The Dual Defib Trial
A randomised trial on early double external sequential defibrillation in out-of-hospital cardiac arrest

Sponsor
Clinic of Emergency Medicine and Prehospital services, St. Olavs University Hospital

Funder
Norwegian Air Ambulance Foundation

Chief investigator
Dr Jostein Rødseth Brede, MD, PhD

Other investigators

Dr Vegard Nordviste, MD
Prof Andreas Jørstad Krüger, MD, PhD
Prof Marius Rehn, MD, PhD

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1. Contact details

Sponsor

Name	Clinic of Emergency Medicine and Prehospital services, St. Olavs University Hospital
Contact person	Kjetil Karlsen, Head of Clinic
Address	Postboks 3250 Torgarden, 7006 Trondheim, Norway

Chief Investigator

Name	Jostein Rødseth Brede
Professional position	MD, PhD, Consultant Anaesthesiologist
Address	Luftambulansen Trondheim, Vestre Rosten 114, 7075 Trondheim, Norway.
E-mail address	Jostein.brede@norskluftambulanse.no
Phone number	+47 994 45 914

PhD candidate

Name	Vegard Nordviste
Professional position	MD
Address	Luftambulansen Trondheim, Vestre Rosten 114, 7075 Trondheim, Norway.
E-mail address	Vegard.nordviste@norskluftambulanse.no
Phone number	+47 90777686

Main funder

Name	Norwegian Air Ambulance Foundation
Contact person	Tom Hanssen, Director of Research and Development
E-mail address	tom.hanssen@norskluftambulanse.no

2. Project management

Jostein Rødseth Brede, MD, PhD

[1] Department of Emergency Medicine and Pre-hospital Services, St. Olavs University Hospital, Trondheim, Norway
[2] Department of Anaesthesiology and Intensive care, St. Olavs University Hospital, Trondheim, Norway
[3] Department of Research, Norwegian Air Ambulance Foundation, Oslo, Norway

Vegard Nordviste, MD

[3] Department of Research, Norwegian Air Ambulance Foundation, Oslo, Norway

Andreas Jørstad Krüger, MD, PhD

[1] Department of Emergency Medicine and Pre-hospital Services, St. Olavs University Hospital, Trondheim, Norway
[3] Department of Research, Norwegian Air Ambulance Foundation, Oslo, Norway
[4] Department of Circulation and Medical Imaging, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Trondheim, Norway

Marius Rehn, MD, PhD

[3] Department of Research, Norwegian Air Ambulance Foundation, Oslo, Norway
[5] Air Ambulance Department, Division of Prehospital Services, Oslo University Hospital, Oslo, Norway
[6] Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Jostein Dale, MD

[1] Department of Emergency Medicine and Pre-hospital Services, St. Olavs University Hospital, Trondheim, Norway

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4. Abbreviations

ACLS	Advanced Cardiovascular Life Support
CPR	Cardiopulmonary resuscitation
CRF	Case Report Form
DSED	Double Sequential External Defibrillation
mRS	Modified Rankin Scale
OHCA	Out of Hospital Cardiac Arrest
REC	Regional Ethics Committee
ROSC	Return of Spontaneous Circulation
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
VF	Ventricular fibrillation
VT	Ventricular tachycardia

5. Background

Out-of-hospital cardiac arrest (OHCA) carries a high mortality rate, and the most frequent aetiology is cardiac disease (1,2). The 30-day survival rate in Norway is 14% (3) Cardiopulmonary resuscitation (CPR) is a means to deliver partially oxygenated blood to vital organs such as the brain and the heart, to prevent irreversible hypoxic damage (4). Anoxic brain damage is the most common cause of mortality after admission to hospital in these patients (5).

The gold standard treatment of out-of-hospital cardiac arrest are advanced cardiovascular life support (ACLS) as described in the guidelines from resuscitation authorities such as the Norwegian Resuscitation Council (6) or the European Resuscitation Council (7) (Figure 1).

