Available online at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Vasopressin and steroids in addition to adrenaline in cardiac arrest (VAST-A) – A randomised pilot study

Malin Albert[a,1,*], *Sune Forsberg*[a,b,1], *Mattias Ringh*[a], *Frida Lindgren*[b], *Marie Thonander*[c,d], *Meena Thuccani*[c,d], *Araz Rawshani*[c], *Therese Djärv*[e], *Jacob Hollenberg*[a], *Leif Svensson*[a], *Johan Herlitz*[f], *Martin Jonsson*[a], *Per Nordberg*[a,g,h], *Peter Lundgren*[c,d,f]

Abstract

Background: The potential benefit of combining adrenaline, vasopressin, and corticosteroids in in-hospital cardiac arrest (IHCA) needs to be confirmed in a large clinical trial. This pilot study assesses feasibility and safety of randomising patients to this combination therapy compared to standard care.

Material and methods: A randomised, double-blind, placebo-controlled pilot study was conducted from December 2022 to June 2024 across three Swedish hospitals (NCT05139849). Witnessed IHCAs meeting criteria for adrenaline were randomised 1:1 to adrenaline, vasopressin, and corticosteroids (intervention) or adrenaline and placebo (control). Primary outcomes included feasibility (e.g., protocol adherence, event times, enrolment rate), and safety. Secondary outcome was return of spontaneous circulation.

Results: Of 183 screened IHCAs, 39 patients (median age 77, 64% male) were randomised (16 intervention, 23 control), with an enrolment rate of 0.8 patients/hospital bed/month. Most cardiac arrests occurred in general wards (n = 17/39, 44%). In the feasibility analysis, four patients at the scene of the arrest and three patients in the intensive care unit experienced protocol deviations. Median time (minutes) from cardiac arrest to rapid response team arrival was similar between groups. Median time to adrenaline administration was 7:00 (IQR 3:00–10:00) (intervention) vs 5:00 (IQR 2:30–8:30) (control) and to vasopressin/placebo 10:30 (IQR 9:30–12:15) vs 9:00 (IQR 5:00–11:00). Return of spontaneous circulation occurred in 38% (6/16) in the intervention group and 17% (4/23) in controls.

Conclusion: In this IHCA pilot study, randomisation to adrenaline, vasopressin, and corticosteroids compared to controls was safe, but feasibility needs improvement for adequate enrolment in the VAST-A main study.

Keywords: RCT, Vasopressin, Corticosteroids, IHCA, Randomized clinical trial, Cardiac arrest

Introduction

The European Resuscitation Council (ERC) guidelines recommend adrenaline and amiodarone as part of advanced cardiac life support, although studies have not demonstrated clear benefits for survival with good neurological outcomes.[1] Furthermore, these recommendations are primarily based on studies of out-of-hospital cardiac arrest (OHCA). Time from cardiac arrest to advanced cardiopulmonary resuscitation (CPR) is typically shorter in in-hospital cardiac arrest (IHCA) than in OHCA. Previous studies have emphasised that early drug administration during CPR is crucial, suggesting that the effectiveness of drug treatment may be enhanced in IHCA.[2]

Three studies have suggested a potential role for combining vasopressin and corticosteroids with adrenaline in CPR. Two studies by Mentzelopoulos et al. demonstrated improved return of

* Corresponding author.
E-mail address: malin.albert@ki.se (M. Albert).
[1] These authors contributed equally to this work.
https://doi.org/10.1016/j.resuscitation.2025.110593
Received 30 January 2025; Received in Revised form 18 March 2025; Accepted 19 March 2025

spontaneous circulation (ROSC), 30-day survival, and survival with good neurological outcome, although this was not a pre-specified outcome measure.[3,4] In 2021, Andersen et al. confirmed improved ROSC with this drug combination but did not observe significant improvements in 30-day survival or neurological outcome.[5] However, Andersen's study was not powered to detect differences in 30-day survival and the results should be interpreted with this limitation in mind. A subsequent *meta*-analysis of these three trials demonstrated improved ROSC, and after the correction of one misclassified patient the outcome for improved neurological outcome reached statistical significance.[6,7] Moreover, the corrigendum to this *meta*-analysis indicated that the effectiveness of vasopressin and steroids may be influenced by the timing of drug administration, suggesting that their benefits could be time-dependent.[7,8]

