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Clinical paper

Recognizing the causes of in-hospital cardiac arrest — A survival benefit☆

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ABSTRACT

Background: The in-hospital emergency team (ET) may or may not recognize the causes of in-hospital cardiac arrest (IHCA) during the provision of cardiopulmonary resuscitation (CPR). In a previous 4.5-year prospective study, this rate of recognition was found to be 66%. The aim of this study was to investigate whether survival improved if the cause of arrest was recognized by the ET.
Methods: The difference in survival if the causes were recognized versus not recognized was estimated after propensity score matching patients from these two groups.
Results: Overall survival to hospital discharge was 25%. After propensity score matching, the benefit of recognizing the cause regarding 1-hour survival of the episode was 29% ($p < 0.01$), and 19% regarding hospital discharge, respectively. Variables commonly known to affect the outcome after cardiac arrest were found to be balanced between the two groups. The largest difference was found in patients with non-cardiac causes and non-shockable presenting rhythms. Patient records and pre-arrest clinical symptoms were the information sources most frequently utilized by the ET to establish the causes of arrest.
Conclusions: Patients suffering an IHCA showed a substantial survival benefit if the causes of arrest were recognized by the ET. Patient records and pre-arrest clinical symptoms were the sources of information most frequently utilized in these instances.

Introduction

In-hospital cardiac arrest (IHCA) is the ultimate complication to critical illness among hospitalized patients. If the triggering causes of arrest are recognized by the in-hospital emergency team (ET), this may have crucial consequences for survival.

Improvements of the cardiac arrest (CA) chain-of-survival (COS) have contributed to increased survival in many regions: early recognition of CA, immediate and good quality cardiopulmonary resuscitation (CPR), early defibrillation in cases of pulseless and shockable cardiac arrhythmias, and proper care of immediate survivors.[1–7] Further elements for improvement should be sought.

From the early days of 'modern resuscitation' to the current guidelines for advanced life support (ALS) and in-hospital resuscitation, encouragement has been given to 'recognize & treat' and 'correct reversible causes during CPR'.[8–11] In a recent prospective and observational study from our institution we found the 'rate of recognition' of causes to be 198 of 302 episodes (66%).[12] To what extent the recognition of cause of cardiac arrest influences survival has not been thoroughly investigated. While return of spontaneous circulation (ROSC) ought to be improved by recognizing and treating the underlying cause, survival to hospital discharge is likely to be less affected — depending on additional factors such as comorbidity.

The aim of this study was to investigate whether recognition of causes during the provision of ALS led to improved survival, and to describe the sources of information utilized by the ET to establish the causes.

☆ A Spanish translated version of the summary of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2015.09.395.

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Table 1
Episode- and patient variables with/without recognized causes of arrest.

Episodes ($n = 302$)	Causes recognized by the ET ($n = 198$)		Causes not recognized by the ET ($n = 104$)	
	n	Percent	*n*	Percent
1-Hour survival	130	66%	34	33%
Age (mean, SD)	69y	±12y	71y	±12y
Male	128	69%	66	66%
Presenting rhythm				
PEA	93	47%	51	49%
Asystole	38	19%	32	31%
VF/VT	63	32%	20	19%
Unknown	4	2%	1	1%
Witnessed	181	91%	76	73%
Monitored	128	65%	30	29%
Delay to CPR, 75th% percentile	1 min		1 min	
Delay to defib., 75th% percentile	2 min		3 min	
CPR end; median, IQR	17 min	7–30 min	17 min	10–29 min
Epinephrine	124	63%	75	72%
Localization				
Ward	80	40%	71	68%
Intermediate	73	37%	16	15%
Emergency dep.	15	8%	7	7%
Cardiac lab.	7	4%	0	
Radiology dep.	6	3%	5	5%
ICU	4	2%	2	2%
Other dep.	13	7%	3	3%
Patients ($n = 285$)	Causes recognized by the ET ($n = 185$)		Causes not recognized by the ET ($n = 100$)	
	n	Percent	*n*	Percent
Survival to hospital discharge	61	33	10	10

ET: emergency team; PEA: pulseless electrical activity; VF/VT: ventricular fibrillation/ventricular tachycardia; CPR: cardiopulmonary resuscitation; defib.att.: defibrillator attached; IQR: inter-quartile range; ICU: intensive care unit; dep.: department; lab.: laboratory.