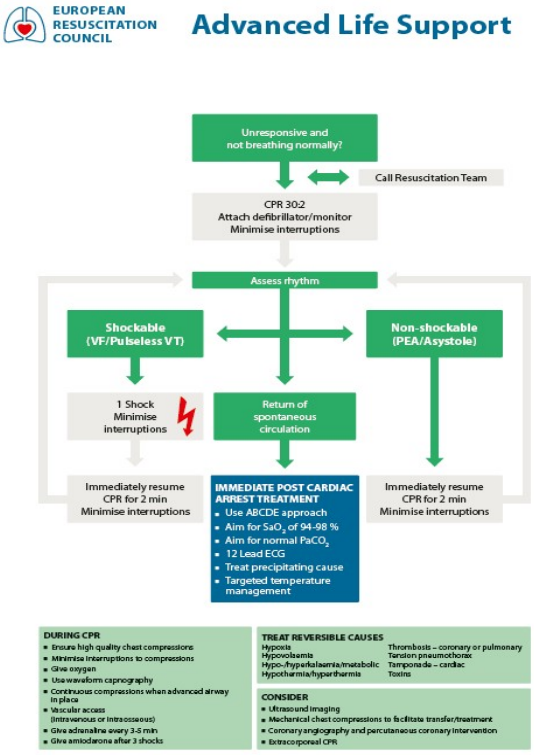


Figure 1. Guidelines from the European Resuscitation Council

In Norway, approximately 22% of OHCA present with a shockable rhythm – ventricular fibrillation (VF) or ventricular tachycardia (VT) (8). In the cardiac arrest setting, it is well documented that immediate defibrillation is important if the presenting cardiac rhythm is VT or VF. According to the Norwegian national guidelines for CPR, a shock should be delivered every third minute if the rhythm is shockable (6). However, multiple attempts with defibrillation may be necessary to achieve return of spontaneous circulation (ROSC).

In double sequential external defibrillation (DSED) two defibrillators are used simultaneously to convert the malignant arrhythmia (9). The first set of defibrillator pads are placed in the standard anterior-lateral position and the second set in the anterior-posterior position (Figure 2). The shocks are administered manually in quick succession, preferably less than one second apart (10).

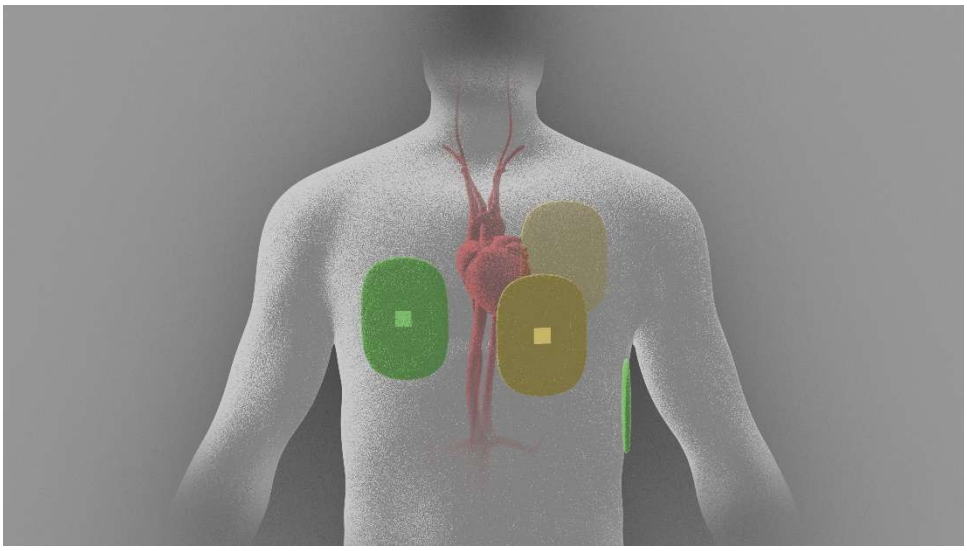


Figure 2. Position of defibrillator pads in dual defibrillation.

DSED has been described in case reports and observation studies without control groups (11–18) and in review papers (19,20). Lately, a randomized controlled trial (RCT) assessed the use of DSED in the prehospital setting (10), where either DSED or anterior-posterior placement of the defibrillation pads were compared to standard defibrillation strategy. In this study, the DSED strategy demonstrated significant increase in survival. However, in this RCT, DSED or anterior-posterior placement of defibrillation pads was not performed until 3 failed attempts, so-called refractory VF, resulting in a delay until alternative defibrillation strategy was attempted.

Studies suggest that more than 50% of patients with shockable rhythm require more than 2 shocks to convert the malignant arrhythmia (21). It is well established that reduced time to ROSC is associated with improved outcome (22–24). Hence, DSED as the initial defibrillation strategy may seem reasonable.

This study therefore aims to assess the use of early DSED as the strategy for defibrillation of OHCA patients with shockable rhythm.

This protocol is designed according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 guidelines and will be reported according to the Consolidated Standards Of Reporting Trials 2010 Guidelines (25,26).