Vasopressin, a non-adrenergic peripheral vasoconstrictor, has a longer duration of action than adrenaline and may enhance coronary and cerebral perfusion pressure during CPR. Post-cardiac arrest shock activates a systemic inflammatory response, which corticosteroids can mitigate by reducing inflammatory response and reduce reperfusion injuries.[9–14] Additionally, corticosteroids potentiate drug-induced vasoconstriction, further enhancing their efficacy.[15–17]

Despite the results of the three studies, the ERC guidelines emphasise the need for further replication and validation of results before recommendations can be revised.[1] The primary objective of the VAST-A main study is to determine whether vasopressin and corticosteroids, in addition to adrenaline, improves 30-day survival in IHCA patients. Recognising the anticipated challenges associated with randomisation, study drug preparation, and administration within minutes of cardiac arrest, this pilot study was conducted to evaluate feasibility and safety of these processes. Moreover, the pilot phase provided a crucial opportunity to evaluate and refine the study protocol in preparation for the VAST-A main study.

Thus, the specific aims of this pilot study were to evaluate the feasibility and safety of randomising and administering a combination of adrenaline, vasopressin, and corticosteroids during CPR compared to standard care with adrenaline alone, focusing on protocol adherence and adverse events.

Methods

Study design and ethics

This was an investigator-initiated, multicentre, randomised, double-blind, placebo-controlled study enrolling adult patients with IHCA. Due to the emergency nature of the intervention, randomisation was performed without prior informed consent. Written consent was obtained from patients who regained consciousness, while presumed consent was applied for those who did not. Ethical approval was obtained from the Swedish Ethical Review Authority (registration number: 2019/04238) and the Swedish Medical Products Agency (initial number: 5.1-2019-59308, EU-number 2022-500137-89-00). The study was registered at ClinicalTrials.gov (NCT05139849). The study protocol can be accessed via the website vast-a.org.

Settings

The pilot study was conducted in three Swedish hospitals. Norrtälje Hospital is a secondary care facility with 96 hospital beds. Södersjukhuset is a tertiary care centre with 600 hospital beds, and Sahlgrenska University Hospital is a tertiary care centre with approximately 700 hospital beds. Patients with cardiac arrest occurring in any ward (including emergency department, intensive care unit (ICU), and operating rooms) at Södersjukhuset and Norrtälje Hospital, except paediatric and maternity/gynaecology wards, were eligible for inclusion in the study. At Sahlgrenska University Hospital, for logistical reasons, patients with cardiac arrest were eligible for inclusion only if it occurred in cardiology wards, medical wards, or the emergency department. The pilot study was planned to run for one year, beginning in December 2022 at Norrtälje Hospital, followed by Södersjukhuset in February 2023, and Sahlgrenska University Hospital in June 2023. The pilot concluded in June 2024.

Patients

Inclusion criteria were: 1) men $\geq$ 18 years and women $\geq$ 50 years (to avoid patients with childbearing potential), 2) witnessed cardiac arrest, 3) no prior "do not attempt CPR" (DNACPR) order, and 4) meeting criteria for adrenaline administration according to ERC guidelines.[1] Patients needed to be included in the study before the first dose of adrenaline was administered. Due to the emergency nature of the intervention patients were screened for post-randomisation exclusion criteria including: 1) ongoing intravenous corticosteroid treatment, 2) a later discovered pre-existing DNACPR order, and 3) unwitnessed cardiac arrest.

Randomisation and study intervention

Randomisation was performed in blocks of 2, 4, 6, or 8 patients by an investigator not involved in recruitment, using SAS statistical analysis software (Cary, NC, USA) version 9.4. The sequences were transferred to hospital pharmacies, where site-specific, blinded treatment packs were prepared, stored in a dedicated ICU fridge, and delivered to the cardiac arrest by a non-clinical rapid response team member.

A physician (anaesthesiologist or cardiologist) led the rapid response team, screened patients, and determined study enrolment. Patients were assigned to the intervention or control by opening the pre-randomised treatment pack, which contained either five doses of vasopressin (20 IU) and one dose of methylprednisolone (40 mg) or corresponding doses of placebo (sodium chloride 9 mg/mL). Study drugs were identical in appearance to placebo, and treating personnel were blinded to allocation.

Vasopressin and methylprednisolone or placebo were administered as soon as possible after the first adrenaline dose. Subsequent doses of vasopressin or placebo were given after each adrenaline dose, up to a maximum of five doses. Patients admitted to the ICU continued their assigned treatment. Those with post-cardiac arrest circulatory shock four hours after the cardiac arrest received 300 mg hydrocortisone in 100 mL of sodium chloride 9 mg/mL or placebo once daily until vasopressors were no longer required or for a maximum of seven days. Hydrocortisone was tapered as shown in Fig. 1.

