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Clinical paper

Hospitalized patients' attitudes towards participating in a randomized control trial in case of a cardiac arrest

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Abstract

Background: No previous study has evaluated patients attitudes towards inclusion in an ongoing cardiac arrest clinical trial. The aim of this study was to assess patients´ willingness and motives to participate in the ongoing randomized controlled drug trial "Vasopressin and Steroids in addition to Adrenaline in cardiac arrest" (VAST-A trial) in case of an in-hospital cardiac arrest (IHCA).

Objectives: Hospitalized patients, men $\geq$ 18 and women $\geq$ 50 years, were asked for informed consent for inclusion in the VAST-A trial in case of an IHCA, the reason for approving or declining inclusion in the trial and baseline characteristics.

Methods: Patients admitted to hospital were asked to give informed consent of inclusion in VAST-A in case of an IHCA during their hospital stay. Patients were also asked why they approved or declined inclusion as well as baseline characteristics questions.

Results: 1,064 patients were asked about willingness to participate in the VAST-A trial, of these 902 (84.8%) patients approved inclusion. A subgroup of 411 patients were, except willingness, also asked about motives to participate or not and basic characteristics. The main reason for approving inclusion was to contribute to research (n = 328, 83.9%). The main reason for declining inclusion was concerns regarding testing the drug treatment (n = 6, 30%).

Conclusion: Among hospitalized patients the vast majority gave informed consent to inclusion in an ongoing randomized cardiac arrest drug trial. The main reason for approving inclusion was to contribute to research.

Keywords: Informed consent, Waiver informed consent, Cardiac arrest

Introduction

Research in critically ill patients is difficult, challenging, and important. The critical state of the disease often requires decision regarding various measures and treatments within minutes. In the case of cardiac arrest and several other critical conditions, the patient is unconscious and unable to give informed consent.

Both the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) allow research without prior consent to enable to include study objects who are physically or mentally incapable of giving consent or during a life-threatening situation.[1,2] However, up until August 2022, the Swedish Medical Products Agency made a stricter interpretation and did not approve any drug studies without informed consent. This made the inclusion of patients to the randomized drug trial "Vasopressin and Steroids in addition to Adrenaline in cardiac arrest" (VAST-A) possible only if patients gave informed consent prior to the occurrence of an in-hospital cardiac arrest (IHCA). This meant that patients admitted to hospital were asked of informed consent to participate in the VAST-A trial in case of cardiac arrest during their hospital stay.

Most published studies assessing patients' attitudes toward inclusion in studies without informed consent have asked for consent of participating in hypothetical studies or proposed studies without informed consent.[3,4] There are, to the authors knowledge no previous

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studies that have evaluated patients attitudes towards inclusion in an ongoing cardiac arrest drug trial. Therefore, in addition to ask patients for informed consent to participate in the VAST-A trial in case of cardiac arrest during their hospital stay, we decided to study the reasons why patients approved or declined inclusion in the VAST-A trial. Thus, the purpose of this study was twofold: first, to measure the willingness of patients to participate in the ongoing randomized controlled drug trial in case of a cardiac arrest. Second, to determine why patients approved or declined participation in the trial and whether the consent procedure was associated with gender, age, comorbidities, socioeconomic status, or quality of life.

Methods

Study design and ethics

This study, CONSENT trial, was a predefined sub study of the VAST-A trial. The study was designed as a prospective observational study of patient's willingness and motives to be included in the randomized control drug trial VAST-A. Patients admitted to hospital were asked to give informed consent of inclusion to the randomized drug trial "Vasopressin and Steroids in addition to Adrenaline in cardiac arrest" (VAST-A) in case of an IHCA during their hospital stay. Patients were also asked why they approved or declined inclusion as well as questions regarding baseline characteristics. The study was approved by the Swedish Ethical Review Authority, (DNR 2021-05692-02).

The VAST-A trial is an ongoing randomized clinical trial where patients with an IHCA who meet criteria for adrenaline administration are randomized to either control group who receive adrenaline and placebo (NaCl) or to intervention group with administration of adrenaline, vasopressin, and steroids during resuscitation. The VAST-A trial was approved by the Swedish Ethical Review Authority (DNR 2019–04238) and the Swedish Medical Products Agency (DNR 2019-59308).

Patients were screened and included in the VAST-A trial between 17th of November 2021 to the 21st of October 2022. In addition, patients included in the VAST-A trial was also, from the 13th of February to the 21st of October 2022, asked why they approved or declined inclusion as well as questions regarding baseline characteristics as part of the CONSENT trial.

