University of Pittsburgh
School of Medicine

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

Restrictive versus Liberal rate of Extracorporeal Volume Removal Evaluation in Acute Kidney Injury (RELIEVE-AKI) Clinical Trial

Person in charge of this study (Principal Investigator):	Dr. Raghavan Murugan MD, MS, FRCP Professor of Critical Care Medicine University of Pittsburgh School of Medicine 300 Halket Street – Suite # 4850 UPMC Magee Womens Hospital Pittsburgh, PA, 15213 muruganr@upmc.edu 412-370-5586 (24 hours)
Co-investigator:	Dr. Paul Palevsky, MD Professor of Medicine University of Pittsburgh School of Medicine Room 7E123 (111F-U) VA Pittsburgh Healthcare System University Drive, Pittsburgh, PA, 15240 palevsky@pitt.edu Pager: 888-210-5884 (24 hours)
Person organizing this study (Contact Person):	Dr. Raghavan Murugan (412-370-5586) (24 hours)
The sponsor of this study:	**National Institute of Health - National Institute of Diabetes and Digestive and Kidney Diseases**
Questions about this study:	If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668.

This form talks about the Restrictive versus Liberal Rate of Extracorporeal Volume Removal Evaluation in Acute Kidney Injury (RELIEVE-AKI) clinical trial. RELIEVE-AKI is a research study.

Joining RELIEVE-AKI research study is voluntary. You can choose to join or not. No matter what you decide, you will still get the best medical care possible.

- Review this form carefully, if you want to join. We will give you a copy of this form to keep. If you have questions, please ask us.
- Your trial doctor or a member of the clinical trial team will also talk to you in detail about the information in this document. Ask your trial doctor or a member of the clinical trial team to explain anything that is not clear to you.
- If you choose to take part in this clinical trial, you will be asked to sign and date this document. You will get a signed and dated copy of this document.

What is the KEY INFORMATION about the RELIEVE-AKI clinical trial?

- If you join, we will be removing fluid from your body during continuous dialysis using one of two different methods, as tolerated by your body. The first method involves removing fluid at a slow speed and the second method involves removing fluid at a slightly faster speed.
- The most common risk to slow fluid removal is build-up of excess fluid in your body resulting in swelling of the body. Swelling may also affect organs inside your body and the organs may not work well. The benefit to removing fluid slowly is that you may tolerate fluid removal better without a drop in blood pressure.
- The most common risk to fast fluid removal is low blood pressure and irregular heartbeats that may result in decreased oxygen supply to your organs. The benefit to removing fluid fast is that your body could be free from fluid overload quickly and your organs may work better.
- If you join the study, you will be helping researchers identify which fluid removal method is feasible and is better tolerated during continuous dialysis. This may help patients with fluid overload who need continuous dialysis in the future. However, participating in this clinical trial may or may not help you to get better. We will also collect your health information during your hospital stay.

To learn more, please read the rest of this form.

What is RELIEVE-AKI clinical trial?

- RELIEVE-AKI is a research study. You are being invited to voluntarily take part in this research study. Our goal is to find out which fluid removal method during continuous dialysis in patients with kidney disease is feasible and helps to treat fluid overload better. We hope the discoveries we make will help healthcare providers take better care of patients with kidney disease in the future.
- Fluid overload develops in ICU patients due to a couple reasons:

  - the kidneys failing to remove fluid because of acute kidney injury and
  - fluid build-up from fluids given for various treatments.

- Fluid overload can cause many problems such as:
  - swelling of the body,
  - high blood pressure,
  - poor wound healing,
  - difficulty breathing due to fluid build-up in the lungs, as well as in other organs, and can lead to death.

Thus, when fluid overload develops, doctors start continuous dialysis to remove fluid until the kidney function improves.

- Currently, doctors do not know the best way to remove fluid during continuous dialysis. In this clinical trial, the researchers are studying whether it is possible to maintain fluid removal using two different methods during continuous dialysis in ICU patients with acute kidney injury: a slower rate of fluid removal and a slightly faster rate of fluid removal.

- The slower or faster rate of fluid removal from your body will be determined randomly depending upon the month at which continuous dialysis is started and the ICU to which you are admitted.

- The researchers will study 112 patients. This study is being conducted in 5 intensive care units (ICU) at University of Pittsburgh Medical Center, Pittsburgh, PA, and 5 ICUs at Mayo Clinic, Rochester, MN.

