PEARL Study

A Pilot Randomized Clinical Trial of Early Coronary Angiography Versus No Early Coronary Angiography for Post-Cardiac Arrest Patients Without ECG ST Segment Elevation

Questions and Answers About the PEARL Study

A Pilot Randomized Clinical Trial of Early Coronary Angiography Versus No Early Coronary Angiography for Post-Cardiac ARrest Patients Without ECG ST Segment ELevation (NCT02387398)

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What is the PEARL study?

Cardiac arrest, also known as sudden death, occurs when the heart suddenly stops or when it can't pump enough blood to make a pulse. Even in patients who receive prompt treatment and resuscitation, damage to vital organs, such as the brain and heart, may occur, potentially leading to death.

Heart attack is one of the most common causes of cardiac arrest. A heart attack occurs when one of the arteries that feed blood to the heart closes suddenly.

Coronary angiography (heart catheterization, or heart cath) can identify and treat a heart attack, but doctors don't know how to best identify patients who would benefit from an angiogram after cardiac arrest.

About 1 patient out of every 3 to 4 patients who would be eligible for the PEARL study after cardiac arrest has a completely blocked artery that could be treated if identified by coronary angiography. These patients seem to be more likely to survive if they have a coronary angiogram, but it's not known if all patients who receive coronary angiography after cardiac arrest will benefit or how soon after cardiac arrest the coronary angiography procedure should be performed.

The PEARL study will help answer the question, "Does an early heart cath improve survival and prevent heart muscle damage after a cardiac arrest without ST segment elevation on the ECG?"

Who will be included in the PEARL study?

Patients who are resuscitated from cardiac arrest outside the hospital will be included in the PEARL study if they meet all the eligibility criteria. Eligibility criteria describe patient characteristics that are required to be included in the study as well as characteristics that exclude patients from the study.

Inclusion criteria

PEARL study participants must meet all these criteria:

- Successfully resuscitated out-of-hospital cardiac arrest patients with a suspected cardiac etiology for their nontraumatic arrest
- Patients must be 18 years or older
- The post-resuscitation electrocardiogram (ECG) shows no evidence of ST segment elevation
- Patients must be considered clinically stable without an indication for emergent coronary angiography according to the treating cardiologist

Exclusion criteria

Patients are ineligible for the PEARL study if they meet one or more of these criteria:

- Nonresuscitated (no sustained pulse or blood pressure)
- Presence of ST segment elevation or new left bundle branch block present on the post-resuscitation ECG
- Suspected noncardiac etiology for the arrest, such as respiratory failure, asphyxia, pulmonary embolus, shock, trauma, drug overdose or central nervous system bleed, as the likely cause of the cardiac arrest
- Known do not resuscitate (DNR) status
- Minors (less than 18 years old)
- Prisoners
- Significant bleeding or blunt trauma
- Known pregnancy or pregnancy confirmed by urinalysis
- Received any other investigational therapies within the 30 days prior to enrollment or at the time of screening for study inclusion
- Known opt-out choice — that is, wearing an opt-out wristband for any exception from informed consent (EFIC)-approved study or on an opt-out list
- Clinical instability warranting emergent coronary angiography

What is the PEARL study treatment?

Patients enrolled in the PEARL study will be randomized into one of two groups: either to receive immediate coronary angiography (within 120 minutes of hospital arrival) or to receive initial medical stabilization in the intensive care unit prior to delayed coronary angiography (more than six hours after hospital arrival).

The rest of the care will be determined according to current standards of care independent of the PEARL study or group assignment.

Where will the PEARL study be conducted?

PEARL is a multicenter study performed at Mayo Clinic and other hospitals in the United States and internationally. The University of Arizona is coordinating the PEARL study.

How many patients will be enrolled in the PEARL study?

The PEARL study plans to enroll 240 patients across all the study sites.

When will the PEARL study start?

The PEARL study is expected to begin enrollment at Mayo Clinic in the fall or winter of 2016, depending on the timing of approval by the local Institutional Review Board (IRB).

How long will it take to complete the PEARL study?

PEARL study enrollment is expected to last for about two years, plus an additional six months of follow-up for enrolled patients.

How do patients become enrolled in the PEARL study?

Patients enrolled in the PEARL study will have had a cardiac arrest, a condition that often leads to brain injury.

Cardiac arrest occurs unexpectedly, and because of the inability to predict when a cardiac arrest will happen, people can't sign up for PEARL ahead of time. Patients may be unconscious or comatose and unable to speak when they are enrolled in the PEARL study because of brain injury, or they may be too sick to consent to PEARL study enrollment because of cardiac arrest.

Patients who are awake and able to consent will be asked if they want to participate in the PEARL study. For patients who can't consent, a family member or legally authorized representative will be asked to consent for the patient. If no legally authorized representative can be contacted, the patient will be enrolled in the PEARL study.

How can research be done on a person without the person's consent?