Participants

Inclusion and exclusion criteria were the same for both the VAST-A and CONSENT trial. Men $\geq$ 18 years and women $\geq$ 50 years who were admitted to the Cardiology wards at Sahlgrenska University hospital or any general ward at Norrtälje hospital were eligible for inclusion. Exclusion criteria were patients with do not resuscitate (DNR) decision, patients not able to comprehend information to decide about participation in the studies, or inability to express themselves or understand the Swedish language. Women < 50 years of age were excluded to avoid inclusion of pregnant women.

Procedures

Screening and inclusion of eligible patients were carried out Monday-Friday by a research nurse in collaboration with a nurse at the hospital ward. Eligible patients were informed written and orally and asked for written and oral consent to participate in the VAST-A. They were also asked about inclusion in the CONSENT trial including data acquisition regarding reason for accepting or declining participation in the VAST-A trial as well as baseline characteristics such as gender, age, comorbidities, socioeconomic status, and quality of life (EQ5D questionnaire). The case report form (CRF) was printed so patients could complete it independently. In case of fatigue the research nurse helped the patient fill in the CRF by having the questions and answer options read out loud. Data regarding past and present illnesses, demographics, and reason for hospital admission were checked with patient's medical record. The data was manually entered into the electronic-CRF in the study database, REDCap by research nurses.

The intention was to ask all patients for both participation in the VAST-A trial and the additional data collection for the CONSENT trial. All patient were not able to consent to both trials due to availability or ability to fill out the form. We do not have reliable data on how many patients who were not asked for participation in the additional data collection for the CONSENT trial and how many patients who declined participation in the CONSENT trial.

Statistical analysis

Patients included in the CONSENT trial were divided into patients who approved inclusion in the VAST-A trial (yes group) and patients who declined inclusion in the VAST-A trial (no group). Baseline characteristics were reported using means or median with appropriate dispersion measures. The two groups, the yes group and the no group were compared using Chi square test for dichotomous variables and Wilcoxon two-sample test for continuous variables. A p-value < 0.05 was considered significant. Due to imbalance between the two groups, we present both p-value and standardized mean difference (SMD). Missing data was excluded from the analysis. We also performed analyse of patients who were only asked about their willingness to participate in the VAST-A trial.

Role of the funding source

The funder had no role in study design, data collection and analysis, interpretation, decision to publish, or preparation of the manuscript.

Funding

The study was funded by independent research grants from the Swedish Heart-Lung Foundation

Results

Screening process and included patients

A total of 1,064 patients were asked about their willingness to participate in the VAST-A trial, without the follow-up questions of motives and basic characteristics (Fig. 1). A total of 411 patients were included in the additional data collection for the CONSENT trial and asked about their willingness to participate in the VAST-A trial as well as questions regarding, motives, basic characteristics, and socioeconomic status (Fig. 2).

Patient's willingness to participate in the VAST-A trial

Of the 1,064 patients asked to participate in the VAST-A trial 902 (84.8%) accepted inclusion in the trial and 162 (15.2%) declined inclusion in the VAST-A trial. No one of the 902 patients experienced a cardiac arrest during their hospital stay.

Basic characteristics among patients included in the CONSENT trial

Among the included patients, median age were 72 years and 41% were women. Most patients were included in the cardiology depart-