- Some of the procedures performed for this clinical trial will be in addition to your standard medical care. If you have questions about any of the procedures, you should ask your doctor or a member of the clinical trial team.

Why are you asking me to join the RELIEVE-AKI clinical trial?

- Your kidneys are not working as well they should right now, and you are making no or very little or no urine. You have a condition called acute kidney injury. As a result, fluid has accumulated in your body resulting in fluid overload.

- The fluid overload has resulted in swelling of your body and possibly of your internal organs making it hard for them to work.

- Thus, your ICU and kidney doctors are thinking about removing fluid using continuous dialysis. Removing fluid using continuous dialysis may help your internal organs work better by treating fluid overload.

How long will RELIEVE-AKI clinical trial last?

- If you decide to participate in the study, fluid removal during continuous dialysis may last several days.

- We will follow you during your stay in the hospital, up to 28 days. We will be seeing you every day and collecting data until ICU discharge.

What will you ask me to do?

There are two main parts to the RELIEVE-AKI clinical trial:

1. We will remove fluid from your body during dialysis

- Since your ICU and kidney doctors are planning to remove fluid during continuous dialysis, we can remove fluid either slow or fast as allowed by your body. This is a medical procedure.

- The decision to remove fluid either slow or fast will be determined by the ICU you are admitted to and the month you participate in the study.

- The fluid will be removed using an existing dialysis catheter inserted into your vein and connected to a continuous dialysis machine. An ICU nurse with specialized training in continuous dialysis will be removing the fluid using the dialysis machine under the direction of your doctors.

- Your doctors will determine when fluid removal should be started while you are on dialysis and when it should be stopped.

- Fluid removal will be started slowly and gradually increased as tolerated by your blood pressure. Fluid will be removed continuously either slow or fast as per the study protocol and continued for several days while you are on the continuous dialysis.

- Fluid removal will be stopped if your blood pressure becomes too low. The doctors will treat your low blood pressure using medications and fluids, as necessary. Fluid removal will be restarted slowly when your blood pressure becomes normal again and continued for the duration of the continuous dialysis.

- Fluid removal may also be slowed or completely stopped if your doctor thinks your body has no excess fluid.

- During fluid removal, we will be closely monitoring and recording your vital signs including your heartbeat and blood pressure. We will also be collecting data on other treatments given to you.

- If your doctor decides to take you off the continuous dialysis and switch you over to a different form of dialysis to remove fluid, we will stop this study protocol.

2. We will gather information from you:

- We will ask your permission to study your medical records to obtain health information about you.
- We will ask what medicines you are taking and about your past medical history.
- We will measure your height, weight, blood pressure, and temperature, and will collect other clinical data.
- We will examine you for swelling caused by fluid overload and kidney problems.
- We will continue to follow you during your hospital stay up until discharge.

What will you do with my medical information?

- Your medical information will not have your name recorded. We will replace your name with a code. We will limit who has the key that links codes to names.
- We will keep your medical information with the records from all the people who join RELIEVE-AKI clinical trial. We will store all these records securely in a password protected computer server.
- We will put a copy of your records in a database managed by the National Institute of Health (NIH). Researchers use these databases to make discoveries about health. The NIH will store your medical records securely.
- The researchers who use your medical records may be from anywhere in the world. They may or may not be part of the RELIEVE-AKI team. They may work at universities or hospitals. They may work for a government. They may work for companies to make new medicines or devices.
- There will be an approval process for researchers who want to work with your medical information. They will have to tell RELIEVE-AKI study team about the research they want to do. They will have to have ethics training. They will have to sign an agreement stating they will not try to find out who you are.
- If you sign this form, you consent to future researchers using your data. There is no limit on the length of time we or the NIH will store your medical information.

Are there any risks to joining RELIEVE-AKI?

- Yes, there are risks to joining RELIEVE-AKI clinical trial. Review these risks carefully. Ask any questions you may have. The main risk of joining RELIEVE-AKI is from fluid removal.

- As with any experimental procedure, there may be adverse events or side effects that are currently unknown and some of these unknown risks could be permanent, severe or life-threatening.

Risk from removing fluid slowly

- When doctors remove fluid slowly, you will be exposed to fluid overload for a long time. Building of excess fluid may result in your heart, lungs, brain, bowels, liver, and kidneys not working well.

- You may end up staying on the breathing machine for a longer time if there is excess fluid build-up in your lungs.

