

N-Terminal Pro-B-Type Natriuretic Peptide as a Prognostic Indicator for 30-Day Mortality Following Out-of-Hospital Cardiac Arrest: A prospective observational study.

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Abstract

Background: Early risk stratification applying cardiac biomarkers may prove useful in sudden cardiac arrest patients. We investigated the prognostic utility of early-on levels of high sensitivity cardiac troponin-T (hs-cTnT), copeptin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in patients with out-of-hospital cardiac arrest (OHCA).

Methods: We conducted a prospective observational unicenter study, including patients with OHCA of assumed cardiac origin from the Southwestern part of Norway from 2007 until 2010. Blood samples for later measurements were drawn during cardiopulmonary resuscitation or at hospital admission.

Results: A total of 114 patients were included, 37 patients with asystole and 77 patients with VF as first recorded heart rhythm. Forty-four patients (38.6%) survived 30-day follow-up. Neither hs-cTnT ($p = 0.49$), nor copeptin ($p = 0.39$) differed between non-survivors and survivors, whereas NT-proBNP was higher in non-survivors and significantly associated with time to death, with a hazard ratio (HR) for patients in the highest compared to the lowest quartile of 4.6 (95% CI 2.1 – 10.1), $p < 0.001$. This association was attenuated in the multivariable analysis [HR 2.18 (95% CI 0.83 – 5.72)], $p = 0.11$. NT-proBNP was significantly higher in asystole- as compared to VF-patients, $p < 0.001$.

Conclusions: In OHCA, NT-proBNP was significantly associated with 30-day survival in univariate analysis, but associations were attenuated after multivariable adjustment. Hs-cTnT and copeptin did not provide prognostic information following OHCA.

Clinical Trial Registration: ClinicalTrials.gov, NCT02886273.

Background

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death and represents a major health problem in western countries. In Europe, the annual incidence of Emergency Medical Services (EMS) attended OHCA is estimated to 84 per 100 000 inhabitants [1]. The mortality rate is high, with an overall rate of survival to hospital discharge of only 10% [1, 2]. Early and precise risk stratification of cardiac arrest patients is important to guide further treatment decisions. On-scene observations [3] and 24-hour intensive care follow-up recordings [4, 5] are currently being used to predict survival from OHCA.

Heart disease is a major risk factor for sudden cardiac arrest [6], with coronary artery disease and cardiomyopathies as the two most common causes of sudden cardiac death [6, 7]. Cardiac arrest with global ischemia and subsequent resuscitation may contribute to myocardial injury and dysfunction [8, 9]. Cardiac troponin (cTn) and copeptin are biomarkers used for early diagnosis of acute myocardial infarction (AMI) [10, 11] and may also serve as prognostic indicators following an acute coronary syndrome (ACS) [10, 12]. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a well-established diagnostic marker of heart failure [13] and an important predictor of mortality in patients with heart

failure [13] or ACS [14]. Both NT-proBNP [15, 16] and copeptin [17, 18] have been found to predict mortality in critically ill patients admitted to a medical intensive care unit (ICU).

Although cardiac biomarkers may be useful for prognostication in OHCA-patients, available data regarding the predictive value of high-sensitivity cardiac troponin-T (hs-cTnT) [9, 19-21], copeptin [21-23] and NT-proBNP [19, 21, 24, 25] diverge. The inconsistency in previously reported results may be related to heterogeneity in patient population regarding cause of cardiac arrest and primary heart rhythm, timing of blood sampling and follow-up time. Previous studies have mainly focused on resuscitated patients admitted to the ICU. In our study, we included patients with OHCA of assumed cardiac origin, both with and without return of spontaneous circulation (ROSC). In a previous publication [21], we have assessed the prognostic utility of hs-cTnT, copeptin and NT-proBNP in OHCA patients with ventricular fibrillation (VF). We also compared ischemic- with non-ischemic cardiac arrest. In the present manuscript we have evaluated these three biomarkers as prognostic indicators in OHCA patients with both shockable- and non-shockable heart rhythm. As VF and asystole are considered as different prognostic entities, we also compared the level of biomarkers between these two cardiac arrest groups.

Methods

Study subjects and design

From February 2007 until November 2010 we collected blood samples from patients ≥ 18 years of age with OHCA of assumed cardiac origin in the Southwestern part of Norway. All patients recruited in this study received out-of-hospital advanced cardiac life support according to the 2005 European Resuscitation Council guidelines with Norwegian modifications [26]. Blood sampling was performed by the EMS paramedics, 20 ml of blood was collected into ethylenediamine tetra acetic acid (EDTA) -tubes, using a venous cannula, during or immediately after termination of cardiopulmonary resuscitation (CPR). In patients with ROSC without a prehospital blood sample, blood was collected immediately after hospital admission.

OHCA-patients were divided into two groups according to first recorded heart rhythm, asystole or VF. We applied clinical information from hospital records and collected additional information from electrocardiograms, echocardiography and coronary angiography for classification of patients [21]. VF-patients were further categorized according to an acute ischemic or non-ischemic mechanism for sudden cardiac arrest, and whether or not they had previously known heart disease.