Potential eligible patients

The number of OHCA incidents in Norway in 2022 was 3 881, which correlates to an incidence of 71/100 000 inhabitants per year, increasing from 60/100 000 in 2017 (3,8). The number of patients with OHCA that present with a shockable rhythm in Norway is more than 650 (3). The annual number of patients in Norway that receive 2 or more defibrillations by ambulance personnel, and therefore eligible to a strategy of early DSED, is currently unknown. However, according to the findings by Hasegawa et al (21), more than 400 patients may be eligible every year in Norway. The exact number

of potential eligible patients will be sought investigated in cooperation with the Norwegian Cardiac Arrest Registry.

Study rationale

The aim of the study is to assess use of early DSED as part of the ACLS treatment in OHCA. The study will assess survival and neurological outcome in surviving patients. The trial does not test specific medical equipment, nor compares the effect of different defibrillators.

The use of DSED is already investigated in a randomised controlled trial setting (10). Safety of both patient and medical equipment has also been investigated, without clear evidence for patient or equipment harm (10,27,28).

DSED may be a superior defibrillation strategy due to several reasons, or combinations of these (10,29):

1) increased energy (Joule) delivered at each defibrillation
2) lowered threshold in the myocytes for the second shock
3) a current vector change that may result in higher amount of energy (Joule) to the posterior parts of the heart muscle where cardiac fibrillation is more likely to originate.

This trial will supplement the data from earlier trials (10), however will potentially be the first to assess early DSED as defibrillation strategy, to all patients with shockable rhythms. Hence, the trial seeks to contribute as research to improve current best practice.

Academic study

This study is not part of an application for regulatory approval of medical devices. It is not conducted to establish or verify the clinical benefits of a defibrillator device as specified by its manufacturer. No defibrillator manufacturer is involved in the design of the trial or the trial itself, nor will any manufacturer gain access to data or results other than those publicly published. The Sponsor retain ownership of all data and results generated through this trial. The trial is not designed to report any alteration of CE-markings or any other regulatory application for any defibrillator devices.

6. Objectives and endpoints

Primary objective

The primary objective is to assess the efficacy of DSED as an initial treatment in patients with out-of-hospital cardiac arrest (OHCA), measured as primary endpoint: Survival with admission to hospital.

Secondary objective

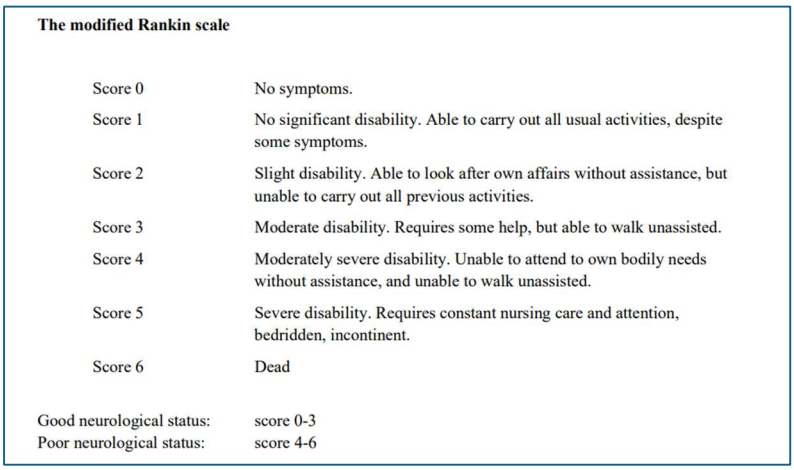
Secondary objectives of this trial are to evaluate the effect of DSED on 30-day survival and neurological status at 30 days.

Primary endpoint

The primary endpoint of this study is the proportion of patients admitted to hospital.

Secondary endpoints

- 30-day survival with neurological status defined as modified Rankin scale (mRS) score 0-3 (Figure 3)
- Successful termination of the arrhythmia



The modified Rankin scale

Score 0	No symptoms.
Score 1	No significant disability. Able to carry out all usual activities, despite some symptoms.
Score 2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
Score 3	Moderate disability. Requires some help, but able to walk unassisted.
Score 4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
Score 5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
Score 6	Dead
Good neurological status:	score 0-3
Poor neurological status:	score 4-6

Figure 3. The modified Ranking scale.

Exploratory endpoints

- All-cause mortality one year after randomisation
- Incidence of all patient-related adverse effects
- Incidents of malfunction of defibrillators after DSED

7. Study population

Selection of participants

The patient population is adult patients (18 or older, as estimated by medical personnel on-scene) suffering from an out-of-hospital cardiac arrest.

