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Clinical paper

Long-term survival and health-related quality of life after in-hospital cardiac arrest

Marc Schluep[a,d,*], *Sanne Elisabeth Hoeks*[a], *Michiel Blans*[c], *Bas van den Bogaard*[d], *Ankie Koopman-van Gemert*[e], *Cees Kuijs*[f], *Chris Hukshorn*[g], *Nardo van der Meer*[h], *Marco Knook*[i], *Trudy van Melsen*[j], *René Peters*[k], *Patrick Perik*[l], *Koen Simons*[m], *Gerben Spijkers*[n], *Wytze Vermeijden*[o], *Evert-Jan Wils*[p], *R.J. (Robert Jan) Stolker*[a], *H. (Rik) Endeman*[b]

[a] Department of Anaesthesiology, Erasmus University Medical Centre, Rotterdam, the Netherlands
[b] Department of Intensive Care Medicine, Erasmus University Medical Centre, Rotterdam, the Netherlands
[c] Department of Intensive Care Medicine, Rijnstate Hospital, Arnhem, the Netherlands
[d] Department of Intensive Care Medicine, OLVG, Amsterdam, the Netherlands
[e] Department of Anaesthesiology, Albert Schweitzer Hospital, Dordrecht, the Netherlands
[f] Resuscitation Committee, Maasstad Hospital, Rotterdam, the Netherlands
[g] Department of Intensive Care Medicine, Isala Hospital, Zwolle, the Netherlands
[h] Department of Intensive Care Medicine, Amphia Hospital, the Netherlands
[i] Department of Intensive Care Medicine, Reinier de Graaf Gasthuis, Delft, the Netherlands
[j] Department of Intensive Care Medicine, Haaglanden Medisch Centrum, The Hague, the Netherlands
[k] Department of Cardiology, Tergooi Hospital, Hilversum, the Netherlands
[l] Department of Cardiology, Deventer Hospital, Deventer, the Netherlands
[m] Department of Intensive Care Medicine, Jeroen Bosch Hospital, ‘s Hertogenbosch, the Netherlands
[n] Department of Hospital Medicine, ZorgSaam Zeeuws-Vlaanderen, Terneuzen, the Netherlands
[o] Department of Intensive Care Medicine, Medisch Spectrum Twente, Enschede, the Netherlands
[p] Department of Intensive Care Medicine, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands

Abstract

Introduction: In-hospital cardiac arrest (IHCA) is an adverse event associated with high mortality. Because of the impact of IHCA more data is needed on incidence, outcomes and associated factors that are present prior to cardiac arrest. The aim was to assess one-year survival, patient-centred outcomes after IHCA and their associated pre-arrest factors.

Methods: A multicentre prospective cohort study in 25 hospitals between January 1st 2017 and May 31st 2018. Patients $\geq$ 18 years receiving cardiopulmonary resuscitation (CPR) for IHCA were included. Data were collected using Utstein and COSCA-criteria, supplemented by pre-arrest Modified Rankin Scale (MRS, functional status) and morbidity through the Charlson Comorbidity Index (CCI). Main outcomes were survival, health-related quality of life (HRQoL, EuroQoL) and functional status (MRS) after one-year.

* Corresponding author at: Department of Anaesthesiology, Erasmus University Medical Centre, Rotterdam, the Netherlands.
E-mail address: m.schluep@erasmusmc.nl (M. Schluep).

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Results: A total of 713 patients were included, 64.5% was male, median age was 63 years (IQR 52–72) and 72.8% had a non-shockable rhythm, 394 (55.3%) achieved ROSC, 231 (32.4%) survived to hospital discharge and 198 (27.8%) survived one year after cardiac arrest. Higher pre-arrest MRS, age and CCI were associated with mortality. At one year, patients rated HRQoL 72/100 points on the EQ-VAS and 69.7% was functionally independent.

Conclusion: One-year survival after IHCA in this study is 27.8%, which is relatively high compared to previous studies. Survival is associated with a patient's pre-arrest functional status and morbidity. HRQoL appears acceptable, however functional rehabilitation warrants attention. These findings provide a comprehensive insight in in-hospital cardiac arrest prognosis.

Keywords: In hospital cardiac arrest, Outcome, Long-term survival, Health-related quality of life, IHCA, HRQoL, Prognostication

Introduction

In-hospital cardiac arrest (IHCA) is a serious adverse event that can potentially affect any hospitalized patient. Although it still occurs frequently, evidence is relatively scarce.[1,2] Because of this, there is much interest in long-term outcomes of IHCA and its predictors.[3,4] Several strategies to improve outcomes have been proposed, aimed at both prevention and treatment.[5,6] Prevention focuses on early recognition of patients who are at risk of cardiac arrest, as well as patient-centred counselling to install do-not-resuscitate (DNR) orders for patients in whom cardiopulmonary resuscitation (CPR) is not expected to be successful.[1,7,8] Preferably, the decision to attempt or refrain from CPR is made based on patient preferences and characteristics that are present prior to cardiac arrest.[9] Outcomes should focus on good long-term quality of life, rather than survival to hospital discharge. Studies from different populations will allow for international comparison and increase learning from good practice.[3,9]