Informed consent was collected retrospectively. All survivors gave written, informed consent. If the patient did not regain consciousness before death, the next-of-kin were asked for consent on the patient's behalf. This study was approved by the Regional Board of Research Ethics and the Norwegian Health Authorities, conducted in accordance with the Helsinki Declaration of 1975, as revised in 1989, and registered in ClinicalTrials.gov, identifier: NCT02886273.

Laboratory Methods

After collection, blood samples were centrifuged at 2500 rpm for 10 min. within 24 hours if stored at room-temperature, or within 48 hours if stored at + 4 °C. EDTA-plasma was stored in aliquots at -70 °C. Measurements of hs-cTnT, copeptin and NT-proBNP were performed at the Department of Multidisciplinary Laboratory Medicine and Medical Biochemistry, Akershus University Hospital, applying standardized methods, as previous reported [21]. Hs-cTnT (according to local stability analyses) and NT-proBNP [27] are found to be stable in EDTA-plasma for up to 3 days stored at room-temperature, and even longer when stored at + 4 °C. Ex vivo copeptin stability in EDTA-plasma is shown for at least 7 days at room temperature and 14 days at + 4 °C [28].

Statistical methods

Descriptive statistics are presented as medians with interquartile range (IQR; 25th to 75th percentile) for continuous data and as numbers and percentages for categorical data. Differences in baseline characteristics were assessed by the Kruskal-Wallis Test for continuous data and Fisher's exact test for categorical data. Due to a right-skewed distribution, hs-cTnT, copeptin and NT-proBNP levels were logarithmically transformed to the base-e (\log_e) prior to analysis. Student's independent two-sample t-test was used after \log_e -transformation to assess between-group differences, comparing biomarker-levels in non-survivors with survivors as well as between the asystole- and VF-group. Spearman's rank correlation coefficient was calculated to identify a possible relation between biomarker levels and time of blood sampling.

Patients were divided into quartiles (Q1-4) according to the hs-cTnT, copeptin and NT-proBNP concentrations. The Kaplan-Meier product limits were used for plotting the times to event and the log rank test was used to test for the equality of the survival curves. A Cox regression model was fitted for each of the biomarkers for the analysis of death within 30 days. We employed three different models for the multivariable analysis, including age, gender and \log_e -creatinine for Model 1, adding witnessed cardiac arrest, bystander-initiated CPR and VF as first recorded heart rhythm for Model 2 and included duration of resuscitation for Model 3. Hazard ratios (HR) with 95% confidence intervals were calculated for each of the higher quartiles as compared to quartile 1. The predictive ability during follow-up was also explored by univariable and multivariable Cox regression analysis applying \log_e -transformed continuous values of the biomarkers. Statistical analyses were performed using the statistical package SPSS version 25 (IBM Corp. Armonk, NY). All tests were 2-sided with a significance level of 5% without multiplicity adjustment.

Results

During the study period, 361 patients suffered cardiac arrest of assumed cardiac origin, defined according to the Utstein definitions [29], and were eligible for inclusion in this study [21]. Out of these, 155 patients were sampled. Retrospectively, a total of 41 patients had to be excluded for different reasons (Fig. 1). The final population of 114 OHCA-patients was further divided into two groups according to the first recorded heart rhythm; 37 patients with asystole and 77 patients with VF. The group of VF-patients was further classified according to the presence of an acute ischemic event, by which 53 patients had

signs of an AMI [21], and 10 of these had previously been diagnosed with heart disease. Twenty-one patients suffered sudden cardiac arrest without signs of an AMI [21], of whom 18 had evidence of prior heart disease, including coronary artery disease and/or chronic heart failure.

The baseline characteristics of the patients stratified according to 30-day mortality are presented in Table 1. Out of 114 patients, 70 (61.4%) died on scene or before hospital discharge. All patients (38.6%) surviving to hospital discharge were still alive at 30-day follow-up. Compared to 30-day survivors, non-survivors were older, had increased prevalence of heart failure and diabetes and worse kidney function. Asystole as first recorded heart rhythm was more frequent in non-survivors (53%), they also had worse cardiac arrest conditions with a significant lower proportion of witnessed cardiac arrest and bystander-initiated CPR, and longer duration of resuscitation.

Blood samples were drawn from 75 patients during resuscitation and from 39 patients at hospital admission, with a median time from cardiac arrest until blood sampling of 31 and 73.5 minutes, respectively. We found no correlation between biomarker levels and time of blood sampling, except for hs-cTnT ($r = 0.31$, $p = 0.001$). Median hs-cTnT concentration was 71 (IQR; 26 – 231) ng/L, ranging from 6.0 to 8333 ng/L. Hs-cTnT levels did not differ significantly between survivors [median 100 (IQR; 21 – 289) ng/L] and non-survivors [66 (26 – 207) ng/L], $p = 0.49$. Furthermore, we found no significant association between hs-cTnT quartiles and time to death, log-rank test $p = 0.57$. Results of univariate- and multivariable cox regression analysis are presented in Suppl. Table 1. These results were confirmed using log-transformed continuous values.

