Comparison of three management strategies for de novo supraventricular arrhythmias in septic shock: a randomised controlled trial.
CAFS (Control Atrial Fibrillation during Septic shock) study

This research is promoted by *Assistance Publique - Hôpitaux de Paris*
Represented by the Director of
***Direction de la Recherche Clinique et de l'Innovation* (DRCI)**
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75010 Paris

INVITATION TO PARTICIPATE

Dear Madam, dear Sir

Dr./Pr. (delete as appropriate) ..... (First name, Surname), working at …….. Hospital, invites you to participate in a research study conducted to examine your disease.
We highly encourage you to read this document carefully before making any decision. Do not hesitate to ask for further information.
If you agree to participate in this research, you will be asked to sign a written consent.

1) What is the objective of this research?

You are admitted in intensive care to be treated for a septic shock. Septic shock is a critical infection that leads to a decrease in blood pressure (acute circulatory failure) and organ damage. This situation has been complicated by cardiac arrhythmia (irregular, faster and less efficient heartbeats), which may worsen your condition.
To limit this risk, there are three alternatives: attempting to reduce the heart rate, or to stop the arrhythmia with a return to normal rhythm (sinus rhythm) by managing its risk factors (risk control); slowing the heart rate (rate control) as a complement to risk factor management; or stopping the arrhythmia and returning to a normal heart rate (rhythm control), also as a complement to risk factor management. At present, there are no data to show which of these three strategies is the best to prevent deterioration in the health of patients with arrhythmia during septic shock, as is the case for you.
The aim of our research is to compare the three strategies (risk control, rate control, rhythm control) in patients with arrhythmia during septic shock. The strategy applied to each patient will be determined by random selection.
To perform this research study, we intend to include 240 patients with arrhythmia during septic shock who are admitted to French and Belgium hospitals.

2) What does the research consist in?

In the present study, we will compare the efficacy of risk control, rate control and rhythm control strategies. You will be treated for 7 days according to the strategy selected by random draw.
The aim of the risk control strategy is either to reduce the heart rate, or to stop the arrhythmia with a return to normal rhythm (sinus rhythm), by controlling the arrhythmia's risk factors (such as low serum magnesium, low serum potassium, fever...), without specific arrhythmia treatment which may cause side effects.
The aim of the rate control strategy is to reduce the heart rate by using a low dose of amiodarone in addition to the risk control strategy. When specific arrythmia treatment is prescribed for patients with septic shock, such as yourself, amiodarone is the most commonly used in France and Belgium. Amiodarone is an anti-arrhythmic drug, which have an action on the heart's electric impulsion. Its action varies according to the dose used: reduction in heart rate at low doses, or arrest of arrhythmia with return to normal heart rhythm at high doses. For rapid action, amiodarone is first administrated intravenously, then orally if available.

The aim of the rhythm control strategy (in addition to the risk control strategy) is to stop the arrhythmia and restore a normal heart rhythm using high-dose amiodarone. If high-dose amiodarone fails, one or more external electrical shocks may be administered if you are under sedation (general anesthesia), with intubation and mechanical ventilation to treat septic shock.

If you are not under sedation, an electric shock will not be given, even if high-dose amiodarone fails. External electrical shock consists of passing a brief electric current through the heart to restore a normal heart rhythm. The current is delivered to the chest through two paddles connected to a device called an external defibrillator. The procedure is carried out under general anesthesia.
In all cases, you will also receive the usual treatment for septic shock as recommended during your stay in hospital.

3) What is the work schedule of the research?

The study is expected to last 43 months and your participation will last 28 days. The trial will not involve any additional tests other than those performed as part of routine care. Your participation in the study will begin after you sign the consent form at your first visit.
Once you have read and signed the consent form, you will be randomised to the risk control, rate control or rhythm control strategy, which will start immediately. This randomisation corresponds to the first day of the trial (D1). You will receive the randomised strategy for 7 days, from D1 to D7. Your monitoring data (routine clinical examinations and blood tests) will be collected daily during your hospital stay.
If you leave the hospital before day 28, a clinical trial technician will contact you on day 28 to check your health.

4) What are the benefits of your participation?

The expected benefit is a reduction in the duration of acute circulatory failure during the 7 days of treatment to reduce the risk of organ failure. In addition, your participation will help us to improve our knowledge of the treatment of arrhythmias in septic shock.

5) Which treatments are authorized and which are not?

Drugs that can cause a cardiac arrhythmia called "torsades de pointes" are not approved for use with amiodarone and are prohibited for research purposes. The most common of these are: erythromycin, levofloxacin, moxyfloxacin and spiramycin.

6) What are the anticipated risks and constraints added by the research?

If you agree to take part in this study, you should take the following into account

- Take your treatment as prescribed by your doctor.
- Inform the research physician of any medication you are taking and of any events that occur during the research (hospitalisation, etc.).
- To be covered by or benefit from any social security scheme.
- Not to participate in another research project without your doctor's permission, in order to protect yourself from any health problems that may arise, for example, from possible incompatibilities between the drugs being studied or from other exposures.
- If you are a woman of childbearing potential, you should have a pregnancy test before starting this study.

7) What are the potential medical alternatives?

If you choose not to participate in this research, you will receive appropriate medical care according to your condition, in accordance with standard clinical practice.

8) What kind of medical care to have after participation?

