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Israelsson, J., Bremer, A., Herlitz, J., Axelsson, Å. B., Cronberg, T., Djärv, T., Kristofferzon, M., Larsson, I., Lilja, G., Sunnerhagen, K. S., Wallin, E., Ågren, S., Åkerman, E., Årestedt, K., (2017), Health status and psychological distress among in-hospital cardiac arrest survivors in relation to gender, *Resuscitation*, 114, 27-33. https://dx.doi.org/10.1016/j.resuscitation.2017.02.006

Original publication available at:
https://dx.doi.org/10.1016/j.resuscitation.2017.02.006

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ABSTRACT

Aim: To describe health status and psychological distress among in-hospital cardiac arrest (IHCA) survivors in relation to gender.

Methods: This national register study consists of data from follow-up registration of IHCA survivors 3-6 months post cardiac arrest (CA) in Sweden. A questionnaire was sent to the survivors, including measurements of health status (EQ-5D-5L) and psychological distress (HADS).

Results: Between 2013 and 2015, 594 IHCA survivors were included in the study. The median values for EQ-5D-5L index and EQ VAS among survivors were 0.78 (q1-q3=0.67-0.86) and 70 (q1-q3=50-80) respectively. The values were significantly lower ($p<0.001$) in women compared to men. In addition, women reported more problems than men in all dimensions of EQ-5D-5L, except self-care. A majority of the respondents reported no problems with anxiety (85.4%) and/or symptoms of depression (87.0%). Women reported significantly more problems with anxiety ($p<0.001$) and symptoms of depression ($p<0.001$) compared to men. Gender was significantly associated with poorer health status and more psychological distress. No interaction effects for gender and age were found.

Conclusions: Although the majority of survivors reported acceptable health status and no psychological distress, a substantial proportion reported severe problems. Women reported worse health status and more psychological distress compared to men. Therefore, a higher proportion of women may be in need of support. Health care professionals should make efforts to identify health problems among survivors and offer individualised support when needed.

Word-/reference count

Abstract 229

Manuscript 3000

References 40

KEYWORDS

Anxiety, Depression, Health Status, Heart arrest, Hospitals, Gender, Survivors

INTRODUCTION

In Europe, approximately 275 000 people suffer an out-of-hospital cardiac arrest (OHCA) annually,[1] while the prevalence of in-hospital cardiac arrest (IHCA) is unknown. Major improvements in survival have been reported over the last decades. In Sweden, more than 1 300 people survive cardiac arrest (CA) annually. The majority of patients suffering CA with a resuscitation attempt in Sweden are men (OHCA 69% and IHCA 62%).[2]

Brain injury develops within minutes after the cessation of blood flow[3] and may explain several complications often seen after CA.[4] Cognitive problems and psychological distress (e.g., anxiety and depression) are some of the most reported complications.[5-8]

According to the WHO definition, health is multidimensional and can be defined as "a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity".[9] However, the definition has been questioned for its´ "absoluteness" and the inclusion of "adapting to and self-management of challenges" have been proposed.[10] Patient reported outcome measures (PROMs) of health are widely used to describe the impact of disease/illness and to evaluate health-care interventions from a patient perspective.[11]

Knowledge about health status and psychological distress among CA survivors is scarce. Some studies have reported negative effects on health and poorer outcome among CA survivors compared to a general population,[7,12] while others have reported no differences.[13,14] A review on psychological distress reported high prevalence of anxiety and depression.[8] Another review reported that health and quality of life (QoL) among survivors appear to be acceptable, but with major variations in methodology and results between studies.[15] A review of outcome measures in clinical CA trials reported a considerable lack of health related outcomes and highlighted the need for a core outcome set for CA survivors, including PROMs of health and QoL to capture the patient perspective.[16]

Recent studies in larger populations have confirmed the findings of high prevalence of psychological distress but acceptable health and QoL among survivors.[6,14] However, most studies on health-related outcomes are performed in populations where the CA occurred in an out-of-hospital context, with only a few small studies including IHCA survivors.[17,18] Compared to those suffering OHCA, the IHCA population is older, has more comorbidity and is resuscitated earlier.[2] Therefore, IHCA survivors may experience other health problems.