Although 1-year long-term survival data is available, there is limited knowledge on long-term functional outcomes and factors that predict these outcomes. As previously reported, survival in European studies is 20.0% (95% prediction interval: 16.0–26.0%) and we reported a one-year survival rate of 23.0% from a single-centre retrospective study.[2,10] The majority of evidence has been derived from retrospective single-centre studies or studies that do not assess the relationship between pre-arrest variables and long-term outcomes.[2] We therefore initiated a prospective cohort study to describe IHCA epidemiology in the Netherlands. The overall goal of our endeavour is to provide information in order to establish patient-centred CPR-directives. This also means that patients can then make an informed decision about their CPR-directive. The primary objective of the current study is to assess the one-year survival of adult patients after IHCA. The secondary objectives are to determine pre-arrest factors for prognostication of outcome and to describe overall functional outcome and health-related quality of life after IHCA. In this paper we report on variables that are present prior to cardiac arrest (age, functional status, comorbidity) and hospital factors (patient monitoring, admission specialty, post-arrest treatment).

Methods

Design and setting

A multicentre prospective cohort study was performed in 25 hospital localizations. The call for participation were done through the Dutch Society for CPR-coordinators (NVCR). Data were collected through an online registration system (OpenClinica, Walton, MA, USA). CPR practice and hospital characteristics of all Dutch hospitals were assessed through a prior nationwide survey.[11] The study was registered at clinicaltrials.gov (NCT03120507) and the Dutch trial registry (NTR6145).

Patient population and follow-up process

The population included were adults (≥18 years of age), who received cardiopulmonary resuscitation, defined by starting manual chest compressions for a circulatory arrest occurring in-hospital. The inclusion period was January 1st 2017–May 31st 2018. Patients from all hospital wards, departments, outpatient clinics and common areas were included. This means we also included patients from the intensive care (ICU) and cardiac care units (CCU), as well as the emergency room (ER). Exclusion criteria were: OHCA < 24 hours prior to IHCA, purposely induced arrhythmia (e.g. electrophysiological interventions) or cardiac arrest (e.g. cardioplegia in cardiac surgery) or refusal to participate. The CPR-team generally attends all cases of IHCA, except for some peri-operative cases in the OR. Therefore all patients were prospectively included through registrations done by each hospital's CPR-team and crosschecked with ICU-admissions for cardiac arrest. In-hospital follow-up was done by the local investigator in each hospital until hospital discharge. After discharge survival was checked with the Dutch Personal Records Database (BRP) at 3 months and 12 months after cardiac arrest. Surviving patients received questionnaires addressing their functional status and quality of life. Up to two reminders were sent and subsequently patients received a phone call to ask for follow-up data.

Ethical considerations

Study participants were asked to provide informed consent, unless they did not survive initial CPR. For patients who survived CPR and died subsequently in-hospital without regaining consciousness, a letter was sent to the next of kin to inform of inclusion. Patients who regained consciousness received information about study participation. At this point informed consent was obtained to participate in follow-up. Patients were informed of the non-interventional design and were given the possibility to opt-out at any time. Patients were only able to refuse or opt-out of follow-up. This study was considered subject to the Dutch Medical Research Involving Human Subjects act (WMO) and was approved by the Erasmus University Medical Centre Medical Ethics Committee (ABR55661.078.16).

Data collection

Data was collected from the Electronic Medical Records of patients, according to the Utstein-template and the Core Outcome Set for Cardiac Arrest (COSCA) recommendations.[12,13] Pre-arrest data were gathered retrospectively.

Outcome measures

The primary outcome measure was one-year survival. Secondary outcome measures were return of spontaneous circulation (ROSC), survival to hospital discharge, 3-month survival, quality of life, functional status and psychological distress at 3 and 12 months after cardiac arrest. Functional status was determined through a Modified Rankin Scale (MRS) score. MRS was assessed by the local investigators after cardiac arrest had occurred, either through a proxy, general practitioner or extensive chart review. Post-discharge MRS was reported via questionnaires. At follow-up CCI was assessed via self-reporting, as were new health issues. Patients were asked if they had prior employment and what their current employment status was. Quality of life and psychological distress was determined through validated questionnaires, including the EQ-5D-5L (EuroQoL). This questionnaire has been used before in cardiac arrest research and allows for good comparison. The EQ-5D measures the HRQoL on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) in which patients can report problems in 5 severity levels. EQ-5D-5L Utility Index scores (EQ-Index) were calculated from the five dimensions of the EQ-5D-5L, with a standard set of population based weights validated for the Netherlands.[14,15] Calculated index scores range from 1 (best health state) to −0.446 for the worst health state possible. Additionally, part of the EQ-5D-5L is a visual analogue scale (EQ-VAS) where patients score their current health state from 0 (indicating worst health state imaginable) to 100 (indicating best health state imaginable).[16] The EQ VAS provides a quantitative measure of the patient's perception of their overall state of health. We compared the EQ-5D-5L dimensions to the Dutch referent population and to the population of hospitalized patients we studied in our previous study to assess advance care directives.[17] Other outcome measures that were used are the Short Form 12 SF-12 with its physical and mental component scale (PCS and MCS), and the hospital anxiety and depression scale (HADS). Strain on the relationship between the patient and his/her partner or next of kin was assessed using the caregiver strain index (CSI). In the design of this study we described using Telephonic Interview of Cognitive Status (TICS), but this was not feasible.