- You may also be dependent on dialysis as your kidneys may not recover due to swelling from fluid overload.

- Fluid build-up in other organs such as heart may result in irregular heartbeat.

- Your body swelling may also persist for a long time.

- You may have high blood pressure due to excess fluid in your blood vessels. If this happens, doctors may start removing fluid rapidly.

- Your wound healing may be impaired if you had an accident or underwent a surgical procedure.

- You may have bowel edema, dilatation or breakdown resulting in intolerance to feeding.

- You may also develop wound infections and pressure ulcerations due to fluid overload.

- You may develop new infections due to fluid overload

- Rarely, surgical incision wounds need to be left open if there is tissue swelling due to fluid overload.

- Rarely, the oxygen levels in your blood may drop due to fluid build-up in the lungs and you may have difficulty breathing, in which case, we may have to place you temporarily on a breathing machine.

- Rarely, fluid overload can cause cardiac arrest and/or death.

Risk from removing fluid rapidly

- When doctors remove fluid rapidly, your blood pressure may drop suddenly and unexpectedly. If this happens, doctors will stop removing fluid, give back more fluids, and treat with other medications, as necessary.
- Low blood pressure may result in decreased oxygen supply to internal organs resulting in the organs not working well.
- Injury to the kidney may prolong dialysis dependence as your kidneys may not improve or completely recover kidney function.
- Injury to the heart may result in irregular heartbeats.
- You may develop electrolyte abnormalities such as low potassium, phosphate or calcium levels.
- You may develop clots in the arteries or veins, anemia, low platelets and rarely destruction of red cells.
- Rarely, rapid fluid removal may also rarely cause cardiac arrest and/or death.

Risk of collecting and storing your private health information

- A risk of participating in RELIEVE-AKI clinical trial is that someone could see or use your private medical information that we collect for the study without permission. There is a chance they could figure out who you are. They could use information from your medical record against you. It could impact your employment, insurance, or family relationships. This risk is called a breach of confidentiality.
- Your confidentiality is very important to us. We will take great care to protect it. We believe the risk to your privacy is low, but it is not zero.
- RELIEVE-AKI has a Certificate of Confidentiality from the National Institutes of Health. This is another way your information is protected. It means we do not have to release private information requested by court order. This means researchers can refuse to give out information that identifies you except if:
    - there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others
    - you give permission to disclose your information, including as described in this consent form
    - it is used for other scientific research allowed by federal law

Other risks:

- There may be other risks that we don't know about yet. We will tell you if we learn anything that might change your decision to be part of the RELIEVE-AKI clinical trial.

Will you ever give my name or other information that identifies me?

There are few times when we might need to give out your name or other information that identifies you.

- We will give out information about you to protect your health or the health of others if:
    - we learn or suspect that you are being abused
    - we learn or suspect you are abusing, neglecting, or have abandoned someone who depends on you for care, like a child or dependent adult
    - we learn that you plan to harm yourself or someone else
    - we learn that you have a disease that is a risk to public health, like measles or COVID-19
    - we learn that you have a condition that is urgent
- We *may* give out any data that the people who oversee U.S. research laws and regulations need to make sure we are following the law. This may include information that identifies you. The people who oversee research are from:
    - The National Institutes of Health (NIH)
    - The University of Pittsburgh Office of Research Protections, including the Institutional Review Board (a committee that oversees the conduct of research involving human participants). The Institutional Review Board has reviewed and approved this study.
- See the related information on your HIPAA authorization on page 11.

Are there any benefits?

- You may benefit from participation
- Slow fluid removal may be better tolerated by your body and dialysis doesn't have to be stopped. There is a chance you may also recover quickly.

- Fast fluid removal may result in rapid correction of fluid overload. You may come off the breathing machine and dialysis quickly.

- You may also get no benefit from either slow or fast removal of fluid.

- If you join, you will be helping researchers make discoveries. This may help people with kidney disease in the future.

Are there alternative treatments available to treat my condition?

- If you do not participate in this study, your doctors will still remove fluid from your body using continuous dialysis as this is a standard medical treatment. However, fluid will be removed at a speed determined by your doctors and nurses and not according to the study protocol. The risks and benefits described above with slow and fast fluid removal may also still be present.

- If you have any questions related to standard of care fluid removal during dialysis, please talk to the investigator listed on the front page of this form.