Follow-up is not specific to this trial. You will continue to receive care that is appropriate to your condition, whether that is usual care in the event that the research is stopped early, or care at the end of your participation.
Your doctor can decide to stop your participation at any time and should explain the reasons to you.

9) If you participate, how will your collected data be used in the research?

In the context of the research in which you are invited to participate, your personal data will be processed by AP-HP, the research promoter in charge of data management, in order to analyse the results.

This data processing is necessary in order to carry out research of public health interest, in line with AP-HP's mission as a public university hospital.

To this end, your medical and lifestyle data will be communicated to the promoter or to persons or partners working on its behalf, in France or abroad, and will be kept for 15 years. This data will be identified by a registration number. These data may also be communicated to French or foreign health authorities under conditions that guarantee their confidentiality.

Your data may be used for further research or complementary analysis in collaboration with private or public partners in France or abroad, under conditions that guarantee their confidentiality and the same level of protection as required by European legislation.
You may at any time object to any further analysis of your data by informing the doctor who is following you in this research.

Your data will only be kept for as long as is strictly necessary and justified by the purpose of the research. It will be kept on the data manager's information systems for two years after the last publication of the research results. Your data will then be archived in accordance with the regulations in force.

The database used for this research is created in accordance with French law (modified "Informatique et Libertés" law) and European law (Règlement Général sur la Protection des Données - RGPD). You have the right to access, modify, limit and object to the processing of data covered by professional secrecy and used in the context of this research. These rights can be exercised with the doctor in charge of the research, who is the only person who knows your identity (identified on the first page of this document).

If you decide to discontinue your participation, the data collected prior to this decision will be used in accordance with the regulations and exclusively for the purposes of this research. Deletion of this data would compromise the validity of the research results. However, from that point on, your data will no longer be used in this research or in any other work.

If you have a problem concerning your rights, you can contact the AP-HP Data Protection Officer at the following address: protection.donnees.dsi@aphp.fr, who will be able to explain the channels available to you with the CNIL. You may also exercise your right to complain directly to the CNIL (for more information on this subject, please visit www.cnil.fr).

10) How is this research supervised?

AP-HP has taken all the measures necessary to carry out this research in compliance with the public health regulations applicable to research involving human volunteers.

AP-HP has taken out an insurance policy (number 0100518814033 200013) with its insurance broker BIOMEDICINSURE, whose address is Parc d'Innovation, Bretagne Sud C.P.142 56038 Vannes Cedex, to cover its civil liability and that of all its collaborators.

AP-HP has been approved by the Ethics Committee (CPP Sud-Ouest et Outre-Mer III) on [29/07/2020] and by the Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) on 21/02/2020.

11) What are your rights ?

Your participation in this research is free and voluntary. Your decision will not affect the quality of care and treatment you receive.

Before you agree to take part in this research, you will undergo an appropriate medical examination, the results of which will be reported to you.

Throughout the study, and at any time, you can ask your investigator for further information about your health and explanations of the research process.

You can withdraw from the research at any time without explanation, without any impact on your treatment or the quality of care you receive, and without any impact on your relationship with your doctor. After this withdrawal, you may be followed by the same medical team. In this case, the data collected up to the time of withdrawal will be used to analyse the research results.

Your medical file will remain confidential and can only be consulted under the responsibility of the doctor in charge of your treatment, as well as by the health authorities and persons authorised by AP-HP for research and bound by professional confidentiality.

At the end of the study and its data analysis, you will have access to the overall results by contacting the doctor treating you in the study.

You can also access all your medical data directly or through a doctor of your choice, in accordance with article L 1111-7 of the Public Health Code.

If, after reading all this information, discussing it with your doctor and having time to think about it, you agree to take part in the research, you will be asked to sign and date the informed consent form at the end of this document.

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

CONSENT FORM

I, the undersigned, Mrs, Mr [delete as appropriate] (first name, surname) ..... agree to voluntarily participate in the study entitled
"Comparison of three management strategies for de novo supraventricular arrhythmias in septic shock: a randomised controlled trial." sponsored by Assistance Publique - Hôpitaux de Paris and I was informed by Dr./Pr. (name, surname, telephone)....., investigator of this study.

- I have read the Invitation to Participate version 3.0 dated 19.6.2023 (4 pages), which explains the purpose of this study, how it will be conducted, and what my participation will entail;
- I will keep a copy of the invitation to participate and the informed consent form:
- I have received adequate answers to all my questions;
- I have had enough time to make my decision;
- I understand that my participation is free of charge and that I can stop my participation at any time without any liability and without affecting the quality of care I receive;
- I have been informed that the data collected in the research may be used for other studies and that I may object to this at any time;
- I understand that my participation may also be interrupted at any time by the doctor, who should explain the reasons;
- I have undergone a medical examination appropriate to the research prior to taking part in this research, the results of which have been communicated to me;
- I am aware that, in order to participate in this research, I must be affiliated to or a beneficiary of a social security scheme. I confirm that this is the case;
- I have been informed that my participation in this research will last for 28 days, during which time I cannot consider taking part in any other research without informing the investigating physician in charge of my case in this study,
- My consent does not in any way relieve the doctor following me in the research or AP-HP of any responsibility, and I retain all the rights guaranteed to me by law.

Signature of the participating person		**Signature of the doctor**	
First name, Surname:		Fist name, Surname:	
Date:	Signature:	Date:	Signature:

This document must be produced in three copies: one copy must be kept by the investigator for 15 years, the second given to the consenting person, and the third sent to AP-HP in a sealed envelope at the end of the study.