Statistical analysis

Data were reported using mean (standard deviation) or median (interquartile range) where appropriate. Comparison between groups was done using designated statistic tests. Kaplan-Meier survival analysis was used. Survival differences were assessed for predefined subgroups: 1) shockable and non-shockable arrest rhythm 2) an Age-combined Charlson Comorbidity Index (ACCI) stratified for low (0–4 points), medium (5–7 points) or high (8+ points) burden of age and disease; 3) pre-admission functional status by Modified Rankin Scale scores. We assessed ACCI because a high ACCI was previously associated with lower survival in IHCA patients.[10,18] The method of ACCI calculation is summarized in supplemental Table 1. Incidences of IHCA were calculated in two ways: (1) by division of the number of IHCA by the total number of hospital admissions during the study period, (2) by division of the number of IHCA by the sum of days of inclusion of all hospitals. For survival differences Log-Rank tests were calculated and hazard ratios (HR) were calculated through Cox regression. Variables that were univariately associated with survival ($p < 0.05$) were included in multivariate survival analysis. Data were analysed using SPSS statistics v25.0 (IBM, Chicago, IL, USA) and R. (R Foundation for Statistical Computing, Vienna, Austria).

Results

Fourteen hospital organizations participated, comprising 25 hospital locations (25.3% of Dutch hospitals). Compared to all Dutch hospitals, participating hospitals were mostly classified as teaching hospitals, trauma centres and thoracic/aortic surgery centres when compared to the overall characteristics of Dutch hospitals. A total of 713 patients were included between January 1st 2017 and May 31st 2018, of whom 64.5% was male, median age was 63 years (IQR 52–72) and 72.8% had a non-shockable rhythm (Table 1). Of these patients 394 (55.3%) achieved ROSC, 231 (32.4%) survived to hospital discharge and 198 (27.8%, 95 %CI 23.9%–30.5%) survived one year after cardiac arrest. If death occurred within one year after IHCA, 93.6% occurred while patients were in hospital versus 6.4% after hospital discharge. The inclusion period contained 5867 hospital days and a total of 529,679 admissions were done. This yields an IHCA incidence of 0.12 per hospital day and 1.3 per 1000 admissions. A flowchart of survival is displayed in Fig. 1 and patient characteristics are displayed in Table 1.

Survival plots for the total population and for predefined subgroups are depicted in Fig. 2. Lower survival was found in patients with a non-shockable cardiac arrest rhythm, an ACCI $\geq$ 5 points and/or higher pre-admission MRS, indicative of functional disability. One-year survival for patients with no disability prior to admission was 38.2%, for non-significant disability 26.8% and for moderate or severe disability 18.0% (Fig. 2c). After adjustment for peri-arrest factors several pre-admission variables were associated with a higher mortality: age (HR 1.01 per year increase, 95 %CI 1.00–1.02, $p = 0.007$) and a higher Charlson Comorbidity Index (HR 1.07 per point increase, 95 %CI 1.03–1.10, $p < 0.001$). The adjusted HR's are displayed in Table 2.

One-year survival varied between patients who were resuscitated in different hospital areas. One-year survival was highest for IHCA in the operation room (50.0%), followed by the emergency room (31.4%) the intensive/cardiac care units (31.9%), the catheterization laboratory (28.6%) and the non-monitored wards (23.0%) ($p = 0.005$). Survival also varied when patients were stratified for the specialty to which they were admitted. The highest probability of survival was found in cardiac surgical admissions (56.3%) and the lowest in medical non-cardiology admissions (17.4%).

Of survivors to discharge 77.5% scored CPC1-2 (none-mild disability), 16.5% CPC3 (severe disability) and 0.9% CPC4 (comatose), and 17.3% was considered to be in need of daily assistance. Need of daily assistance was more numerically prevalent in patients who died in the following year (32.1% vs. 15.7%, $p = 0.085$).

After discharge, 212 (29.7%) patients survived 3 months and 198 (27.8%) patients survived one year, of whom 136 (64.2%) and 110 (55.6%) answered the follow-up questionnaires respectively. Median time for first follow-up time was 94 days (IQR 82–132) and for final follow-up it was at least $\geq$ 12 months. The majority of surviving patients reported having no or a slight disability in functional status (MRS 0–1): 62.7% at 3 months, and 69.7% at 1 year as displayed in supplemental Fig. 1. At one-year follow-up 65.5% of surviving patients retained the same MRS score, and 30.0% had no more than 1-point decrease in MRS, compared to their status before cardiac arrest. Of the patients with a decrease in MRS (n = 49) at 12 months

Table 1 – Characteristics of all in-hospital cardiac arrests; one-year survivors vs. non-survivors. *patients who were lost to follow-up were excluded from analysis (n = 8) (Fig. 1).

