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Good quality of life before cardiac arrest predicts good quality of life after resuscitation

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1 **Good quality of life before cardiac arrest predicts good quality of life after**
2 **resuscitation**

3 **Short title:** Quality of life remains good after CA

4
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28

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30 organizing committee for SuPARnostic (Virogates, Copenhagen, Denmark) and co-founder and
31 shareholder of SenSem Technologies (Tampere, Finland) and Medieta Ltd (Helsinki, Finland).

32

33 **Abstract**

34 **Background:** The survival rate of cardiac arrest (CA) patients is increasing. Our aim was to
35 compare the quality of life (QoL) before and after CA and analyse the factors associated with
36 outcome.

37 **Methods:** During the years 2009-2011 all adult CA patients admitted to Tampere University
38 Hospital ICU were included in a retrospective follow-up study if surviving to discharge and
39 returning a questionnaire after six months. Data on patient demographics and pre-arrest quality of
40 life were retrieved from medical records. Data are given as means (SD) or medians (Q₁, Q₃). We
41 used logistic regression to identify factors associated with better QoL after CA.

42 **Results:** Six months after CA 36% (79/222) were alive and 70% (55/79) of those patients
43 completed the follow-up EuroQoL (EQ-5D) quality of life questionnaire. Median values for the EQ-
44 5D before and after CA were 0.89 [0.63, 1] and 0.89 [0.62, 1] respectively (p=0.75). Only the EQ-
45 5D prior to CA was associated with better quality of life afterwards (OR 1.2; 95% CI 1.0 - 1.3;
46 p=0.02).

47 **Conclusions:** Quality of life remained good after CA especially in those patients who had good
48 quality of life before the incident.

49

50 **Introduction**

51 Although the survival rate of cardiac arrest (CA) patients may be increasing at least in expert
52 centres, wide variation between centres persists.¹ Reports suggest that cardiac arrest survivors have
53 good or at least acceptable quality of life.²⁻⁶ Factors predicting better survival at hospital discharge
54 and good quality of life are ventricular fibrillation (VF) as an initial rhythm and short delay to the
55 return of spontaneous circulation (ROSC).⁷

56 Quality of life is a complex and multidimensional term based on four different elements, namely
57 socioeconomic factors, health and ability to function in daily living, self-awareness and life
58 satisfaction.⁸ The term health-related quality of life (HRQoL) was coined for research purposes,
59 comprising mental, physical and social components of well-being.^{9,10} Numerous different scales can
60 measure quality of life,¹¹⁻¹³ many of which have been used to analyse quality of life after CA.² In
61 the 1990's the EuroQoL Group developed a quality of life questionnaire based on five domains of
62 everyday living and self-care.¹⁰ EuroQoL (EQ-5D) has also been used to report CA patients' quality
63 of life.¹³⁻¹⁵ Quality of Life Index (EQIndex) is calculated from the scores of the five domains given
64 by the patient. The range of the score varies from 0 to 1, 1 being the best possible quality of life.

65 This study was aimed to assess the quality of life before and six months after CA using EuroQoL
66 (EQ-5D) questionnaire as a health-related quality of life (HRQoL) scale (primary endpoint). We
67 also wanted to identify possible factors associated with good quality of life (secondary endpoint).

68 **Methods**

69 *Study design*

70 This retrospective observational study was approved by Pirkanmaa Hospital District Science Center
71 and the Ethics Committee of Tampere University Hospital (Approval no: R08116, 22.2.2011;
72 clinicaltrials.gov NCT00951704). Data on the EuroQoL (EQ-5D) questionnaire before and after
73 CA, medical histories, cause of CA, initial rhythm, return of spontaneous circulation (ROSC), the
74 possible use of therapeutic hypothermia (TH), other treatments or procedures undertaken (e.g.
75 coronary artery bypass surgery (CABG), percutaneous coronary intervention (PCI) or implantable
76 cardioverter-defibrillator (ICD)/cardiac pacemakers (PAMA) implanted) were collected
77 retrospectively from patients' medical files. Charlson's weighted index of comorbidities (CCI)¹⁶ and
78 estimated ten-year survival percentages were calculated using the medical histories.

79 *Source population*

80 From 1.1.2009 to 31.12.2011 we screened all adult patients admitted to ICU after successful
81 resuscitation from in-hospital cardiac arrest (IHCA) or out-of-hospital cardiac arrest (OHCA).
82 Those successfully resuscitated and alive six months after resuscitation received the EQ-5D
83 questionnaire by mail and patients who responded to the follow-up EQ-5D questionnaire constituted
84 the study population.