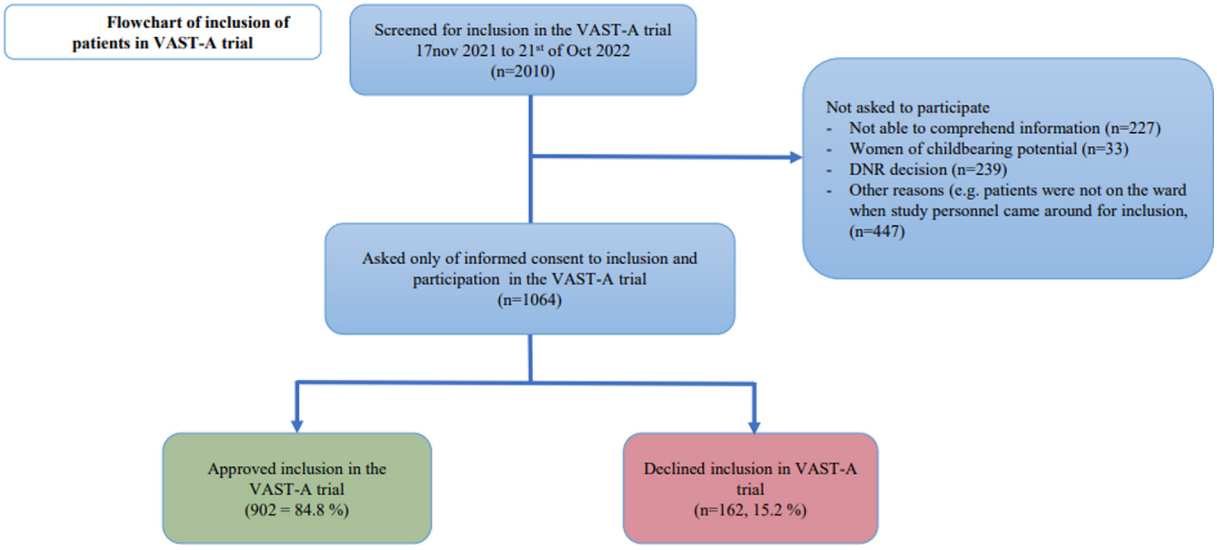

Fig. 1 – Flowchart of inclusion of patients VAST-A trial.

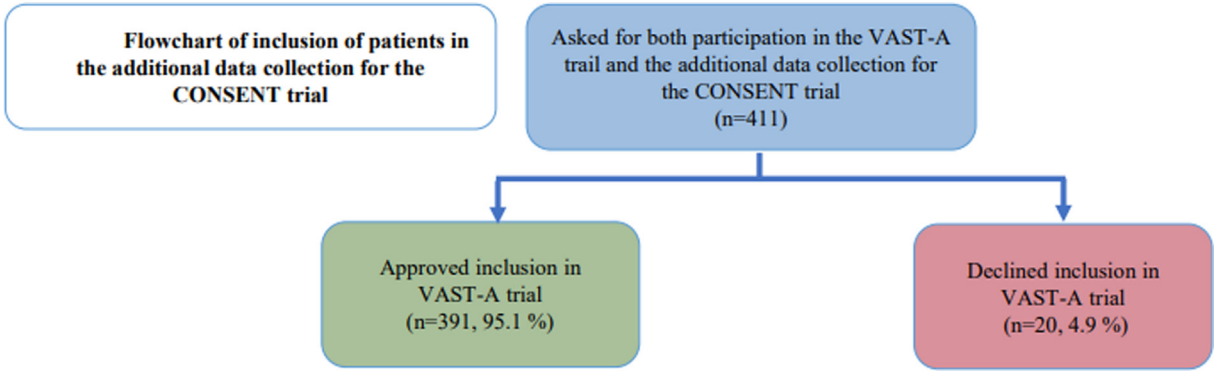

Fig. 2 – Flowchart of inclusion of patients in the additional data collection for the CONSENT trial.

ment and cardiac cause was the major reason for hospital admission. The yes group compared to the no group significantly more often had a comorbidity of atrial fibrillation (27.6% versus 5.0%, *p*-value 0.048) and significantly less often diabetes mellitus type 1 (1% versus 10%, *p*-value 0.021). There was a significant difference between the groups regarding reason for hospital admission (*p*-value 0.047). The yes group significantly more often had a cardiac cause for hospital admission (69.7% versus 50%) and significantly less often a respiratory cause (4.9% versus 15%) or planned admission (4.6% versus 20%) compared to the no group (Table 1).

Socioeconomic factors and quality of life among patients included in the CONSENT trial

There was no difference between the groups in regard to socioeconomic factors or quality of life (Tables 2 and 3).

Patient's motives to not participate in the VAST-A trial

Of the 411 patients who were included in the CONSENT trial, 391 (95.1%) accepted inclusion in the VAST-A trial. All patients were not able to consent to both studies due to availability or ability to fill out the form.

Of the 411 patients, 20 (4.9%) patients declined inclusion in the VAST-A trial. There were several reasons for this, six patients (30%) expressed concerns regarding testing the drug treatment and two patients (10%) did not want to be part of a time-consuming follow up after the cardiac arrest. Ten patients (50%) stated, "other reasons" and made comments in free text. These answers included, too tired to decide, do not want to be resuscitated, and do not want to have treatment with steroids (Supplementary Table 4).

In the adjusted analysis, primary educational level affected the probability of a patient accepting inclusion in the VAST-A trial, OR 0.22 (CI 0.05–0.79) (Fig. 3).