Inclusion criteria

The subject must meet all the following criteria to be included in the trial:

- Estimated age 18 or older
- Out-of-hospital cardiac arrest with shockable rhythm

Exclusion criteria

Fulfilling one criterion excludes the subject to be included in this trial.

- Known do-not-resuscitate order
- Obvious ethical reasons not to initiate or continue resuscitation
- Pregnancy, obvious or suspected
- Incarcerated patients

Criteria for withdrawal or discontinuation

Patients can withdraw from the clinical study at any time without the need of a rationale and without compromise to their future medical care. If the patient has not regained ability to give consent, the next-of-kin can withdraw the patient from the study at any time. All patients will receive the same standard of care.

Any safety data on adverse events registered in patients that withdraw from the study will be stored in the database in an anonymized form, to ensure that no safety information is lost.

Patients that withdraw or are withdrawn from the study after randomisation will be replaced.

Enrolment

Subjects with out-of-hospital cardiac arrest in the areas serviced by the study centres are candidates for enrolment into the study. Patients who develop cardiac arrest while being treated for other causes by ambulance personnel are also eligible.

8. Informed consent process

Eligible patients cannot provide informed consent before inclusion due to the cardiac arrest. Hence, inclusion to study will be performed before the patient or next-of-kin can provide informed consent or withdraw from the study.

In accordance with national regulations and as currently applied in studies on cardiac arrest patients, the patient's next-of-kin will be asked for an informed consent. However, during the resuscitation informed consent cannot be obtained, both because ambulance personnel are occupied with resuscitation of the patient and because it is expected that the next-of-kin is in a mental state where such information may be difficult to process. The next-of-kin will therefore be asked for a deferred consent, and they will be contacted as soon as possible after the incident. All information will be given

by someone experienced in communication with next-of-kin to patients with critical illness. If the patient regain capacity to provide an informed consent within 90 days, he/she will be asked for a deferred consent. Informed consent may be signed on paper or by a digital solution, as approved by the regional ethical committee (REC).

This adheres to the ethical principles that have their origin in the Declaration of Helsinki (30). Prior to study start, all written information intended to subject or next-of-kin has been approved by the REC. The responsible investigator at the study site and/or a designee (collectively named site investigator (SI)) will explain the clinical study to the subject/next-of-kin as well as provide a copy of the subject information sheet. This sheet will include all aspects of the clinical study that are relevant to the subject's/next-of-kin's decision to participate. The sheet will be written in a non-technical and easily understood language.

The SI is instructed to avoid coercion, not to appear to waive the subject's legal rights in any way, to allow sufficient time for questions about study details and allow the subject/next-of-kin to make an informed decision to participate or not in the clinical study.

In case of consent to participation, the informed consent form is signed and dated, and a copy is provided to the subject. A digital solution for informed consent will be available, through the eFORSK solution, handled by KlinForsk, the Clinical Research Unit, Central Norway. The information in this digital solution is identical as the written consent forms.

9. Statistics

The study will follow a group sequential design with adaptive sample size modification. This allows possible early stop of the study, in case of significant differences in the primary endpoint or 30-day survival rate between the groups. It also allows re-estimation of the sample size at the interim analyses to maintain the desired statistical power. Adaptive design is used in clinical research because it may contribute to study cost-effectiveness regarding time and money, may require fewer participants and is a safety aspect hence an important ethical argument (31–34).

Statistical hypothesis

Null hypothesis H_0: There is no difference in survival to hospital admission between the control group (single defibrillation strategy) and the intervention group (dual sequential external defibrillation strategy).

Alternative hypothesis H_A: There is a difference in survival to hospital admission between the control group (single defibrillation strategy) and the intervention group (dual sequential external defibrillation strategy).

Sample size

In Norway, 3881 patients suffered an OHCA in 2022, of which 22 % presented with a shockable rhythm (3). It is reported that 50% of patients receive more than one defibrillation shock (21), which results in 420 patients in Norway annually.

The number of patients with both two or more defibrillation shocks and survival to hospital admission in Norway is not reported in known literature. A need assessment study to investigate this will be sought performed during 2024, as part of Dr Vegard Nordvistes PhD thesis.

However, preliminary estimates using available data from the Norwegian Cardiac Arrest Registry indicate that expected survival to hospital admission in this patient cohort is approximately 50%. The sample size needed to demonstrate a clinically relevant increase from 50% to 65% survival to hospital admission, with 0,80 power and a significance level of 0,05 is 169 patients in each group, total 338 patients.