New information

- You will be promptly notified if any new information we learn during this research study may cause you to change your mind about continuing to participate in this study.

Does it cost anything to participate in RELIEVE-AKI?

- You do not have to pay any money to participate in RELIEVE-AKI clinical trial. That said, if you have any complications because of participating, your hospital stay, or recovery may be longer. This could mean more time off work. If you must take extra time off, you may lose wages.

Will I receive payment?

- You will not receive any compensation for participating in this study.

Will I find out the results of the research?

- On completion of the clinical trial, results and data from the trial that will not include any personal information about you may be published in accordance with the regulatory requirements.

- Although information about this clinical trial, including the results, may be published for scientific purposes, presented or posted electronically (for example, in a clinical studies registry/database) or presented to scientific groups, your name and personal information will not be used, and your identity will not be revealed.

- During the clinical trial, new information about the risks and benefits of slow and fast fluid removal may become known. The research team will talk to you and your doctor about any important new information that is learned during this clinical trial that may affect your willingness to continue to take part in the clinical trial. This new information may also mean that you can no longer take part in this clinical trial. In any case, you will be offered all available care to treat your underlying medical condition.

Do I have to join?

- Joining RELIEVE-AKI clinical trial is voluntary. You can choose to join or not. No matter what you decide, now or in the future, it will not affect your medical care. You will not lose any benefits or rights. You will not be penalized.

- If you join RELIEVE-AKI clinical trial, you can change your mind at any time and you won't be penalized or lose any benefits for which you otherwise qualify. If you decide you want to withdraw (quit), we ask that you tell us. You can tell us by calling Dr. Murugan at 412-370-5586 or writing to us at muruganr@upmc.edu or by mail at 200 Lothrop Street, Pittsburgh, PA, 15213.

Can I be taken out of RELIEVE-AKI?

- Yes, the RELIEVE-AKI team can take you out of the study. They could remove you if they think it is necessary for your safety. The RELIEVE-AKI team will tell you if they remove you from the research study.

What if I have questions?

- We encourage you to ask questions. If you have any questions about RELIEVE-AKI, please contact Dr. Murugan at 412-370-5586 or using muruganr@upmc.edu.

- If you have questions, concerns or complaints or would like to talk to someone outside of RELIEVE-AKI about your rights as a research participant or about your experience in the study, contact the University of Pittsburgh Human Research Protection Office at 866-212-2668.

- If you experience a research-related injury, please contact: the Principal Investigator who is listed on the first page of this form. If the Principal Investigator is not available, please call the hospital operator at 412-647-2345 for 24/7 service or toll-free at 1-800-533-8762 and tell them that you are a research participant.

HIPAA Authorization for Disclosure of Protected Health Information (PHI)

- As part of this research study, we are requesting your authorization or permission to review your medical records to determine whether you meet the conditions for participation in this study. This authorization is valid for an indefinite period.

- We will document the following information in your medical record:
  - whether you agreed to speak with the research team
  - study procedures were explained to you
  - you were enrolled in the RELIEVE-AKI trial
  - a copy of the consent form was provided to you
  - name of the investigator who obtained consent from you

- We will obtain the following information from your medical records: your name and medical record number; age and date of birth; sex, race and ethnicity; home address including zip code; phone numbers and email address; history and physical examination; height and weight; past medical history; medical diagnosis; diagnostic and treatment procedures; results of laboratory tests including clinical chemistry, blood counts, and blood gasses; vital signs such as heart rate and blood pressure; fluid balance; dialysis and ventilator data; rate of fluid removal during dialysis; number of days without organ failure; clotting of dialysis machine resulting in stopping of dialysis; medications given; length of hospital and intensive care unit stay; death or dependence on dialysis and/or ventilator at hospital discharge; low and high blood pressure; abnormal heart beats; fluid overload requiring rapid dialysis; findings of organ swelling during surgery; results of X ray, CT scan, scan of the heart, and blood vessels; and any new infections occurring during your hospital stay.

- As part of this research study, some information that we obtain from you will be placed into your medical records held at UPMC. This identifiable medical record information will be made available to members of the research team for an indefinite period.

- Your medical information, as well as information obtained during this research study, *may* be shared with authorized officials from the University of Pittsburgh Office of Research Protections or the National Institutes of Health for the purpose of monitoring the study. Authorized representatives of UPMC, or affiliated healthcare providers may also have access to this information to provide services and address billing and operational issues.