Patient characteristics upon admission		Death <1 year* n = 507		One-year survivors* n = 198		Total n = 713		p=
Age	*Median (IQR)*	69	(62–77)	67	(56–73)	63	(52–72)	0.036
Male sex	n (%)	327	(64.5)	125	(63.1)	460	(64.5)	0.734
BMI (kg/m^2)	*Median (IQR)*	25.7	(23.4–29.4)	26.6	(23.9–30.1)	25.7	(23.0–30.0)	0.039
Charlson comorbidity index	*Median (IQR)*	2	(0–3)	1	(0–2)	1	(0–3)	<0.001
Functional status at home								
(Modified Rankin Scale)**/†	*n(%)*							<0.001
0–1 – none/slight disability		325	(67.0)	157	(82.2)	488	(68.4)	
2–3 – moderate disability		143	(29.5)	30	(15.7)	174	(24.4)	
4–5 – severe disability		17	(3.5)	4	(2.1)	22	(3.1)	
Cerebral performance cat.1–2**	n(%)	438	(86.4)	188	(95.0)	634	(88.9)	0.010
Presence of malignant disease	*n(%)*							<0.001
None		402	(79.3)	172	(86.9)	582	(81.6)	
Solid tumour		43	(8.5)	23	(11.6)	66	(9.3)	
Solid tumour with metastases		35	(6.9)	1	(0.5)	36	(5.0)	
Hematologic		27	(5.3)	2	(1.0)	29	(4.1)	
Type of ward	*n (%)*							0.005
Non-monitored ward		288	(56.8)	87	(43.9)	378	(53.0)	
Intensive/cardiac care unit		128	(25.2)	61	(30.8)	191	(26.8)	
Operation Room		15	(3.0)	16	(8.1)	32	(4.5)	
Emergency Room		48	(9.5)	22	(11.1)	70	(9.8)	
Catheterization laboratory		28	(5.5)	12	(6.1)	42	(5.9)	
Type of admission	*n(%)*							<0.001
Cardiology		178	(35.1)	89	(44.9)	272	(38.1)	
Cardiac surgery		14	(2.8)	18	(9.1)	32	(4.5)	
Medical non-cardiology		211	(41.6)	45	(22.7)	258	(36.2)	
Surgical non-cardiac		104	(20.5)	46	(23.2)	151	(21.2)	
No. of cardiac arrest events	*n(%)*							0.652
One event		477	(94.1)	183	(92.4)	667	(93.5)	
Two events								
Current admission		12	(2.4)	7	(3.5)	19	(2.7)	
In prior medical history		18	(3.6)	8	(4.0)	27	(3.8)	
Arrest-related factors								
Time of day	*n(%)*							
07:00–14:59		191	(37.7)	91	(46.0)	284	(39.8)	
15:00–22:59		172	(33.9)	55	(27.8)	230	(32.3)	
23:00–06:59		144	(28.4)	52	(26.3)	199	(27.9)	
Day of the week								
weekday		370	(73.0)	158	(79.8)	536	(75.2)	
weekend		137	(27.0)	40	(20.2)	177	(24.8)	
Witnessed arrest	*n(%)*	372	(73.4)	182	(91.9)	561	(78.7)	0.000
Time to (min.)	*Median (IQR)*							
basic life support		0	(0–0)	0	(0–0)	0	(0–0)	0.127
advanced life support		2	(1–4)	1	(0–2)	1	(0–3)	0.414

Cause of arrest - cardiac	*n (%)*	237	(46.9)	120	(60.3)	357	(50.7)	0.001
Primary Arrest Rhythm	*n (%)*							0.000
Asystole		171	(33.7)	32	(16.2)	205	(28.8)	
PEA		237	(46.7)	65	(32.8)	304	(42.6)	
VF		71	(14.0)	65	(32.8)	140	(19.6)	
VT		27	(5.3)	27	(13.6)	54	(7.6)	
No rhythm analysis		1	(0.2)	9	(4.5)	10	(1.4)	
After ROSC		**n = 194**	**n = 200**	**n = 394**				
Time to ROSC (min)	*Median (IQR)*	10	(5–20)	5	(3–10)	9	(5–15)	0.393
Glasgow Coma Scale								
(after ROSC)*	*Median (IQR)*	3	(3–14)	9	(3–15)	3	(3–14)	<0.001
Serum lactate (mmol/L)	*Median (IQR)*	6.6	(2.8–10.8)	3.3	(1.8–6.5)	5.9	(2.8–10.0)	<0.001
Coronary intervention†	*n(%)*	25	(11.8)	50	(24.4)	79	(11.1)	<0.001
ICU admissions	*n(%)*	168	(88.9)	124	(62.9)	299	(75.9)	<0.001
At discharge		**n = 28**	**n = 203**	**n = 231**				
Cognitive performance Cat.**	*n(%)*							0.116
1–2 none/slight disability		17	(60.7)	156	(78.8)	179	(77.5)	
3 – severe disability		9	(32.1)	29	(14.6)	38	(16.5)	
4 – coma		0	(0)	2	(1.0)	2	(0.9)	
Unknown‖		2	(7.1)	11	(5.6)	12	(5.2)	
In need of daily assistance§	*n(%)*	9	(32.1)	31	(15.7)	40	(17.3)	0.085
Discharge destination	*n(%)*							0.084
home or family		19	(69.2)	128	(65.0)	150	(64.9)	
rehab centre		3	(11.5)	26	(13.2)	31	(13.4)	
nursing home		1	(3.8)	14	(7.1)	16	(6.9)	
other hospital (for long-stay ward)		3	(11.5)	29	(14.7)	34	(14.7)	

**data was missing for the following categories (n): MRS at admission (29), CPC at admission (25), CPC at discharge (13). †For 35 patients, there was no MRS score reported; non-survivors (22), survivors (7). ‖CPC was unknown for patients who were discharged to other hospitals earlier than scheduled, therefore CPC at discharge was not known. §Patients requiring assistance for daily activities such as bathing, getting dressed or cooking.

