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Clinical paper

A nationwide overview of 1-year mortality in cardiac arrest patients admitted to intensive care units in the Netherlands between 2010 and 2016

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Abstract

Aim: Worldwide, cardiac arrest (CA) remains a major cause of death. Most post-CA patients are admitted to the intensive care unit (ICU). The aim of this study is to describe mortality rates and possible changes in mortality rates in patients with CA admitted to the ICU in the Netherlands between 2010 and 2016.

Methods: In this study, we included all adult CA patients registered in the National Intensive Care Evaluation (NICE) registry who were admitted to ICUs in the Netherlands between 2010 and 2016. The primary outcome was 1-year mortality which was analysed by Cox regression. The secondary outcomes were ICU mortality and hospital mortality. Hospital mortality was analysed by binary logistic regression analysis. Patients were stratified by whether they experienced in-hospital cardiac arrest (IHCA) or out-of-hospital cardiac arrest (OHCA). Finally, the outcome over calendar time was assessed for both groups.

Results: We included 26,056 CA patients: 10,618 (40.8%) IHCA patients and 14,482 (55.6%) OHCA patients. The 1-year mortality rate was 57.5%: 59% for IHCA and 56.4% for OHCA, $p < 0.01$. This mortality rate remained stable between 2010 and 2016 for IHCA ($p = 0.31$) and declined for OHCA patients ($p = 0.01$). The hospital mortality rate was 50.3%: 50.5% for IHCA and 50.2% for OHCA, $p = 0.66$. This mortality rate remained stable between 2010–2016 for IHCA ($p = 0.21$) and decreased for OHCA patients ($p < 0.01$). An additional analysis with calendar year as a continuous variable showed a mortality decline of 1.56% per calendar year for 1-year mortality.

Conclusion: This nationwide registry cohort study reported a 57.5% 1-year mortality rate for CA patients admitted to the ICU between 2010 and 2016. We reported a decline in 1-year mortality for OHCA patients in these years.

Keywords: Cardiac arrest, Heart arrest, Intensive care units, ICU, Mortality, 1-year mortality

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Introduction

Sudden cardiac arrest (CA) remains a major cause of death worldwide (World Health Organization, WHO). In Europe, approximately 375,000 adults suffer annually from CA.[1,2] Mortality rates in patients admitted to the hospital due to CA have been reported to be between 58−61%.[3−5] If these CA patients are admitted to the intensive care unit (ICU), mortality rates vary between 53−66 %.[6−8] Of all surviving CA patients 25−75% have poor neurological outcomes and a large portion suffers from long-term side effects,[9−11] such as post-traumatic stress disorder (PTSD),[12,13] impaired quality of life,[14] and lower physical and mental functioning.[15]

Recent studies have examined characteristics that are associated with the mortality of CA patients. More specifically, these studies focused on differences in patient characteristics,[16,17] the location of the CA (in- or out-of-hospital),[18−20] and hospital characteristics.[4,6] Generally, these studies provide data on all CA patients, including patients who died before hospital admission. However, there is no recent study showing a nationwide overview of CA patients admitted to the ICU.

In the Netherlands, 4.6% of all patients admitted to the ICU have CA as primary diagnosis.[21] The outcomes of these patients are highly interesting because they survived the first episode of CA (namely, cardiopulmonary resuscitation). However, they are prone to haemodynamic deterioration/instability, ischaemia/reperfusion injury, and neurological damage. In addition, large-scale data on the outcomes in this patient group are lacking. This information would be particularly relevant given recent changes in guidelines and treatments, such as targeted temperature management (TTM).[22] Therefore, we analysed a large national database to investigate the mortality rates in CA patients (both IHCA and OHCA) admitted to ICUs in the Netherlands.