Previous studies have demonstrated differences in age and survival between men and women in CA populations.[19,20] Despite the fact that a vast majority of existing research, independent of disease, shows that women have poorer health[21,22] and more psychological distress,[23,24] few studies

have investigated health status and psychological distress among CA survivors in relation to gender. Women surviving OHCA report more health problems and psychological distress than men.[6,14] To our knowledge, no studies have investigated these aspects in IHCA survivors.

The aim of the current study was therefore to describe health status and psychological distress among IHCA survivors in relation to gender.

METHODS

Design

This register study had a cross-sectional design and was approved by the Regional Ethical Review Board in Gothenburg (No. 406-13).

Sample and procedure

The sample for the present study was taken from the Swedish national register of cardiopulmonary resuscitation (https://www.hjartstoppsjh.se). This Internet-based register includes data from 95% of Swedish emergency hospitals. Data is registered on three occasions. The first registration includes data on patient characteristics and the CA event. The second is a follow-up registration performed at 30-days post CA and includes data on aetiology, comorbidity, post resuscitation care, survival and cerebral performance. As of August 2013, a third registration is performed 3-6 months after resuscitation and includes PROMs of health status and psychological distress in survivors. For this third registration, a questionnaire and an invitation to a telephone follow-up interview are sent to the survivors. The survivors are instructed to complete the questionnaire during the interview while data are entered in a web-form by the interviewer. The interviews are performed by resuscitation coordinators or cardiac rehabilitation nurses per a written

manual. In addition, a scoring of cerebral performance is conducted based on information from the interview using the Cerebral Performance Category (CPC) scale.

Data for the present study was collected between August 2013 and December 2015 in 47 emergency hospitals (64% of all eligible hospitals in Sweden). During this period, 1 061 30-day survivors were initially identified for the third registration. After exclusion 773 survivors remained eligible and 594 (76.8%) were included in the study (Figure 1).

The questionnaire

The questionnaire included the EQ-5D-5L[25] and the Hospital Anxiety and Depression Scale (HADS).[26]

The EQ-5D-5L

The EQ-5D-5L questionnaire includes the EQ-5D-5L descriptive system and the EQ VAS. The descriptive system measures health status in five dimensions; mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[25] Each dimension is rated on a five-point scale, ranging from 1 “no problems” to 5 “extreme problems”. A score of ≥2 indicate problems (regardless of severity). These dimensions can be used to describe a health state profile and to calculate a preference-based utility index. The index value is based on value sets for the EQ-5D-3L version. Higher index values indicate better health status. The index values in this study were calculated by a crosswalk procedure using the Danish value set (no Swedish available) and the EQ-5D-5L Crosswalk Index Value Calculator (www.euroqol.org). Using this crosswalk calculator, the possible index values range between -0.624 and 1, where 1 is perfect health and a value less than 0 is a health state worse than death. The EQ-5D-5L also includes a visual analogue scale (the EQ

VAS) for self-rated health, ranging from “the worst health you can imagine” (0) to “the best health you can imagine” (100). The EQ-5D-5L has not previously been applied in the CA population.

The Hospital Anxiety and Depression Scale

The HADS was developed to detect anxiety and/or symptoms of depression.[26] It consists of 14 items, of which seven measure anxiety and seven depression. Each item has four response categories, from 0-3. The item responses within each domain are summarized, with a total score ranging between 0 and 21 for anxiety and depression respectively. Higher values indicate more anxiety and/or symptoms of depression. Different cut-off scores have been suggested.[8] In the present study the following were used: normal (0-7), mild (8-10), moderate (11-14) and severe (15-21).[26] HADS has shown acceptable measurement properties for medical patients [27] and has been used in CA research.[6] However, HADS has not been robustly evaluated in CA survivors. The internal consistency in the present study was satisfactory according to Cronbach’s alpha for both anxiety (0.87) and depression (0.87).

Statistics

Descriptive statistics were used for sample characteristics and study variables. Mann-Whitney U test, with eta square (η^2) as effect size measure, was used to compare health status and psychological distress between women and men.

