



Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: [www.journals.elsevier.com/journal-of-critical-care](http://www.journals.elsevier.com/journal-of-critical-care)

## In-depth assessment of health-related quality of life after in-hospital cardiac arrest

M. Schluep (Marc), MD <sup>a,\*</sup>, H. Endeman (Rik), MD, PhD <sup>b</sup>, B.Y. Gravesteijn (Benjamin), MSc <sup>a</sup>, C. Kuijs (Cees), RN <sup>c,d</sup>, M.J. Blans (Michiel), MD <sup>e</sup>, B. van den Bogaard (Bas), MD, PhD <sup>f</sup>, A.W.M.M. Koopman Van Gemert (Ankie), MD, PhD <sup>g</sup>, C.J. Hukshorn (Chris), MD, PhD <sup>h</sup>, B.J.M. van der Meer (Nardo), MD, MBA, PhD <sup>i</sup>, A.H.M. Knook (Marco), MD, MBA <sup>j</sup>, T. van Melsen (Trudy), MD <sup>k</sup>, R. Peters (René), MD, PhD <sup>l</sup>, K.S. Simons (Koen), MD, PhD <sup>m</sup>, G. Spijkers (Gerben), MD <sup>n</sup>, J.W. Vermeijden (Wytze), MD, PhD <sup>o</sup>, E.-J. Wils (Evert-Jan), MD, PhD <sup>p</sup>, R.J. Stolker (Robert Jan), MD, PhD <sup>a</sup>, S.E. Hoeks (Sanne), PhD <sup>a</sup>

<sup>a</sup> Department of Anesthesiology, Erasmus University Medical Center, Rotterdam, the Netherlands

<sup>b</sup> Department of Intensive Care Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands

<sup>c</sup> Department of Intensive Care Medicine, Maasstad Hospital, Rotterdam, the Netherlands

<sup>d</sup> Resuscitation Committee, Maasstad Hospital, Rotterdam, the Netherlands

<sup>e</sup> Department of Intensive Care Medicine, Rijnstate Hospital, Arnhem, the Netherlands

<sup>f</sup> Department of Intensive Care Medicine, OLVG, Amsterdam, the Netherlands

<sup>g</sup> Department of Anesthesiology, Albert Schweitzer Hospital, Dordrecht, the Netherlands

<sup>h</sup> Department of Intensive Care Medicine, Isala Hospital, Zwolle, the Netherlands

<sup>i</sup> Department of Intensive Care Medicine, Amphibia Hospital, the Netherlands

<sup>j</sup> Department of Intensive Care Medicine, Reinier de Graaf Gasthuis, Delft, the Netherlands

<sup>k</sup> Department of Intensive Care Medicine, Haaglanden Medisch Centrum, The Hague, the Netherlands

<sup>l</sup> Department of Cardiology, Tergooi Hospital, Hilversum, the Netherlands

<sup>m</sup> Department of Intensive Care Medicine, Jeroen Bosch Hospital, 's Hertogenbosch, the Netherlands

<sup>n</sup> Department of Hospital Medicine, ZorgSaam Zeeuws-Vlaanderen, Terneuzen, the Netherlands

<sup>o</sup> Department of Intensive Care Medicine, Medisch Spectrum Twente, Enschede, the Netherlands

<sup>p</sup> Department of Intensive Care Medicine, Franciscus Gasthuis & Vlietland, Rotterdam, the Netherlands

### ARTICLE INFO

Available online xxxx

#### Keywords:

In-hospital cardiac arrest  
Health-related quality of life  
Psychological wellbeing  
Patient-reported outcome measures

### ABSTRACT

**Introduction:** Evidence on physical and psychological well-being of in-hospital cardiac arrest (IHCA) survivors is scarce. The aim of this study is to describe long-term health-related quality of life (HRQoL), functional independence and psychological distress 3 and 12 months post-IHCA.

**Methods:** A multicenter prospective cohort study in 25 hospitals between January 2017 – May 2018. Adult IHCA survivors were included. HRQoL (EQ-5D-5L, SF-12), psychological distress (HADS, CSI) and functional independence (mRS) were assessed at 3 and 12 months post-IHCA.

**Results:** At 3-month follow-up 136 of 212 survivors responded to the questionnaire and at 12 months 110 of 198 responded. The median (IQR) EQ-utility Index score was 0.77 (0.65–0.87) at 3 months and 0.81 (0.70–0.91) at 12 months. At 3 months, patients reported a median SF-12 (IQR) physical component scale (PCS) of 38.9 (32.8–46.5) and mental component scale (MCS) of 43.5 (34.0–39.7) and at 12 months a PCS of 43.1 (34.6–52.3) and MCS 46.9 (38.5–54.5).

**Discussion:** Using various tools most IHCA survivors report an acceptable HRQoL and a substantial part experiences lower HRQoL compared to population norms. Our data suggest that younger (male) patients and those with poor functional status prior to admission are at highest risk of impaired HRQoL.

© 2021 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

\* Corresponding author at: Department of Anesthesiology, Erasmus University Medical Center, P.O. Box 2040, 3000CA Rotterdam, the Netherlands.  
E-mail address: [m.schluep@erasmusmc.nl](mailto:m.schluep@erasmusmc.nl) (M. Schluep).

## 1. Introduction

In-hospital cardiac arrest (IHCA) is a major adverse event in hospitalized patients. Its outcome has improved over the past decades, although survival rates remain low [1–3]. Outcome assessment after cardiac arrest traditionally focuses on survival rates and clinician-based description of functional outcome. Historically, good outcome was defined as a Cognitive Performance Category of 1 or 2, indicating none to mild neurologic disability [4]. The 2018 International Liaison Committee On Resuscitation (ILCOR) statement on reporting in cardiac arrest research advocates the use of patient-reported outcome measures. In this regard, the Core Outcome Set for Cardiac Arrest research (COSCA) contains a well-constructed set of recommendations of which outcome measures to use [5]. The principal recommendation is to use health-related quality of life (HRQoL) and functional status at 90 days and 1 year via validated instruments, in addition to the use of a Cognitive Performance Category (CPC) scale to measure neurologic performance. To date, determinants of HRQoL in ICU patients and cardiac arrest survivors have not been studied extensively [6–10].

To survive a cardiac arrest is a close encounter with death and many patients report some form of existential suffering, alongside physical symptoms resulting from cardiopulmonary resuscitation and hospital treatment [11,12]. Identifying patients in need of (more specific and intensive) rehabilitation can help increase HRQoL among cardiac arrest survivors, but evidence is scarce [11,13–17]. Moreover, the role of age, sex and functional status on quality of life are not well described. We started the Resuscitation Outcomes in the Netherlands (ROUTINE) project to establish the characteristics of IHCA and its outcomes [2,3,18–20]. In a prior publication we presented a one-year survival rate of 27.8% and we described the influence of comorbidity and functional status on survival. The current manuscript adds a more in-depth analysis of HRQoL and its association with pre-arrest factors. [3]. As mentioned earlier, reported outcomes in cardiac arrest research need to focus more on what matters to patients [5,10]. The primary aim of this study is to describe HRQoL, anxiety, depression, and caregiver strain 3 and 12 months after IHCA. The secondary aim is to determine factors associated with HRQoL.

## 2. Methods

### 2.1. Design and setting

A nationwide multicenter prospective cohort study was performed. [3]. Our previous article contains more information on the follow-up in terms of survival and HRQoL in general. A call for participation was done through the Dutch Society for CPR-coordinators (NVCR). This resulted in 14 participating hospital organizations, comprising 25 hospital locations (25.3% of all Dutch hospitals). Data were collected through an online registration system (OpenClinica, Walton, MA, USA).