Copeptin levels were elevated in all patients [436 (216 – 825) pmol/L], and did not differ between the two outcomes, $p = 0.38$. In survival analysis, copeptin quartiles did not separate survivors and non-survivors after 30 days, log-rank test $p = 0.67$. There was no statistically significant association, neither between copeptin quartiles and time to death, (Suppl. Table 2), nor between log-transformed continuous values of copeptin and time to death in the univariate analysis and in multivariable models.

NT-proBNP was the only biomarker demonstrating a significant difference between non-survivors [105 (35 – 495) pmol/L] and survivors [30 (12 – 98) pmol/L], $p < 0.001$. Patients were grouped into quartiles according to NT-proBNP levels; Quartile 1 (Q1): < 24 pmol/L, Q2: 25 - 60 pmol/L, Q3: 62 - 218 pmol/L, and Q4: > 250 pmol/L. The median NT-proBNP level in Q4 was 720 (IQR; 371 – 2506). Q4-patients were significantly older with increased prevalence of heart failure and reduced kidney function, and there was a larger proportion with asystole as first recorded heart rhythm, Table 2. NT-proBNP quartiles were significantly associated with time to death (log-rank test $p < 0.001$). Survival curves for NT-proBNP quartiles are shown in Fig. 2. In univariate analysis, the HR for patients with NT-proBNP in Q4 compared to Q1 was 4.61 (95% CI; 2.10 – 10.1), $p < 0.001$. Adding age, gender and \log_e -creatinine value in a multivariable Cox regression model (Model 1) resulted in loss of a significant association between the upper NT-proBNP quartile and 30-day mortality, $p = 0.11$ (Fig. 3), but the association remained significant when applying \log_e -transformed continuous values of NT-proBNP, $p = 0.024$. In Model 2, which also contained witnessed cardiac arrest, bystander-initiated CPR and VF, the association became further

attenuated for NTproBNP-Q4 ($p = 0.32$) and was no longer significant for \log_e NT-proBNP ($p = 0.96$). By adding duration of resuscitation (Model 3), the attenuation became even more evident for NT-proBNP-Q4, $p = 0.50$ (Fig. 3), and remained non-significant for \log_e NT-proBNP ($p = 0.57$).

Among the clinical variables, increasing age was associated with death in all three models (Model 3; $p = 0.010$). Witnessed cardiac arrest, VF as first recorded heart rhythm and duration of resuscitation were also significantly associated with outcome (Fig. 3).

At 30-day follow-up, all patients in the asystole-group had died, as compared to 43% in the VF-group. Baseline characteristics of patients with asystole versus VF as first recorded heart rhythm are presented in Table 3. NT-proBNP was the only biomarker that differed between these two groups, with a significantly higher median value of 250 (42 – 1305) pmol/L in the asystole group compared to 51 (18-111) pmol/L in the VF-group, $p < 0.001$. This difference is driven by VF-patients presenting with ischemic cardiac arrest (68.8 % of the VF-population), $p < 0.001$, and was not evident when comparing non-ischemic cardiac patients with the asystole group, $p = 0.74$. Hs-cTnT and copeptin were elevated in both asystole- and VF patients, but there was no significant difference between the two groups. These findings are illustrated by applying \log_e -transformed values of the biomarkers as shown in Suppl. Fig. 1.

Discussion

We evaluated the prognostic utility of early-on levels of hs-cTnT, copeptin and NT-proBNP for all-cause death at 30-day follow-up in clinically characterized patients with OHCA of assumed cardiac origin, presenting with asystole or VF.

The upper quartile of NT-proBNP was found to be significantly related to death in the univariate analysis, whereas hs-cTnT and copeptin were not associated with outcome. Adjusting for demographic and clinical variables, the prognostic value of NT-proBNP was attenuated and no longer statistically significant.

These findings are consistent with two previous studies [24, 25], reporting a similar association between admission levels of NT-proBNP and outcome in resuscitated OHCA patients. There are several possible mechanisms for increased NT-proBNP/BNP secretion during cardiac arrest and CPR, including hypoxemia [30], ischemia [31], ischemia-reperfusion induced inflammation [32], therapeutic interventions with administration of fluids [33] and vasopressors [34], and mechanical ventilation with supplementary oxygen administration [35]. Myhre et al. 2016 [24] demonstrated an increase in NT-proBNP levels from admission up to 96 hours after hospitalization in OHCA-VT/VF patients. Longer time to ROSC and higher admission levels of hs-cTnT were found to be associated with high NT-proBNP concentrations after 24 hours in multivariable analysis. Furthermore, 24-hour NT-proBNP levels provided additional prognostic information for the prediction of 1-year mortality. These associations may reflect myocardial changes brought about by the cardiac arrest, whereas earlier on-site levels of NT-proBNP in our study most likely will reflect the pre-cardiac arrest condition, as patients in Q4 as compared to lower quartiles were more

prone to heart failure, were older and presented with worse renal function. The prognostic value of comorbidity has previously been claimed to be of less importance in OHCA patients [36, 37].

As NT-proBNP concentrations are known to be related to age and kidney function [13], we adjusted for these variables in addition to gender in our first multivariable model. This attenuated the association between the upper NT-proBNP quartile and survival ($p = 0.11$), leaving only age related to outcome, which is in accordance with previous studies [38-40], although the association remained significant when applying \log_e -transformed continuous values of NT-proBNP, $p = 0.024$.