Data collection

Screened IHCA patients were recorded on-site in a screening log with details including screening ID number, date, time, inclusion criteria, initial rhythm, and randomisation status. For randomised patients, a mini-Case Report Form (CRF) was completed on-site by the rapid response team, documenting the timing of drug administration as well as ROSC status and time. Paper records were later digitised into the REDCap database by the research team. Additional eCRFs were completed by research nurses using data extracted from medical records.

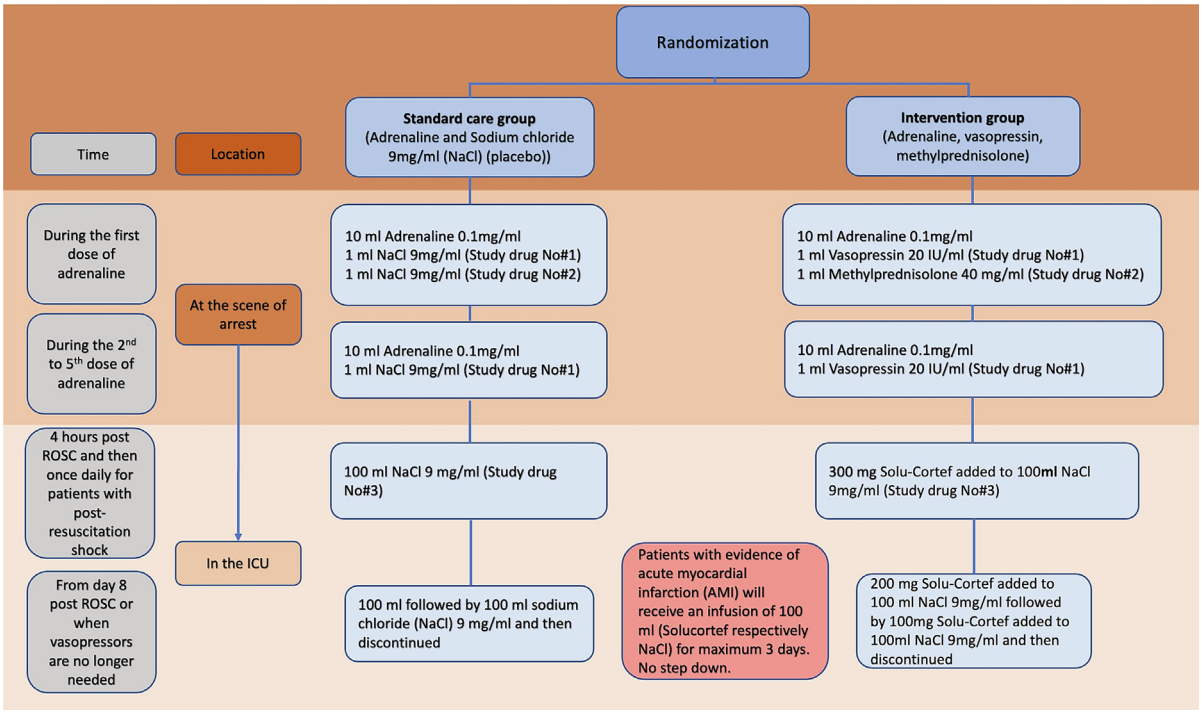

Fig. 1 – Study drug administration in the VAST-A pilot study (Vasopressin and steroids in addition to adrenaline).

Some patients were not screened at the time of the cardiac arrest due to the absence of the additional team member responsible for delivering the treatment pack. To address this, patients with IHCA during their hospital stay were retrospectively screened (Fig. 2).

Outcomes

The primary outcomes of the pilot study were feasibility and safety. Feasibility was defined as adherence to study protocol for study drug administration. To be considered compliant, all drug doses had to be administered as described in the protocol. Other feasibility measures included the rate of inclusion, time from recognition of the cardiac arrest to rapid response team arrival, and time to adrenaline and study drug administration.

The safety outcome was assessed by whether adrenaline was administered before the study drug. Other safety aspects included predefined adverse events. These were categorised as general adverse events/reactions, serious adverse events/reactions, suspected unexpected serious adverse events/reactions, or the need for treatment of specific adverse events. The definitions and management of adverse events are described in detail in the supplementary material.