### 2.2. Patient population

Patients eligible for inclusion were adults ( $\geq 18$  years of age), who received in-hospital cardiopulmonary resuscitation, defined as the start of manual chest compressions for a circulatory arrest. The inclusion period was January 1st 2017 – May 31st 2018. Patients from all hospital wards, departments and outpatient clinics were included. Patients from the intensive care (ICU) and cardiac care units (CCU), as well as the emergency room (ER) were also included. Exclusion criteria were: OHCA  $< 24$  h prior to IHCA, purposely induced arrhythmia (e.g. electrophysiological interventions) or cardiac arrest (e.g. cardioplegia in cardiac surgery), or refusal to participate. Last follow-up was completed August 1st 2019.

### 2.3. Follow-up process

All patients were prospectively included through registration 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. At discharge, the Cognitive Performance Category (CPC) score was assessed and the discharge destination was registered. After 3- and 12-months post-discharge the survival status was checked using the Dutch Personal Records Database (Basis Registratie Personen; BRP). Survivors received questionnaires addressing their functional status and HRQoL. Up to two reminder questionnaires were sent and, in case of no response, patients were contacted by telephone.

### 2.4. Outcome measures

The primary outcome measure was health-related quality of life (HRQoL) measured by the EQ-5D-5L Visual Analogue Scale (EQ-VAS, explained below). Secondary outcome measures comprised an in-depth examination of HRQoL (EQ-5D-5L, Short Form-12) and measures of psychological distress (Hospital Anxiety and Depression Scale/HADS, Caregiver Strain Index/CSI) at 3 and 12 months after cardiac arrest, and survival rates.

### 2.5. Functional status and comorbidity

Functional status was determined through a self-reported Modified Rankin Scale (mRS) [21]. The mRS is a 5-point disability scale describing severity of functional disability: 0 means no disability and 5 means the patient is bedridden. Furthermore, reported functional status was confirmed by the SF-12 Physical Component Scale (PCS) and EQ-5D-5L mobility and usual activities domains. The Charlson Comorbidity Index was established at hospital admission and cross-checked with self-reported comorbidities at 3 and 12 months [22].

### 2.6. Health-related quality of life

#### 2.6.1. EuroQol: EQ-5D-5L

The EQ-5D-5L questionnaire measures 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 [23]. Calculated index scores range from 1 (best health state) to  $-0.59$  for a health state deemed worse than death. The visual analogue scale (EQ-VAS), a part of the EQ-5D-5L questionnaire, allows patients to score their perceived health state from 0 (indicating worst health state imaginable) to 100 (indicating best health state imaginable). [24] The EQ VAS provides a quantitative measure of the patient's perception of their overall state of health. In a previous study we assessed patients' experiences with CPR-directive counselling and as a general demographic we gathered EQ-5D data on these 1136 hospitalized patients from all types of hospital wards in fifteen hospitals, which we now used for comparison with our study population [20]. The hospitals in this cross-sectional cohort have an 85.7% overlap (12/14 hospitals) with the current study. Normative data for the Dutch population were obtained through the EuroQoL project [23].

#### 2.6.2. Short-form 12

The Short Form-12 is validated standardized questionnaire that uses a mental component scale (MCS) and physical component scale (PCS) [25]. SF-12 scores are standardized and result in composed scores for physical and mental health ranging from 0 (worst) to 100 (best health imaginable). Normative data for the Dutch population were obtained through Tilburg University [26].

**Table 1**

Characteristics of the study population. All variables are presented as n(%), unless stated otherwise. BMI: body mass index; CCI: Charlson Comorbidity Index; LOS: length of stay; HADS: Hospital Anxiety and Depression Scale; SF-12: short form 12 question quality of life questionnaire MCS: mental component scale of SF-12; PCS: physical component scale of SF-12; CSI: caregiver strain index; IQR interquartile range; EQ: EuroQoL or EQ-5D-5L; FU: follow-up. \*patients who were not admitted to ICU were admitted to coronary care units.

Patient characteristics	All IHCA patients		3-month responders		12-month responders	
During hospital admission	<i>n</i> = 713		<i>n</i> = 136		<i>n</i> = 110	
Age, median (IQR)	63	(52–72)	68	(58–73)	69	(59–73)
Male gender	460	–64.5	91	–66.9	77	–70
BMI (kg/m <sup>2</sup> ), median (IQR)	25.7	(23.0–30.0)	26.7	(23.9–30.3)	26.5	(24.1–26.5)
CCI, median (IQR)	1	(0–3)	1	(0–2)	1	(0–2)
Cerebral performance category 1–2	634	–88.9	131	–96.3	107	–97.3
Modified Rankin Scale (at home)						
0–1 – none/slight disability	488	–68.4	112	–82.4	90	–81.1
2–3 – moderate disability	174	–24.4	21	–15.4	16	–14.5
4–5 – severe disability	22	–3.1	1	–0.7	1	–0.9
Unknown	29	–4.1	2	–1.5	3	–2.7
After ROSC	<i>n</i> = 394					
Time to ROSC (min), median (IQR)	9	(5–15)	5	(2–10)	5	(2–10)
ICU admission*	299	–75.9	89	–65.9	72	–65.5
ICU LOS (days), median (IQR)	5	(2–15)	12	(6–21)	11	(5–22)
After hospital discharge	<i>n</i> = 231					
Cerebral performance category 1–2	179	–77.5	111	–81.6	90	–81.8
Discharge destination						
home or family	150	–64.9	92	–67.6	75	–68.2
medical facility	81	–35.1	44	–32.4	35	–31.8
Modified Rankin Scale at FU			missing <i>n</i> = 3		missing <i>n</i> = 1	
0–1 – none/slight disability			84	–62.7	76	–69.7
2–3 – moderate disability			42	–31.3	27	–24.8
4–5 – severe disability			8	–6	6	–5.5
Charlson Comorbidity Index (CCI) at FU			missing <i>n</i> = 1		missing <i>n</i> = 1	
0–1 – none/mild comorbidity			94	–69.6	70	–64.2
2–3 – moderate comorbidity			35	–25.9	32	–29.4
≥4 – severe comorbidity			6	–4.5	7	–6.4
EQ – visual analogue scale, median (IQR)			70	(60–80)	75	(65–85)
EQ – utility index score, median (IQR)			0.77	(0.65–0.87)	0.81	(0.70–0.91)
Short-Form 12 (SF-12)			missing <i>n</i> = 19		missing <i>n</i> = 7	
PCS, median (IQR)			38.9	(32.8–46.5)	43.1	(34.6–52.3)
MCS, median (IQR)			43.5	(34.0–39.7)	46.9	(38.5–54.5)
HADS – Anxiety			missing <i>n</i> = 11		missing <i>n</i> = 2	
Normal (0–7)			84	–67.2	73	–67.6
Minor (8–10)			26	–20.8	19	–17.6
Moderate (11–14)			14	–11.2	16	–14.8
Major (15–21)			1	–0.8	0	0
HADS – Depression			missing <i>n</i> = 11		missing <i>n</i> = 4	
Normal (0–7)			103	–82.4	89	–84
Minor (8–10)			15	–12	5	–4.7
Moderate (11–14)			5	–4	12	–11.3
Major (15–21)			2	–1.6	0	0
CSI – Caregiver strain indicated, <i>n</i> (%)			28	–23.9	18	–20.5