85

86 *Hospital and Intensive Care Unit*

87 Details of Tampere University Hospital (Tays) and incidence of IHCA have been published in our
88 previous study.¹⁷ The incidence of OHCA in Tampere region is 52/100,000/year.¹⁸ The mixed ICU
89 has 22 beds, 12 primarily reserved for critically ill patients. The remaining beds provide a high
90 dependency unit with special monitoring and treatment for patients with single organ dysfunction.

91 *Health-related Quality of Life, Charlson's weighted index of comorbidities*

92 Quality of life before and after resuscitation was measured on EuroQoL (EQ-5D), with five

93 dimensions of quality of life (mobility, self-care, usual activities, pain/discomfort and

94 anxiety/depression) assessed in one simple score (EQIndex). The version of EQ-5D questionnaire

95 used in this study has three grades in each dimension: no / some / major problems on the

96 dimensions describing quality of life.¹¹ Score one equals full health and zero death in the EQIndex.

97 A change of 0.05 points is considered significant. The second part of the questionnaire is a self-

98 rated visual analogue scale (VAS) ranging from 0 to 100, 100 being the best possible overall health.

99 In this study VAS was omitted from the analysis due to missing data. All patients admitted to ICU

100 were interviewed with EuroQoL (EQ-5D) questionnaire upon arrival or later during the stay,

101 depending on the condition of the patient. If the patient was too sick to respond, the next of kin

102 served as a reliable proxy.^{19,20} Therefore the EQ-5D questionnaire was chosen as a method to report

103 quality of life after CA.

104 The Charlson Comorbidity Index (CCI) was used to characterise the burden of diseases.¹⁶

105 International Classification of Diseases (ICD) diagnosis codes were used to calculate CCI.

106 Diagnoses included in the score in weight category 1 are myocardial infarction, congestive heart

107 failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease,

108 connective tissue disease, ulcer disease, mild liver disease and diabetes. Weight category 2 includes

109 hemiplegia, moderate and severe renal disease, diabetes with end-organ damage, any tumour,

110 leukaemia and lymphoma. Weight category 3 includes moderate and severe liver diseases.

111 Metastatic tumours and AIDS have weight 6. The weight in each category is associated with the

112 adjusted risk of mortality or resource use. A patient's comorbidity score is formed by summing all

113 weight results. No comorbidities are scored as 0. Charlson's index has been shown to predict

114 hospital mortality in critically ill patients and also 1-year survival.²²⁻²⁴ Charlson Comorbidity Index

115 is used to calculate the estimated 10-year survival percentage.²⁵

116 *Statistical analysis*

117 IBM SPSS Statistics for Windows (SPSS Version 22.0. Armonk, NY: IBM Corp.) was used for the
118 statistical analyses. Independent sample t-test and Mann-Whitney U-test were used for comparison
119 of continuous data and paired EQIndexes were analysed using Wilcoxon test. Binomial variables
120 were analysed with χ^2 -test. Quality of life index (EQIndex) after CA was dichotomized from 0.885
121 into two equal-sized groups. Forward stepwise binary logistic regression was used to explain higher
122 post-resuscitation EQIndex using initial rhythm (VF vs. ASY/PEA); CCI; ROSC (min); TH; age;
123 PCI/CABG; and EQIndex before CA as explanatory variables. Results are shown as percentages
124 and numbers of patients, as medians with interquartile range (Q₁, Q₃) or as means with standard
125 deviations (SD) as appropriate. Results for the binary logistic regression analyses are shown as odds
126 ratios (OR) and 95% confidence intervals (95% CI). Two-sided $p < 0.05$ was considered
127 statistically significant.

128

129 **Results**

130 *Patients' Demographics*

131 During the study period, a total of 222 patients received post-resuscitation care in the ICU. After six
132 months 79/222 (36%) were alive and 55/79 (70%) made a post-discharge follow-up visit to the ICU
133 or replied by mail to the EQ-5D questionnaire. Flowchart of the patients admitted to ICU (Fig 1.).

134 Patients' mean age was 66 (14) years and 42/55 (76%) were male. The percentages of CCI were 0:
135 33%, 1-2: 48%, ≥ 3 : 19%. 56% of all the patients were estimated to survive 10 years according to
136 CCI. ROSC was achieved in 13 (8, 25) minutes. TH was used for 28 (51%), CABG/PCI was done
137 for 15 (27%) and ICD/PAMA was implanted for 17 (31%) patients. There were no statistically
138 significant differences in age, gender dispersion, number of comorbidities, estimated 10-year
139 survival, EQIndex prior to cardiac arrest and time to return of spontaneous circulation between
140 patients who answered to the questionnaire and patients who did not. Patients' characteristics are
141 shown in Table 1.