Other factors, such as witnessed cardiac arrest, bystander-initiated CPR, time to ROSC and primary heart rhythm, may also influence outcome [3, 38-42]. In our second model, we chose to add witnessed cardiac arrest, bystander-initiated CPR and VF, not including duration of cardiac arrest, as bystander attention and time of EMS-arrival on scene was uncertain in some patients. These adjustments weakened the prognostic value of NT-proBNP, and in line with previous studies [3, 39-41], we found that witnessed cardiac arrest and VF was significantly associated with outcome. In contrast to previous reports [3, 39], bystander-initiated CPR was not found to be an independent outcome-predictor in our study, probably cancelled by a larger proportion of VF-patients and a short EMS response-time between 8 to 15 minutes in our recruitment area.

In our third multivariable model we also included the duration of resuscitation, and in accordance with previous observations [41, 42], we found that longer CPR-duration was significantly associated with increased risk of death (Fig. 3).

Furthermore, we found that NT-proBNP differentiated between ischemic VF patients and those presenting with asystole. This could be explained by a difference in baseline risk variables, as previously reported [21]. Patients in the asystole group were older and a higher proportion suffered from prior cardiac morbidity, including established coronary artery disease and heart failure. However, no difference in NT-proBNP was observed when comparing non-ischemic VF patients with those presenting with asystole. These groups had similar baseline characteristics and differed mainly by the presenting arrhythmia, which may relate to prognosis. Accordingly, all patients in the asystole group died as compared to 50% in the non-ischemic VF group.

The two other biomarkers, hs-cTnT and copeptin, were not related to outcome, neither in univariate, nor in multivariable analysis. As previously demonstrated [9], we found that essentially all resuscitated OHCA-patients had elevated levels of hs-cTnT. Gilje et al. [20] found that hs-cTnT peaked 24 hours after admission following OHCA, but only hs-cTnT at 48 and 72 hours, respectively, was independently associated with all-cause mortality. In our study, we analysed only one blood sample very close to the cardiac arrest, which may not reflect the peak values of hs-cTnT, and the prognostic utility may have been missed. This assumption is supported by the FINNRESUSCI substudy by Røsjø et.al [9], where admission levels of hs-cTnT failed to differ between hospital non-survivors and survivors and did not yield independent prognostic information at 1-year follow up in OHCA-VF/VT patients.

Copeptin levels were markedly increased in all patients in our study and did not differ between 30-day non-survivors and survivors. Admission levels of copeptin have previously been demonstrated to independently predict organ dysfunction and death in the ICU following OHCA [22]. As a predictor of long-term mortality, copeptin levels at day 3 were shown to perform better than copeptin measured at ICU-admission [23]. In our early-on sample, elevated copeptin may largely reflect the stress response during cardiac arrest, rather than outcome related hemodynamic instability following ROSC. The prognostic utility of copeptin claimed in the FINNRESUSCI population [22], is based on samples harvested up to 6 hours after admission and did not include on-scene non-ROSC patients.

Strengths

Blood was collected very early after OHCA and includes non-admitted patients without ROSC, a patient category usually missed out in previous studies. Also, the initial cardiac rhythm was recorded in all patients. Pre-hospital data were collected in accordance with the Utstein guidelines [29], and advanced cardiac life support was performed by the EMS paramedics according to current guidelines [26].

Limitations

The small study population is one of the limitations. Inclusion of patients was restricted to the largest ambulance centres in the area located closest to the hospital and to the medical support helicopter to ensure timely delivery of blood samples, limiting the potential recruitment area. Furthermore, patient recruitment could only be performed when there was enough EMS crew present at the OHCA-scene. Samples were obtained during resuscitation and not after death was declared. Unfortunately, there was a selection bias due to unbalanced blood sampling in the ROSC and non-ROSC group of patients. A few patients lacked detailed information regarding the OHCA. Our study is limited to 30-days observations of outcome.

Conclusions

High NT-proBNP plasma concentrations in samples collected very close to the OHCA were associated with increased 30-day mortality in univariate analysis, but the association was attenuated and no longer statistically significant in multivariable analysis after adjusting for age and cardiac arrest conditions. Early-on levels of hs-cTnT and copeptin did not provide prognostic information following OHCA.

List Of Abbreviations

ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
CI	Confidence interval
CPR	Cardiopulmonary resuscitation

cTn	Cardiac troponin
EDTA	Ethylenediamine tetra acetic acid
EMS	Emergency Medical Services
HR	Hazard ratio
Hs-cTnT	High-sensitivity cardiac troponin-T
ICU	Intensive care unit
IQR	Interquartile range
NT-proBNP	N-terminal pro-B-type natriuretic peptide
OHCA	Out-of-hospital cardiac arrest
ROSC	Return of spontaneous circulation
VF	Ventricular fibrillation

Declarations

Ethics approval and consent to participate

Informed consent was collected retrospectively. All survivors gave written, informed consent. If the patient did not regain consciousness before death, the next-of-kin were asked for consent on the patient's behalf. This study was approved by the Regional Board of Research Ethics and the Norwegian Health Authorities, conducted in accordance with the Helsinki Declaration of 1975, as revised in 1989.