- We will protect your privacy and the confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records, once your personal information is disclosed to others outside UPMC or the University of Pittsburgh.

By signing this form, you consent to participate in this research study and provide authorization to share medical records with the research team.

- We will share deidentified data with the study Data Safety and Monitoring Board. We may share deidentified data with other researchers and federal repositories in the future.

A description of this clinical trial will be available on *http://www.clinicaltrials.gov*, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

This form is not a contract. It tells what will happen if you decide to join the RELIEVE-AKI clinical trial. You are not waiving any legal rights by agreeing to participate in this study.

Remember:

- You have the right to as much time as you need to decide if you want to join. Nobody is allowed to pressure you.
- You have the right to understand all the information in this form.
- You have the right to ask questions and get answers you can understand.

If you decide to join RELIEVE-AKI clinical trial:

- You have the responsibility to participate as best as you can.
- You have the responsibility to tell us if you want to stop participating.
- You have the responsibility to tell us accurate and complete information.
- You have the responsibility to tell us right away if you are having any problems related to the RELIEVE-AKI trial.

You have a right to withdraw from this research study

- You can, at any time withdraw from this research study; you can also withdraw your authorization for us to use your identifiable medical information for the purposes described above. This means that you will also be withdrawn from further participation in this research study. Any identifiable research or medical information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.
- If you withdraw from the study intervention during the treatment period, the study intervention will be stopped but we will continue to follow up with you as part of the trial. We will ask your permission to continue to access your medical records for up to 28 days or hospital discharge (whichever comes first) for data related to the study. If you wish to withdraw from the study after completion of the study intervention, we will ask your permission to continue to access your medical records for up to 28 days or hospital discharge (whichever comes first) for the data related to the study.

- To withdraw from this research study, you should inform the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh, your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

- It is possible that you may be removed from the research study by the researchers if, for example you do not tolerate fluid removal as per the study protocol or for safety reasons. The investigator may also request follow-up for safety reasons.

- If a complication arises from this study protocol, your doctor may treat you as needed. You will still be getting all your standard medical treatment if you withdraw from the study.

Compensation for injury

- If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC.

- Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. You do not, however, waive any legal rights by signing this form.

Participation in this research is voluntary

- Your participation in this research study is entirely voluntary. You may want to discuss this study with your family and friends and your personal physician before agreeing to participate.

- As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

Informed Consent to Participate:

The above information has been explained to me and all my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any part of this research study during this study. Any future questions, concerns or complaints will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given.

I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the Human Research Protection office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation.

By signing this form, I consent to participate in this research study and provide authorization to *use and share my medical records. If I decide later to withdraw from this study, I still consent to allow for the collection of my medical record data until 28 days post-intervention or until my hospital discharge. (Check one) ___Yes ___No. A copy of this consent form will be given to me.*

_____

Signature of Participant Date / Time

_____

Printed Name of Participant

LEGALLY AUTHORIZED REPRESENTATIVE CONSENT:

_____ Participant's Name (Print)

The above-named individual is unable to provide direct consent for study participation

because: _____

Therefore, by signing this form, I give my consent for his/her participation in this research study.

_____

Signature of Legally Authorized Representative *(if applicable)* Date/Time

_____

Printed Name of Legally Authorized Representative *(if applicable)*

Statement of the Investigator who Obtained Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was started until after this consent form was signed.

Signature of Investigator	Date /Time
Printed Name of Investigator	Role in the Research Study

CONSENT FOR CONTINUED RESEARCH PARTICIPATION

I understand that I am currently participating in a research study. I further understand that consent for my participation in this research study was initially obtained from my authorized representative since I was unable to provide direct consent at the time that this initial consent was requested. I am now able to provide direct consent for continued participation in this research study and because I am still in the hospital during the 28-day post-intervention period of the study, I am being asked to self-consent to continue participation.

The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any part of this research study during the course of this study. Future questions, concerns or complaints will be answered by a qualified person or by an investigator listed on the first page of this consent document at the telephone number(s) given.

I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable. I agree to participate in this research study and provide my authorization for the use of my medical records.

By signing below, I agree to continue my participation in this research study. A copy of this consent form will be given to me.

_____

Signature of Participant Date / Time

_____

Printed Name of Participant

Statement of the Staff who Obtained Consent

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was started until after this consent form was signed.

_____ _____

Signature of Staff Obtaining Consent Date /Time

_____

Printed Name of Staff