Methods

Patient data

In this study, we used patient data included in the National Intensive Care Evaluation (NICE) registry.[21] This is a national quality registry in the Netherlands for ICU care, in which demographics, physiological and diagnostic data, patient outcomes, and ICU characteristics are registered. The data are prospectively collected with a primary focus on monitoring the quality of care in the ICU. We retrospectively analysed the data from approximately 85% of ICU departments in 2010 to 100% of ICU departments in 2016 in the Netherlands.[21,23]

We included all adult CA patients (≥18 years) who were admitted to the participating ICUs from 2010 to 2016. This period was selected because starting in 2010, we were able to determine 1-year mortality.[21,23] The Scientific Board of the NICE Foundation (number 2018-01) and the Medical Ethics Committee of the Erasmus MC, Rotterdam, the Netherlands (number MEC-2018-1228) approved this study and the need for informed consent was waived.

Characteristics and clinical outcomes

We included patient characteristics (i.e., sex, age, body mass index (BMI), and history (e.g., renal insufficiency/dialysis, chronic obstructive pulmonary disease (COPD)/chronic respiratory insufficiency, cardiovascular insufficiency, liver cirrhosis, (haematologic) malignancy, and immunologic insufficiency)), admission characteristics (i.e., Acute Physiology and Chronic Health Evaluation (APACHE IV) score, estimated mortality rate and diagnoses within 24 h of ICU admission (e.g., acute kidney injury (AKI), the use of mechanical ventilation, infection, the administration of thrombolytic therapy, vasoactive medication use, and academic/non-academic hospital), and clinical outcomes (length of stay, ICU mortality, hospital mortality, and 1-year mortality). Supplementary Material Table A shows the definitions of these variables.

First, we included all patients (henceforth referred to as CA patients) registered with an admission diagnosis of CA or cardiopulmonary resuscitation (CPR). Next, we stratified the characteristics and clinical outcomes for IHCA and OHCA patients. However, IHCA and OHCA were not encoded in the NICE registry. Therefore, we defined IHCA as an admission diagnosis of CA or CPR, with admission origin within the hospital, excluding the emergency department (ED). OHCA was defined as an admission diagnosis of CA or CPR, with an admission origin in the ED or home. Hospital and 1-year mortality rates were calculated, and hazard ratios (HRs) per year were assessed relative to the year 2010. We determined the 1-year mortality by using an administrative claims database that is linked to the NICE registry (i.e., Vektis data).[23,24]

Statistical analysis

All characteristics and clinical outcomes were described as counts (%) and medians (interquartile range, IQR), as appropriate. The data are shown for the total sample and were stratified by IHCA and OHCA. Patients with unknown locations of CA were excluded from the stratified analyses. To test for differences between IHCA and OHCA patients, we used Chi-square and Wilcoxon tests for categorical and continuous variables, respectively.

The primary outcome was 1-year mortality. We examined the mortality trend over time using a Cox proportional hazard model with calendar years from 2010 to 2016 as an independent variable. For each calendar year, a dummy variable was included. The variables we included in each of the regression models are stated in the Supplementary Material Appendix 1. We built these regression models in two ways: (1) univariable analysis and (2) multivariable analysis adjusting for demographic and clinical characteristics and including a random intercept for hospital. This was done to take the correlation between patients from the same hospital into account. To check whether the selection of different hospitals across the calendar years might have influenced the results, we performed a sensitivity analysis restricted to hospitals that registered their patients in each calendar year of the study period (2010−2016). We present the hazard ratios (HR) and 95% Confidence Intervals (95% CI) of model (2), as this was the best possible representation of all the available data. The adjusted effect of calendar year as a categorical variable on the hazard of death was tested by means of a post-estimation Wald test with number of degrees of freedom equal to the number of calendar years minus 1 (for the reference category = 2010). In this test, calendar year was included as categorical variable without assuming a linear trend. As an additional analysis, we performed Cox proportional hazards regression, including calendar year as a continuous variable for the different outcomes. These analyses enabled us to estimate the average change in mortality rates per year over time. All models were analysed for IHCA and OHCA separately. IHCA and OHCA were not compared in these analyses because of the non-registered characteristics relevant to CA.