We estimate a 5% drop-out from the study and therefore choose to include a total of 356 patients in the study, 178 patients in each group.

Interim analyses

One interim analysis will be performed, after 90 patients in both the intervention and the control group are included. There is no specific time schedule for the interim analysis. The variables that should be assessed is the primary endpoint and 30-day survival with good neurologic outcome.
An external data monitoring committee will perform the interim analysis and may consider a recommendation to the Sponsor to stop the trial if a difference in primary endpoint or 30-day survival between the groups, with a significance level following the O´Brien-Fleming approach is found (35,36).
At the interim analysis, we will re-estimate the sample size. Based on an assumption that any difference in the primary endpoint between the two groups will persist, we will recommend the sponsor to consider stopping the trial due to futility if the new sample size needed to prove a difference is more than three times the planned sample size (with 0.80 power and a significance level of 0.05).

Measures to minimize bias

Selection bias

This is a randomised study, which is important to minimise selection bias. Randomisation procedure is described in the section "*Randomisation procedure*".

Performance bias

The treatment post-ROSC or after hospital admission will not differ between the groups. This will minimize performance bias.

Exclusion bias

Exclusion bias is mitigated using limited number of personnel to obtain informed consent and to check survival and other patient data. The same personnel are used for registration of data into the case report form (CRF).

Statistical design

Statistical analysis will follow the intention-to-treat (ITT) principle. The outcome between participants randomised to the intervention group (DSED strategy) and the control group (single defibrillation strategy) will be analysed, for all patients where defibrillation has been performed. Per-protocol analyses will be considered if more than 10% of patients in the intervention group that received defibrillation did not receive DSED but single defibrillation. This means that a considerable amount in the intervention group has deviated from protocol and may therefore undermine the validity of the ITT analysis.

Hypothesis testing will be used to analyse the primary endpoint and other dichotomous secondary endpoints. Any continuous variables will be analysed by regression methods.

The level of significance and power of the clinical study

One RCT demonstrate that DSED improve survival (10), however it is possible that DSED, and the inclusion to a study itself, may contribute to decrease the chance of good outcome. Therefore, we will use a two-sided test with significance level of 0.05 for the analyses. A significance level following the O´Brien-Fleming approach is chosen on the interim analysis (35,36).

Expected drop out rates

Inclusion to study is performed prior to informed consent. Based on earlier experience with cardiac arrest studies in Norway we expect a low dropout rate, estimated to 5%.

Specification of exploratory subgroups

Subgroups of patients may have enhanced or reduced effect of the intervention. To assess possible modifiers of the intervention effect, exploratory analyses will be used:

- Age
- Sex
- Time from debut of arrest to defibrillation
- Study site

The subgroups will be analysed by generalised linear models, which includes multiple regression analyses. This enables multiple imputation if necessary.

Treatment of missing data

Missing data will be reported in the publication and multiple imputation may be considered.

Min/max number of subjects per centre

There is no minimum or maximum number of subjects per study site.

10.Project methodology and overall design

The purpose of the study is to assess the efficacy of DSED as a strategy as part of the ACLS provided in treatment of OHCA. This trial will not test any medical device, nor compare the effect of different medical devices.

This is a prospective, cluster randomised, parallel group, crossover, multi-centre, clinical trial. Study sites are randomised in a 1:1 ratio to include patients to either the control group or the intervention group. After 6 months, crossover to the other study arm will be performed. After these 6 months a re-randomisation is performed, and the study site will be allocated to either the control group or intervention group. This will continue to the end of study or to the study site withdraw from the study (Figure 4).
The control group will receive ACLS according to national guidelines. The intervention group receives ACLS according to national guidelines, with defibrillations performed as DSED.

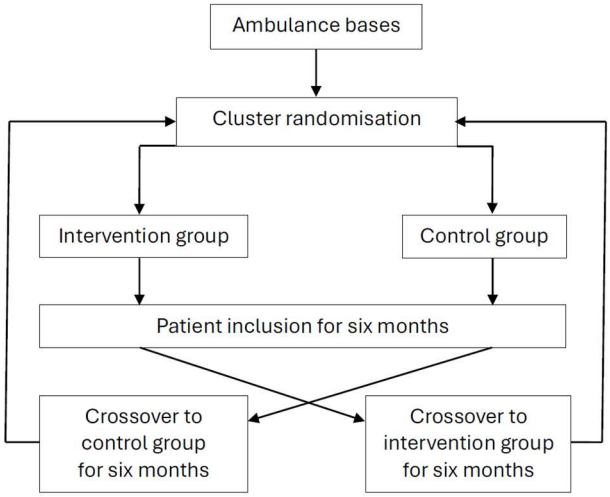


Figure 4. Flow-chart of patient allocation and inclusion

Blinding of the ambulance crew to the intervention is impossible due to the nature of the intervention. The study is estimated to last for 8 years. This includes start-up and education of the study centres, enrolment of patients, evaluation of last included patient one year after randomisation and a period of five years for retention of study documentation.

