Clinical trial fails to disclose risk of death, repeat heart attacks, advocacy group says

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A clinical trial testing blood transfusion therapies for heart attack patients may place participants in danger of death or a repeat heart attack without fully disclosing those risks, a Washington, D.C.-based consumer advocacy group said Tuesday in a letter asking federal health officials to immediately suspend enrollment in the study, which is recruiting patients at dozens of hospitals, including Mount Sinai Medical Center in Miami Beach.

The nonprofit consumer advocacy group, Public Citizen, claims the clinical trial, which is designed to compare two red blood cell transfusion strategies for heart attack patients with anemia, fails to inform participants of previous studies that strongly suggest one method is more likely to result in death or a repeat heart attack.

"Those are serious end points," said Michael Carome, a physician and director of Public Citizen's health research group. "This isn't measuring what your appetite is or how far you can walk. This is measuring serious outcomes that have tremendous importance for the subjects."

Carome added that the patient consent form should explicitly state the risk of death, repeat heart attack or cardiac surgery as a result of participating in the study. "The consent form is completely silent on that," he said.

But the principal researcher for the study, Dr. Jeffrey Carson of Rutgers University in New Jersey, said in a written statement that he stands

behind the science and the ethics of the study, called the Myocardial Ischemia and Transfusion or MINT trial. The study is being funded through a $16.1 million grant from the National Institutes of Health.

The clinical trial "seeks to answer an important question about the optimal amount of blood transfusion that we give to patients with low red blood cell counts who have had a heart attack," Carson's statement read. "Previous small trials do not provide adequate data for accurate predictions, which is why the NIH funded this high-quality large trial. The health and safety of our participants is our top concern."

He added that the MINT trial's research methods have been vetted by his peers at Rutgers and other institutions.

"Our protocols have been reviewed by more than 35 institutional review boards across the country, as well as the Data Safety Monitoring Board, which is an independent organization comprised of physicians and ethicists," he said.

According to a brief description of the study posted on the NIH-sponsored website, clinicaltrials.gov, Carson and other researchers aim to recruit 3,500 heart attack patients with anemia at dozens of hospitals across the country, including Mount Sinai.

Jackie Kaplan, a spokeswoman for Mount Sinai, said the hospital was selected to participate in the study but has not yet begun to recruit patients. The hospital sees about 1,500 heart attacks patients a year.

Patients participating in the study will be randomly assigned to one of two blood transfusion therapies based on their red blood cell or hemoglobin levels. Some patients will be assigned to a "liberal" group, which means they will receive red blood cell transfusions whenever their hemoglobin level falls below 10 grams per deciliter.

The second group will be assigned to a "restrictive" group, which means they will receive red blood cell transfusions only when their hemoglobin level falls below 8 grams per deciliter.

Researchers will then measure how many subjects in each group die, have another heart attack, or require cardiac surgery within 30 days, according to a detailed description of the clinical trial.

The study's primary hypothesis states that a liberal transfusion strategy reduces adverse outcomes compared with a restrictive approach. But Carome, with Public Citizen, said previous studies already provide "strong signals" that a liberal approach is less likely to harm patients.

An NIH analysis of 16 randomized trials comparing liberal and restrictive transfusion strategies for heart attack patients found a higher risk of death and major cardiac events associated with a restrictive approach.

A pilot study for the MINT trial published in the American Heart Journal in June 2013 also suggested that patients were more likely to die from a restrictive approach compared with a liberal one. Of the 110 patients recruited for the study, seven died after a restrictive strategy compared with one who died after a liberal approach.

"It's not a definitive proof," Carome acknowledged, "but it certainly is very strongly suggestive, and the data is consistently suggestive that there is harm with a restrictive transfusion group."

Still, the question of whether a liberal or restrictive blood transfusion strategy works best for heart attack patients with anemia remains unanswered - and that uncertainty is all researchers need to justify a randomized clinical trial, said William Allen, a University of Florida medical ethicist who reviewed Public Citizen's letter to federal

regulators at the Miami Herald's request.

"One of the big problems in evidence-based medicine is to eliminate variability in practice," he said.

But while studies help doctors determine the best treatments, randomized clinical studies like the MINT trial can blur the lines between a physician, who is obligated to do what is best for the patient, and a researcher, who is trying to find the answer to an unresolved question.

When the roles of physician and researcher intertwine, Allen said, patients can get confused.

"If you're randomizing people to two arms of a protocol, obviously the physician isn't using their best judgment about what's best for that patient because you're deciding randomly," Allen said. "Normally, when you go to a doctor, you don't expect him to do by chance what's best for us."

That's one reason why researchers should clearly state the risks for patients who want to participate in the MINT trial. He noted that the consent form states the purpose of the study is to determine if patients who receive blood transfusions "do better or worse."

"Well, that's pretty vague," Allen said. "It doesn't clearly say they're trying to figure out which one results in less death and heart attacks in the next 30 days."