Our secondary outcomes were ICU mortality and hospital mortality. For ICU mortality, we only present a percentage to make a rough comparison with hospital mortality. For hospital mortality, we analysed the data using a binary logistic regression model and presented the Odd Ratios (ORs) and 95% CIs. All analyses were performed using R-studio. A p-value < 0.05 was considered statistically significant.

Results

Between 2010 and 2016, a total of 567,856 patients were included in the NICE registry, and 26,056 (4.6%) of those patients were admitted due to CA: 10,618 (40.8%) IHCA patients and 14,482 (55.6%) OHCA patients. Data from 956 (3.6%) patients were excluded from the comparison of OHCA versus IHCA due to an unknown location of the CA.

Descriptive statistics

Table 1 presents the patient characteristics of all CA patients and then those of the patients stratified into the IHCA and OHCA groups. The majority of the CA patients were male, with an average age of 67 years at the time of the arrest. IHCA patients were older and had overall more comorbidities than OHCA patients. Table 2 presents the admission characteristics. The median APACHE IV estimated mortality probability was 0.75. The majority of patients had a Glasgow coma scale (GCS) at admission of $\leq$5 (61.7%). At admission, 87.1% of the patients were mechanically ventilated. Table 3 presents the clinical outcomes. The median length of ICU stay was 64 h (IQR 21-134) and the median hospital length of stay was 6 days (IQR 2-15).

Primary outcome: 1-year mortality

Within one year after ICU admission, 14,974 (57.5%) CA patients died. This 1-year mortality was significantly higher in IHCA patients (59.0%) versus OHCA patients (56.4%, p < 0.01). In Supplementary Material Fig. A, we present the Kaplan–Meier curve for 1-year mortality for IHCA and OHCA patients. Fig. 1 presents the analysis of model (2), as described in the methods section, of 1-year mortality for IHCA and OHCA patients separately. In IHCA patients no significant differences over time were observed. In OHCA patients a significant decrease in 1-year mortality between 2010 and 2016 was observed (all p < 0.02). The sensitivity analyses restricting to hospitals that recruited patients the full study period gave similar results.

Secondary outcomes: ICU mortality, hospital mortality, and additional analyses

Of the total sample, 11,681 (44.8%) CA patients died in the ICU. The ICU mortality rates were slightly lower for IHCA than for OHCA patients (44.2% versus 45.4%, respectively, p = 0.05). During their hospital admission, 13,072 (50.3%) CA patients died. This hospital mortality rate was comparable in IHCA and OHCA patients (50.5% versus 50.2%, respectively, p = 0.66).

For hospital mortality, there was no significant trend in IHCA patients over time (Wald test (df) 8.39 (6), p = 0.21). However, the analysis for hospital mortality in OHCA patients with calendar year as a categorised variable showed significant differences between the calendar years Wald test (df) 22.78 (6), p < 0.01). Inspecting the Odds Ratios we found a decreasing trend, as shown in Fig. 2.

Next, the results of the additional analysis with calendar year as a continuous variable showed no significant trend in 1-year mortality over time for IHCA patients (HR 0.99, 95% CI 0.98-1.00, p = 0.13). Furthermore, it confirmed the observed decline in 1-year mortality over time for OHCA patients (HR 0.98, 95% CI 0.97-1.00, p < 0.01). This HR shows a reduction in 1-year mortality of 1.56% per year over the study period.

As we found a decreasing trend in 1-year mortality for OHCA patients, we decided to perform an additional Cox regression using left truncation at the time of hospital discharge (i.e., only selecting the hospital survivors), see Supplementary Material Fig. B. This shows that a significant trend over time remains present (p < 0.01).

Discussion

This is the first large nationwide study on 1-year mortality rates of CA patients admitted to the ICU, and it was performed in the Netherlands between 2010 and 2016. The secondary outcomes we described were ICU mortality and hospital mortality. Overall, we found reasonable mortality rates and a significant decrease in 1-year mortality of OHCA patients between 2010 and 2016.

