radcliffe cardiology

Title: ACC.24: Preventing Chemotherapy-Related Heart Damage in Patients with Breast Cancer and Lymphoma: PROACT
Faculty: Dr David Austin
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Dr David Austin

"My name is David Austin. I'm a consultant cardiologist at the James Cook University Hospital in Middlesbrough. I'm an honorary clinical senior lecturer at Newcastle University in the UK.

Study Significance

This is an important study for the survivors of breast cancer and non-Hodgkin's lymphoma. These patients receive cardiotoxic medications as part of the management of their primary disease. And really, this is about trying to reduce the impact of these important therapies on the quality of the patient's survival.

Study Overview

PROACT is a study aimed at preventing the myocardial injury or cardiac damage associated with anthracycline chemotherapy. Anthracycline chemotherapy, such as doxorubicin or epirubicin, is commonly used in conditions such as breast cancer and non-Hodgkin's lymphoma. The study is a multicenter randomised control trial assessing the ACE inhibitor enalapril to determine whether enalapril can prevent the myocardial injury that occurs during chemotherapy and prevent what's called cancer therapy-related cardiac dysfunction (CTRCD).

Primary and Secondary Endpoints

The primary endpoint of the PROACT clinical trial was the detection of myocardial injury, as determined by highly sensitive cardiac troponin T. We also had secondary endpoints, including cardiac troponin I and cardiac function assessed by echocardiography. These

were all done in a blinded fashion in core laboratories to ensure the quality of the findings.

Findings

We found that enalapril, when titrated to 20 milligrammes daily, did not impact the myocardial injury caused by anthracycline chemotherapy. This was consistent across both troponin T, troponin I, and across the cardiac function measured by LV global longitudinal strain and left ventricular ejection fraction.

Implications

What we have are negative findings, but this provides a definitive answer in this particular area, particularly because we recruited patients receiving the highest dose anthracycline chemotherapy, a main risk factor for developing heart failure at a later stage. This study suggests that we should not be studying enalapril further in this setting for prevention. Although current guidelines suggest monitoring these patients closely, it might be that if they develop cardiotoxicity subsequently, these therapies can still be useful, but perhaps not in a preventative fashion given prior to the commencement of chemotherapy.

Future Directions

The next steps for the PROACT trial involve following up the patients for longer with late echocardiography and late clinical follow-up to ensure there is no delayed effect or even a delayed benefit of enalapril in this setting. It's also important that we, as a cardio-oncology research community, look at pooling our data. These clinical trials are very challenging to perform, and understanding some of the event rates, such as moderate or more severe cancer therapy-related cardiac dysfunction, can help us plan future trials."