Discussion

The main finding in this study was that among hospitalized patients the vast majority gave informed consent to inclusion and participation in an ongoing randomized cardiac arrest drug trial. The main reasons for a positive attitude toward participation was to contribute to research and to receive the opportunity of a promising drug treatment. The main reasons for declining participation in the VAST-A trial was concerns about negative effects of the drug treatment and because patients were too tired to decide. There was a significant difference between the groups in terms of reason for hospital

Table 1 – Baseline characteristics among patients included in the CONSENT trial.

	Overall	Confirmed inclusion in VAST-A[1] trial (Yes group)	Declined inclusion in VAST-A[1] trial (No group)	*P*-value	SMD[2]
n	411	391	20		
Age (median [IQR])	72 [61—80]	72 [61–80]	72 [67–77.5]	0.539	0.272
Sex, women (%)	163 (41.0)	152 (40.2)	11 (55.0)	0.281	0.299
Reason for accepting participation in the VAST-A trial					
Possibility of receiving new potential effective drug therapy (%)	–	222 (56.8)	0 (0.0)	<0.001	
Contribute to research (%)	–	328 (83.9)	0 (0.0)	<0.001	
Possibility of better follow-up (%)	–	125 (32.0)	0 (0.0)	0.005	
Other reason (%)	–	28 (7.2)	0 (0.0)	0.433	
Reason for declining participation in the VAST-A trial					
Concerns regarding new unproven drug treatment (%)	–	0 (0.0)	6 (30.0)	<0.001	
Concerns regarding storage of personal data (%)	–	0 (0)	0 (0)	NA	
Time-consuming follow-up (%)	–	0 (0.0)	2 (10.0)	<0.001	
Other reason (%)	–	0 (0.0)	10 (50.0)	<0.001	
Reason for admission (%)				0.047	0.730
Respiratory	22 (5.4)	19 (4.9)	3 (15.0)		
Cardiology	281 68.7)	271 (69.7)	10 (50.0)		
Planned admission	22 (5.4)	18 (4.6)	4 (20.0)		
Trauma	10 (2.4)	10 (2.6)	0 (0.0)		
Infection	15 (3.7)	14 (3.6)	1 (5.0)		
Neurology	3 (0.7)	3 (0.8)	0 (0.0)		
Surgical	7 (1.7)	7 (1.8)	0 (0.0)		
Other reason	49 (12.0)	47 (12.1)	2 (10.0)		
Comorbidity					
Ischemic heart disease (%)	89 (21.7)	86 (22.0)	3 (15.0)	0.644	0.181
Hypertension (%)	207 (50.4)	199 (50.9)	8 (40.0)	0.471	0.220
Cardiac failure (%)	72 (17.5)	70 (17.9)	2 (10.0)	0.545	0.230
Atrial fibrillation/flutter (%)	109 (26.5)	108 (27.6)	1 (5.0)	0.048	0.643
Other cardiac arrythmia (%)	37 (9.0)	36 (9.2)	1 (5.0)	0.810	0.164
Diabetes mellitus type 1 (%)	6 (1.5)	4 (1.0)	2 (10.0)	0.021	0.401
Diabetes mellitus type 2 (%)	62 (15.1)	57 (14.6)	5 (25.0)	0.342	0.264
Cerebrovascular disease (%)	39 (9.5)	37 (9.5)	2 (10.0)	1.000	0.018
Chronic renal failure (%)	22 (5.4)	20 (5.1)	2 (10.0)	0.662	0.186
Chronic liver failure (%)	0 (0)	0 (0)	0 (0)	NA	NA
Cancer (%)	34 (8.3)	34 (8.7)	0 (0.0)	0.337	0.436
Asthma/COPD (%)	55 (13.4)	51 (13.0)	4 (20.0)	0.579	0.188

[1] Vasopressin and Steroids in addition to Adrenaline in cardiac arrest (VAST-A trial).
[2] Standardized mean difference (SMD).

admission. The yes group were more often admitted to the hospital due to cardiac cause meanwhile the no group more often had a planned hospital admission. Also, patients with primary education were less prone to accept inclusion in the study.

To our knowledge there is no previous trial investigating pre-consent in patients at risk of inclusion in a cardiac arrest trial. Studies assessing the willingness to participate in a hypothetical study of a new drug treatment in case of a cardiac arrest reported that 55–83% of patients were willing to participate without informed consent.[4,5] Patients were less willing to be included if the hypothetical trial involved randomization between placebo and the study drug but, more willing to accept inclusion if asked to personally be involved in a proposed study without informed consent.[4,6–9]

In the US, around 55% (34–80%) in general agree with research without informed consent.[10–12,5,6] Studies have shown that the willingness to participate in a study decreased with increased risk of the intervention.[4,7,9,13] In the study by Smithline et al. 73% would approve inclusion in a study without informed consent if the risk of the intervention were minimal, e.g. an extra blood sample but, decreased to 50% if the study involved testing a new drug.[13] Surprisingly, patients were more willing to accept experimental treatment 'outside' of a research protocol. In the study by Abboud et al.[4] 84% of patients asked in the ED were willing to receive a new drug treatment without consent.