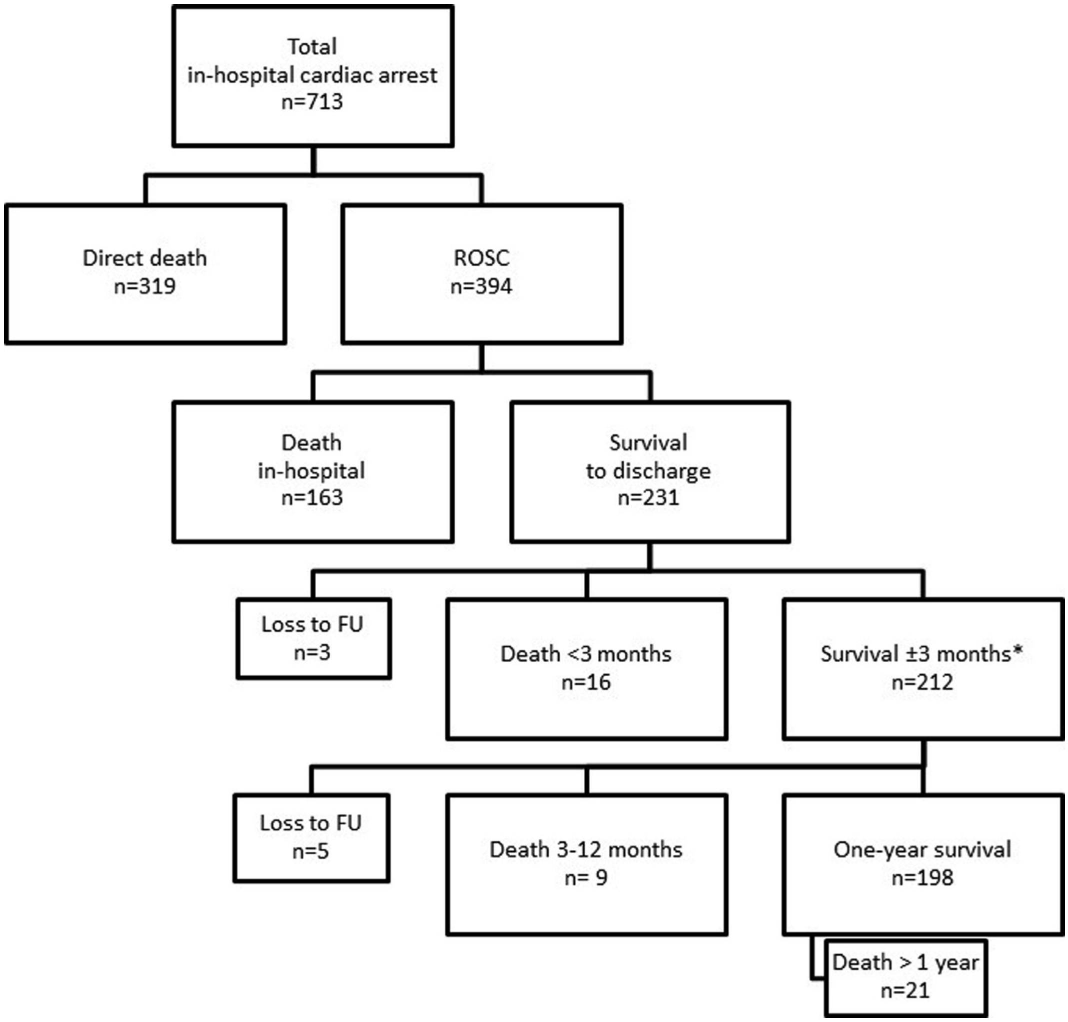

Fig. 1 – Survival flowchart for all-in-hospital cardiac arrest cases. *survival at this time point was assessed through patients' responses to the questionnaire and was therefore variable with a median follow-up of 94 days (IQR 82–132).

only 23.4% reported having been admitted to a nursing or rehab facility. The change in MRS scores before admission and at follow-up is summarized in supplemental Fig. 1. Of patients who answered the questionnaire at 1-year follow-up reported several problems: readmission to hospital (15.5%), chest pain (8.2%), heart failure (11.8%), heart rhythm disturbances (10.0%) and syncope (4.5%). The proportion of comorbidities in terms of CCI was the similar pre-arrest and at 3- and 12-month follow-up. Of patients who were employed at time of the cardiac arrest, 17.1% had quit working. Caregiver strain was present in 17.1% of patients' partners or family members. These data are displayed in supplementary Table 3.

HRQoL was assessed using the EQ-5D VAS score and EQ-5D index score at 3 and 12 months post-IHCA. Median EQ-VAS was 70 (IQR 60–80) at 3 months and 75 (IQR 65–85) at 12 months. Patients reported a median EQ-5D index score of 0.77 (IQR 0.65–0.87) at 3 months and 0.81 (IQR 0.70–0.91) at 12 months. The reported items (scores $\geq$ 1 point severity) stratified by the EQ-5D-5L domains are displayed in Fig. 3. The most frequent reported problems at 12 months were: *usual activities* (56.9%), followed by *mobility* (55.0%), *pain* (53.2%), *anxiety/depression* (43.2%) and *self-care* (17.4%). Only a small proportion of patients ($\leq$2.4%) reported severe problems (score $\geq$ 4 points severity) for each domain. The percentage of patients reporting severe problems is separately mentioned in Fig. 3. Results from SF-12 and HADS questionnaires are summarized in supplemental Table 3.