Table 1 – Patient characteristics.

	Total sample[a]	IHCA	OHCA	p-value
Patients 2010–2016	26,056	10,618	14,482	
Age (IQR)	67 (57–76)	69 (59–77)	66 (55–75)	<0.01
Gender, male (%)	17,320 (66.5)	6731 (63.4)	9967 (68.8)	<0.01
BMI (IQR)	25.7 (23.4–28.7)	25.7 (23.4–28.9)	25.7 (23.4–28.4)	0.99
BMI missing (%)		711 (6.6)	985 (6.8)	
History (N = 26,056)				
Cardiovascular insufficiency (%)	2291 (8.8)	1160 (10.9)	1030 (7.1)	<0.01
COPD /respiratory insufficiency (%)	4070 (15.6)	1894 (17.8)	2042 (14.1)	<0.01
Renal insufficiency (%)	1802 (6.9)	976 (9.2)	765 (5.3)	<0.01
Liver cirrhosis (%)	273 (1)	138 (1.3)	125 (0.9)	0.01
(Hematologic) malignancy (%)	1092 (4.2)	692 (6.5)	374 (2.6)	<0.01
Immunodeficiency(%)	1316 (5.1)	779 (7.3)	500 (3.5)	<0.01

[a] In 956 patients, it was unknown if the cardiac arrest occurred in- or outside the hospital; these patients were excluded from the analyses.

Table 2 – Admission characteristics in CA patients admitted to the ICU between 2010–2016.

	Total sample[a]	IHCA	OHCA	p-value
APACHE IV estimated mortality rate (IQR)	0.75 (0.45–0.89)	0.71 (0.32–0.90)	0.77 (0.54–0.88)	<0.01
Admission type				<0.01
Medical	23,156 (88.9)	7968 (75)	14,291 (98.7)	
Urgent surgical	1682 (6.5)	1517 (14.3)	122 (0.8)	
Elective surgical	1103 (4.2)	1088 (10.2)	6 (<1)	
Diagnosis on admission				
GCS ≤ 5 (%)	16,066 (61.7)	5333 (50.2)	10,167 (70.2)	<0.01
GCS 6–14 (%)	4057 (15.6)	1736 (16.3)	2148 (14.8)	
GCS 15 (%)	5391 (20.7)	3327 (31.3)	1851 (12.8)	
GCS missing (%)		222 (2.1)	316 (2.2)	
Dysrhythmia (%)	13,343 (51.2)	5138 (48.4)	7676 (53)	<0.01
Mechanical ventilation (%)	22,701 (87.1)	8696 (81.9)	13,189 (91.1)	<0.01
CVA (%)	1053 (4.1)	455 (4.3)	558 (3.9)	0.10
Intracranial mass (%)	708 (2.7)	264 (2.5)	421 (2.9)	0.04
Gastro intestinal bleeding (%)	480 (1.8)	277 (2.6)	189 (1.3)	<0.01
Diabetes (%)	4438 (17)	2045 (19.3)	2221 (15.3)	<0.01
Diagnosis at 24 h of ICU admission				
GCS ≤ 5 (%)	13,541 (52)	4615 (43.5)	8420 (58.1)	<0.01
GCS 6–14 (%)	4198 (16.1)	1621 (15.3)	2407 (16.6)	
GCS 15 (%)	7664 (29.4)	4095 (38.6)	3312 (22.9)	
AKI (%)	4617 (17.7)	2263 (21.3)	2188 (15.1)	<0.01
Mechanical ventilation (%)	23,666 (90.8)	9229 (86.9)	13,592 (93.9)	<0.01
Infection (%)	2768 (10.6)	1641 (15.5)	1062 (7.3)	<0.01
Vasoactive medication (%)	18,962 (72.8)	7640 (72)	10,652 (73.6)	<0.01
Thrombolytic therapy (%)	1354 (5.2)	560 (5.3)	756 (5.2)	0.87
Academic hospital (%)	7956 (23.9)	3102 (22.2)	4656 (26.1)	<0.01

[a] In 956 patients, it was unknown if the cardiac arrest occurred in- or outside the hospital; these patients were excluded from the analyses.