Methods

Material

From January 2009 to August 2013, we prospectively observed all IHCA episodes at the St Olav University Hospital in Norway. The details concerning patients, inclusion strategy and the thorough investigation of the IHCA causes, were described in recent papers.[12,13] The ET consist of one resident anaesthesiologist, one resident cardiologist and one nurse anaesthetist and responds to every location of the hospital, including the emergency department. The ET are set up to provide respiratory and circulatory stabilizing measures at any time of the day. The ET may obtain further support from the intensive care physician or interventional cardiologist, among others.

The study was registered at clinicaltrials.gov (NCT00920244). The regional committee for medical and health research ethics in central Norway approved the study: REK 4.2008.2402, ref. no: 2009/1275.

Table 2
Adjusted effect estimates if causes of arrest were recognized by the ET.

	1-Hour survival	Hospital discharge
coef	0.285	0.190
se	0.103	0.086
p	0.006	0.026
N	195	184
n0	65	63
n1	130	121

A coefficient (coef) of 0.285 means 28.5% estimated increased survival if causes were recognized by the emergency team (ET). se: standard errors; *p*: *p*-values. *N*: number of cardiac arrest episodes (1-hour survival) and number of patients (hospital discharge) respectively; n0: the group with unrecognized causes of arrest; n1: the group with recognized causes of arrest.

Data analysis and statistical methods

To investigate the consequences of recognizing the causes by the ET and ROSC, we tabulated both the observed 1-hour survival and the survival to hospital discharge, against recognition of the underlying cause(s); yielding unadjusted estimates of this association. To further investigate potential causality, we applied a 'treatment effect' estimator based on propensity score matching (teffects psmatch in STATA IC 13.1 for Windows, StataCorp LP, Texas, USA). Propensity score matching reduces the bias due to confounding variables in estimates of the effect of treatment in observational data sets. In this analysis we defined 'treatment' as the underlying cause of CA being recognized by the ETs. The 'treatment effect' was defined as the average difference in survival between the 'treated' patients and propensity score matched patients who *did not* receive the 'treatment', i.e. patients whose causes *were not* recognized by the ET. The propensity of a cardiac arrest episode is the estimated probability (between 0 and 1) that the causes of arrest were recognized by the attending ET, conditional on the variables included. The following episode variables were included in the estimation of the propensity scores: witnessed arrest, monitored arrest, delay to CPR, presenting cardiac rhythm, delay to attachment of a defibrillator, duration of CPR, whether or not intravenous epinephrine (adrenaline) was administered, and age. To closer identify subgroups of patients where the 'effect' of recognition was most pronounced, we stratified the analysis according to cardiac/non-cardiac causes and shockable/non-shockable presenting rhythms, and calculated two-sided Fischer's exact test statistics.

An essential assumption regarding treatment effect estimation from observed data is the 'overlap assumption'. It states that all individuals in the analysis must have a positive and overlapping probability of being exposed to the treatment — in this case the recognition of causes. We constructed overlap plots

Table 3
Survival according to recognition of causes. Stratified according to cardiac aetiology and shockable arrhythmia.

Table 3. Survival according to recognition of causes. Stratified according to cardiac aetiology and shockable arrhythmia.

1-hour survival in 302 episodes			Recog.	Not recog.	Crude benefit	p
CARDIAC	VF/VT	Survival	49	9		
		Dead	12	3		
		Total	61	12		
		% survival	80 %	75 %	5 %	0.7
	Non-VF/VT	Survival	26	6		
		Dead	35	18		
		Total	61	24		
		% survival	43 %	25 %	18 %	0.14
NON-CARDIAC	VF/VT	Survival	2	5		
		Dead	0	3		
		Total	2	8		
		% survival	100 %	63 %	37 %	1.00
	Non-VF/VT	Survival	53*	14		
		Dead	21	46		
		Total	74	60		
		% survival	72 %	23 %	49 %	< 0.01
Hospital discharge in 285 patients			**Recog.**	**Not recog.**	**Crude benefit**	**p**
CARDIAC	VF/VT	Survival	31	5		
		Dead	20	6		
		Total	51	11		
		% survival	61 %	45 %	16 %	0.5
	Non-VF/VT	Survival	8	1		
		Dead	52	22		
		Total	60	23		
		% survival	13 %	4 %	9 %	0.67
NON-CARDIAC	VF/VT	Survival	0	2		
		Dead	2	5		
		Total	2	7		
		% survival	0 %	29 %	-29 %	1
	Non-VF/VT	Survival	22*	2		
		Dead	50	57		
		Total	72	59		
		% survival	31 %	3 %	28 %	< 0.01