Consent for publication

Not applicable.

Availability of data and materials

Local database. The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

T.O. and H.R. are partners in a patent application filed by the University of Oslo regarding the use of secretoneurin as a biomarker in cardiovascular disease and in patients with critical illness. H.R and T.O. have financial interests in CardiNor AS, which holds the license to commercialize secretoneurin. T.O. and H.R. have also received personal payments from CardiNor AS. H.R have also received personal fees from

Novartis and Thermo Fisher BRAHMS. T.O has received honoraria and research support from Roche Diagnostics via Akershus University Hospital.

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Authors' contributions

R.A: investigation, formal analysis, writing – original draft. T.O: resources, writing – review and editing. H.R: resources, writing – review and editing. He.S: resources, writing – review and editing. T.L: investigation, resources, writing – review and editing. HA: methodology, investigation, writing – review and editing. Ha.S: formal analysis, writing – review and editing. D.N: conceptualization, methodology, writing – review and editing.

All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics and laboratory values of patients suffering out-of-hospital cardiac arrest.

Data are presented as median (interquartile range) or numbers (%).

^a n = 110 (96%), ^b n = 111 (97%), ^c n = 112 (98%).

Abbreviations: CPR, cardiopulmonary resuscitation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CRP, C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table 2: Baseline characteristics and laboratory values of patients suffering out-of-hospital cardiac arrest, arranged according to Quartiles of NT-proBNP.

	All patients (n= 114)	Survivors (n = 44)	Non-survivors (n= 70)	P-value
Age, y	67 (56 - 78)	61 (51 - 68)	72 (62 - 83)	<0.001
Male gender	95 (83)	36 (82)	59 (84)	0.80
Previous history				
Angina pectoris	17 (18)	6 (14)	11 (22)	0.42
Myocardial infarction	33 (31)	10 (23)	23 (36)	0.20
Previous PCI	12 (11)	5 (11)	7 (11)	1.00
Previous CABG	12 (11)	2 (5)	10 (16)	0.12
Heart failure	28 (26)	7 (16)	21 (34)	0.046
Hypertension	53 (52)	19 (43)	34 (58)	0.17
Diabetes mellitus	17 (17)	2 (5)	15 (25)	0.007
Hypercholesterolemia	44 (42)	22 (51)	22 (36)	0.16
Smoking				0.81
Current smoker	27 (32)	13 (33)	14 (31)	
Ex-smoker	40 (47)	20 (50)	20 (44)	
Cardiac arrest conditions				
Witnessed cardiac arrest	87 (77)	39 (89)	48 (70)	0.022
Bystander-initiated CPR	93 (82)	40 (91)	53 (76)	0.049
Duration of resuscitation, min	23 (10 - 38)	9 (5 - 15)	32.5 (23 - 45)	<0.001
Initial rhythm				<0.001
VF	77 (68)	44 (100)	33 (47)	
Asystole	37 (33)	0 (0)	37 (53)	
Baseline blood samples				
Creatinine (µmol/L)	102 (87 - 122)	93 (82 - 116)	110 (92 - 125)	0.013
Total cholesterol (mmol/L)	4.2 (3.6 - 5.3)	4.9 (4.1 - 6.5)	3.9 (3.4 - 5.0)	0.002
CRP (mg/L)	2.5 (1.1 - 9.9)	2.1 (1.2 - 4.6)	3.9 (1.0 - 18.0)	0.15
Glucose (mmol/L)	12.6 (8.0 - 16.9)	12.6 (8.8 - 14.7)	12.6 (6.6 - 17.8)	0.94
Copeptin (pmol/L) ^a	436 (216 - 825)	388 (195 - 825)	445 (244 - 879)	0.39
hs-cTnT (ng/L) ^b	71 (26 - 231)	100 (21 - 289)	66 (26 - 207)	0.49
NT-proBNP (pmol/L) ^c	61 (25 - 234)	30 (12 - 98)	105 (35 - 495)	<0.001

Data are

presented as median (interquartile range) or numbers (%).

^a n = 110 (96%), ^b n = 111 (97%), ^c n = 112 (98%).

Abbreviations: OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CRP, C- reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table 3. Baseline characteristics and laboratory values of patients suffering out-of-hospital cardiac arrest, arranged according to first recorded heart rhythm.

Data are presented as median (interquartile range) or numbers (%).

^a n = 110 (96%), ^b n = 111 (97%), ^c n = 112 (98%).