Table 3 – Clinical outcomes in CA patients admitted to the ICU between 2010–2016.

	Total sample[a]	IHCA	OHCA	p-value
Length of ICU stay in hours (IQR)	64.2 (21.4–133.8)	52.1 (17.2–135.2)	69 (26.4–133.2)	<0.01
Hospital length of stay in days (IQR)	5.9 (1.8–14.8)	6.1 (1.5–15.1)	5.9 (2–14.6)	0.27
ICU mortality (%)	11,681 (44.8)	4690 (44.2)	6579 (45.4)	<0.05
Hospital mortality (%)	13,072 (50.3)	5346 (50.5)	7256 (50.2)	0.66
1-year mortality (%)	14,974 (57.5)	6263 (59.0)	8169 (56.4)	<0.01

[a] In 956 patients, it was unknown if the cardiac arrest occurred in or outside the hospital; these patients were excluded from the analyses.

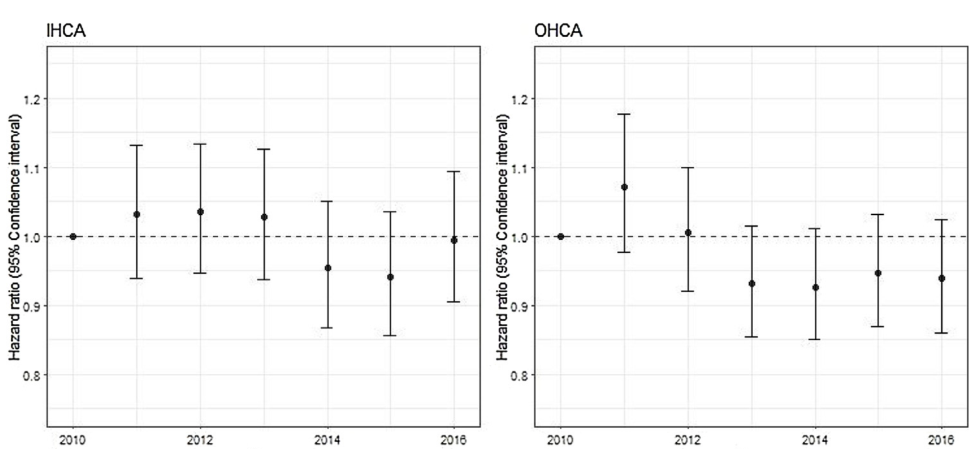

Fig. 1 – Multivariable Cox regression analysis of 1-year mortality for IHCA (p = 0.31) and OHCA (p = 0.01) over calendar time.