Our study reported a higher willingness to participate compared to other studies, there are several reasons why. First and foremost, the question differ, previous studies have asked about the willingness to participate in either a hypothetical study or the willingness to participate in a proposed study without informed consent. In our study patients are asked to participate in an ongoing study with informed consent. Second, even with optimal care patients with cardiac arrest have a high mortality rate, this has previously been sug-

Table 2 – Information regarding social activity, physical activity, tobacco habits, and education among patients included in the CONSENT trial.

	Overall	Confirmed inclusion in VAST-A[1] trial (Yes group)	Declined inclusion in VAST-A[1] trial (No group)	*P*-value	SMD[2]
n	411	391	20		
Living together (%)	247 (60.1)	234 (59.8)	13 (65.0)	0.822	0.107
Accommodation (%)				0.968	0.077
Independent living	363 (89.0)	345 (88.9)	18 (90.0)		
Independent living with homecare	44 (10.8)	42 (10.8)	2 (10.0)		
Special accommodation	1 (0.2)	1 (0.3)	0 (0.0)		
How often do you meet up with friends and family (%)				0.465	0.243
More than once a week	347 (87.2)	331 (87.6)	16 (80.0)		
More than once a month	31 (7.8)	28 (7.4)	3 (15.0)		
Less than once a month	20 (5.0)	19 (5.0)	1 (5.0)		
How often do you experience lack of companionship (%)				0.321	0.430
Almost never	293 (71.5)	276 (70.8)	17 (85.0)		
Sometimes	95 (23.2)	92 (23.6)	3 (15.0)		
Often	22 (5.4)	22 (5.6)	0 (0.0)		
How often do you feel alone/excluded (%)				0.532	0.321
Almost never	330 (81.3)	312 (80.8)	18 (90.0)		
Sometimes	64 (15.8)	62 (16.1)	2 (10.0)		
Often	12 (3.0)	12 (3.1)	0 (0.0)		
How often do you feel isolated from others (%)				0.587	0.308
Almost never	330 (82.9)	312 (82.5)	18 (90.0)		
Sometimes	54 (13.6)	52 (13.8)	2 (10.0)		
Often	14 (3.5)	14 (3.7)	0 (0.0)		
Tobacco habits					
Active smoker (%)	33 (8.1)	30 (7.7)	3 (15.8)	0.409	0.252
Previous smoker (%)	197 (53.0)	185 (52.1)	12 (70.6)	0.214	0.386
Daily use of snuff (%)	68 (16.8)	66 (17.1)	2 (10.0)	0.599	0.210
Alcohol habits					
Female > 9 standard glasses per week (%)	9 (5.6)	9 (6.0)	0 (0.0)	0.933	0.356
Male > 14 standard glasses per week (%)	17 (6.9)	17 (7.1)	0 (0.0)	0.813	0.392
Can walk without aids (%)	328 (81.4)	311 (81.2)	17 (85.0)	0.896	0.102
Engaged in pulse raising activity (%)	262 (64.7)	250 (64.9)	12 (60.0)	0.833	0.102
Engaged in pulse raising activity > 2.5 h a week (%)	184 (68.7)	179 (69.9)	5 (41.7)	0.081	0.593
Born in Sweden (%)	347 (85.7)	332 (86.0)	15 (78.9)	0.601	0.187
Education				0.133	0.453
Primary school/community school	125 (30.5)	115 (29.5)	10 (50.0)		
High school	117 (28.5)	112 (28.7)	5 (25.0)		
University/College	168 (41.0)	163 (41.8)	5 (25.0)		
Main occupation (%)				0.952	0.412
Work fulltime	102 (25.1)	97 (24.9)	5 (27.8)		
Work part time	32 (7.9)	31 (8.0)	1 (5.6)		
Unemployed	5 (1.2)	5 (1.3)	0 (0.0)		
Early retiree	9 (2.2)	9 (2.3)	0 (0.0)		
Pensioner	245 (60.2)	233 (59.9)	12 (66.7)		
Sick leave	12 (2.9)	12 (3.1)	0 (0.0)		
Student	2 (0.5)	2 (0.5)	0 (0.0)		

[1] Vasopressin and Steroids in addition to Adrenaline in cardiac arrest (VAST-A trial).
[2] Standardized mean difference (SMD).

gested to increase the willingness to accept inclusion without informed consent.[14] Third, patients were asked to be personally involved in our study, as mentioned above this too has been shown to increase willingness to accept inclusion.[7–9] One can also speculate if Swedes have a higher trust in government and medical research compared to other countries. For example, the Swedish Covid-19 strategy was based more on trust than on compulsory measures. We believe that the fact that this study assesses patients' willingness to participate in an ongoing trial makes our results more reliable and more relevant to real life compared to previous studies assessing patients' willingness to participate in a hypothetical trial.