## 2.7. Psychological well-being

Symptoms of depression and anxiety are assessed using the Hospital Anxiety and Depression scale, or HADS. The HADS is a 14-item scale that generates ordinal data and is commonly used to determine the levels of anxiety and depression that a person is experiencing. Seven of the items relate to anxiety and seven relate to depression. The HADS yields a depression and anxiety sum score, ranging from 0 to 21 with higher scores indicating more severe symptoms. A cumulative score above 8 of either the depression or anxiety subscale is classified as clinically significant symptoms of depression or anxiety. HADS scoring permits dividing into categories of severity according to its original manual: less than 7 no symptoms; 8–10 mild; 11–14 moderate; 15–21 major [27]. The Caregiver Strain Index (CSI) can be used to quickly identify families with potential caregiving concerns. It is a 13-question tool that measures strain related to care provision. There is at least one item for each of the following major domains: Employment, Financial, Physical, Social and Time. Positive responses to 7 or more items on the index indicate a greater level of strain. This instrument can be used to assess individuals of any age who have assumed the role of caretaker. Because HADS and

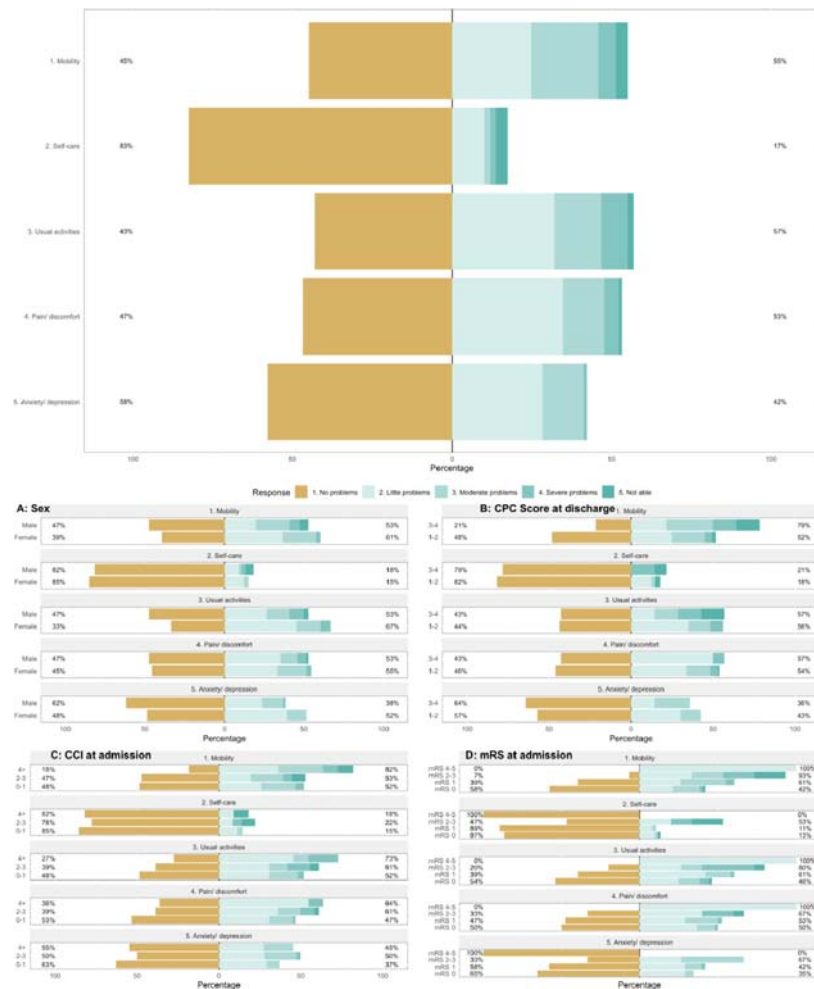
CSI have not been evaluated for cardiac arrest patients, we calculated Cronbach's alpha to test their internal validity [28].

## 2.8. Ethical considerations

Patients who survived to hospital discharge received study information at the hospital of admission. Prior to discharge patients were informed of the non-interventional design and informed consent was obtained for the use of their medical data, and for being approached within 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). The study was registered with [clinicaltrials.gov](https://clinicaltrials.gov) (NCT03120507) and the Dutch trial registry (NTR6145).

## 2.9. Statistical analysis

Data were summarized with descriptive statistics in terms of mean (standard deviation) or median (interquartile range) when appropriate. Normal distribution was visually assessed through histograms and Q-Q



**Fig. 1.** EQ-5D-5L quality of life domains with the reported levels of problems patients experience at 12-month follow-up. Pre-specified subgroups were used. EQ-5D-5L: EuroQoL 5 dimensions/5 level quality of life questionnaire, CPC: cognitive performance category, CCI: Charlson comorbidity index, mRS: modified Rankin scale.

plots. Comparisons between responders and non-responders (e.g., age, comorbidity, or admission specialty) were made by the  $\chi^2$ -test or Fisher exact (categorical) Mann-Whitney-U/Wilcoxon test (non-normal distribution). For comparison of SF-12 scores to normative standardized mean differences (SMD; *Cohen's d*) were calculated. For this goal the mean PCS and MCS scores were used as this was advised in the SF-12 manual. To investigate the influence of age and gender on EQ-5D-5L index score, Tobit regression was performed and right censored at 1. This censoring was performed because of skewed data on the one hand and a maximum performance limit of 1 on the other. Regression coefficients are presented along with their 95% confidence interval (CI). To determine the associations of CPC, functional status, and comorbidity with HRQoL, we performed subgroup analyses on the EQ-5D5L index scores and SF-12 PCS/MCS scores. The predefined subgroup analyses were made for age, the Charlson Comorbidity Index (CCI) (0–1; 2–3; 4 and higher) and the Modified Rankin Scale (0–1; 2–3; 4–5) at admission and at follow-up and the Cognitive Performance Category (1–2 and 3–4) at hospital discharge. Association between EQ-5D-5L index scores/SF-12 scores and subgroups were tested using a Kruskal-Wallis test. For effect size  $\epsilon^2$  was calculated [29]. Epsilon-squared ( $\epsilon^2$ ) is the equivalent of  $R^2$ , but rather for the Kruskal-Wallis test. An  $\epsilon^2$  of >0.16 is considered a relatively strong effect size, >0.36 is considered strong. For normally distributed data ANOVA was used. For all tests, a probability value for significance of less than 0.05 (two-sided) was used. Data

were analyzed using SPSS statistics v25.0 (IBM, Chicago, IL, USA) and R (The R Foundation for Statistical Computing, Vienna), using the 'censReg' package.