A series of nested multiple linear regression analyses in three blocks were conducted to explore if gender was associated with health status, anxiety and symptoms of depression. In these models, EQ-5D-5L index, EQ VAS, HADS anxiety and HADS depression were included as outcome variables. Since all outcome variables deviated from a normal distribution (D’Agostino test $p<0.001$), all regression models were based on robust standard errors.[28] Gender was included

as predictor variable in block I. As women were significantly older than men, age was included as a covariate in block II. To further evaluate interaction effects of gender and age, a multiplicative interaction term (gender × age) was included in block III. No problems with multicollinearity between predictor variables were detected according to the variance inflation factor (VIF mean = 1.02).

The significant level was set to $p<0.05$. All statistical analyses were performed using Stata 13.1 for Windows (StataCorp LP, College Station, TX, USA).

RESULTS

Description of the participants in relation to gender

During the study period, 594 IHCA survivors completed the questionnaire. There were no significant differences in gender ($\chi^2(1)=0.01$, $p=0.935$) and age ($Z=0.53$, $p=0.599$) between participants (n=594) and non-participants (n=179). However, non-participants had significantly worse CPC score ($Z=6.90$, $p<0.001$) at hospital discharge.

Among survivors, the median age was 70 years (q1-q3 = 62-78 years), and the majority were men (63.3%). The women were significantly older (median 73 vs. 69 years, $p<0.001$), more often suffered CA with non-cardiac or unknown aetiology (33.5% vs. 17.6%, $p<0.001$), and had lower proportions of cardiac ischaemic aetiology (21.6% vs. 40.2%, $p<0.001$) and shockable initial rhythm (51.5% vs. 63.3%, $p=0.007$). In addition, women had worse CPC score at 3-6 months than men ($p=0.006$). There were no significant differences between women and men in the proportion of witnessed CA, location of CA or comorbidities (Table 1).

Health status

The median values for EQ-5D-5L index and EQ VAS among survivors were 0.78 (q1-q3=0.67-0.86) and 70 (q1-q3=50-80) respectively, with significantly lower ratings ($p<0.001$) in women compared to men (Table 2).

The EQ-5D-5L index and EQ VAS were negatively skewed distributed and ceiling effects were detected among 18% and 4% for EQ-5D-5L index and EQ VAS respectively.

Pain/discomfort was the dimension of EQ-5D-5L where most survivors reported health problems (n=363, 61.1%) regardless of severity (score ≥2). Problems with anxiety/depression was reported by more than half of the survivors (n=300, 50.5%), while problems with usual activities, mobility and self-care were reported by less than half (n=282, 47.5%, n=279, 47.0% and n=126, 21.2% respectively). Pain/discomfort was also the dimension where survivors reported most severe problems (2.03±1.01), followed by usual activities (1.89±1.14), mobility (1.88±1.12), anxiety/depression (1.75±0.86) and self-care (1.36±0.83). Women reported poorer health status than men in all dimensions except self-care (Figure 2).

Psychological distress

A majority of the survivors reported no problems with anxiety (85.4%) and/or symptoms of depression (87.0%), i.e. HADS score <8. A minority of the survivors reported moderate to major problems (>10) with anxiety (n=30, 5.0%) and/or depression (n=28, 4.8%) (Table 3). Women reported significantly more problems with anxiety (median 3 vs. 2, $p<0.001$) and symptoms of depression (median 3 vs. 2, $p<0.001$) compared to men (Table 2).

HADS were positively skewed distributed and floor effects were detected among 26% and 18% for HADS anxiety and HADS depression respectively.

Associations between gender, health status and psychological distress

Gender was significantly associated with health status and psychological distress. In block I, women reported poorer health status, and more problems with anxiety and symptoms of depression compared to men. This association remained after age was included as covariate in block II. No interaction effects for gender and age were found in block III (Table 4).

DISCUSSION

To or knowledge, this is the largest study describing health status and psychological distress among IHCA survivors. Overall, health problems and psychological distress among the survivors were common. Although the majority reported minor problems there was great variation and a significant percentage reported severe problems. Women reported poorer health status and more problems with psychological distress than men.