Expected study duration

The trial period is one year after inclusion for each study participant. The survival rate after 30 days will be registered and all-cause mortality one year after inclusion will be registered, after a chart review.

Part I

The first part of the trial will commence summer 2024 and last for two months. Three ambulance bases in Trondheim, Norway, will include patients to the intervention group during these two months.

Any modifications to the trial's operating procedure and/or changes in the CRF will be performed before the second part of the trial can start. If Part I demonstrate need for significant change to the study protocol or lack of compliance to protocol by the ambulance bases, the included patients in Part I will not be added to the intervention group in the main part of the study, Part II.

Part II

This is the main part of the trial and will include no more than 50 ambulance bases, 25 to the intervention group and 25 to the control group.
We estimate that the second part of the trial will start 1st September 2024 and estimate that 3 years is necessary to include patients. This includes the time needed for education and training of ambulance and study personnel.

Randomisation procedure

Study sites will be randomly allocated in a 1:1 ratio between the two study groups. The study site will then include all eligible patients into the study group assigned, for 6 months. After 6 months cross-over will be performed, so the study site will include patients to the other study arm for the next 6 months. After these 6 months a re-randomisation will be performed (Figure 4).

The study site randomisation will be performed by KlinForsk, Clinical Research Unit, Central Norway. The random allocation sequence is generated using a Microsoft Access data base by KlinForsk. No investigator has access to the allocation sequence.

Medical devices in the study

During ACLS, several medical devices are used for treatment and diagnosis. These devices will be used in both groups of this trial, as part of the normal set-up in ground ambulances. This includes several devices, such as mechanical chest compressions devices, monitoring equipment, ultrasound, venous catheters, intraosseous needles, supraglottic airways and other.

The study sponsor takes no responsibilities in the funding, provision, approval, or other aspects regarding these devices.

Each study site will use two identical defibrillators, Corpulse 3 (Corpuls, GS Elektromedizinsche Geräte, Germany).
Other available defibrillators may be used during the trial.

11.Study procedures

Treatment 1 – the control group

The control group will receive ACLS as described in the guidelines from the Norwegian Resuscitation Council (6).

Treatment 2 – the intervention group

The intervention group will receive the same treatment as the control group, with the exception that defibrillations will be as DSED. The standard operating procedure is described in the chapter "*Outline of the DSED procedure*" (Figure 5).

Education and training of personnel

All personnel involved in this study that will include patients are regularly part of resuscitation teams both in real life and in scenario training. Therefore, no mandatory training program for ACLS is necessary for this trial.

All personnel that will include patients, must participate in a training program to ensure compliance to the DSED standard operating procedure. Participants must complete and pass this training program to include patients into the intervention group. Participants without proper training in DSED may still include patients in the control group.

Outline of the DSED procedure

Two defibrillators are placed side by side, preferably on the patients left side. The first ambulance worker identifies cardiac arrest and initiates CPR. The second ambulance worker turns on the defibrillators and readies two sets of pads. The first two pads are placed according to existing guidelines, i.e., in anterolateral position while chest compressions are ongoing. The third pad is placed in sternal position. The patient is logrolled, the left side of the posterior torso is exposed, and the fourth pad is placed in subscapular position before the patient is returned to supine position. To enable this, a maximum of 20 second pause in chest compression is allowed. The cardiac rhythm can be identified, and shocks delivered if appropriate (Figure 5).

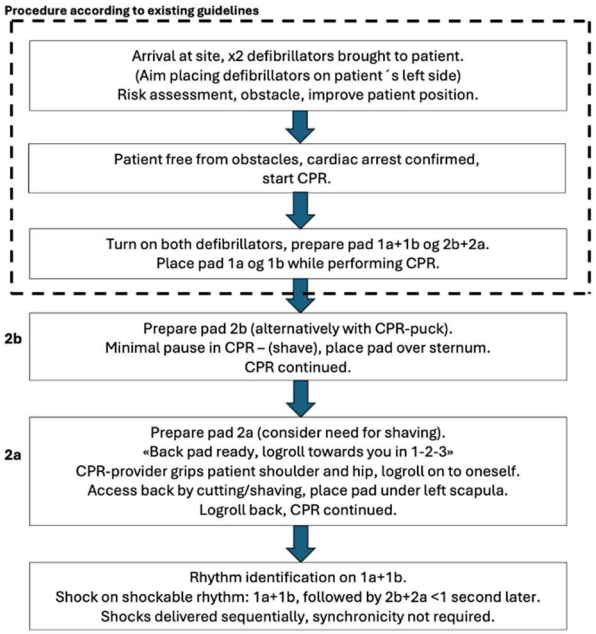


Figure 5. Standard operating procedure for dual defibrillation set-up.