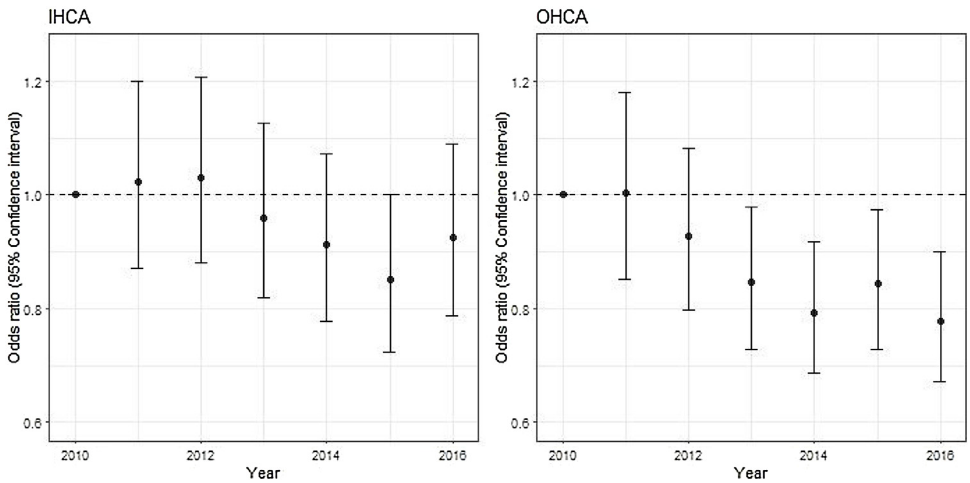

Fig. 2 – Binary logistic regression analysis of hospital mortality for IHCA (p = 0.21) and OHCA (p < 0.01) over calendar time.

As a primary outcome, we reported a 1-year mortality rate of 57.5% in the total cohort. This 1-year mortality rate was slightly higher in IHCA patients than in OHCA patients. Though in a smaller sample, Engsig et al.[25] investigated long-term outcomes and showed comparable 1-year mortality rates, which were similar for IHCA and OHCA patients (47% and 51%, respectively). We found a stable 1-year mortality rate between 2010 and 2016 for IHCA patients. Remarkably, the 1-year mortality of OHCA patients decreased in this time period, and this decrease persisted after limiting the analysis to the hospital survivors (see Supplementary Material Fig. C). This could point to a healthier discharged CA patient population.

As a secondary outcome, we studied hospital mortality, which was approximately 50% in the total cohort, as well as for both IHCA and OHCA patients separately. In addition, we found that hospital mortality was stable for IHCA patients between 2010 and 2016. For OHCA, we found a decreasing trend in hospital mortality in this time period. These mortality rates are in line with those in previous studies reporting hospital mortality rates in CA patients.[7,26–28]

In this study, we found a median APACHE IV estimated mortality rate of 0.75, which is much higher than the observed hospital mortality rate. Zimmerman et al.[29] validated this APACHE IV score for CA patients in the United States. However, Brinkman et al.[30] showed poor APACHE IV score performance in CA patients in the Netherlands. Our study was performed with the same data registry as was the study by Brinkman et al.[30] Because the APACHE IV score is not validated for CA patients in the Netherlands, this difference in expected and observed mortality could be explained.

Given the limitations of a nationwide observational dataset, we could not fully study the underlying cause for the reduction in mortality among the OHCA patients. However, we would like to discuss possible explanations for the differences in mortality rates between IHCA and OHCA patients and the decline in 1-year and hospital mortality of OHCA patients.

First, although we have corrected our analyses for relevant patient characteristics, CA characteristics may have changed during the study period. For example, in the Netherlands public awareness of CA is increasing over time due to nationwide education.[31] This could have resulted in a higher percentage of bystander life support and automated external defibrillator (AED) use. In turn this may have resulted in a shorter time to the return of spontaneous circulation (ROSC), which we were unable to examine in the present study.

Second, AED use may have contributed to the decrease in the mortality rate in OHCA patients. Despite the promising results, worldwide AED use is still quite limited compared to the Netherlands.[18,20,32,33] Blom et al.[32] showed that in the Netherlands, the use of AEDs and hospital survival both increased over time in the period 2006–2012. In this same period, Ringh et al.[34] reported an increase in the number and use of public AEDs and its effect on mortality rates in Sweden. Taken together, in our opinion, the widespread use of AEDs in the Netherlands probably contributed to the decrease in 1-year mortality in OHCA patients found in our study.