### 3. Results

A total of 713 patients suffered an in-hospital cardiac arrest during the inclusion period. Two hundred-thirty-one (32.4%) patients were discharged alive after cardiac arrest of whom 212 (29.7%) survived to 3 months and 198 (27.8%) to 12 months. The survival flow-chart is depicted in supplemental fig. 1. At follow-up 136/212 (64.1%) at 3 months and 110/198 (55.5%) of patients at 12 months responded to the questionnaires (i.e. responders). Table 1 summarizes data on responders. Demographics, cardiac arrest characteristics and hospital treatment were comparable between responders and non-responders (supplemental table 1). Functional disability prior to cardiac arrest (at home) was higher in non-responders vs. responders when evaluated at the 3-month time point (mRS  $\geq 2$  at home: 22.3% vs. 16.1%;  $p = .032$ ), and also at the 12-month time point (19.3% vs. 15.4%;  $p = .243$ ), albeit not significantly. The proportion of patients with a CPC score of 1–2 at discharge was similar between responders and non-responders, at 3 months (81.6% vs. 75.0%,  $p = .158$ ) and 12 months (81.8% vs. 75.0%,  $p = .332$ ). The majority of responders reported none to slight functional disability (mRS 0–1)



**Table 2**

Health-related quality of life index scores at 12-month follow-up for the complete group of responders and for various predefined subgroups. EQ-5D-5L; EuroQoL 5 dimensions/5-layer quality of life questionnaire, SF-12; short form 12 question quality of life questionnaire, med; median score. Range indicates the lowest and highest reported score. Group differences were assessed using the Kruskal-Wallis tests and variance is expressed as  $\epsilon^2$  (epsilon squared).

Health-related quality of life scores at 12-month follow-up												
	EQ-5D-5L index score				SF-12 physical component scale				SF-12 mental component scale			
	Med	range	$\epsilon^2$	p=	Med	range	$\epsilon^2$	p=	Med	range	$\epsilon^2$	p=
<b>Group total</b>	.81	.08-1.0	-	-	43.1	23.4-58.8	-	-	46.9	18.0-62.2	-	-
<b>Subgroups</b>			.006	.41			.006	.41				.54
Male gender	.82	.08-1.0			44.3	23.4-58.8			47.1	18.0-62.2		
Female gender	.81	.10-1.0			40.5	24.6-57.3			44.2	19.0-58.5		
<b>Modified Rankin Scale upon admission</b>			.133	.001			.114	.003			.009	.62
0-1	.85	.10-1.0			43.7	24.6-57.3			47.1	18.0-62.2		
2-3	.70	.08-.92			32.6	23.4-58.8			41.1	21.2-58.8		
4-5	.81	.81-.81			26.1	26.1-26.1			52.7	52.7-52.7		
<b>Charlson Comorbidity Index Upon admission</b>			.199	<.001			.172	<.001			.027	.26
0-1	.86	.50-1.0			46.6	24.6-58.8			48.8	18.0-62.2		
2-3	.80	.08-1.0			36.5	23.4-56.9			41.8	24.5-57.5		
4 or higher	.14	.08-.22			31.6	24.6-39.9			52.1	21.2-58.8		
<b>Cognitive Performance Cat. at discharge</b>			.003	.59			.009	.34			.001	.79
1-2	.81	.08-1.0			39.7	23.4-55.1			46.9	24.5-62.2		
3-4	.81	.08-1.0			43.4	24.6-58.8			56.9	18.0-58.8		
<b>Modified Rankin Scale at 12 months</b>			.500	<.001			.410	<.001			.136	<.001
0-1	.88	.65-1.0			49.1	26.1-58.8			49.9	18.0-58.8		
2-3	.66	.10-.87			34.1	23.4-43.3			38.7	19.0-62.2		
4-5	.14	.08-.22			30.0	25.7-33.1			28.7	21.2-58.8		

at 3 months (62.7%) and at 12 months (69.7%). For a longitudinal evaluation of mRS a Sankey plot is provided in supplemental fig. 2. This figure shows the transition of patients to other states of functional capacity over time.

3.1. HRQoL: EQ-5D-5L

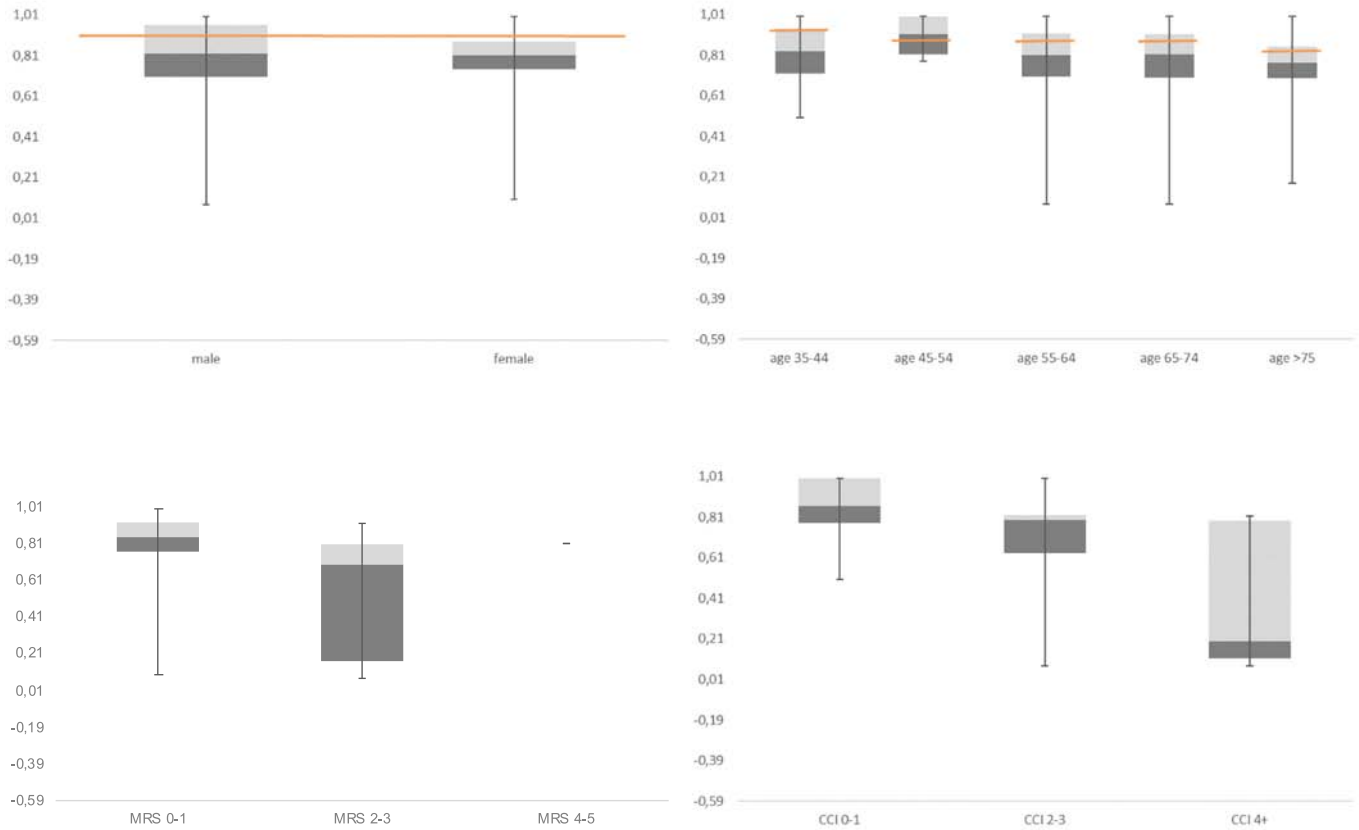
Median EQ-VAS was 70 (IQR 60–80) at 3 months and 75 (IQR 65–85) at 12 months ( $p = .022$ ). The reported EQ-5D-5L domains are displayed in Fig. 1. The most frequent reported problems at 12 months were: *usual activities* (56.9%), followed by *mobility* (55.0%), *pain* (53.2%), *anxiety/depression* (43.2%) and *self-care* (17.4%). Only a small proportion of patients ( $\leq 2.4\%$ ) reported severe problems (score  $\geq 4$ ) for each domain. Patients with higher pre-admission mRS and CCI, reported more and more severe problems in the EQ-5D-5L domains at 12-month follow-up (Fig. 1C-D). 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 ( $p = .007$ ).