Discussion

One-year survival after in-hospital cardiac arrest in this prospective multicentre study is 27.8%. Of all patients who die within one year after cardiac arrest the majority of deaths occurred in hospital (93.6%). In our study the incidence of IHCA is 1.3 per 1000 admissions. We found several pre-arrest variables to influence one-year survival, most notably pre-arrest functional status (MRS) and the combination of age and comorbidity (ACCI).

Survival in this study is relatively high compared to other studies in populations comprising all hospital wards (including critical care wards).[2,3,10] One-year survival rates from a systematic review range from 9-29% globally, and 16–26% in European studies.[2] The survival rate of 27.8% from this study borders the upper margins of both ranges. Our study population was not notably younger or healthier

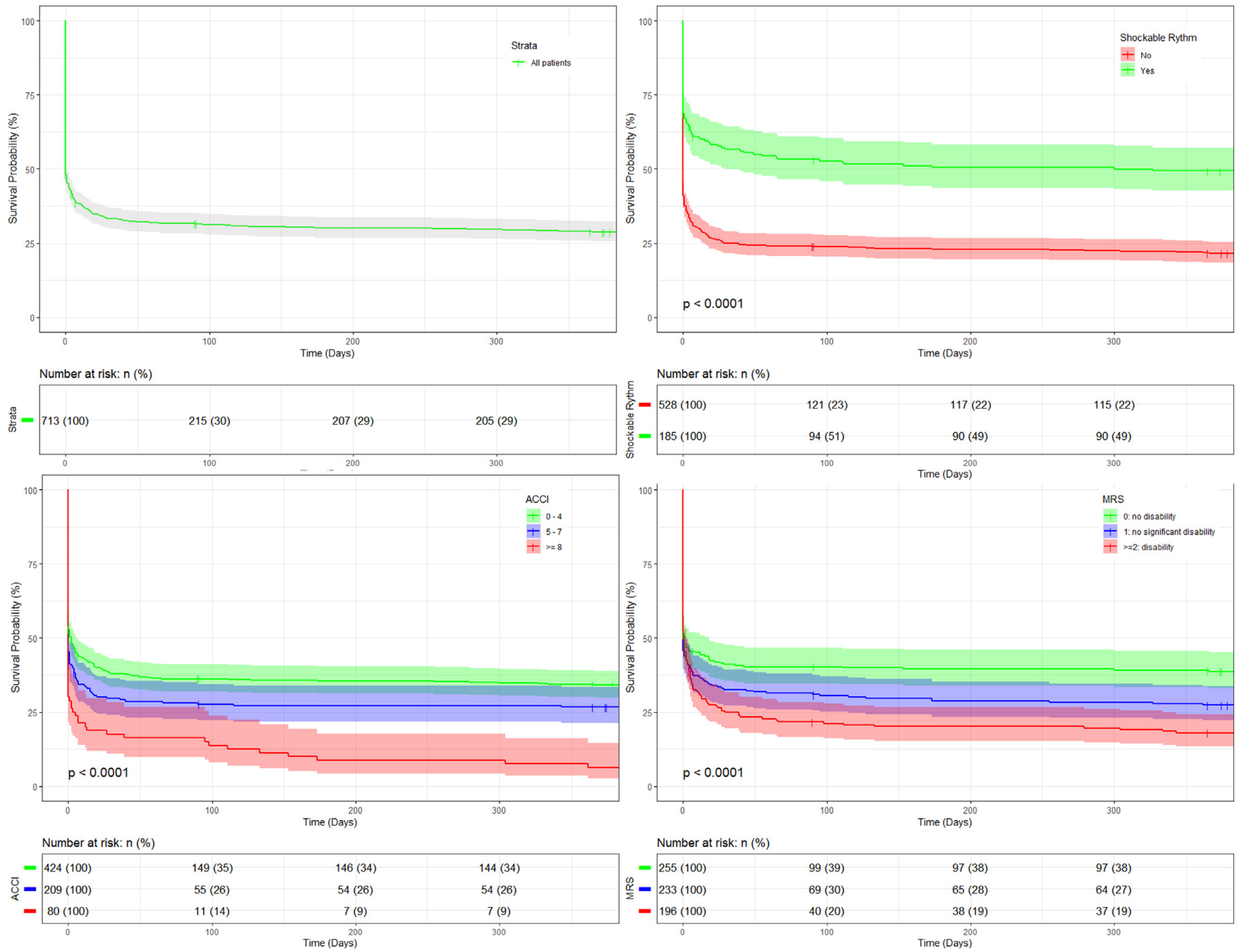

Fig. 2 – Long-term survival. Survival function is stratified for shockable rhythm, pre-admission functional status (Modified Rankin Scale) and for Age-Combined comorbidity index (ACCI). Log-rank tests were performed: shockable rhythm p < 0.001, MRS p < 0.001, ACCI p < 0.001.

and did not comprise a larger proportion of shockable rhythms than in prior studies. Furthermore all patients suffering IHCA were included and loss to follow-up was low.