Abbreviations: VF, ventricular fibrillation; OHCA; out-of-hospital cardiac arrest; CPR, cardiopulmonary

	NT-proBNP Quartiles				
	Quartile 1 (N = 28)	Quartile 2 (N = 28)	Quartile 3 (N = 28)	Quartile 4 (N = 28)	P- value
Age, y	53 (47 - 62)	68 (60 - 79)	65 (57 - 78)	78 (69 - 87)	< 0.001
Male sex	24 (86)	23 (82)	24 (86)	22 (79)	0.95
Death at 30 days					0.007
Died on scene	4 (14)	9 (32)	6 (21)	16 (57)	
Died in hospital	7 (25)	7 (25)	12 (43)	7 (25)	
Cardiac arrest conditions					
Initial rhythm					< 0.001
Asystole	4 (14)	8 (29)	5 (18)	18 (64)	
Ventricular fibrillation	24 (86)	20 (71)	23 (82)	10 (36)	
Witnessed OHCA	22 (79)	24 (86)	18 (64)	21 (78)	0.33
Bystander-initiated CPR	23 (82)	23 (82)	25 (89)	20 (71)	0.45
Duration of resuscitation, (min.)	15.0 (6.0 - 44.0)	15.0 (5.0 - 35.0)	37.0 (18.0 - 64.0)	25.0 (15.0 - 33.0)	0.043
Previous history					
Angina pectoris	4 (16)	3 (13)	3 (14)	7 (32)	0.39
Myocardial infarction	5 (19)	7 (28)	10 (36)	11 (41)	0.35
Previous PCI	4 (15)	1 (4)	4 (14)	3 (11)	0.58
Previous CABG	1 (4)	2 (8)	4 (14)	5 (19)	0.36
Heart failure	1 (4)	3 (12)	9 (33)	15 (58)	< 0.001
Hypertension	11 (44)	14 (56)	11 (42)	17 (68)	0.23
Diabetes mellitus	2 (8)	9 (35)	1 (4)	5 (19)	0.016
Hypercholesterolemia	14 (54)	11 (44)	10 (37)	9 (36)	0.56
Smoking					0.26
Current smoker	12 (50)	5 (29)	4 (19)	5 (23)	
Ex-smoker	7 (29)	10 (59)	11 (52)	12 (55)	
Baseline blood samples					
Creatinine (µmol/L)	98 (84 - 117)	102 (84 - 115)	98 (88 - 113)	126 (96 - 198)	0.013
Total cholesterol (mmol/L)	5.1 (3.8 - 6.9)	4.4 (4.0 - 5.2)	4.1 (3.4 - 4.9)	3.9 (3.1 - 4.9)	0.022
CRP (mg/L)	1.7 (1.1 - 4.3)	1.8 (1.0 - 4.6)	2.0 (1.1 - 6.1)	14.5 (3.8 - 51.0)	< 0.001
Glucose (mmol/L)	11.8 (8.0 - 16.8)	13.5 (11.3 - 16.9)	14.2 (8.2 - 19.4)	12.2 (5.8 - 14.4)	0.47
Copeptin (pmol/L) ^a	461 (295 - 925)	389 (216 - 882)	366 (138 - 793)	425 (286 - 688)	0.58
hs-cTnT (ng/L) ^b	36 (15 - 118)	42 (23-197)	127 (45 - 314)	93 (57 - 254)	0.011
NT-proBNP (pmol/L) ^c	11 (7 - 16)	36 (28 -51)	105 (84 - 168)	720 (371 - 2506)	< 0.001

resuscitation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CRP, C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T;

NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Figures

	Asystole-patients (n = 37)	VF-patients (n = 77)	P-value
Age, y	75 (66 - 86)	63 (54 - 75)	< 0.001
Male sex	26 (70)	69 (90)	0.015
Death at 30 days	37 (100)	33 (43)	< 0.001
Died on scene	26 (70)	9 (12)	
Died in hospital	11 (30)	24 (31)	
Cardiac arrest conditions			
Witnessed cardiac arrest	26 (70)	61 (80)	0.24
Bystander-initiated CPR	26 (70)	67 (87)	0.040
Duration of resuscitation, min	28.5 (20 - 35)	15 (6 - 43)	0.082
Previous history			
Angina pectoris	9 (32)	8 (12)	0.037
Myocardial infarction	11 (32)	22 (30)	0.82
Previous PCI	4 (12)	8 (11)	1.00
Previous CABG	5 (15)	7 (10)	0.51
Heart failure	11 (33)	17 (23)	0.34
Hypertension	21 (64)	32 (46)	0.097
Diabetes mellitus	7 (21)	10 (14)	0.40
Hypercholesterolemia	12 (36)	32 (44)	0.53
Smoking			0.56
Current smoker	10 (39)	17 (29)	
Ex-smoker	10 (39)	30 (51)	
Baseline blood samples			
Creatinine (µmol/L)	101 (92 - 130)	102 (87 - 121)	0.42
Total cholesterol (mmol/L)	4.1 (3.5 - 5.0)	4.3 (3.7 - 5.4)	0.16
CRP (mg/L)	12.0 (2.0 - 50.0)	1.9 (1.1 - 4.1)	< 0.001
Glucose (mmol/L)	10.7 (3.7 - 15.7)	13.7 (9.6 - 17.2)	0.034
Copeptin (pmol/L) ^a	402 (244 - 939)	453 (210 - 765)	0.82
hs-cTnT (ng/L) ^b	67 (28 - 226)	73 (26 - 231)	0.77
NT-proBNP (pmol/L) ^c	250 (42 - 1305)	51 (18 - 111)	< 0.001