We compared mean EQ-index scores stratified for predefined subgroups, as displayed in Table 2. EQ-index scores at follow-up were lower in patients with a lower mRS ( $\epsilon^2 = 0.133$   $p = .001$ ) and a higher CCI score ( $\epsilon^2 = 0.199$   $p = .001$ ) at admission. Patients who were discharged with none to mild neurologic disability (CPC 1–2) had the same median EQ-index as patients discharged with

moderate-severe neurologic disability (CPC 3–4) ( $\epsilon^2 = 0.003$   $p = .598$ ) (Table 2). In addition, median EQ-5D-5L index score did not differ when patients were subdivided based on age ( $\epsilon^2 = 0.02$ ) or sex ( $\epsilon^2 = 0.06$ ) (Fig. 2). Similar results were obtained when these variables were analyzed using a Tobit regression model (age  $-0.003$ , 95%CI  $-0.007$ ; 0.001,  $p = .173$ ; male sex:  $-0.01$ , 95% CI  $-0.1$ ; 0.01,  $p = .826$ ).

3.2. HRQoL: Short Form-12

At 3 months, patients reported a median (IQR) PCS of 38.9 (32.8–46.5) and MCS of 43.5 (34.0–39.7) and at 12 months a PCS of 43.1 (34.6–52.3) and MCS 46.9 (38.5–54.5). Median MCS ( $p = .002$ ) and PCS ( $p = .001$ ) scores increased between 3 and 12 months (Table 1 and Fig. 3). Overall, at 12 months patients reported a lower MCS (SMD  $-1.422$ , 95% CI  $-1.691$  to  $-1.152$ ) and PCS ( $-1.102$ , 95% CI  $-1.536$  to  $-0.507$ ) compared to a Dutch norm population. Fig. 3 displays the SMD for patients, subdivided for sex at both the 3- and 12-month follow-up. Men reported significantly lower scores than women on MCS at both 3 months (SMD  $-1.950$ , 95%CI  $-2.222$  to  $-1.686$ ) and 12 months (SMD  $-1.422$ , 95%CI  $1.691$  to  $-1.152$ ). Stratified for the predefined groups, there was a significant decrease in reported quality of life on both the physical and mental component scale for patients with a lower Modified Rankin Scale (Table 2).

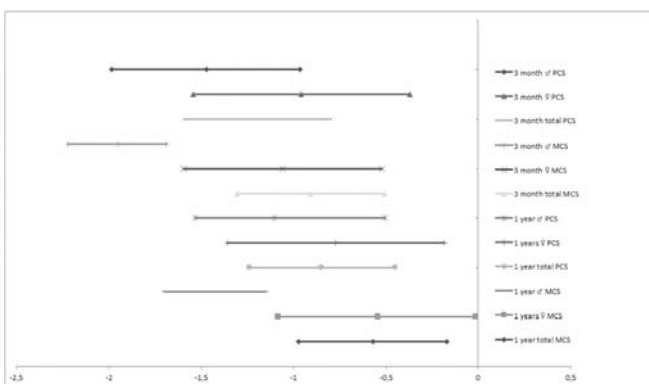


**Fig. 2.** EQ5D-5 L utility index scores stratified for sex, age, functional capacity and comorbidity index. All categories were measured upon hospital admission (pre-arrest). Presented are median utility index scores with the boxplot indicating the 25th and 75th (Q1-Q3) percentile and the whiskers indicating the lowest and highest (range) reported index score for each category. The reference median utility index score for the Dutch population is 0.89. Reference scores of the Dutch population per category are indicated by the orange line. For MRS 4–5 the score is 0.81 at  $n = 1$ , as described in supplemental fig. 2 & supplemental table 1. MRS: modified Rankin scale for functional capacity. CCI: Charlson Comorbidity Index score.

### 3.3. Hospital Anxiety and Depression Scale

Reliability of HADS questionnaire at 3 months and 12 months after IHCA was assessed by Cronbach's alpha and was questionable for the anxiety subscore (respectively 0.60 and 0.71) and good for the depression score (respectively 0.86; 0.90) [30]. Table 1 summarizes the results on the HADS questionnaire at 3 months and 12 months. Moderate-major problems on the anxiety scale (i.e.  $\geq 11$  points) were reported

by 12.0% (15/125) at 3 months and 14.8% (16/108) at 12 months. Moderate-major problems on the depression scale (i.e.  $\geq 11$  points) were reported by 5.6% (7/125) at 3 months and 11.3% (12/106) at 12 months. No significant association was observed between pre-arrest, hospital-related factors or CPC-score at discharge and the occurrence of anxiety or depression at 12 months. Moderate-major symptoms of depression at 12 months were more prevalent in male patients (Table 2).



**Fig. 3.** Perception of health state as assessed by SF-12. Standardized mean difference (SMD) of SF-12 scores at 3 months and 12 months for survivors in comparison with Dutch population norms, calculated according to domain (mental/physical) and sex. MCS indicates Mental Component Scale; PCS, Physical Component Scale.

### 3.4. Caregiver strain index

The Caregiver strain index evaluates the burden among patient's caregivers. Cronbach's alpha for the caregiver strain index was good (0.89; 0.88). At 3 months caregiver strain was reported by 23.9% of responders' caregivers and by 20.5% at 12 months, respectively (Table 3). Caregiver strain was more prevalent in patients with moderate-major depression symptoms versus none-mild symptoms (44.4% vs. 15.6%,  $p = .035$ ) as described in Table 3. A separate analysis showed caregiver strain was also more prevalent in patients with higher mRS scores  $\geq 2$  points versus 0–1 points as well (45.8% vs. 11.3%,  $p < .001$ ),

## 4. Discussion

In this large multicenter cohort study various tools were used to measure HRQoL and psychological wellbeing of In-Hospital Cardiac Arrest survivors. Most survivors report an acceptable HRQoL. Still a number of patients reported moderate or severe problems, mostly in usual

**Table 3**

Anxiety and depression in relation to patient characteristics at 12-month follow-up divided into none-mild and moderate-severe symptoms on the Hospital Anxiety and Depression Scale (HADS). HADS was divided into validated subgroups according to the scoring system: less than 7 no symptoms; 8–10 mild; 11–14 moderate; 15–21 major. *p*-values have been calculated for the differences between severity groups.