The secondary outcome was sustained ROSC (for at least 20 min).

Statistical analysis

Data were analysed according to intention-to-treat. Patients achieving ROSC after adrenaline but before receiving study drug were included, as were those meeting post-randomisation exclusion criteria.

Baseline characteristics were reported using either median or mean with appropriate measures of dispersion. Dichotomous variables were reported as counts and percentages with comparisons made using chi-square tests or Fisher's exact test for small cell sizes. Continuous variables were compared using t-tests. Analyses were made using R version 4.1.3.

Results

Patient characteristics

In total, 183 IHCA patients were screened at the scene of the arrest or retrospectively during the 18-month study period. Among them, 39 patients (21%) were randomised to receive either adrenaline, vasopressin, and methylprednisolone (intervention) or adrenaline and sodium chloride (9 mg/mL) (standard care). Of the excluded patients, 97 did not meet the inclusion criteria, 47 were excluded due to other reasons, of whom 42 patients were retrospectively screened and identified as eligible (Fig. 2).

As seen in Table 1, the median age was 77 years (IQR 68–79), and 25/39 (64%) of the patients were male. The IHCA occurred in general wards in 17/39 (44%), in cardiac wards in 11/39 (28%), and in the ICU/coronary care unit in 7/39 (18%). A majority (90%, 36/39) of the cardiac arrests presented with an initial non-shockable rhythm. Fewer males were found in the intervention group compared to the standard care group (38%, 6/16, vs 83%, 19/23). No other baseline characteristics showed significant differences between the groups (Tables 1 and 2).

Primary outcomes – Feasibility and safety

In the feasibility analysis, 4 out of 39 (10%) patients experienced protocol deviations at the scene of the cardiac arrest. Three patients received multiple doses of adrenaline without corresponding doses of vasopressin or the corresponding placebo and one patient

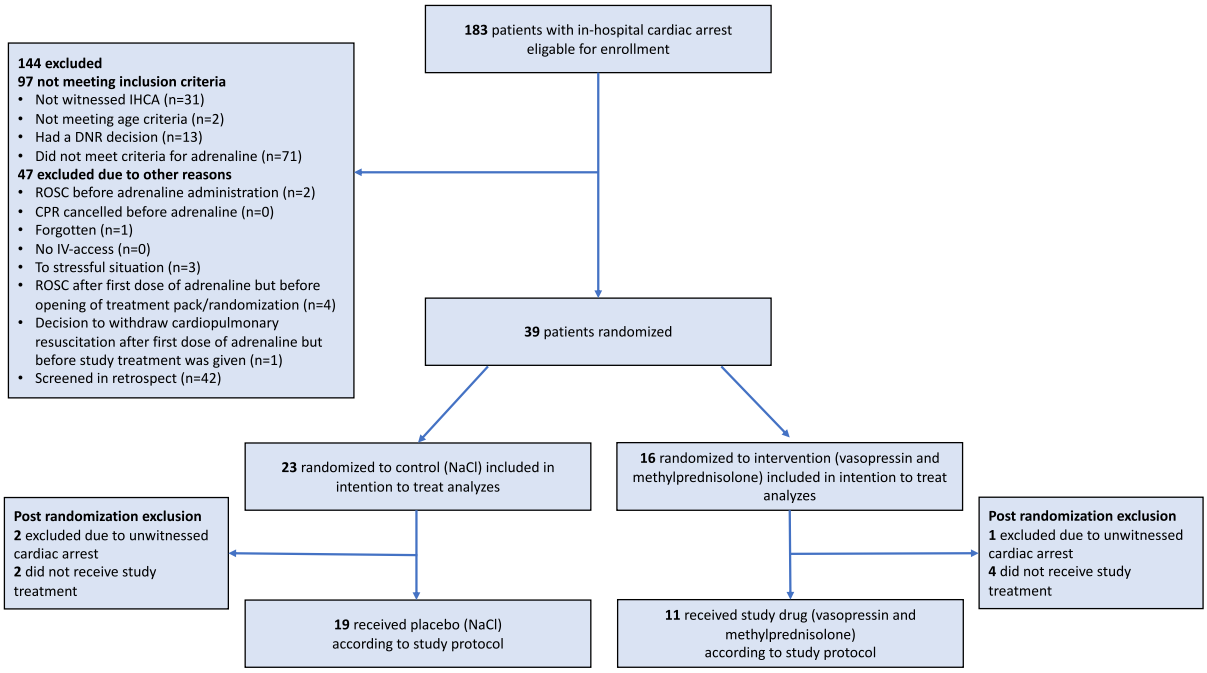

Fig. 2 – Screening and randomisation of patients in the VAST-A pilot study (Vasopressin and steroids in addition to adrenaline).