Follow-up

The SI (principle investigator at study site or research employee) will follow up patients admitted to hospital until 30 days after inclusion.

The SI will perform a chart review after one year to assess one-year mortality and register the result in the CRF.

Follow-up medical care

All patients will receive standard care after inclusion to the study.

Discontinuation of the study

The trial may be stopped by the sponsor in the event of any of the following:

- Occurrence of adverse event (unknown to date) in respect of their severity, nature or duration.
- Loss of study funding
- Low inclusion rate
- Ethical or medical reasons that affect the continuation of the study

If the interim analysis demonstrates significant group difference in the primary endpoint or 30-day survival with good neurologic prognosis, the sponsor may decide to stop the study. Recommendation to stop the study should only happen after a face-to-face meeting with the project management.

The study site primary investigator may stop or terminate the study at his/her study site, at any time.

The data monitoring committee (DMC) can recommend the sponsor to stop or terminate the study if they find severe or unsolvable safety issues.

Laboratory test

We will not analyse blood samples in this study.

12.Data collection and handling

Data handling

Data will be registered into a web-based case report form (CRF),through the *eFORSK* solution, (https://www.klinforsk.no/info/Informasjon) handled by the department KlinForsk, Clinical Research Unit, Central Norway. KlinForsk is authorised as data processors by the Norwegian Centre for Research Data. KlinForsk will set up necessary accounts to permit access to the CRF.

Source data

Data may be gathered from:

- Ambulance journal and air ambulance journal
- Utstein prehospital cardiac arrest journal
- Data file from the defibrillator used
- Electronic patient journal
- Interview with the patient/next-of-kin

Storage of study documentation

Electronically data (i.e., ultrasound images, pictures, patient monitor files) will be stored in a separate folder in the Microsoft Teams application, connected to the users at St. Olavs Hospital. Access to this folder will be restricted to authorized users only on a need to know and need to do basis.

Hard copies of any patient documents that may include identifiable information will be stored at the investigator site file (ISF), at a locked location at each study site or at the coordinating study site at Rosten, Trondheim. Only the site investigator and study employee at the study site have access to this ISF.

Original study trial documents will be stored at the study sites or at the coordinating study site at Rosten, Trondheim, for five years to allow for inspection by relevant authorities. The site investigator will maintain confidentiality of the data and prevent accidental destruction of such documents.

Data collection

Data will be registered according to this schedule:

	Study period					
	Randomisation	Enrolment	Post-randomisation			
TIMEPOINT	**T**	**T=0**	**Hospitalization**	**T < 2 weeks**	**T +30 days**	**T +1 year**
ENROLMENT						
Inclusion criteria		X				
Exclusion criteria		X				
Allocation	X					
Informed consent			X	X		
INTERVENTIONS						
Intervention or control group		X				
ASSESSMENT						
ROSC		X				
Survival			X	X	X	X
Pre-hospital registrations						
Utstein-styled documentation		X				
Defibrillation-related data		X				
All relevant dispatch/procedure times		X	X			
In-hospital registrations						
Modified Rankin scale			X	X	X	
Adverse effects		X				

Table 1. SPIRIT data schedule.

These data points will be registered:

All patients - data reported after inclusion	
Age	
Gender	
Location of the incident	*Public outdoors, public indoors, private indoors*
Medication and dose used during resuscitation	

Route of administration	*Intravenous, intraosseous*
All relevant times Time of dispatch Time of arrival Time of first defibrillation Time of first termination of shockable rhythm Time of first ROSC Time of sustained ROSC	*DD.MM.YYYY: hh:mm*
Number of defibrillations, DSED or single	*n*
Number of defibrillations before DSED	*n*
Compression machine used	*yes/no*
Airway management (main method)	*Supraglottic airway, Endotracheal intubation*
ROSC more than 20 minutes	*yes/no*
Data file from monitor used	
Signs of life during CPR	*yes/no*

Delivered to hospital - additional data	
Survival to hospital discharge	*Yes/no*
Modified Rankin scale at day 30	*0 to 6*
Survival one year after randomisation	*yes/no*

Data review and editing

Each included patient will be given a unique study number and data will be identified only by the study number. The site investigator or designee will handle an enrolment log (*Subject ID log* and *Screening log*, in Appendix) which include the patients name, date of birth and study number. These logs will be stored separately at each study site. Identifiable data will not be registered in the CRF.