The 1-hour survival among 302 episodes (upper table), and survival to hospital discharge among 285 patients (lower table), stratified according to cardiac or non-cardiac aetiology, shockable or non-shockable presenting rhythms and whether the causes of arrest were recognized or not.
*The causes identified among these survivors are tabulated in Table 4.
ET: Emergency team; VF/VT: ventricular fibrillation/ventricular tachycardia; Recog.: recognized, *p*: *p*-value from two-sided Fischers' exact test.

based on the propensity scores to assess if this assumption was met.

Heterogeneity regarding the 'treatment effect' within the cohort was investigated using the 'test_condate' function based on the treatment effect estimator.[14,15] It is a test of the null-hypothesis that the 'treatment effect' within the cohort is equal for all individuals. It uses the same variables as for the 'treatment effect' estimation above. The appendix contains extended information about propensity score matching and treatment effect estimation. A *p* value of 0.05 or less was considered statistically significant.

Table 4
Causes recognized in survivors from non-cardiac non-shockable arrest.

1-Hour survival: 56 causes in 53 episodes	Number	%
Hypoxia	35	63
Hypovolaemia	7	13
Pulmonary embolus	6	11
Cerebral seizure	4	7
Cerebral infarction/haemorrhage	2	4
Cardiac tamponade	1	2
Hyperkalaemia	1	2
Survival to hospital discharge: 22 causes in 22 patients	**Number**	**%**
Hypoxia	17	77
Pulmonary embolus	3	14
Cerebral seizures	2	9

Causes recognized by the emergency team in survivors from non-cardiac, non-shockable cardiac arrests (marked with * in Table 3). One episode may have more than one cause.

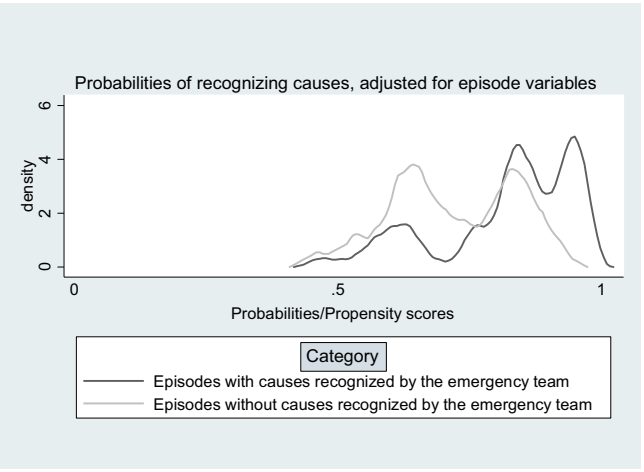

Fig. 1. Estimated probabilities ('propensity scores') that the causes of arrest could be recognized by the emergency team, for the two groups of in-hospital cardiac arrest patients whose causes were *recognized* (dark grey curve) and *not recognized* (light grey curve), conditional on observed variables; first documented rhythm, witnessed arrest, monitored arrest, delay to CPR, delay to defibrillator attached, whether epinephrine (adrenalin) was administered or not, CPR duration and age. ALS: Advanced life support.

Results

Two-hundred and eighty-five patients experienced 302 IHCA episodes (17 patients experienced two episodes). Overall survival to discharge was achieved in 71/285 patients (25%), as recently published.[12] Table 1 shows overall survival and episode variables for patients with and without recognized causes of arrest. The 'crude' unadjusted difference in 1-hour survival according to whether or not the causes were recognized, were 33%. The corresponding difference regarding survival to hospital discharge was 23% (Table 1).

The 'treatment effect' estimates are presented in Table 2. Regarding the 1-hour episode survival, the coefficient was 0.285 which means a 28.5% increased survival if causes were recognized. The corresponding coefficient regarding survival to hospital discharge was 0.19 meaning a 19% increased survival (Table 2). The estimates are statistically significant and roughly correspond to the unadjusted differences reported above.

The results from the 'test_condate' analysis were statistically significant, both regarding 1-hour survival and to hospital discharge (Appendix). This means that the estimated survival difference was unevenly distributed within the cohort. By stratification on cardiac/non-cardiac causes and shockable/non-shockable rhythms, the largest survival difference was found among patients with non-cardiac aetiologies and non-shockable initial rhythms (Table 3). This applied both for 1-hour episode survival and survival to hospital discharge. The actual causes recognized in this subgroup of survivors are presented in Table 4.