received more doses of the study drug (vasopressin or corresponding placebo) than adrenaline (Table 3). For three of the patients, the reason for protocol deviation was unclear. For one patient, the reason for protocol deviation was explained by an overly stressful situation due to cardiac tamponade in a young adult. Among the nine patients admitted alive to the ICU, three patients (33%) did not receive the post-circulatory shock study treatment according to protocol. The study treatment in the ICU was forgotten for two patients, and one patient received a reduced dose of hydrocortisone or the corresponding placebo despite circulatory shock lasting less than four hours.

The inclusion rate was 0.8 patients per hospital bed/month (39 randomised out of 183 screened patients). The number of included patients per hospital is described in supplementary material.

The median time from cardiac arrest to adrenaline administration was 7:00 min (IQR 3:00–10:00) in the intervention group and 5:00 min (IQR 2:30–8:30) in the standard care group (Table 2). The median time from arrest to study drug administration was 10:30 min (IQR 9:30–12:15) in the intervention group and 9:00 min (IQR 5:00–11:00) in the standard care group.

In the safety analysis, no patients received the study drug before adrenaline administration.

Predefined treatment-specific serious adverse events were reported for three patients. One patient in the intervention group experienced a bleeding event requiring transfusion and an infection requiring antibiotic treatment. Additionally, two patients (one patient in the intervention group and one patient in standard care group) developed infection requiring antibiotic treatment. No other serious adverse events were reported.

Secondary outcome – ROSC

The median time from cardiac arrest to ROSC was 11:00 min (IQR 6–15:15) in the intervention group and 8:30 min (IQR 4:30–15:15) in the standard care group. In the intervention group 6/16 (38%) achieved ROSC compared to 4/23 (17%) in the standard care group ($p = 0.30$) (Table 4).

Discussion

The purpose of this pilot study was to evaluate the feasibility and safety of conducting the VAST-A main study within a nationwide Swedish healthcare setting. The goal of the VAST-A main study is to determine if the addition of vasopressin and corticosteroids to adrenaline is associated with improved survival among patients with IHCA. The primary finding in this pilot study suggests that the administration of the study drugs was safe, with the correct sequence of adrenaline and study drug administration, and no major adverse events reported. However, the feasibility analysis revealed a high proportion of protocol deviations in the ICU and a tendency for delays in adrenaline and study drug administration in the intervention group compared to the standard care group. Additionally, enrolment was lower than expected. Ensuring adequate enrolment, feasibility, and drug administration without delay in the VAST-A main study will require adjustments to the study protocol regarding randomisation and study drug preparation and administration. Suggestions include an open label design, placing the study drug in the rapid response team kit alongside adrenaline, and the possible use of pre-prepared syringes. These adjustments should aim to enable faster

Table 1 – Basic characteristics.

	Placebo (n = 23)	Intervention (n = 16)
Randomised patient	23	16
Hospital (%)		
Norrtälje Hospital	8 (34.8)	5 (31.2)
Södersjukhuset	12 (52.2)	10 (62.5)
Sahlgrenska University Hospital	3 (13.0)	1 (6.2)
Initial rhythm (%)		
Asystole	8 (34.8)	6 (37.5)
PEA	11 (47.8)	10 (62.5)
VT/VF	4 (17.4)	0 (0.0)
Sex (%)		
Men	19 (82.6)	6 (37.5)
Women	4 (17.4)	10 (62.5)
Age median, [IQR]	77.00 [70.5, 80.5]	75.50 [67.5, 79]
Past medical history (%)		
Ischemic heart disease	9 (39.1)	5 (31.2)
Hypertension	14 (60.9)	10 (62.5)
Congestive heart failure	11 (47.8)	4 (25.0)
Atrial fibrillation or flutter	9 (39.1)	4 (25.0)
Other cardiac arrhythmia	3 (13.0)	1 (6.2)
Diabetes mellitus type 1	0 (0)	0 (0)
Diabetes mellitus type 2	8 (34.8)	7 (43.8)
Cerebrovascular disease or TIA	1 (4.3)	2 (12.5)
Chronic renal failure	3 (13.0)	3 (18.8)
Chronic hepatic failure	0 (0)	0 (0)
Cancer	4 (17.4)	5 (31.2)
COPD/Asthma	4 (17.4)	3 (18.8)
Reason for hospital admission (%)		
Dyspnoea/respiratory	8 (34.8)	4 (25.0)
Trauma	1 (4.3)	1 (6.2)
Neurological	2 (8.7)	1 (6.2)
Cardiological	8 (34.8)	5 (31.2)
Infection	2 (8.7)	2 (12.5)
Surgical (ortho, general surgery, gynaecology)	4 (17.4)	1 (6.2)
Planned intervention	0 (0)	0 (0)
Other	1 (4.3)	1 (6.2)
mRS pre cardiac arrest (%)		
mRS 0–3	14 (60.9)	11(73.3)
mRS 4–5	9 (39.1)	4 (26.7)

