics and/or the traits of the index hospital. We hypothesize that the long length of stay and the low number of patients that are directly discharged home, may also (at least partly) be attributable to the high adverse event rates. Namely, some adverse events such as a stroke might have disabling consequences, resulting in an extended length of stay or even another discharge destination (e.g. a rehabilitation centre instead of home). In addition, a prolonged hospital stay can also be a risk factor for hospital-acquired infections.[33]

In summary, our study shows that VA-ECMO therapy is associated with a higher degree of invasiveness and adverse events when compared with Impella. Prospective randomized trials comparing Impella and/or VA-ECMO are unreservedly needed to define the best treatment strategy for patients suffering from AMICS. The ANCHOR trial (NCT04184635) which evaluates VA-ECMO in AMICS, is recruiting. Of note, the very recently published ECLS-SHOCK trial ($n = 420$) showed no improvement on 30-day mortality of VA-ECMO compared to medical treatment alone.[12] The DanGer Shock trial (NCT01633502) compares Impella versus no Impella in AMICS patients and is well underway.[34] The effects of Impella versus no Impella will also be evaluated by the ULYSS trial (NCT05366452) and the RECOVER IV trial (NCT05506449).[35]

In this current era, in which evidence of beneficial effects is lacking and the results of the upcoming trials are yet unknown, the results of our study support a careful and individualized assessment of the potential benefits, risks, and resource demands before device initiation.

Limitations

This study has some inherent limitations. First, treatment selection bias can be assumed. Second, although these data represent a very complete, contemporary, and unselected population, generalizability might be comprised due to the single-nation nature of this study. Part of these data is however in line with previously published data from other nations and the contemporary and unselected nature of this study is of great value for clinical applicability in such a rapidly developing landscape. Third, case selection and data extraction were based on ICD-10 coding, with a risk of underestimating the prevalence of diagnoses and procedures. Also, confirmation of diagnoses and adverse events were not submitted to adjudication, haemodynamic data were not available and rare diagnoses and procedures (less than four per cohort) were not available to ensure privacy. Moreover, differentiation between iterative use, (de)escalation and unloading in the Impella + VA-ECMO group was impossible due to the lack of data on timing, causing a heterogeneous cohort. Likewise, eCPR patients could not be excluded due to the lack of granular patient data. However, the sensitivity analysis with and without OHCA did not importantly change the outcomes. Last but importantly, the reported costs should be interpreted as indicative and minimal costs. The InEK GmbH database does not provide the DRG codes and procedures that occur less than four times per cohort, to prevent public availability of traceable information. Therefore, these DRGs and procedures are omitted from

the calculation, very likely resulting in an underestimation of the total costs.

Conclusion

This is the most current and largest European AMICS cohort that described outcomes, adverse events, and resource demands based on claims data in AMICS patients with Impella and/or VA-ECMO support. Overall, mortality, adverse event rates and resource consumption were high. Compared to patients receiving Impella support, those receiving VA-ECMO support have higher in-hospital mortality, higher adverse event rates, higher index in-hospital costs, and a longer length of stay. However, these results should be interpreted in the presence of confounders. Given the current lack of beneficial evidence, our study reinforces the urgent need for prospectively established, high-quality evidence to guide clinical decision-making.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Conflict of interest: none declared.

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