We have two hypotheses to explain this survival rate. The first is that advanced directives are becoming increasingly important. The prevalence of Do Not Resuscitate orders among hospitalized patients is relatively high in the Netherlands: 27.5%.[17] As a consequence, CPR with a low chance of success may be attempted less frequently. As mentioned, our population was not younger or healthier in means of comorbidity (ACCI), compared to other cohorts. Perhaps this means the relation between functional performance (MRS) and poor outcome is more important. We have no data to substantiate this hypothesis. Secondly Dutch hospitals have a 96% adherence to ERC guidelines, 91% availability of rapid response systems and all hospitals have dedicated CPR-teams with frequent team training.[11,19] The exact role of these factors needs to be elucidated further in future research. Our hypothesis is supported by the fact that incidence of IHCA in our sample is in the lower margin of what is described in literature, i.e. 1–6 cases per 1000 admissions.[2] Compared to studies from the US and Denmark, the incidence of IHCA is relatively low in our study.[3,20] A likely explanation of this effect is the widespread availability of rapid response systems.[11] Rapid response systems may lower the incidence of IHCA, although its influence on mortality has yet to be proven.[21] As expected, pre-arrest morbidity and functional status in this study is associated with survival after cardiac arrest.[1,10,22] One-year survival for patients with no previous disability in daily life (MRS 0) is 38.2% and for patients with a low burden of age and disease (ACCI 0–4 points) one-year survival is 33.7%. Inversely, survival was low for patients who suffered disability or had a high burden of disease before hospital admission.

At discharge, 77% of patients had a CPC score of 1–2 and were therefore expected to be able to live independently or with minor assistance. Self-reported functional status at 3 months and 12 months was less than reported by physicians at hospital discharge. In general the health status of IHCA survivors is lower than that of a Dutch norm populations, as reflected by the EQ-5D domains and the EQ-5D index score.[15] IHCA survivors reported a median EQ-5D index score of 0.77. When compared to the Dutch population mean of 0.89, there is a gap that indicates that HrQoL is lower for cardiac arrest survivors. EQ-5D index score compares well to other studies done in IHCA and OHCA patients, where HRQoL was mea-

Table 2 – Cox regression of factors associated with death <1 year after cardiac arrest, meaning not achieving ROSC, death in-hospital or death after discharge in the year after surgery. Two analyses were performed for pre-arrest variables, both with and without adjustment for peri-arrest variables.

Patient characteristics	Pre-arrest variables			Pre and peri-arrest variables		
	Hazard ratio at death	95% CI	p=	Hazard ratio at death	95% CI	p=
Age, per year increase	1.01	1.00–1.02	0.003	1.01	1.00–1.02	0.007
Body Mass Index (kg/m^2) (BMI) per point increase	0.98	0.98–1.01	0.722	1.00	0.98–1.01	0.583
Charlson comorbidity index (CCI) per point increase	1.07	1.03–1.10	<0.001	1.07	1.03–1.10	<0.001
Modified Rankin Scale (MRS) per point increase	1.05	0.96–1.14	0.290	1.02	0.94–1.12	0.616
Cognitive Performance Category score (CPC) per point increase	1.11	0.97–1.27	0.124	1.06	0.92–1.21	0.436
Non-shockable rhythm				1.89	1.46–2.36	<0.001
Non-cardiac cause of arrest				0.94	0.75–1.17	0.571
Non-cardiac admission specialty				1.11	0.87–1.40	0.354
Non-monitored ward				1.00	0.81–1.23	0.968
Non-witnessed arrest				1.50	1.19–1.89	0.001

sured after discharge.[4,23–25] EQ-5D-5L visual analogue score was on average 70 at 3 months and 75 at 12 months, where the Dutch population norm is 82 and 62 in Dutch hospitalized patients as described in our previous cross-sectional study.[15,17] Perceived HrQoL (EQ-VAS) in cardiac arrest survivors was lower compared to the Dutch population, but higher than in patients during hospitalization. IHCA survivors perceive less HrQoL than the general population with at least minor problems in all domains of the EQ-5D, but mainly with regard to mobility and daily activities.[15,26] The same results are reflected in the SF-12 and HADS outcome measures. Notably, the majority of patients with a decrease in MRS did not attend a rehabilitation program. This would imply that cardiac arrest survivors might benefit from rehabilitation programs to improve neurological status and exercise capacity.[27] It is known that better neurologic status leads to more work participation.[28] This poses interesting goals for future post-resuscitation care.