The health status of the majority of the IHCA survivors may be considered acceptable and is comparable to patients with myocardial infarction,[29] but lower compared to OHCA survivors,[13,14,17] and to a general Swedish population.[30] In a large study on health status among Australian OHCA survivors, EQ VAS was considerably higher than among our participants and equal to a general British population.[14] This can possibly be explained by the different timing of measurements (12 months post CA), i.e. a longer recovery time. Other possible explanations could be differences in culture or post CA care between Sweden and Australia. However, as a preliminary report from Sweden indicates similar health status among OHCA survivors (at 3-6 months) as in the Australian study,[2] it is more likely that the differences are due to other factors, e.g. higher age and more comorbidity among the IHCA survivors in our study.

The EQ-5D-5L is a generic measure of health status and can be criticized for lacking evidence of content validity in the CA population. There is a need for instruments specifically developed for

this group of patients.[16] Further, a recently published review acknowledged the need for qualitative studies to explore survivors´ experiences and what they consider to be important aspects of health and QoL.[31]

Health differences between genders have not previously been studied in IHCA populations. In our study, women reported more health problems compared to men. This corresponds to earlier research on OHCA survivors[14] and general populations.[30] One possible explanation is that women may experience worse health due to more responsibility in social activities.[32] In addition, as women generally live longer than men, women of high age are more likely to live alone and are therefore at risk of experiencing loneliness.[33] Problems in anxiety/depression, mobility and usual activities may partly be explained by the consequences of being alone, e.g. due to dependency on others to participate in social activities. Feelings of loneliness have been reported to be more common among women in a Swedish general population aged 65-80 years.[34] Furthermore, loneliness has been reported to be associated with widowhood, depression and mobility problems uniqely among women.[35]

A minority reported psychological distress. The proportion of survivors with anxiety and symptoms of depression in this study are comparable to general populations[34] and to most previous studies on OHCA survivors using the HADS.[6,8] More problems with psychological distress were identified with EQ-5D-5L compared to HADS, even when using a HADS cut-off score of >7. This may be explained by the EQ-5D-5L single item construct, combining anxiety and depression with no validated cut-off scores, which could lead to overestimation of the prevalence of psychological problems. However, although many survivors reported psychological distress measured by EQ-5D-5L, the problems were not reported to be severe. This highlights the necessity of reporting prevalence and severity when studying psychological distress, and also the importance of using more than one instrument to capture different aspects of psychological distress to understand the

actual effects on patients' everyday life. Further, lower cut-off score for HADS may be more suitable for identifying those at risk of suffering psychological distress.

Women reported more psychological distress which cannot be explained by higher age. This has previously been described in OHCA survivors,[6] and in general populations.[24]

Our results may have implications for post cardiac arrest care and follow-up. Structured follow-up for CA survivors has shown positive effects on psychological distress.[18] However, a recently published survey describing post CA care in Sweden reported a lack of structured follow-up.[36] Since a vast majority of the survivors in our cohort scored good cerebral performance (CPC=1), their health problems might be at risk of being ignored, especially when follow-up care lack structure. Knowledge of health status and psychological distress among IHCA survivors, and differences between men and women, is important when testing follow-up interventions, creating guidelines, and when offering targeted support to CA survivors. Until there are disease specific instruments, a combination of EQ-5D-5L and HADS may be suitable measures for clinical and research use. However, both instruments need to be robustly validated in CA survivors.

Methodological considerations

This study has some limitations. The design does not support any causal conclusions, e.g. we cannot say anything about health status and psychological distress prior to CA. However, the large number of included survivors is a major strength and the results will help increase the knowledge of this group of patients.

The number of non-participants could be a potential threat against external validity. In addition, the reasons for some survivors declining participation are unknown. However, there were no differences in age or gender between participants and non-participants. In contrast, there was a significant difference in CPC score between the groups, which is an important limitation.

Therefore, our findings cannot be generalized to survivors with the poorest cognitive outcome. Failure to include such participants may result in overestimation of health among survivors.