drug administration and improve the inclusion process, ensuring enough patients are enrolled to meet the statistical power required to address the primary research question, whether vasopressin and corticosteroids, in addition to adrenaline, improve 30-day survival in patients with IHCA.

At the scene of the arrest, the protocol deviations were primarily due to discrepancies between the number of adrenaline doses and the corresponding doses of the study drug (vasopressin or its corresponding placebo). This proportion was comparable to the 7.4% of patients with protocol deviations reported by Andersen et al.[5] However, adherence to post-circulatory shock study treatment in the ICU was also lower. Miscommunication regarding study inclusion at the scene of the arrest probably contributed to two of the three patients with protocol deviations in the ICU, as they achieved ROSC after adrenaline but before receiving vasopressin and methylprednisolone or the corresponding placebo. To address these challenges, adjustments to the study protocol are planned to improve clarity and minimise deviations in the ICU.

The inclusion rate and randomisation of patients were lower compared to the study by Andersen et al. but, the proportion of randomised patients relative to those eligible in our study closely aligns with their findings. When examining the number of screened patients per hospital bed per month, we screened and randomised more patients compared to Andersen et al. To achieve the statistical power needed to evaluate 30-day survival in the VAST-A main study it is crucial to recruit additional hospitals and streamline the randomisation process.

Several studies highlight the critical role of early drug administration during CPR, with shorter times improving effectiveness.[5,7,8,18] In our study, the time from cardiac arrest to adrenaline and study drug administration was comparable to Andersen et al. but longer than in the study by Mentzelopoulos et al.[3–5] A key difference is that Mentzelopoulos et al. used preprepared syringes and dedicated study personnel, whereas in our study and in the study by Andersen et al., the rapid response team prepared and administered the drugs at the scene of the arrest. This pragmatic approach better reflects real-life clinical scenarios and explains the 3–4-minute delay between the administration of adrenaline and vasopressin (or corresponding placebo) observed in both our study and that of Andersen et al. In our study, this delay was longer in the intervention group and

Table 2 – At the scene of the arrest.

	Placebo (*n* = 23)	Intervention (*n* = 16)
Place of cardiac arrest (%)		
ICU	5 (21.7)	2 (12.5)
Cardiac ward	7 (30.4)	4 (25.0)
General ward	8 (34.8)	9 (56.2)
Emergency department	2 (8.7)	1 (6.2)
Other	1 (4.3)	0 (0.0)
At the scene of the arrest		
Monitored	13 (59.1)	4 (25.0)
Defibrillated	5 (21.7)	3 (18.8)
Intubated	13 (56.5)	9 (56.2)
Time (min:sec) median (IQR)		
Cardiac arrest – CPR	0:00 [0:00–0:30]	0:00 [0:00–0:00]
Cardiac arrest – rapid response team	3:00 [2:00–4:00]	2:00 [0:45–7:15]
Cardiac arrest – adrenalin	5:00 [2:30–8:30]	7:00 [3:00–10:00]
Cardiac arrest – vasopressin/placebo	9:00 [5:00–11:00]	10.30 [9:30–12:15]
Rapid response team – adrenalin	2:00 [0:00–0:25]	3:00 [1:30–6:00]
Rapid response team – vasopressin/placebo	4:00 [2:00–7:15]	5:30 [3:00–9:30]
Cardiac arrest – ROSC	8:30 [4:30–15:15]	11:00 [6:00–15:15]

Table 3 – Protocol deviations.