In previous studies there are conflicting results whether gender, education level, and socioeconomic factors affect the attitude toward inclusion in studies.[6,11] In our study there were no significant difference in gender, age, education level, socioeconomic factors, or quality of life. However, due to the imbalance between the groups with only 20 patients in the no group it is difficult to draw any conclusions of a p-value <0.05. This is why we also present the standardized

Table 3 – EQ5D, Quality of life among patients included in the CONSENT trial.

	Overall	Confirmed inclusion in VAST-A[1] trial (Yes group)	Declined inclusion in VAST-A[1] trial (No group)	*P*-value	SMD[2]
n	411	391	20		
Mobility (%)				0.404	0.462
1. No problem to walk	210 (52.6)	203 (53.6)	7 (35.0)		
2. Slight problem to walk	74 (18.5)	68 (17.9)	6 (30.0)		
3. Moderate problem to walk	64 (16.0)	59 (15.6)	5 (25.0)		
4. Severe problem to walk	48 (12.0)	46 (12.1)	2 (10.0)		
5. Unable to walk	3 (0.8)	3 (0.8)	0 (0.0)		
Self-care (%)				0.826	0.373
1. No problem washing and dressing	333 (83.5)	315 (83.1)	18 (90.0)		
2. Slight problem washing and dressing	29 (7.3)	28 (7.4)	1 (5.0)		
3. Moderate problem washing and dressing	21 (5.3)	21 (5.5)	0 (0.0)		
4. Severe problem washing and dressing	15 (3.8)	14 (3.7)	1 (5.0)		
5. Unable to wash and dress myself	1 (0.3)	1 (0.3)	0 (0.0)		
Usual activities (%)				0.772	0.278
1. No problem doing my usual activity	288 (72.2)	275 (72.6)	13 (65.0)		
2. Slight problem doing my usual activity	47 (11.8)	44 (11.6)	3 (15.0)		
3. Moderate problem doing my usual activity	31 (7.8)	30 (7.9)	1 (5.0)		
4. Severe problem doing my usual activity	24 (6.0)	22 (5.8)	2 (10.0)		
5. Unable to do my usual activities	9 (2.3)	8 (2.1)	1 (5.0)		
Pain/discomfort (%)				0.813	0.342
1. No pain or discomfort	132 (33.1)	124 (32.7)	8 (40.0)		
2. Slight pain or discomfort	94 (23.6)	91 (24.0)	3 (15.0)		
3. Moderate pain or discomfort	110 (27.6)	104 (27.4)	6 (30.0)		
4. Severe pain or discomfort	53 (13.3)	50 (13.2)	3 (15.0)		
5. Extreme pain or discomfort	10 (2.5)	10 (2.6)	0 (0.0)		
Anxiety/depression (%)				0.135	0.731
1. No anxious or depression	217 (54.4)	202 (53.3)	15 (75.0)		
2. Slight anxious or depression	116 (29.1)	113 (29.8)	3 (15.0)		
3. Moderate anxious or depression	46 (11.5)	46 (12.1)	0 (0.0)		
4. Severe anxious or depression	18 (4.5)	16 (4.2)	2 (10.0)		
5. Extreme anxious or depression	2 (0.5)	2 (0.5)	0 (0.0)		
Your health today 0–100 (median [IQR])	60 [50, 75]	60 [50, 75]	75 [61.25, 80]	0.934	0.020
EQ5D – INDEX (median [IQR])	0.90 [0.81, 0.96]	0.90 [0.81, 0.96]	0.90 [0.81, 0.95]	0.083	0.420

[1] Vasopressin and Steroids in addition to Adrenaline in cardiac arrest (VAST-A trial).
[2] Standardized mean difference (SMD).

mean differences (SMD). With this in mind, there is a tendency that patients in the no group had lower level of education, less often felt a lack of companionship, more often were an active or former smoker, and less often did pulse raising activity. In the EQ5D there was a tendency of patients in the no group having more problem with mobility but less anxiety. The adjusted analyses reflected the tendency seen that primary level of educational affected the attitude toward inclusion in the VAST-A trial.