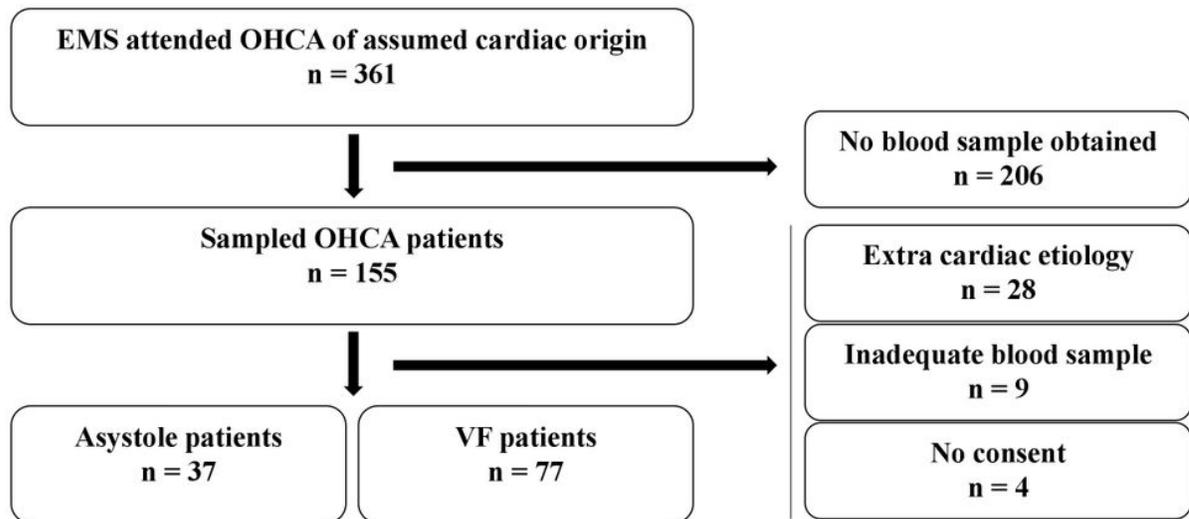


Figure 1

Flow chart displaying selection and classification of patients with out-of-hospital cardiac arrest recruited between February 2007 and November 2010