	Placebo (*n* = 23)	Intervention (*n* = 16)
Fulfilled exclusion criteria		
Randomised but not eligible, Not witnessed	2	1
At the scene of the arrest		
More adrenaline than study drug	2	1
More study drug than adrenaline	1	
In the ICU	**Placebo (*n* = 4)**	**Intervention (*n* = 5)**
Received reduced dose of hydrocortisone or corresponding placebo but did not have vasopressor need for > 4 h.		1
Did not receive hydrocortisone or corresponding placebo in the ICU	1	1

Table 4 – Sustained ROSC.

	Placebo (*n* = 23)	Intervention (*n* = 16)	P-value
Outcome			
Sustained ROSC	4 (17.4)	6 (37.5)	0.30
Alive at ICU admission	4 (17.4)	5 (31.2)	0.53

may have contributed to the longer time from cardiac arrest to ROSC in the intervention group compared to the control group in our study.

This delay may also partly explain the differences in the proportion of ROSC between the three trials. In our study, 38% of the patients in the intervention group achieved ROSC, comparable to 42% in Andersen's study, while the standard care group achieved ROSC in 17% of cases compared to 33% in Andersen's study.[5] However, Mentzelopoulos et al. reported a substantially higher proportion of ROSC, with 81% and 83% in the intervention group compared to 52% and 65% in the standard care group in the 2009 and 2013 studies, respectively.[3,4] This difference is likely due to their shorter time from cardiac arrest to drug administration as well as a higher proportion of patients with an initial shockable rhythm. Given the small sample size in our pilot study, statistical conclusions should be interpreted cautiously. However, these findings underscore the importance of minimising delays in drug administration in the VAST-A main study. To achieve this, improvements in the randomisation process and study drug preparation and administration are needed to minimise delays and maximise the potential benefits of the intervention in the VAST-A main study.

Limitations

This study has several limitations. First, the low inclusion rate may indicate selection bias, as fewer than 50% of eligible patients were enrolled. While this does not affect internal validity, it may limit the generalisability of the results in the VAST-A main study. We are considering an open-label approach in the main study to improve the inclusion rate. Second, the number of protocol deviations in the ICU needs to be addressed, and adjustments to the study protocol will be considered to minimise the likelihood of deviation in the ICU. Third, given the low numbers of included patients, any statistical conclusions regarding outcomes – e.g., time from cardiac arrest to adrenaline and study drug administration, time to ROSC, as well as the proportion of ROSC – should be interpreted with caution. Due to the small sample size, any observed imbalance between the groups is expected and is most likely due to random variation. Fourth, although no serious adverse events were recorded, the low number of randomised patients prevents us from drawing any definitive conclusions regarding the safety of the treatment. However, the pilot study provided an opportunity to assess and refine the study protocol regarding the randomisation process and drug administration, thereby identifying areas for potential improvement and optimisation. This aligns with the primary goal of the pilot, which was to evaluate feasibility and enhance these processes in preparation for the VAST-A main study.

Conclusion

In this IHCA pilot study, randomisation to a strategy of combining adrenaline, vasopressin, and corticosteroids compared to standard care was safe. The protocol requires minor adjustments to ensure adequate enrolment in the VAST-A main study. The inclusion rate was lower than anticipated, highlighting the need to streamline the randomisation process and study drug administration to ensure sufficient enrolment in the VAST-A main study, which is planned to expand nationwide in 2025.

Conflicts of interest

TD is member of the editorial board of Resuscitation Plus. No other conflicts of interest to declare.

CRediT authorship contribution statement

Malin Albert: Writing – review & editing, Writing – original draft, Validation, Software, Investigation, Formal analysis, Data curation. **Sune Forsberg:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Mattias Ringh:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Frida Lindgren:** Writing – review & editing, Validation, Data curation. **Marie Thonander:** Writing – review & editing, Validation, Data curation. **Meena Thuccani:** Writing – review & editing, Validation, Data curation. **Araz Rawshani:** Writing – review & editing, Methodology. **Therese Djärv:** Writing – review & editing, Methodology. **Jacob Hollenberg:** Writing – review & editing, Methodology, Conceptualization. **Leif Svensson:** Writing – review & editing, Methodology, Conceptualization. **Johan Herlitz:** Writing – review & editing, Methodology, Conceptualization. **Martin Jonsson:** Writing – review & editing, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Per Nordberg:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Peter Lundgren:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Funding

The study was funded by independent research grants from Swedish resuscitation council and the Swedish Heart and Lung foundation as well as from the Swedish state under the agreement between the Swedish government and the county councils, the ALF agreement (ALFGBG-933899).