There are serious emergency medical situations in which patients are unconscious or are too sick and can't give permission to be enrolled in a study. Cardiac arrest is one of those situations. The PEARL study will be conducted under federal regulations that allow an exception from informed consent (EFIC).

What is exception from informed consent (EFIC)?

In 1996, the Food and Drug Administration (FDA) developed specific regulations to permit emergency research without prospective consent under carefully controlled circumstances. This

is in recognition of the unique kind of emergency medical situations in which patients or family members can't give informed consent before treatment, as well as the need to allow emergency care to advance through research.

According to FDA regulations, to qualify for EFIC, the research must involve participants with a life-threatening disease process or injury for which the current standard of care is associated with a very high failure or mortality rate, such as cardiac arrest. In addition, there must be reasonable evidence that the research has the potential to provide real and direct benefit to the patient. Studies must be held to the highest ethical standards.

The PEARL study has undergone multiple independent rigorous reviews to ensure that it meets these standards.

The use of a randomized clinical trial such as this is the gold standard for determining what treatment works best. For treatments that must be given immediately to be effective, EFIC research is considered appropriate by federal regulatory bodies and many ethicists who study this field. The obligation to improve standard treatments that yield poor results in life-threatening conditions is also considered an ethical imperative, as is maintaining the individual rights of citizens.

In EFIC trials, citizens receive standard treatment in addition to research treatment. To be tested in this fashion, the research treatment has to have shown promise in earlier studies.

In the case of the PEARL study, both randomized treatment groups are within the current standard of care provided across the United States and internationally.

If a family member is present when the patient has a cardiac arrest, will the family member be asked for permission to allow the patient to be enrolled in the PEARL study?

Yes, if the family member is the patient's legally authorized representative.

After the patient is evaluated and determined to be eligible for the PEARL study but unable to consent, the study team will attempt to contact the patient's family member or legally authorized representative to consent for the patient if feasible. If no legally authorized representative can be contacted within the study time window, the patient will be enrolled in the PEARL study under the EFIC process.

In order to give permission to participate in a research study, it's important that the person giving permission understands what is being said and can make a well-informed decision.

Cardiac arrest is an extreme emergency during which the patient could potentially die if treatment is delayed. Patients who have had a cardiac arrest are usually too sick or are unconscious and can't give permission to discuss their treatment, and any time that's taken to discuss their treatment with the family may deprive the patient of immediately starting life-saving measures. In addition, the family of a cardiac arrest patient may be too upset to discuss

the risks and benefits of study enrollment. For these reasons, patients who have had a cardiac arrest may be enrolled in the PEARL study under the EFIC process.

When will patients or family members be told about the PEARL study?

Patient will be told about PEARL if and when they awaken and are able to understand the discussion. When they're able to provide informed consent directly, they will be approached about consent.

If patients deny consent, they will no longer be followed for study purposes, but their data obtained prior to refusing consent can be included in the study. If they provide consent, they will be followed for six months, including at least two clinical follow-up visits and follow-up testing appropriate for cardiac arrest survivors who aren't enrolled in a research study.

The family member or legally authorized representative will be informed about the PEARL study as soon as he or she can be contacted by study staff, although this may not occur until after the patient is enrolled and randomized. Patients and their family members or legally authorized representatives will be given the opportunity to withdraw from further study participation and will be provided instructions about how to do so.

Are there any risks to patients from PEARL study participation?

The coronary angiography (heart catheterization, or heart cath) procedure has a number of potential risks. The PEARL study is only investigating the timing of when to perform coronary angiography, not whether to perform coronary angiography.

Therefore, it's expected that all patients in the PEARL study (regardless of randomized study group) will undergo a coronary angiography at some time, so all study patients will be exposed to the potential risks of the procedure independent of their study group assignment.

Prior studies have suggested that early coronary angiography in patients with cardiac arrest from a heart attack may reduce injury to the heart and might decrease the risk of death, but this has not been proved. Delaying coronary angiography in a patient with a heart attack may be harmful in this way.

Complications from the coronary angiography procedure (such as bleeding) may be more frequent in patients who receive an emergency procedure (as in the early coronary angiography study group).

The PEARL study is designed to determine the balance between the potential benefits and risks of early coronary angiography. The PEARL study design specifically excludes patients who are felt to require coronary angiography based on clear evidence of a heart attack (ST elevation) or severe illness (unstable), because these patients could not be randomized. The decision to randomize a patient in the PEARL study will require a discussion with the treating cardiac intensive care unit physician.

Can people opt out of this research?

Yes. The PEARL study team will provide an opt-out mechanism for patients who don't want to be enrolled in this research study at Mayo Clinic if they have a cardiac arrest.

To request a free opt-out wristband, email the research team or call 507-538-7178.

Potential study patients who are wearing an opt-out wristband will be automatically excluded from enrollment.

The opt-out wristband must be on at the time of the cardiac arrest or the patient may be enrolled in the study if eligible. If the opt-out wristband is lost during the process of resuscitation from cardiac arrest, the patient may be enrolled in the study if eligible.

Visit the PEARL study website for more information.