Another possible explanation for the decrease in the mortality rate in OHCA patients is the predominant use of targeted temperature management (TTM), compared to its limited use in IHCA patients. Mounting research has been performed on temperature management in CA patients,[8,22,27,28,35–37] mostly these studies have been performed in OHCA patients. As stated in the 2015 guidelines, since 2010, a temperature of 32–34 °C is recommended, which changed in 2015 to 36 °C.[22] Several studies showed different results in goal temperatures for the TTM, but they all recommend using hypothermia or normothermia and preventing hyperthermia.[8,22,35–37] However, Engsig et al.[25] showed no difference in IHCA and OHCA patients. Wang et al.[38] showed a benefit for TTM in IHCA patients, but TTM was performed in only 3.2% of the patients. Chan et al.[39] also showed a low TTM rate in IHCA patients and they found no association between TTM and survival or neurological outcomes. In the Netherlands, it is difficult to pinpoint the exact date of the implementation of the TTM guidelines, as shown by Pickkers et al,[8] while at the same time many hospitals started using TTM for OHCA patients during our study period. Thus, this may have contributed to the differences in mortality trends between 2010 and 2016 in IHCA and OHCA patients found in our study. Taken together, TTM is used more often in OHCA patients and has shown some promising results. However, TTM is not used as often in IHCA patients, although this may actually be a promising treatment strategy for these patients too.

Fourth, in the Netherlands, no studies have been conducted on the effect of cardiac rehabilitation on the mortality rate specifically in CA patients. However, some studies on the effect of cardiac rehabilitationon mortality in acute coronary syndrome and cardiac surgery patients showed a lower mortality rate for those who received cardiac rehabilitation compared to those who did not.[40,41] OHCA patients are more likely to receive cardiac rehabilitation.[10,42] For these patients, a cardiac cause such as coronary disease, was most likely the reason for the CA. Given the decrease in 1-year mortality rates in our study, which persisted after selecting only hospital survivors, it is likely that rehabilitation therapy contributed to this lower 1-year mortality in OHCA patients. It may clarify the difference between IHCA and OHCA outcomes.

Finally, during the last decade the treatment of coronary diseases improved. Advances in coronary revascularization and adherence to secondary prevention guidelines (including internal cardiac defibrillatory therapy) may have contributed to an important improvement in mortality rates in OHCA patients, while this is not the case in IHCA patients.

Future research may study the possible effects of pre-ICU characteristics and in- and post-hospital treatments on short- and long-term mortality rates of CA patients admitted to the ICU. Our linear trend should be regarded as a crude average of various up- and downward movements of the graph. In the restricted time frame of our analysis, these movements are hard to interpret as coincidence or due to specific causes. For this reason, no nonlinear trends were included in the analysis. In case a study can be performed with more data relevant to CA from a longer time period a more specific trend analysis (e.g. non-linear trend) will be informative.

Limitations

As in every (retrospective) study, this research had several limitations. First, as mentioned before, the NICE registry is aimed at quality of care at the ICU and not all characteristics relevant to CA are registered. In particular, we did not have access to the following characteristics: witnessed/unwitnessed CA, CPR delay, time until ROSC, primary cardiac rhythm, cardiac interventions, AED use, mechanical compression device use and cause of arrest. These characteristics are important when studying the determinants of the outcome of CA. Therefore, in future research, these characteristics must be taken into account.

Second, the NICE registry does not record whether the CA took place in- or out-of-hospital. We had to determine this with the best possible approximation. With this method, we expect that some of the IHCA patients were misclassified as OHCA. Most of the patients admitted at the ICU with admission-origin ED were OHCA patients; however, some of them experienced CA while in the ED. We assume that this issue has limited consequences for the results, but we cannot exclude the possibility of some bias.

Third, in this study, we could only report mortality rates. Unfortunately, there were no data available on neurological outcomes; therefore, we were unable to report survival with good neurological outcome.

Finally, in some hospitals in the Netherlands, post-CA patients are admitted to the cardiac care unit instead of the ICU. We were unable to estimate how many patients were in this group as this is not recorded or these data were not available to the authors. As a consequence, this could result in different numbers of patients in comparison to the CA numbers reported in other studies.

Conclusion

This nationwide registry cohort study reported a 57.5% 1-year mortality rate for CA patients admitted to the ICU between 2010 and 2016. We reported a decline in 1-year mortality for OHCA patients in these years.

Conflicts of interest

None.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:10.1016/j.resuscitation.2019.12.029.

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