Patient characteristics	Follow-up at 12 months after cardiac arrest									
	HADS anxiety				<i>p</i> =	HADS depression				<i>p</i> =
	normal or minor		moderate-major			normal or minor		moderate-major		
	<i>n</i> = 92		<i>n</i> = 16		<i>n</i> = 94		<i>n</i> = 12			
Prior to admission										
Age median (IQR)		59 (60–78)	70 (60–78)	0.47	59 (58–73)	70 (59–78)	0.39			
Sex male	n (%)	63 (–82.9)	13 (–17.1)	0.3	62 (–84.9)	11 (–15.1)	0.07			
Female		29 (–90.6)	3 (–9.4)		32 (–97)	1 (–3)				
Charlson comorbidity index	med (IQR)	1 (0–2)	2 (0–3)	0.27	1 (0–2)	2 (0–3)	0.23			
Cerebral performance category 1–2	n (%)	89 (–96.7)	16 (–100)	0.77	92 (–97.9)	11 (–91.7)	0.2			
Modified Rankin Scale (at home)	n (%)			0.1			0.1			
0–1 – none/slight disability		78 (–87.6)	11 (–68.8)		80 (–87.9)	8 (–66.7)				
2–3 – moderate disability		10 (–11.2)	5 (–31.3)		10 (–11)	4 (–33.3)				
4–5 – severe disability		1 (–1.1)	0 (0)		1 (–1.1)	0 (0)				
After ROSC										
ICU admission	n (%)	59 (–64.1)	12 (–75)	0.39	62 (–66)	7 (–58.3)	0.6			
Length of stay after cardiac arrest	med (IQR)	11 (4–22)	14 (9–22)	0.28	11 (4–22)	14 (8–22)	0.49			
After discharge										
Cerebral performance category 1–2	n (%)	75 (–81.5)	13 (–81.3)	0.99	79 (–84)	8 (–66.7)	0.17			
Discharge destination	n (%)			0.21			0.23			
home or family		60 (–65.2)	13 (–81.3)		62 (–66)	10 (–83.3)				
medical facility		32 (–34.8)	3 (–18.7)		32 (–34)	2 (–16.7)				
At 12 month follow-up										
Modified Rankin Scale (at 12 months)	n (%)			<0.001			<0.001			
0–1 – none/slight disability		72 (–78.3)	4 (–25)		73 (–77.7)	3 (–25)				
2–3 – moderate disability		18 (–19.6)	8 (–50)		20 (–21.3)	6 (–50)				
4–5 – severe disability		2 (–2.2)	4 (–25)		1 (–1.1)	3 (–25)				
Caregiver strain indicated	n (%)			0.06			0.04			
Yes		12 (–16.2)	5 (–38.5)		12 (–15.6)	4 (–44.4)				
No		62 (–83.8)	8 (–61.5)		65 (–84.4)	5 (–55.6)				

activities, mobility and depression symptoms. Our findings suggest that HRQoL is lower in patients that are functionally incapacitated and that psychological distress is more prevalent among male survivors. Also, pre-arrest functional disability seems to predispose for impaired HRQoL at follow-up. Our study highlights the existence of problems in all daily aspects of life for cardiac arrest survivors, as well as its relationship with psychological well-being.

In general the HRQoL of IHCA survivors is lower than that of a Dutch norm populations, as reflected by the functional and psychological domains of the EQ-5D, the EQ-5D index score, and both SF-12 domains [23]. Male survivors more frequently reported psychological distress based on the SF-12-MCS and HADS. When we compared the EQ-index score to the Dutch population mean, a gap remains indicative of a lower HRQoL for cardiac arrest survivors. EQ-5D index scores are similar to those found in earlier studies on HRQoL at discharge in IHCA and OHCA patients [13,14,31,32] and in Dutch ICU-survivors [33]. Median EQ-5D-5L visual analogue scale score was 70 at 3 months and 75 at 12 months, as compared to 82 in the Dutch population norm and 62 in the cohort of hospitalized patients as described in our previous cross-sectional study [20,23]. A similar proportion of IHCA survivors reported problems concerning mobility, usual activities and pain as was reported by hospitalized patients, but IHCA survivors more frequently suffered from anxiety and depression [20]. Although IHCA survivors are discharged home in most cases and quality of life was measured while they were no longer in hospital, the reported problems in the ED-5D-5L domains were similar to patients during hospitalization. The proportion of patients with severe problems was however lower than in hospitalized patients, as described earlier [3]. Overall HRQoL, as determined by SF-12 and EQ-5D-5L was lower in IHCA survivors compared to a Dutch cohort of OHCA survivors [34]. The high incidence of caregiver strain and psychological distress was similar when we

compare our cohort to these OHCA survivors [34]. Similar SF-12 scores at 3 month and 12 month follow-up were observed in a Norwegian study [35].

Despite limitations inherent to such comparisons, our data delivers important signals. First, the prevalence of HRQoL problems is relatively high and perceived quality of life is lower compared to a reference population (Fig. 2). Nonetheless, the fraction of severe problems is relatively low (Fig. 1). Second, pre-arrest functional independence and comorbidity appears to resonate in more problems in the quality-of-life domains and lower HRQoL scores at follow-up (Fig. 1 and Table 2). Third, anxiety and depression are frequent in IHCA survivors (Table 3). We can only speculate on possible explanations for the findings on lower HRQoL. First, pre-existing illness and cerebral hypoxia may synergistically create a decline of quality of life in both physical and mental domains. After IHCA, in our cohort, most patients died after cessation of treatment for multi-organ failure (49.7%), or hypoxic brain damage (29.7%) and only a minority died without cessation of treatment (i.e. re-occurrence of cardiac arrest without subsequent medical intervention)(20.5%). It is possible that these number reflect on the survivors, i.e. the presence of both (less severe) multi-organ failure and hypoxic damage. For OHCA cessation of treatment is largely based on the presence of irreversible severe brain damage, whereas multi-organ failure is less common [1]. Secondly, there may be a lack of recognition of the problem of IHCA survivors. IHCA survivors return to the hospital ward after an ICU session to be treated for their underlying disease rather than receiving physical and neurocognitive rehabilitation aimed at cardiac arrest survivors. Lastly, in our own cohort, only 23.4% attended a rehabilitation program. We believe this may also contributed to diminished HRQoL. These findings show the impact of cardiac arrest and subsequent critical illness on patients' lives and indicate the presence of suffering [20]. The relation to functional incapacitation is relevant, as it might prove useful for rehabilitation purposes.

To date, this is the second largest prospective study to describe HRQoL and psychological distress among IHCA survivors [14]. In the heterogeneity of reported outcome measures, our study is one of the first to adhere to the Core Outcome Set for Cardiac Arrest recommendations by the ILCOR. No specific instrument is available for assessing HRQoL in cardiac arrest survivors. As each of the used measurements has its merits and demerits, the simultaneous use of qualitative instruments and functional and survival outcome measures is currently the most practical mode of reporting [36]. Several interactions or the lack thereof, are notable. First, the CPC scores at discharge were not associated with HRQoL at 3 or 12 months, nor with psychological well-being. CPC has often been used to describe “good outcome” [13,36,37]. As CPC does not clearly correlate with HRQoL in our study, this finding expresses once more that quality of life warrants a more in-depth examination. Secondly, patients with more severe depression or anxiety more often reported functional disability. This is in accordance with prior reports from OHCA populations and supports the need for more structured rehabilitation programs aiming at both physical as psychological well-being [16,38,39].

In a prior publication we reported findings from this cohort that focused mainly on survival and observed that survival was associated with pre-admission functional status (mRS) and the level of comorbidity (ACCI) [3]. The current manuscript adds challenges to the topics of cardiac arrest prognostication and subsequent patient counselling. We have now described survival, health-related quality of life and the possible problems IHCA survivors may encounter. We however do not yet have a clear picture of the weight patients attribute to these outcomes and future CPR-directives counselling should take this into account. How and on what specific topics patients need to be informed about during a CPR-directive conversation is not yet fully elucidated but probably requires an individualised approach [10,40]. As patient centred care and advance care planning have become increasingly important, based on our findings, a patient’s condition and functional status at admission should be taken into account when speaking about CPR-directives.