Although female gender was associated with worse health status and more psychological distress, gender explained a minor part of the total variation according to the R2 values. In addition, more women had non-cardiac aetiology and non-shockable rhythm. Therefore, the results should be interpreted with some caution. Covariates like e.g. comorbidity, place of arrest, aetiology and initial rhythm might be of importance. Further studies will have to explore predictors for health problems and psychological distress.

The EQ-5D-5L could be criticized for reporting merely a few and broad dimensions of health status. However, the simplicity makes EQ-5D-5L suitable for register studies and allows for comparisons with other groups of patients and general populations. The EQ-5D-3L version has previously shown acceptable validity and reliability in cardiac patients[37] and has previously been used in CA research.[14,15] However, problems with responsiveness and ceiling effects have been reported.[38] The new 5-level version used in this study has shown improved psychometric properties compared to the 3-level version in other patient groups.[39] As the response scale is extended from 3 to 5 categories, it has potential to constitute a more sensitive and responsive measure.

HADS is a well-validated, widely used screening instrument for psychological distress, recommended in the European guidelines for post resuscitation care.[40] However, further studies will have to investigate the psychometric properties and the most accurate cut-off score for HADS in CA survivors.

Both EQ-5D-5L and HADS could be criticized for having unknown capacity to detect truly relevant aspects of health for CA survivors.

CONCLUSION

Although the majority of survivors reported acceptable health status and no psychological distress, a substantial group reported severe problems. These results support the importance of screening for health problems in follow-up measures to enable individualized post CA care for those in need. Women reported worse health status and more psychological distress compared to men. Therefore, a higher proportion of women may be in need of support. These results are important in order to improve post CA care. In addition, health status among IHCA survivors may be worse compared to earlier results describing OHCA survivors. This should be further investigated. Specific research tools for CA survivors and guidelines for reporting are warranted.

CONFLICT OF INTEREST STATEMENT

None of the authors have any conflicts of interest to declare.

ACKNOWLEDGEMENTS

We would like to thank the Swedish register of cardiopulmonary resuscitation for giving permission to the study and Sofia McGarvey for reviewing the language. A special thanks goes to all participating patients and personnel.

The study was funded by the Swedish Heart and Lung Association and The Medical Research Council of Southeast Sweden.

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LEGENDS TO FIGURES

Figure 1. Flowchart of inclusion.

Figure 2. Dimensions of EQ-5D-5L among IHCA survivors (n=594). Mean values for women and men (p-values based on Mann-Whitney U test, with eta square (η^2) as effect size measure). Higher values indicate more severe problems.