The probability density plot in Fig. 1 shows the influence of episode variables on the conditional probabilities (the estimated propensity scores) that the causes of arrest could be recognized by the ET. The groups are clearly overlapping and the probability mainly above 0.5, indicating proper balance of the variables between the two groups.

One-hour survival was never achieved in 132 episodes. In 22 of these episodes (7% of all 302 episodes), CPR and further life support was actively terminated based on information about underlying critical condition, comorbidity or the immediate cause of arrest.

In the 198 of 302 episodes where the ET correctly identified a cause of arrest (66% 'rate-of-recognition'), several sources of patient data were utilized (Fig. 2). The sources predominantly utilized (i.e. in more than 50% of episodes) were patient records and pre-arrest clinical symptoms.

Discussion

The main finding in this study was that 1-hour episode survival and survival to hospital discharge was substantially better for cardiac arrest patients whose causes were recognized by the emergency teams, also after adjusting for relevant variables via propensity score matching. The benefit was most pronounced among patients with non-cardiac causes and non-shockable presenting rhythms. The causes identified in this subgroup (hypoxia, hypovolaemia, thrombosis/pulmonary embolus, cardiac tamponade and hyperkalaemia) correspond to the ALS guidelines' recommendations to look for potentially reversible '4H4T' causes.[16,17] A similar analysis of survival after IHCA related to the recognition of causes has not been described in the literature. Our findings suggest that a structured search for underlying causes of IHCA during ALS should be encouraged, especially in episodes of non-shockable rhythms. A systematic search for causes may be based on knowledge about the most common causes identified, on information from patient records on scene, and on pre-arrest clinical symptoms.

We wish to emphasize that our findings *do not* indicate that other causes than those listed in Table 4 are less important to recognize. The patients with a *cardiac and shockable* CA already profit from effective diagnosis *and* treatment due to the rapid application of a defibrillator. As the ETs follow current ALS guidelines, VF/VT will not be missed. If not relapsing into arrest after defibrillation, the immediate cause of arrest has been reversed and the probability of surviving a cardiac and shockable arrest is high.[18,19] Among patients suffering a *cardiac and non-shockable* IHCA, we found critical decompensated heart failure and cardiac tamponade. Such conditions have a grave prognosis *even if* correctly recognized and treated. For example, in cardiac tamponade sudden rupture of the free ventricular wall has been shown to be the dominating cause if CA is the presenting symptom.[20] Survival is low, even with prompt recognition and treatment. *Untreated* cardiac tamponade is mainly found in autopsies as a frequent cause of sudden cardiac deaths.[21] IHCA in which the underlying cause carries a very poor prognosis will, even if recognized and properly treated, weaken the relation between recognition of causes and survival, e.g. septic shock, ruptured aortic aneurysm and central pulmonary embolus.

In a retrospective Finnish-Swedish material of 104 IHCAs with initial PEA, Saarinen and co-workers observed that being alive after 30 days was more likely if treatment measures included in the ALS algorithm matched the causes of PEA identified. While this did not independently predict survival in the multivariate analysis — age