Three important caveats need consideration when interpreting our results. Because not all survivors responded, the possibility of response bias is realistic. Notwithstanding, several lines of data suggest non-response bias in our study to be limited. First, baseline demographics, cardiac arrest characteristics and hospital treatment characteristics were similar between responders and non-responders. Second, functional status prior to cardiac arrest was similar in both groups. Third, the proportion of patients with a CPC score of 1–2 was similar between responders and non-responders, at all study time points evaluated. Although the actual impact is not quantifiable, non-participation in itself might be a proxy for psychological distress. Especially non-participation in elderly and frail patients tend to skew the results of HRQoL research. This may lead to the results being more positive than the actual perceived HRQoL of the entire group [41]. If this effect applies to our data, HRQoL for IHCA survivors may actually be lower than we have now described. Future research, with more in-depth follow-up should elucidated this phenomenon. The second caveat pertains to validation. As noted earlier all methods used to quantify HRQoL and psychological distress have not been formally validated for cardiac arrest survivors. They are, however, in itself well-validated, widely used and recommended in current guidelines for post-resuscitation care [5,17]. Also, cardiac arrest survivors are in most cases also ICU survivors. And [35]. HRQoL appears lower in patients with functional disability at home, although it is hard to make a definite conclusion due to the number of responders that was too low. Although we cannot formally determine whether pre-arrest factors, the cardiac arrest itself, or subsequent ICU treatment is the main driver of diminished HRQoL, the message remains unaltered; HRQoL is diminished and requires our attention in the post-resuscitation period. The third caveat pertains to selection. We feel

is it plausible that patients, who report longstanding incapacitation and diminished quality of life at hospital admission, will have been given a Do Not Resuscitate order. In our studies on survival characteristics and on CPR-directives, we report a relatively high survival rate and we explained that one of the causes might be selection of patients for whom CPR is deemed likely to be successful [3,20]. If these patients had been resuscitated, survival might have been lower, as well as HRQoL of the surviving group. This needs to be taken into account when comparing our results to other studies. However, it also stresses even more the importance of CPR prognostication and adequate communication of CPR-directives [10].

This study underlines the added value of more patient-reported outcome measures in cardiac research, confirms the burden of physical and psychological impairments among IHCA survivors and highlights certain groups of survivors at particular risk. We suspect patients suffering from IHCA, unlike OHCA survivors are not recognized as cardiac arrest survivors. IHCA survivors frequently return to the hospital ward after an ICU admission to be treated for their underlying disease. Physical and neurocognitive rehabilitation had less priority in these cardiac arrest survivors. Screening and risk stratification for physical and psychological issues should be implemented in post-cardiac arrest care. Our data suggest that younger (male) patients and those with a pre-existing poor functional status are at highest risk. In these patients, early recognition of problems and subsequent early rehabilitation could prove especially useful with regard to improving quality of life and return to daily life.

#### Credit author statement

M. (Marc) Schluep: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Writing - original draft;

B.Y. (Benjamin) Gravesteijn: Data curation; Formal analysis; Project administration;

S.E. (Sanne) Hoeks, PhD: Data curation; Methodology; Formal analysis; Supervision; Writing - original draft;

C. (Cees) Kuijs, RN - M.J. (Michiel) Blans, MD - B. (Bas) van den Bogaard, MD, PhD - A.W.M.M. (Ankie) Koopman - van Gemert, MD, PhD - C.J. (Chris) Hukshorn, MD, PhD - B.J.M. (Nardo) van der Meer, MD, MBA, PhD - A.H.M. (Marco) Knook, MD, MBA - T. (Trudy) van Melsen, MD - R. (René) Peters, MD, PhD - P.J. (Patrick) Perik, MD, PhD - K.S. (Koen) Simons, MD, PhD - G. (Gerben) Spijkers, MD - J.W. (Wytze) Vermeijden, MD, PhD - E.J. (Evert-Jan) Wils, MD, PhD - Data curation; Writing - review & editing.

R.J. (Robert Jan) Stolker, MD, PhD and H. (Rik) Endeman, MD, PhD - Supervision; Methodology; Writing - review & editing.

#### Declaration of Competing Interest

This study was funded by Departmental Funds of the Participating Hospitals. Licensing of the SF-12 software (€800) was funded by the ESA Air Liquide unrestricted research grant 2017, as well as printing and postage costs (approx. €300).

#### Acknowledgements

We would like to thank all participating hospital organizations for their help in this multicenter project. In particular we would like to thank the following local investigators for their help in data collection: Elke Berger, Andrea Bouts, Mariska Burgmeijer, Ann van Daalen, Merel Erkamp, Benjamin Gravesteijn, Irene Hoekstra, Loes Mandigers, Alice Pap, Patrick Perik, Koen Rijs, Martin Rinket, Francis de Smet, Ramón Soer, Peggy Sorensen, Friso Wesdorp, Hermien van der Wier, Steven Winkel, Mirjam van der Zeijst.



## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jccr.2021.11.008>.