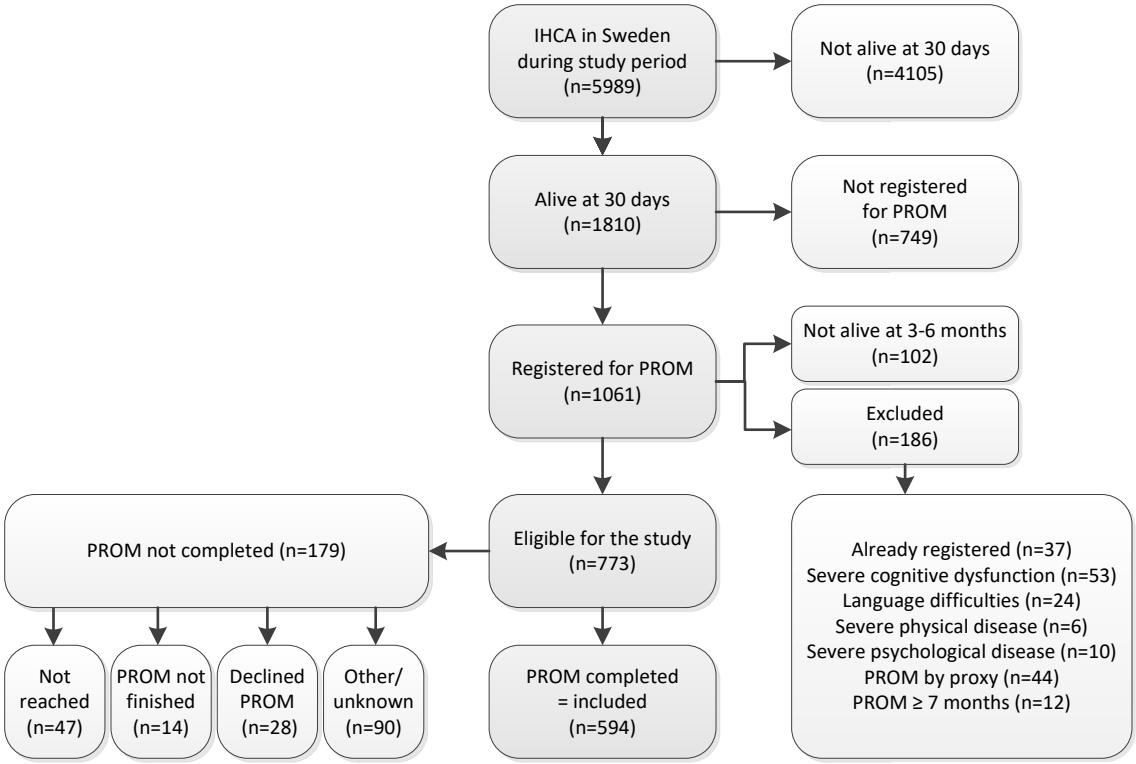

Figure 1. Flowchart of inclusion.