If a SI for any reason must withdraw from the trial, his/her responsibility is transferred to the project management, which, if necessary, will appoint a new investigator.

13.Study management

The study will be performed according to the ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95). All study sites will have a system for data monitoring, and data management and retention. Individual patient data records will be handled according to the legislation of each participating country.

14.Study amendments

This research protocol may require amendments during study. Any amendments will be agreed upon between the project management and sponsor and be approved by REC and other relevant authorities.

15.Ethics Committee Approval

The study will not start before approval by the ethics committee is granted. This approval will apply for all Norwegian study sites.

Any foreign study sites must be approved by their regional or national ethics committee, prior to patient inclusion. All sites must comply with local regulations, national and EU law.

16.Other Regulatory Approvals

Sites outside of Norway may be need national regulations in conjunction to European Union Regulation 2017/745 on medical devices. In such instances, the necessary approvals must be in place prior to site opening. These applications are the responsibility of the foreign site's investigator.

17.Trial insurance

In Norway, all patients who participate in the study are covered by Norwegian System of Patient Injury Compensation (Norsk Pasientskadeerstatning), a government agency subject to the Norwegian Ministry of Health and Care Services. Details are found at http://www.npe.no/en/.

Any foreign study sites must ensure insurance cover for any included patients and provide the project management with documentation prior to opening the study site.

18.Trial organisation

Organisation

The research responsible institution (Sponsor) is the Clinic of Emergency Medicine and Prehospital services, St. Olavs University Hospital. The main funder is the Norwegian Air Ambulance Foundation. An external data monitoring committee is independent from the project management and will communicate directly to the sponsor or the project management as appropriate (Figure 6).

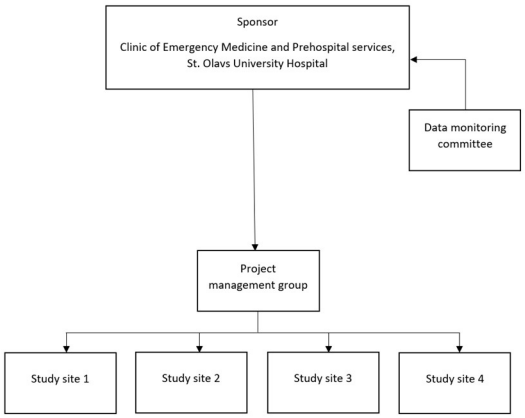


Figure 6. Trial organisation

The project management

These are the personnel most involved with the day-to-day handling of the study. They will have face-to-face meetings at need, no less than every 6 months. Members of the project management are listed in chapter 2, *Project management*.

19.Data monitoring committee

An independent Data Monitoring Committee (DMC) will be established and be governed by a charter based on the NorCRIN standard operating procedure. This charter will describe the roles and responsibilities of the DMC. The charter and DMC should be in place before inclusion of the first patient.

20.Funding

This trial is funded mainly by the Norwegian Air Ambulance Foundation. Research grants or funders may be involved during the study period. None of the funders will contribute to the study design, collection, management, analysis, or interpretation of data, nor writing of the report or decision to submit the report to publication. The sponsor retains full ownership of all data generated in the trial.

21.Conflict of Interest

The sponsor has no conflict of interest in relation to any defibrillator device or manufacturer in this trial.

VN, AJK, MR, JD and JRB have no financial conflict of interest. VN, AJK, MR and JRB are partly funded by the Norwegian Air Ambulance Foundation for research purposes.

22.Publication policy

The study protocol will be submitted for publication in an international peer reviewed journal.
When the study is completed, the results will be submitted for publication in an international peer reviewed journal, as well as submitted to the REC according to national regulations.

Authorship of the primary publication is decided by the project management and granted according to the Vancouver definitions ((37). Personnel with significant contribution, but not fulfilled the criteria to authorship, will be mentioned under “Acknowledgements”. Study sites that recruit > 30 participants will be entitled to one name, > 60 participants will be entitled to one additional name, > 90 two additional names. If a study site includes less than 30 patients, the site will not be entitled to an author name.
The main publication will report the primary and secondary endpoints.

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