## References

- Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-hospital cardiac arrest. *JAMA*. 2019;321:1200. <https://doi.org/10.1001/jama.2019.1696>.
- Schluep M, Gravesteijn BY, Stolker RJ, Endeman H, Hoeks SE. One-year survival after in-hospital cardiac arrest: a systematic review and meta-analysis. *Resuscitation*. 2018;132:90–100. <https://doi.org/10.1016/j.resuscitation.2018.09.001>.
- Schluep M, Hoeks SE, Blans MJ, van den Bogaard B, AWMM Koopman Van Gemert, Kuijs C, et al. Long-term survival and health-related quality of life after in-hospital cardiac arrest. *Resuscitation*. 2021. <https://doi.org/10.1016/j.resuscitation.2021.07.006>.
- Group TH after CAS. Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest, 346; 2009; 549–56. <https://doi.org/10.1056/NEJMoa012689>.
- Haywood K, Whitehead L, Nadkarni VM, Achana F, Beebsems S, Böttiger BW, et al. COSCA (Core outcome set for cardiac arrest) in adults: an advisory statement from the international liaison committee on resuscitation. *Resuscitation*. 2018;127:147–63. <https://doi.org/10.1016/j.resuscitation.2018.03.022>.
- Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of THE outcomes reported in cardiac arrest clinical trials: THE need for a core outcome set. *Resuscitation*. 2015;88:150–7. <https://doi.org/10.1016/j.resuscitation.2014.11.013>.
- Kerckhoffs MC, Kosasi FFL, Soliman IW, van Delden JJM, Cremer OL, de Lange DW, et al. Determinants of self-reported unacceptable outcome of intensive care treatment 1 year after discharge. *Intensive Care Med*. 2019;45:806–14. <https://doi.org/10.1007/s00134-019-05583-4>.
- Elliott VJ, Rodgers DL, Brett SJ. Systematic review of quality of life and other patient-centred outcomes after cardiac arrest survival. *Resuscitation*. 2011;82:247–56. <https://doi.org/10.1016/j.resuscitation.2010.10.030>.
- Djäv T, Bremer A, Herlitz J, Israelsson J, Cronberg T, Lilja G, et al. Health-related quality of life after surviving an out-of-hospital compared to an in-hospital cardiac arrest: a Swedish population-based registry study. *Resuscitation*. 2020;151:77–84. <https://doi.org/10.1016/j.resuscitation.2020.04.002>.
- Djäv T, Lilja G. My quality of life is superb but can you let me die next time? *Resuscitation*. 2021;0. <https://doi.org/10.1016/j.resuscitation.2021.07.030>.
- Haydon G, van der Riet P, Maguire J. Survivors' quality of life after cardiopulmonary resuscitation: an integrative review of the literature. *Scand J Caring Sci*. 2017;31:6–26.
- Whitehead L, Perkins G, Biggerstaff D, Couper K, Haywood K. Exploring the lived experience of surviving an out of hospital cardiac arrest: understanding what health outcomes really matter to patients. *Resuscitation*. 2015;96:108. <https://doi.org/10.1016/j.resuscitation.2015.09.255>.
- Haydon G, van der Riet P, Maguire J. Survivors' quality of life after cardiopulmonary resuscitation: an integrative review of the literature. *Scand J Caring Sci*. 2017;31(1):6–26. <https://doi.org/10.1111/scs.12323> Epub 2016 Jul 21. PMID: 27440375.
- Israelsson J, Bremer A, Herlitz J, Axelsson AB, Cronberg T, Djäv T, et al. Health status and psychological distress among in-hospital cardiac arrest survivors in relation to gender. *Resuscitation*. 2017;114:27–33. <https://doi.org/10.1016/j.resuscitation.2017.02.006>.
- Smith K, Andrew E, Lijovic M, Nehme Z, Bernard S. Quality of life and functional outcomes 12 months after out-of-hospital cardiac arrest. *Circulation*. 2014;131:174–81. <https://doi.org/10.1161/circulationaha.114.011200>.
- Boyce LW, Goossens PH, Moulart VR, Pound G, van Heugten CM. Out-of-hospital cardiac arrest survivors need both cardiological and neurological rehabilitation! *Curr Opin Crit Care*. 2019;25:240–3. <https://doi.org/10.1097/MCC.0000000000000609>.
- Nolan JP, Soar J, Cariou A, Cronberg T, Moulart VRM, Deakin CD, et al. European resuscitation council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care. *Intensive Care Med*. 2015;41:2039–56. <https://doi.org/10.1007/s00134-015-4051-3>.
- Gravesteijn BY, Schluep M, Voormolen DC, van der Burgh AC, Dos Reis Miranda D, Hoeks SE, et al. Cost-effectiveness of extracorporeal cardiopulmonary resuscitation after in-hospital cardiac arrest: a Markov decision model. *Resuscitation*. 2019;143. <https://doi.org/10.1016/j.resuscitation.2019.08.024>.
- Schluep M, van Limpt GJC, Stolker RJ, Hoeks SE, Endeman H. Cardiopulmonary resuscitation practices in the Netherlands: results from a nationwide survey. *BMC Health Serv Res*. 2019;19:333. <https://doi.org/10.1186/s12913-019-4166-2>.
- Schluep M, Hoeks SE, Endeman H, Ijmker S, TMM Romijn, Alisma J, et al. A cross-sectional investigation of communication in do-not-resuscitate orders in Dutch hospitals. *Resuscitation*. 2020. <https://doi.org/10.1016/j.resuscitation.2020.04.004>.
- van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*. 1988;19:604–7. <https://doi.org/10.1161/01.STR.19.5.604>.
- Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2011;173:676–82. <https://doi.org/10.1093/aje/kwq433>.
- Janssen B, Szende A. Population Norms for the EQ-5D. Self-Reported Popul. Heal. An Int. Perspect. Based EQ-5D. Dordrecht: Springer Netherlands; 2014; 19–30. [https://doi.org/10.1007/978-94-007-7596-1\\_3](https://doi.org/10.1007/978-94-007-7596-1_3).
- Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20:1727–36. <https://doi.org/10.1007/s11136-011-9903-x>.
- Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, et al. Cross-validation of item selection and scoring for the SF-12 health survey in nine countries: results from the IQLA project. *International quality of life assessment. J Clin Epidemiol*. 1998;51:1171–8.
- Mols F, Pelle AJ, Kupper N. Normative data of the SF-12 health survey with validation using postmyocardial infarction patients in the Dutch population. *Qual Life Res*. 2009;18:403–14. <https://doi.org/10.1007/s11136-009-9455-5>.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67:361–70. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>.
- Robinson BC. Validation of a caregiver strain index. *J Gerontol*. 1983;38:344–8. <https://doi.org/10.1093/geronj/38.3.344>.
- Rea L, Parker R. *Designing and Conducting Survey Research: A Comprehensive Guide*. 4th ed. Wiley; 2014 [ISBN 978-1-118-76703-0 2014].
- Spinhoven PH, Ormel J, Sloekers PPA, Kempen GJJM, Speckens AEM, Van Hemert AM. A validation study of the hospital anxiety and depression scale (HADS) in different groups of Dutch subjects. . vol. 27Cambridge University Press; 1997.
- Wilder Schaaf KP, Artman LK, Peberdy MA, Walker WC, Ornato JP, Gossip MR, et al. Anxiety, depression, and PTSD following cardiac arrest: a systematic review of the literature. *Resuscitation*. 2013;84:873–7. <https://doi.org/10.1016/j.resuscitation.2012.11.021>.
- Wachelder EM, Moulart VRMP, van Heugten C, Verbunt JA, Bekkers SCAM, Wade DT. Life after survival: long-term daily functioning and quality of life after an out-of-hospital cardiac arrest. *Resuscitation*. 2009;80:517–22.
- Soliman IW, de Lange DW, Peelen LM, Cremer OL, Slooter AJC, Pasma W, et al. Single-center large-cohort study into quality of life in Dutch intensive care unit subgroups, 1 year after admission, using EuroQoL EQ-6D-3L. *J Crit Care*. 2015;30:181–6. <https://doi.org/10.1016/j.jccr.2014.09.009>.
- Beebsems SG, Wittebrood KM, de Haan RJ, Koster RW. Cognitive function and quality of life after successful resuscitation from cardiac arrest. *Resuscitation*. 2014;85:1269–74. <https://doi.org/10.1016/j.resuscitation.2014.05.027>.
- Langerud AK, Rustoen T, Småstuen MC, Kongsgaard U, Stubhaug A. Health-related quality of life in intensive care survivors: associations with social support, comorbidity, and pain interference. *PLoS One*. 2018;13. <https://doi.org/10.1371/journal.pone.0199656>.
- Whitehead L, Perkins G, Clarey A, Haywood K. A systematic review of the outcomes reported in cardiac arrest randomised controlled trials: the need for a core outcome set. *Resuscitation*. 2013;84:S50. <https://doi.org/10.1016/j.resuscitation.2013.08.129>.
- Thai TN, Ebell MH. Prospective validation of the good outcome following attempted resuscitation (GO-FAR) score for in-hospital cardiac arrest prognosis. *Resuscitation*. 2019;140:2–8. <https://doi.org/10.1016/j.resuscitation.2019.05.002>.
- Moulart V, Wachelder EM, Verbunt JA, Wade DT, van Heugten CM. Determinants of quality of life in survivors of cardiac arrest. *J Rehabil Med*. 2010;42:553–8.
- Moulart VRM, van Heugten CM, Winkens B, Bakx WGM, de Krom MCFM, Gorgels TPM, et al. Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: a randomised controlled trial. *Int J Cardiol*. 2015;193:8–16. <https://doi.org/10.1016/j.ijcard.2015.04.229>.
- Fritz Z, Slowther A-M, Perkins GD. Resuscitation policy should focus on the patient, not the decision. *BMJ*. 2017;356:j813. <https://doi.org/10.1136/BMJ.j813>.
- Coste J, Quinquin L, Audureau E, Pouchot J. Non response, incomplete and inconsistent responses to self-administered health-related quality of life measures in the general population: patterns, determinants and impact on the validity of estimates – a population-based study in France using the MOS SF-36. *Heal Qual Life Outcomes*. 2013;11(11):1–15. <https://doi.org/10.1186/1477-7525-11-44>.