Several limitations of our study should be taken into account. Firstly, this is an observational study and may be subject to selection bias. Because the study was voluntary and there are no financial or disciplinary consequences for hospitals, we hope this effect is negligible. Our sample has a relatively high number of teaching hospitals. On the one hand this means the complexity of care increases, e.g. more high-risk surgery, and on the other hand the availability of advanced life support certified doctors increases.[11] This difference could however be small as training level and training frequency does not differ, nor does ICU-level or rapid response team availability; other proxies for the chain of survival. Because our sample of participating hospitals was based on voluntary participation, we might have introduced a sampling bias. Although our sample contains more teaching hospitals, no significant differences were found, regarding hospital size, level of care, guideline adherence, and team training,[11] Secondly, MRS was assessed by the local investigators after cardiac arrest had occurred, either through a proxy, general practitioner or extensive chart review. This could have introduced bias. That pre-arrest MRS estimates still produce a survival effect on long-term indicates that a physician estimate of functional status may be a valuable predictor of long-term mortality. Lastly, the response rates were 64.2% at 3 months and 55.6% at 12 months. These numbers are similar to a recent study from Sweden, with a response rate of 55.0% at 3–6 month follow-up.[26] All patients who were eligible for follow-up received telephonic reminders to fill out the questionnaires. The most heard reason not to respond was that they found it too strenuous or difficult. Furthermore, pre-admission mRS was lower in the non-responder group, than among responders. Differences between these two groups have been summarized in supplemental Table 2. We therefore think the found HRQoL is possibly overestimated.

Regarding our overall goal, this study yields important results. It appears that in our sample, we can identify groups of patients for whom CPR would be less likely to succeed. Moreover these groups could have been identified upon hospital admission, by means of MRS or ACCI. Our study warrants validation in other cohorts, but its data may serve as a basis for discussing CPR-directives with patients.[7] Furthermore, our study yields the positive message that survival after IHCA in our health care system is relatively high, especially in patient categories with a low burden of disease (ACCI $\leq$ 7) or good pre-arrest functional status (MRS < 2). In these categories survival is at least double when compared to the global average.[2] As we have previously assessed, knowledge of CPR-directives is often lacking in

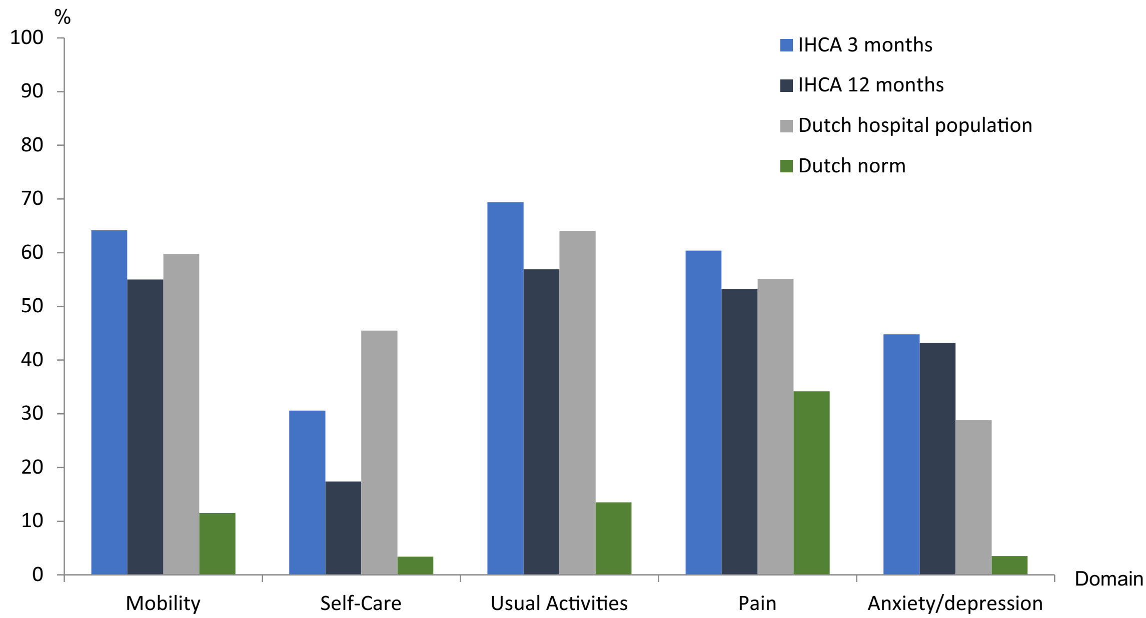

Fig. 3 – EQ-5D-5L percentage of patients who report any problem in one of the five domains at 3 months and 12 months after cardiac arrest. Reporting of problems was compared to a cross-sectional sample from Dutch hospitalized patients and the Dutch norm population.

patients.[17] With our current findings we can improve communication in two ways. First it allows us to reassure young and healthy patients that are overwhelmed by hearing about CPR-directives, that it seldom occurs and that their prognosis is good. Second, it allows us to speak to our older, multimorbid and/or functionally incapacitated patients about their prognosis and it might lower the threshold for clinicians to speak about this subject.

Our study design has several other merits. Patients were included from different hospitals in different regions, providing a variety of health services We provide a comprehensive view of in-hospital cardiac arrest patients with data on pre-admission status following up to 12 months after cardiac arrest. To combine survival, health-related quality of life (HRQoL) and functional status in a prospective cohort aids in improving the external validity of IHCA prognostication and such studies are scarce.[4,23]

We conclude that in this study one-year survival after in-hospital cardiac arrest is 27.8% in this population and survival is associated with pre-admission functional status and morbidity. Outcomes such as cognitive function, daily functionality and work participation warrant more attention in future research. We think future guidelines should incorporate advanced directive planning, of which prognostication and CPR-directive counselling is a vital part.[7,29] Similar studies should be repeated in various populations in order to develop tailor-made prognostication tools.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2021.07.006.

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