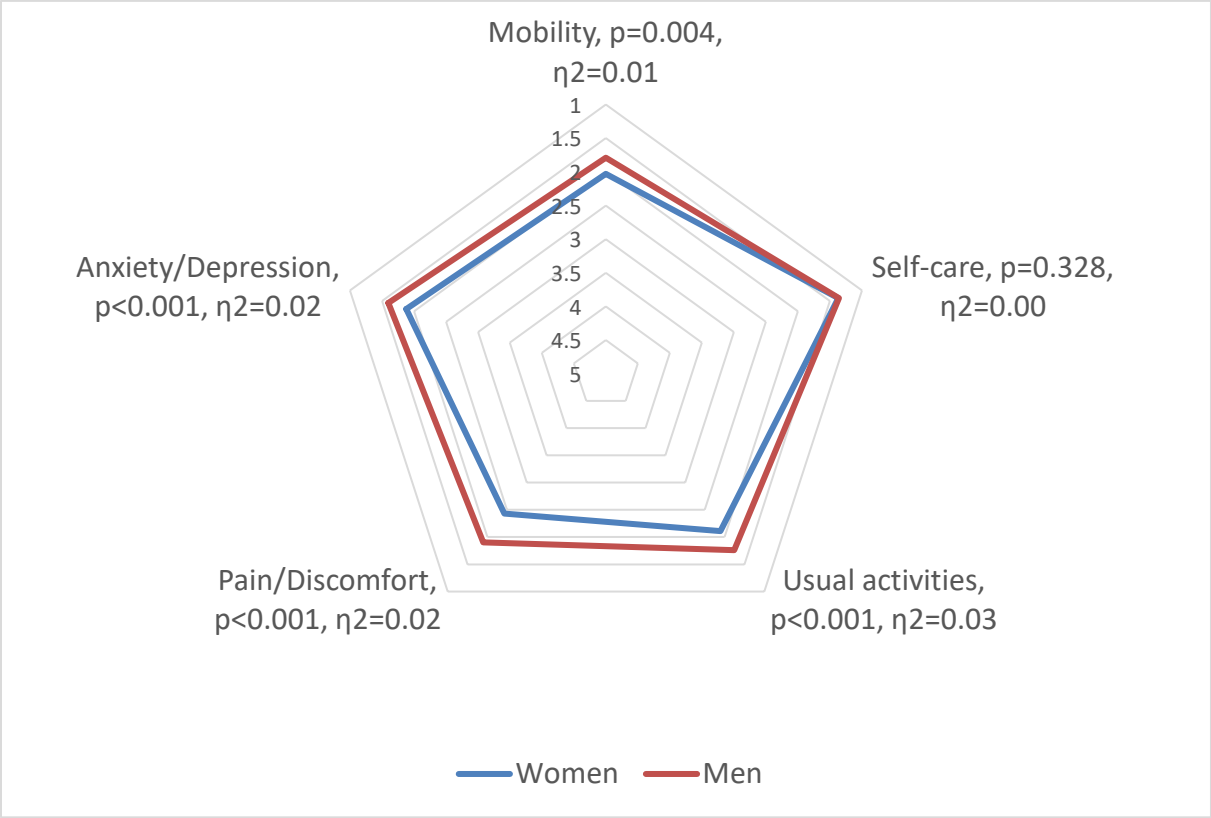

Figure 2. Dimensions of EQ-5D-5L among IHCA survivors (n=594). Mean values for women and men (p-values based on Mann-Whitney U test, with eta square (η^2) as effect size). Higher values indicate more severe problems.

Table 1. Characteristics of participants

Variable	Number of observations	All patients (n=594)	Women (n=218)	Men (n=376)	p-value
Age, md (q1-q3)	594	70 (62-78)	73 (63-80)	69 (60-75)	<0.001[a]
Cardiac ischemic aetiology, n (%)	594	198 (33.3)	47 (21.6)	151 (40.2)	<0.001[b]
Cardiac arrhythmic aetiology, n (%)	594	257 (43.3)	98 (45.0)	159 (42.3)	0.527[b]
Other/unknown aetiology, n (%)	594	139 (23.4)	73 (33.5)	66 (17.6)	<0.001[b]
Shockable initial rhythm, n (%)	543	320 (58.9)	104 (51.5)	216 (63.3)	0.007[b]
Witnessed CA, n (%)	589	560 (95.1)	206 (94.9)	354 (95.2)	0.901[b]
Location of cardiac arrest, n (%)	594				0.347[b]
Cardiac intensive care unit		154 (25.9)	60 (27.5)	94 (25.0)	
Cardiac catheterization unit		123 (20.7)	36 (16.5)	87 (23.1)	
General intensive care unit		60 (10.1)	18 (8.3)	42 (11.2)	
Surgery care unit		23 (3.9)	11 (5.1)	12 (3.2)	
Emergence department		65 (10.9)	24 (11.0)	41 (10.9)	
Hospital ward		126 (19.2)	54 (24.8)	72 (21.1)	
Reception-/diagnostic unit		27 (4.6)	9 (4.1)	18 (4.8)	
Other unit		16 (2.7)	6 (2.8)	10 (2.7)	
Co-morbidity, n (%)					
Prior AMI	587	147 (28.0)	43 (20.0)	104 (27.0)	0.032[b]
Respiratory insufficiency	588	61 (9.4)	26 (12.0)	35 (9.0)	0.314[b]
Stroke	591	40 (7.0)	14 (6.5)	26 (8.6)	0.815[b]
Diabetes	594	124 (20.1)	47 (21.6)	77 (20.5)	0.755[b]
Heart failure	575	147 (25.6)	53 (24.8)	94 (26.0)	0.735[b]
Cancer	591	64 (10.8)	21 (9.7)	43 (11.5)	0.511[b]
Cerebral function at discharge, n (%)	532				0.320[c]
CPC 1		472 (88.7)	166 (86.9)	306 (89.7)	
CPC 2		50 (9.4)	23 (12.0)	27 (7.9)	
CPC 3		8 (1.5)	2 (1.0)	6 (1.8)	
CPC 4		2 (0.4)	0 (0.0)	2 (0.6)	
Cerebral function at 3-6 months, n (%)	594				0.006[c]
CPC 1		528 (88.9)	182 (83.5)	346 (92.0)	
CPC 2		60 (10.1)	33 (15.1)	27 (7.2)	
CPC 3		6 (1.0)	3 (1.4)	3 (0.8)	
CPC 4		0 (0.0)	0 (0.0)	0 (0.0)	

AMI=Acute Myocardial infarction; CPC=Cerebral Performance Category CA=Cardiac Arrest
[a] Mann-Whitney U test, [b] Chi-square test, [c] Fischer's exact test