The difference between 84.8% who gave informed consent when only asked to participate in the VAST-A trial and 95.1% who gave informed consent to participate in the VAST-A trial of patients also included in the CONSENT trial, needs to be commented. Patients who were positive towards inclusion in the VAST-A trial were probably positive towards being included in the CONSENT trial. Hence there is a probable selection bias of more research positive patients included in the CONSENT trial and this might also be important to consider when interpreting results from community consultation surveys.

Regarding the difference of reason for hospital admission between the yes group and the no group one can speculate if patients with a planned hospital admission were more surprised or shocked by the question to participate in a cardiac arrest trial compared to patients who were admitted due to cardiac cause and therefore were more prone to have a negative attitude towards inclusion in the VAST-A trial.

In Sweden, cardiac arrest occurs in approximately 1 of 600 hospital admissions.[15] Of the 902 patients who gave informed consent to participate in the VAST-A trial during the study period no one suffered from a cardiac arrest during their hospital stay and thus no one were included and randomized in the VAST-A trial. This proves how difficult it is to include enough patients to receive statistical power in a study assessing outcome after cardiac arrest if informed consent in demanded before the cardiac arrest occurs. Conducting a randomized control drug trial with informed consent prior to inclusion and randomization in a rare condition such as cardiac arrest is not just time consuming, costly, but makes it difficult to implement, conduct, and complete the study.

Informed consent prior to inclusion in a study is the mainstay in medical research since 1964 when the declaration of Helsinki was developed by the World Medical Association.[16] There are however

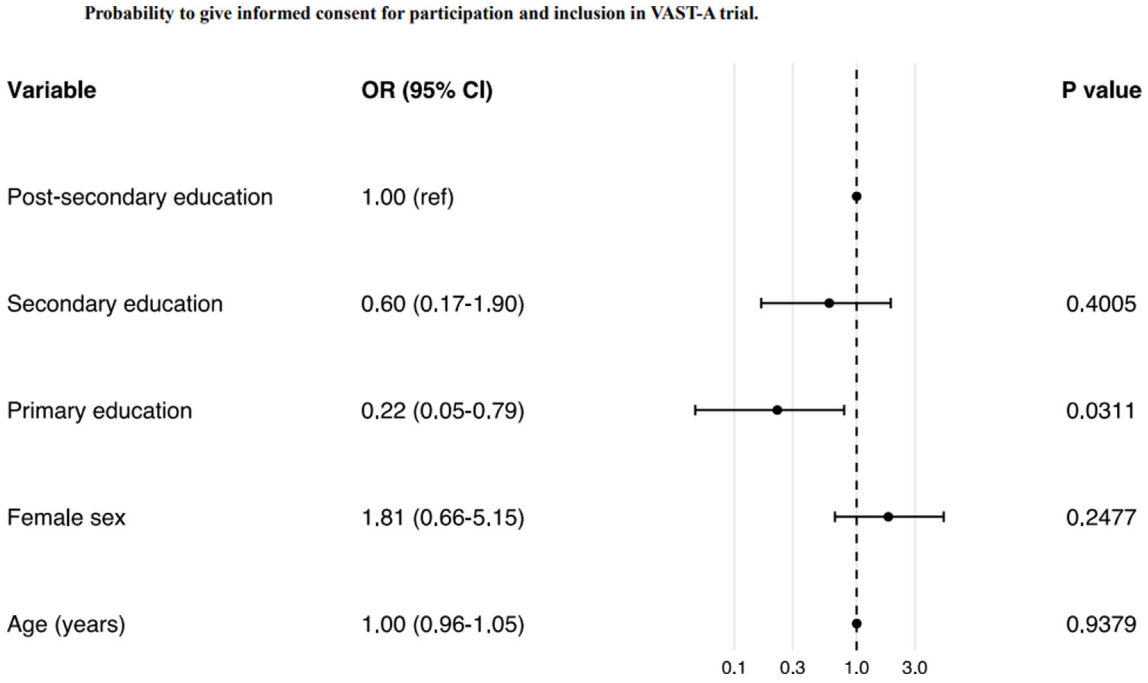

Fig. 3 – Probability to give informed consent for participation and inclusion in VAST-A trail.

situations when informed consent prior to inclusion in studies are difficult to or even impossible to get. Patients with cardiac arrest are by definition unconscious when relevant to be included in a cardiac arrest study. Still, medical care of patients with cardiac arrest must be performed with highest quality evidence and thus research of these patients is important. There are four main options in consent procedure used in research of critically ill patients; prospective informed consent, third-party consent, deferred consent, or waived consent. In cardiac arrest with decision and resuscitation being made within seconds, third party consent is not an option. Prospective informed consent, such as obtained in this trial is difficult in a rare condition such as IHCA. In August 2022 the Swedish Medical Products Agency harmonized the interpretation of the law with the European Medicines Agency (EMA) and approved exceptions of informed consent in special circumstances. In December 2022 the VAST-A trial restarted with deferred consent instead of prospective informed consent.