142 OHCA patients represented 64% (35/55) of the study population. In OHCA patients ROSC was
143 achieved in 19 min [11.0, 31.0] whereas in IHCA patients it was achieved in 7.5 min [5.25, 12.25]
144 ($p<0.001$). OHCA patients had less comorbidities than IHCA patients ($p=0.04$) and 64% of the
145 OHCA patients were estimated to survive 10 years whereas the corresponding percentage for IHCA
146 patients was 41% ($p=0.02$). TH was used for 66% of OHCA and 25% of IHCA patients ($p=0.004$).
147 A similar difference was also seen in revascularization procedures: 14/35 (40%) of OHCA patients
148 had either PCI or CABG, but only 1/20 (5%) of IHCA patients underwent CABG ($p=0.005$).

149 Details of these patient/treatment groups are shown in Table 1. We observed no statistically
150 significant differences in the quality of life, gender or age between the cardiac patients treated with
151 revascularization procedure or therapeutic hypothermia and those who were not.

152

153 *Quality of Life*

154 The values for EQIndex for all the patients before and after CA were 0.89 [0.63, 1] and 0.89 [0.62,
155 1] ($p=0.75$), respectively. Pre- and post-CA QoL parameters are shown in Table 2.

156 Table 3 presents the results from the binomial multivariable logistic regression model assessing the
157 association between post-CA EQIndex and possible predictive factors. Higher EQIndex values prior
158 to CA were associated with increased odds of EQIndex post-CA (OR 1.2; 95% CI 1.0 - 1.3;
159 $p=0.02$). Subgroup analysis of patients with cardiac reasons and non-cardiac reasons for CA yielded
160 similar results.

161

162 **Discussion**

163 This study demonstrates that in survivors responding to the questionnaire the overall quality of life
164 after CA is comparable to the pre-CA evaluation. Our results concur with earlier reports, although
165 direct comparisons are difficult due to differences in quality of life scales and because many studies
166 have not considered pre-CA quality of life.²⁻⁶ Quality of life prior to CA remained the only
167 significant factor predicting better quality of life after CA. Interestingly, patients surviving CA
168 seemed to have a better quality of life before and after CA than their peers in general Finnish
169 population.²⁶

170 Research has shown that OHCA patients presenting with VF as initial rhythm have the best
171 prognoses for survival and good quality of life.²⁷⁻³⁰ In our study the EQIndex values were similar
172 before and after CA in VF patients. Patients with VF had higher EQIndex values after CA than
173 patients presenting with PEA/ASY. However, VF patients had higher EQIndex values than the
174 others already prior to CA.

175 Our study confirms the findings that, compared to surviving IHCA patients, cardiac causes as
176 aetiology and VF as initial rhythm are more common in OHCA patients.³¹⁻³⁵ In a study published by
177 Bergum et al. cardiac causes explained 60% of all IHCA cases and 30% of discharged patients had
178 a cardiac cause for CA.³⁶ Less than half of surviving IHCA patients had a cardiac cause for CA and
179 non-shockable rhythms predominated in the IHCA patients. However, the question remains whether
180 all cardiac patients at risk for CA are properly identified in hospital. Although the patients are of
181 similar age, many diseases are overrepresented in IHCA patients and the estimated 10-year survival
182 is lower in IHCA than in OHCA patients. Majority of IHCA patients had comorbidity index 2 or
183 more predicting increased mortality following intensive care.²⁴

184 Callaway et al. reported in 2014 that early coronary intervention and induced hypothermia were
185 associated with favourable functional status measured with modified Rankin Score in OCHA
186 patients.³⁷ However, this study lacks the vital information on the patients' functional status prior to
187 CA. Subgroup analysis in our study showed that patients selected for invasive cardiac procedures
188 were associated with higher EQIndex after CA compared to those without invasive cardiac
189 procedures. No difference was seen in pre-CA EQIndexes, but the patients selected for TH had
190 higher EQIndex and lower CCI before CA than patients treated without TH. The patients treated
191 with TH had no change in EQIndex after CA, but the patients treated with conservative methods
192 had better EQIndex after than before CA. However, when all possible factors influencing the
193 outcome were considered, the only factor which demonstrably predicted better quality of life after
194 CA in the multivariate analysis was good quality of life prior to CA. It would be very important in
195 future studies to report quality of life and comorbidities before and after any invasive treatment to
196 be able to analyse the possible effect of different interventions on patient outcome.

197 Our study has some limitations. Because this was a retrospective study, we could not retrieve all
198 data pertinent for the study. Furthermore, 24 patients out of 79 did not complete the EuroQoL
199 questionnaire. We can only guess the reasons. Whether the missing data from the 30% of the
200 patients represent a group with poor quality of life with high dependence on continuous support
201 remains unresolved. On the other hand, quality of life was analysed only for those patients with data
202 available both before and after CA. The total number of patients was rather small. Therefore, it is
203 prudent to state that caution should be exercised in the interpretation and extrapolation of the data.
204 It must also be emphasized that EQIndex does not directly correlate with the patient's cognitive
205 outcome.