Table 2. Health status and psychological distress in relation to gender

Variable	All patients (n=594)	Women (n=218)	Men (n=376)	p-value	eta square (η^2)
EQ-5D-5L index, md (q1-q3)	0.78 (0.67-0.86)	0.75 (0.61-0.81)	0.79 (0.69-0.87)	<0.001[a]	0.02
EQ VAS, md (q1-q3)	70 (50-80)	65 (50-80)	75 (55-80)	<0.001[a]	0.02
HADS anxiety, md (q1-q3)	2 (0-5)	3 (1-6)	2 (0-5)	<0.001[a]	0.04
HADS depression, md (q1-q3)	2 (1-5)	3 (1-6)	2 (1-4)	<0.001[a]	0.02

EQ VAS= EQ Visual Analogue Scale, HADS= Hospital Anxiety and Depression Scale
[a] Mann-Whitney U test

Table 3. Cut-off scores of HADS (n=594)

	HADS Anxiety n (%)	HADS Depression n (%)
Normal (0-7)	507 (85.4)	517 (87.0)
Men	326 (86.7)	335 (89.1)
Women	181 (83.0)	182 (83.5)
Minor (8-10)	57 (9.6)	49 (8.2)
Men	36 (9.6)	24 (6.4)
Women	21 (9.6)	25 (11.5)
Moderate (11-14)	18 (3.0)	17 (2.9)
Men	7 (1.9)	11 (2.9)
Women	11 (5.1)	6 (2.8)
Major (15-21)	12 (2.0)	11 (1.9)
Men	7 (1.9)	6 (1.6)
Women	5 (2.3)	5 (2.3)

HADS= Hospital Anxiety and Depression Scale

Table 4. Gender and age as predictors for health status and psychological distress based on robust multiple linear regression models (n=594)

		Block I		Block II		Block III	
Outcome variable	Predictor variable	B (SE)	p-value	B (SE)	p-value	B (SE)	p-value
EQ-5D-5L index	Gender	-0.08 (0.02)	p<0.001	-0.08 (0.02)	p<0.001	-0.06 (0.10)	0.568
	Age			-0.00 (0.00)	0.841	0.00 (0.00)	0.917
	Gender x Age					-0.00 (0.00)	0.858
	Model statistics	F(1, 582)=19.05, p<0.001, R^2=0.03		F(2, 594)=9.52, p<0.001, R^2=0.03		F(3, 590)=6.50, p<0.001, R^2=0.03	
EQ VAS	Gender	-6.03 (1.76)	0.001	-5.58 (1.78)	0.002	2.38 (9.29)	0.798
	Age			-0.13 (0.06)	0.032	0.03 (0.19)	0.886
	Gender x Age					-0.11 (0.13)	0.376
	Model statistics	F(1, 592)=11.71, p<0.001, R^2=0.02		F(2, 591)=8.72, p<0.001, R^2=0.03		F(3, 590)=6.13, p<0.001, R^2=0.03	
HADS Anxiety	Gender	1.01 (0.33)	0.002	1.21 (0.32)	<0.001	0.21 (1.84)	0.908
	Age			-0.06 (0.01)	<0.001	-0.08 (0.04)	0.032
	Gender x Age					0.01 (0.03)	0.571
	Model statistics	F(1, 592)=9.31, p=0.002, R^2=0.02		F(2, 592)=17.49, p<0.001, R^2=0.06		F(3, 590)=12.18, p<0.001, R^2=0.06	
HADS Depression	Gender	0.84 (0.31)	0.007	0.77 (0.30)	0.012	-0.98 (1.47)	0.507
	Age			0.03 (0.01)	0.060	-0.02 (0.03)	0.624
	Gender x Age					0.03 (0.02)	0.227
	Model statistics	F(1, 592)=7.35, p=0.007, R^2=0.01		F(2, 591)=5.00, p=0.007, R^2=0.02		F(3, 590)=3.87, p=0.009, R^2=0.02	

EQ VAS= EQ Visual Analogue Scale, HADS= Hospital Anxiety and Depression Scale