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.

Author details

[a]Department of Clinical Science and Education, Södersjukhuset, Centre for Resuscitation Science, Karolinska Institutet, Sjukhusbacken 10, 11883 Stockholm, Sweden[b]Norrtälje Hospital, Lasarettsgatan, 76145 Norrtälje, Sweden [c]Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg 41345 Gothenburg, Sweden [d]Region Västra Götaland, Sahlgrenska University Hospital, Department of Cardiology, 41345 Gothenburg, Sweden [e]Department of Medicine, Karolinska Institutet, 17176 Stockholm, Sweden [f]Centre for Prehospital Research, University of Borås SE- 501 90 Borås, Sweden [g]Function Perioperative Medicine and Intensive Care, Karolinska University Hospital, 17176 Stockholm, Sweden [h]Department of Physiology and Pharmacology, Karolinska Institutet, 171 76 Stockholm, Sweden

REFERENCES

1. Soar J, Bottiger BW, Carli P, et al. European resuscitation council guidelines 2021: adult advanced life support. Resuscitation 2021;161:115–51.
2. Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-hospital cardiac arrest: a review. JAMA 2019;321(12):1200–10.
3. Mentzelopoulos SD, Zakynthinos SG, Tzoufi M, et al. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. Arch Intern Med 2009;169(1):15–24.

4. Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. JAMA 2013;310 (3):270–9.
5. Andersen LW, Isbye D, Kjaergaard J, et al. Effect of vasopressin and methylprednisolone vs placebo on return of spontaneous circulation in patients with in-hospital cardiac arrest: a randomized clinical trial. JAMA 2021.
6. Holmberg MJ, Granfeldt A, Mentzelopoulos SD, Andersen LW. Vasopressin and glucocorticoids for in-hospital cardiac arrest: a systematic review and meta-analysis of individual participant data. Resuscitation 2022;171:48–56.
7. Mentzelopoulos SD, Chalkias A. A critical reappraisal of vasopressin and steroids in in-hospital cardiac arrest. Crit Care 2024;28(1):191.
8. Holmberg MJ, Granfeldt A, Mentzelopoulos SD, Andersen LW. Corrigendum to "Vasopressin and glucocorticoids for in-hospital cardiac arrest: a systematic review and meta-analysis of individual participant data" [Resuscitation 171 (2022) 48-56]. Resuscitation 2023;190:109929.
9. Chalkias A, Xanthos T. Post-cardiac arrest syndrome: mechanisms and evaluation of adrenal insufficiency. World J Crit Care Med 2012;1 (1):4–9.
10. Adrie C, Adib-Conquy M, Laurent I, et al. Successful cardiopulmonary resuscitation after cardiac arrest as a "sepsis-like" syndrome. Circulation 2002;106(5):562–8.
11. Kim JJ, Lim YS, Shin JH, et al. Relative adrenal insufficiency after cardiac arrest: impact on postresuscitation disease outcome. Am J Emerg Med 2006;24(6):684–8.
12. Miller JB, Donnino MW, Rogan M, Goyal N. Relative adrenal insufficiency in post-cardiac arrest shock is under-recognized. Resuscitation 2008;76(2):221–5.
13. Varvarousi G, Stefaniotou A, Varvaroussis D, Xanthos T. Glucocorticoids as an emerging pharmacologic agent for cardiopulmonary resuscitation. Cardiovasc Drugs Ther 2014;28 (5):477–88.
14. Liu B, Zhang Q, Li C. Steroid use after cardiac arrest is associated with favourable outcomes: a systematic review and meta-analysis. J Int Med Res 2020;48(5)300060520921670.
15. Yang S, Zhang L. Glucocorticoids and vascular reactivity. Curr Vasc Pharmacol 2004;2(1):1–12.
16. Annane D, Bellissant E, Sebille V, et al. Impaired pressor sensitivity to noradrenaline in septic shock patients with and without impaired adrenal function reserve. Br J Clin Pharmacol 1998;46(6):589–97.
17. Fang F, Zhang Y, Tang J, et al. Association of corticosteroid treatment with outcomes in adult patients with sepsis: a systematic review and meta-analysis. JAMA Intern Med 2019;179(2):213–23.
18. Ran L, Liu J, Tanaka H, Hubble MW, Hiroshi T, Huang W. Early administration of adrenaline for out-of-hospital cardiac arrest: a systematic review and meta-analysis. J Am Heart Assoc 2020;9(11) e014330.