206 We conclude that in this highly selected group, the quality of life six months after CA was
207 surprisingly good in CA survivors, even in those with numerous comorbidities. The best predictor

208 for good quality of life after CA was good quality of life prior to CA. In future studies, it is prudent
209 to include pre-CA quality of life into analyses when assessing the possible benefits of targeted
210 temperature management and other invasive treatments, such as coronary interventions.

211

212

213 **Conflicts of Interest**

214 Dr. Jyrki Tenhunen has been a member of the SuPAR-Symposium organizing committee for
215 SuPARnostic (Virogates, Copenhagen, Denmark) and co-founder and shareholder of SenSem
216 Technologies (Tampere, Finland) and Medieta Ltd (Helsinki, Finland).

217 The other authors declare no conflicts of interest.

218

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226

227

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325

326

Table 1 Characteristics of the patients

Variables	Study population n=55 (%)	IHCA n=20 (36)	OHCA n=35 (64)	<i>p</i> -value
Age	68 [60, 77]	72 [64, 80]	65 [60, 73]	0.11
Gender, male (%)	42 (76)	14 (70)	28 (80)	0.51
CCI ^a (%)				
Index value 0	18 (33)	4 (20)	14 (40)	0.04
Index value 1-2	26 (48)	9 (45)	17 (49)	0.05
Index value ≥ 3	11 (19)	7 (35)	4 (11)	0.68
Estimated 10 y survival (%)	56 (33)	41 (36)	64 (29)	0.02
Pre-CA EQIndex ^b	0.89 [0.63, 1]	0.85 [0.63, 0.92]	0.89 [0.72, 1]	0.36
Post-CA EQIndex ^c	0.89 [0.62, 1]	0.85 [0.62, 0.92]	0.89 [0.71, 1]	0.34
ROSC, min	13 [8.0, 25.0]	7.5 [5.3, 12.3]	19.0 [11.0, 31.0]	<0.001
TH ^d (%)	28 (51)	5 (25)	23 (66)	0.004
Revascularization ^e (%)	15 (27)	1 (5)	14 (40)	0.005
ICD/PAMA (%)	17 (31)	3 (15)	14 (40)	0.05
Cause of CA				
- Cardiac origin (%)	37 (67)	8 (40)	29 (83)	0.001
- Non-cardiac origin (%)	18 (33)	12 (60)	6 (17)	0.001
Initial rhythm				
- Shockable rhythm (%)	36 (65)	6 (30)	30 (86)	<0.001
Non-shockable rhythm (%)	19 (35)	14 (70)	5 (14)	<0.001

Table 2

Quality of life index prior to cardiac arrest and six months after cardiac arrest

Variables	Pre-CA EQIndex	Post-CA EQIndex	<i>p-value</i>
All patients, n=55	0.89 [0.63, 1]	0.89 [0.62, 1]	0.75
OHCA patients, n=35	0.89 [0.72, 1]	0.89 [0.71, 1]	0.19
IHCA patients, n=20	0.85 [0.63, 0.92]	0.85 [0.62, 0.92]	0.24
Cause of CA			
- Cardiac, n=37	0.89 [0.75, 1]	0.89 [0.78, 1]	0.62
- Other reason, n=18	0.61 [0.57, 0.85]	0.72 [0.45, 0.92]	0.75
Initial rhythm			
- Shockable rhythm, n=36	0.89 [0.78, 1]	0.89 [0.81, 1]	0.22
- Non-shockable rhythm, n=19	0.63 [0.56, 0.89]	0.75 [0.45, 0.92]	0.68
Therapeutic hypothermia			
- Yes	0.89 [0.63, 1]	0.89 [0.75, 1]	0.35
- No	0.81 [0.70, 0.92]	0.89 [0.53, 0.92]	0.59
Revascularization			
- Yes	0.89 [0.81, 1]	1 [0.92, 1]	0.91
- No	0.89 [0.70, 1]	0.89 [0.81, 1]	0.69

The data presented as medians [Interquartiles].

EQIndex: Quality of life Index (0-1)

Table 3

Association of different variables with post-CA EQIndex

Variable	Univariable regression	
	OR (95% CI)*	p-value
Pre-CA EQIndex	1.2 (1.0 - 1.3)	0.02
Age, Y	1.1 (0.9 - 1.2)	0.09
CCI	1.2 (0.6 - 2.6)	0.62
Initial rhythm, VF or PEA/ASY	0.6 (0.2 - 1.9)	0.25
ROSC (min)	1.1 (0.9 - 1.1)	0.11
Revascularization (PCI/CABG)	2.2 (0.3 - 2.9)	0.38
Therapeutic hypothermia YES NO	1.1 (0.8 - 3.1)	0.09
*Odds ratio with 95% Confidence Interval		

Fig 1. Flowchart of the patients