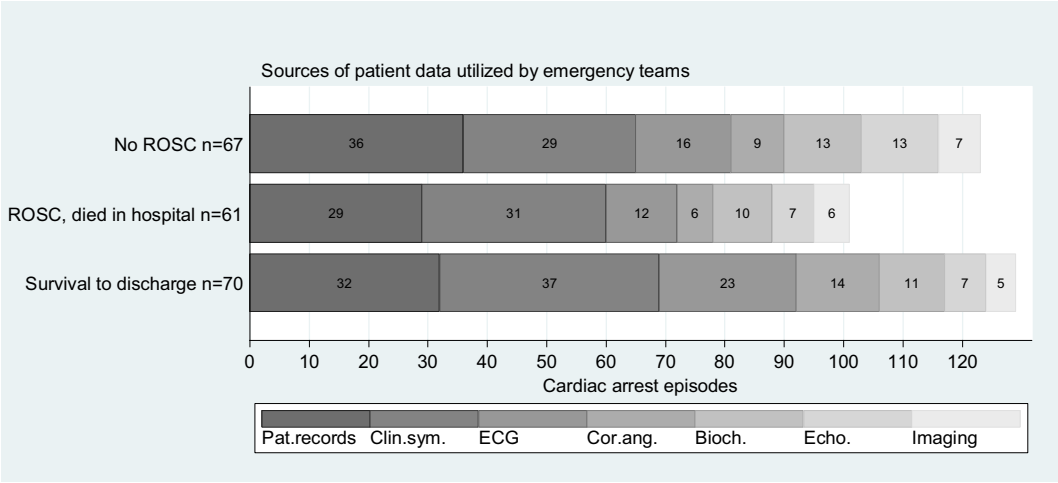

Fig. 2. The sources of patient data utilized by the emergency team in episodes where the causes of arrest were correctly recognized (198 out of 302 episodes; 66%). The sources are not mutually exclusive, and the number thus exceeds both the number of episodes and patients. ROSC: return of spontaneous circulation; Pat.rec.: patient records; Clin.sym.: clinical symptoms; ECG: electrocardiogram; Cor.ang.: coronary angiography; Bioch.: biochemical results; Echo.: echocardiography; Imaging: Medical imaging results.

turned out to be the only significant factor — their study sample was small.[22] As suggested in the present study, if causes of CA are recognized, this may also represent a benefit. This benefit may be related to individual adjustments of therapeutic measures already present in the ALS algorithm or new cause-directed treatments applied during ALS.

One may ask to what extent survival can be further increased by systematically searching for causes during CPR. The unadjusted 1-hour episode survival where the causes were not recognized was 33% (34 of 104 episodes in Table 1). If we assume causality between recognition of causes and the achievement of ROSC, and apply the estimated survival benefit of 29% (coef 0.285 in Table 2), a 1-hour survival of approximately 9 more patients could have been achieved. Based on the same reasoning as above, survival to hospital discharge among the 'unrecognized' might at best increase by 19% (coef 0.19 in Table 2), i.e. from 10 to 12 patients, although these numbers obviously depend on additional factors like comorbidity.

This is the first study that attempts to quantify the potential impact of recognition of IHCA causes on survival. Furthermore the study suggest which IHCA episodes that may benefit most from the recognition of causes beyond the provision of high quality CPR; namely the non-shockable. Finally, the sources of information were often simple; pre-arrest symptoms and patient records. A larger prospective study would be needed to confirm that a structured approach towards identifying and treating the insult actually would improve survival. In the meantime, however, it makes sense to systematically search for the potential causes of arrest — of course without compromising CPR performance.

This study has several limitations. This was not a randomized clinical trial and the association between cause recognition and survival may have been confounded by unobserved clinical factors. Underlying conditions with higher probabilities of survival may also be easier to recognize by the ET during ALS. Thus, recognition of causes by the ET may not have been a causal event leading to increased survival, but rather reflecting the patient's characteristics.

Exactly when during ALS efforts the ETs suspected a certain cause of arrest could not be determined in this study. It may have been the achievement of ROSC in the first place that made it possible for the ETs to gather additional patient information and reason about the causes of arrest. This may be supported by the results demonstrated in Table 1 where a high proportion of patients among those without a recognized cause of arrest never achieved ROSC (67%).

Patients with a restricted treatment level because of severe comorbidity may have received fewer diagnostic measures ahead of the CA episode. Causes in these patients may thus have been difficult to detect because few diagnostic results were available from patient records. Such patients are also likely to have lower survival probabilities from the onset. This may have contributed to the results indicating that inability to detect causes of arrest during ALS is associated with lower survival probability.

The sample size is too small to investigate every possible subgroup. This applies especially to the group of cardiac non-VF/VT episodes where the underlying conditions have a high mortality, and the group of non-cardiac VF/VT which is rarely seen.

The study originates from a single clinical centre, which limits the generalizability, however the patient and episode characteristics are in general comparable to what is being reported in international studies.[12]

The strengths of the study are the prospective design and identification of IHCA episodes, the thorough investigation of CA causes, and consistent data about CPR efforts during the first minutes of ALS.

Conclusions

Patients suffering an in-hospital cardiac arrest where the triggering causes were recognized by the ET had a higher 1-hour survival and survival to hospital discharge. The survival benefit was most pronounced among patients with a non-cardiac cause and a non-shockable presenting rhythm. The information sources most frequently utilized by the ET to identify causes of arrest were patient records and pre-arrest clinical symptoms.

Conflicts of interest statement

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2015.09.395.

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