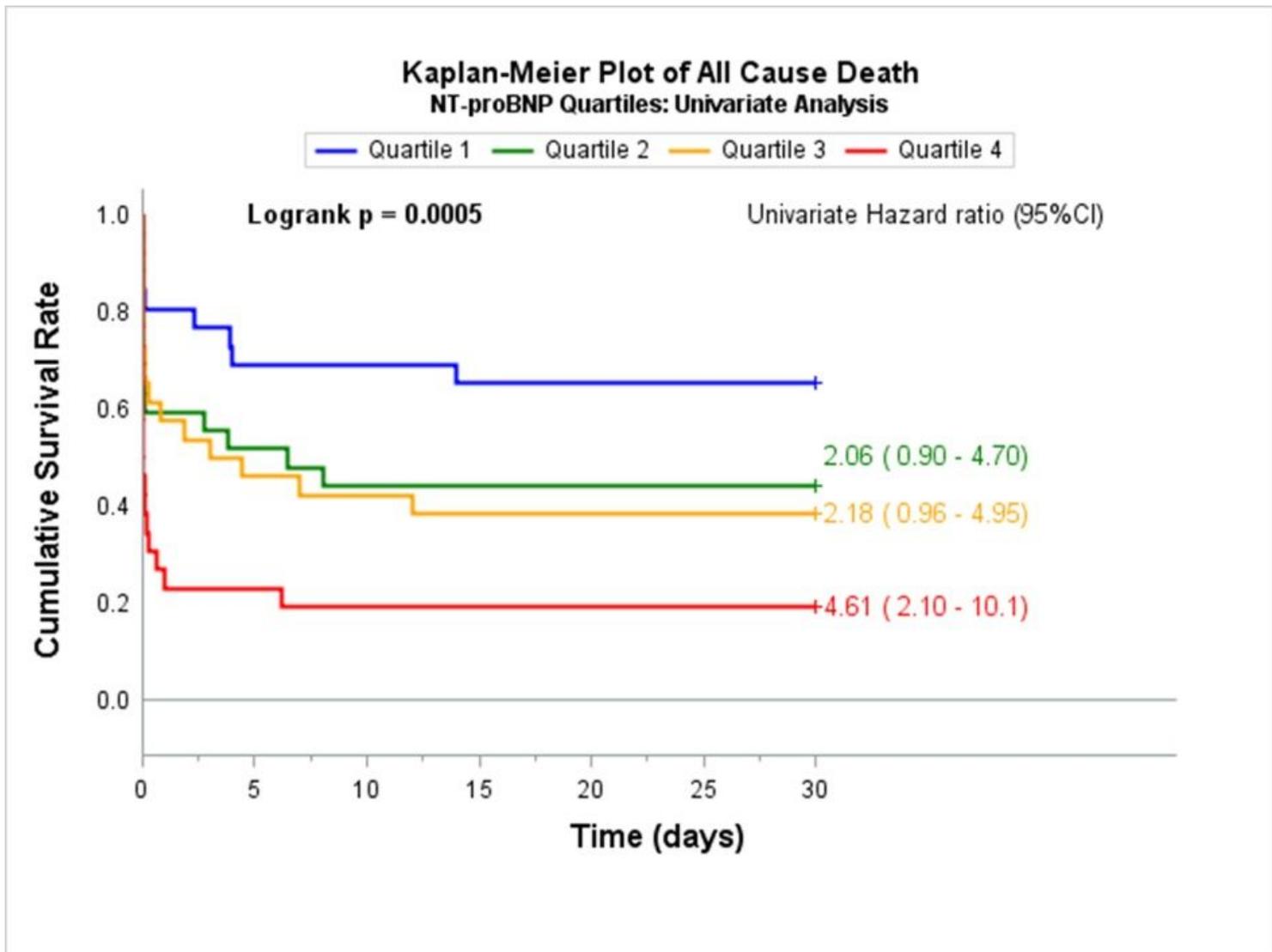


Figure 2

Survival curves up to 30-days in OHCA-patients stratified by NT-proBNP quartiles

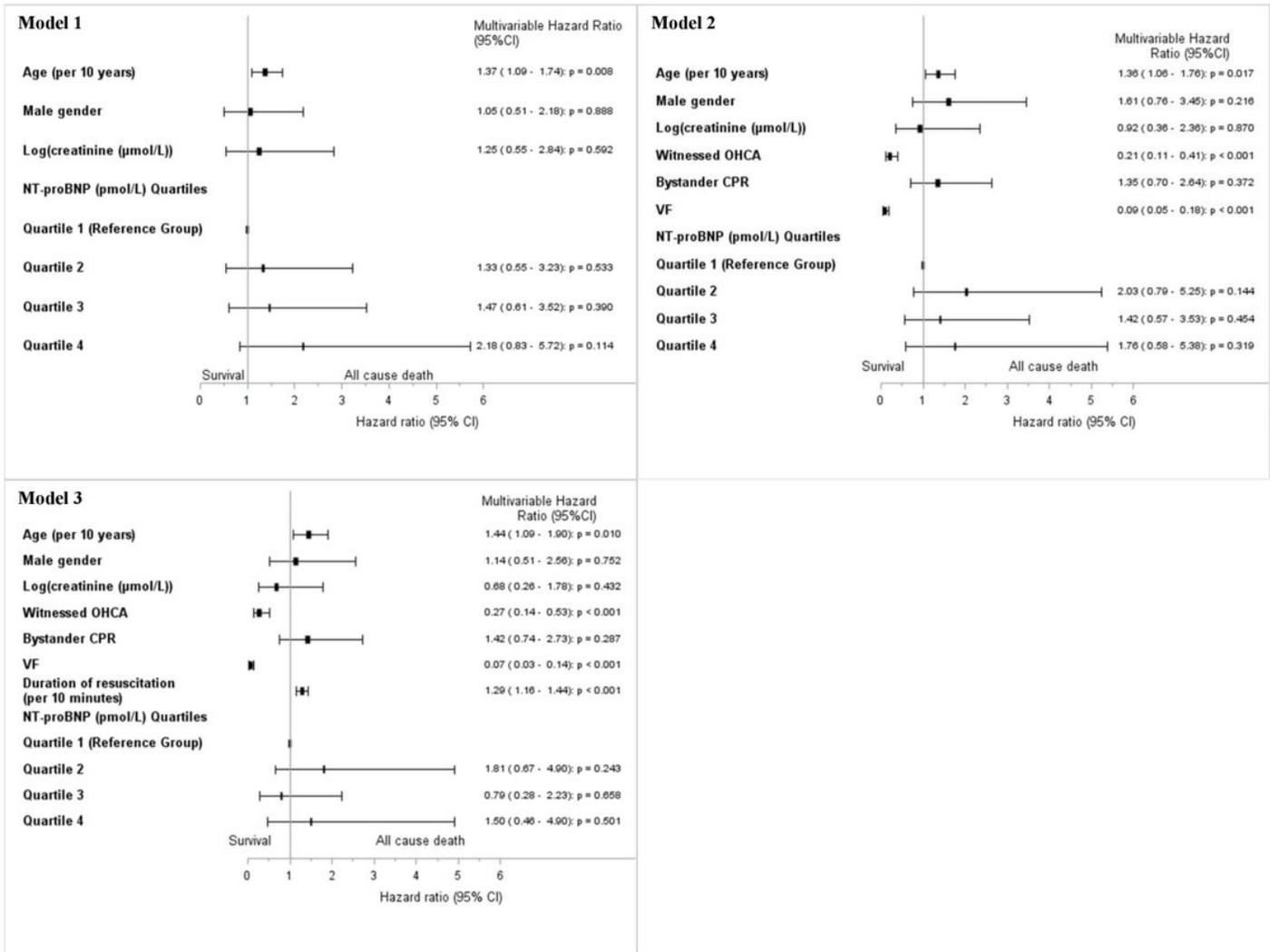


Figure 3

Adjusted hazard ratio and 95% confidence intervals for 30-day mortality according to selected risk factors from three different multivariable models. Hazard ratio (squares), 95% confidence interval (lines)
 Abbreviations: OHCA, out-of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; 95% CI, 95% confidence interval.

Supplementary Files

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