Limitation

The main limitation is that we do not have data on how many patients who declined inclusion in the CONSENT trial nor how many patients who were only asked of participation in the VAST-A trial and not asked for the additional data collection for the CONSENT trial.

Conclusion

In this prospective observational study we have shown that among hospitalized patients the vast majority gave informed consent to inclusion and participation in an ongoing randomized cardiac arrest drug trial. The main reason for approving inclusion was to contribute to research.

CRediT authorship contribution statement

Malin Albert: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Marie Thonander:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Sune Forsberg:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Frida Lindgren:** Writing – review & editing, Methodology, Data curation. **Meena Thuccani:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Annika Odell:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Kristofer Skoglund:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Niklas Bergh:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Jacob Hollenberg:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Mattias Ringh:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Martin Jonsson:** Writing – review & editing, Methodology, Data curation. **Per Nordberg:** Writing – review & editing, Methodology, Data curation. **Peter Lundgren:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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REFERENCES

1. Services. DoHaH. Protection of human subjects: informed consent and waiver of informed consent requirements in certain emergency research Federal Register: October 2, 1996 (volume 61, number 192).
2. The European Parliament and the Council of the European Union. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. Off J Eur Union. 2014;27.5.2014.
3. Furyk J, Franklin R, Watt K, et al. Community attitudes to emergency research without prospective informed consent: A survey of the general population. Emerg Med Australas 2018;30:547–55.
4. Abboud PA, Heard K, Al-Marshad AA, Lowenstein SR. What determines whether patients are willing to participate in resuscitation studies requiring exception from informed consent? J Med Ethics 2006;32:468–72.
5. Goldstein JN, Espinola JA, Fisher J, Pallin DJ, Camargo CA. Public opinion of a stroke clinical trial using exception from informed consent. Int J Emerg Med 2010;3:385–9.
6. Feldman WB, Hey SP, Franklin JM, Kesselheim AS. Public approval of exception from informed consent in emergency clinical trials: A systematic review of community consultation surveys. JAMA Netw Open 2019;2:e197591.
7. McClure KB, DeIorio NM, Gunnels MD, Ochsner MJ, Biros MH, Schmidt TA. Attitudes of emergency department patients and visitors regarding emergency exception from informed consent in resuscitation research, community consultation, and public notification. Acad Emerg Med 2003;10:352–9.
8. Triner W, Jacoby L, Shelton W, et al. Exception from informed consent enrollment in emergency medical research: attitudes and awareness. Acad Emerg Med 2007;14:187–91.
9. Booth MG, Lind A, Read E, Kinsella J. Public perception of emergency research: a questionnaire. Eur J Anaesthesiol 2005;22:933–7.
10. Lecouturier J, Rodgers H, Ford GA, et al. Clinical research without consent in adults in the emergency setting: a review of patient and public views. BMC Med Ethics 2008;9:9.
11. Fehr AE, Pentz RD, Dickert NW. Learning from experience: a systematic review of community consultation acceptance data. Ann Emerg Med 2015;65:162–71 e3.
12. Scotton WJ, Kolias AG, Ban VS, et al. Community consultation in emergency neurosurgical research: lessons from a proposed trial for patients with chronic subdural haematomas. Br J Neurosurg 2013;27:590–4.
13. Smithline HA, Gerstle ML. Waiver of informed consent: a survey of emergency medicine patients. Am J Emerg Med 1998;16:90–1.
14. Richardson LD, Wilets I, Ragin DF, et al. Research without consent: community perspectives from the Community VOICES Study. Acad Emerg Med 2005;12:1082–90.
15. Hessulf F, Karlsson T, Lundgren P, et al. Factors of importance to 30-day survival after in-hospital cardiac arrest in Sweden - A population-based register study of more than 18,000 cases. Int J Cardiol 2018;255:237–42.
16. WMA declaration of Helsinki – ethical principles for medical research involving human subjects. World Medical Association; 2022.