Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/opening-statements-holding-court-in-ph-should-all-adult-fontan-patients-be-placed-on-pah-group-1-therapy/14243/

Released: 10/28/2022
Valid until: 10/28/2023
Time needed to complete: 54m

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Opening Statements - Holding Court in PH: Should All Adult Fontan Patients Be Placed on PAH Group 1 Therapy?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

The views you are about to hear are not necessarily the exact viewpoints of the participating physicians. They are expressed for the purpose of presenting differing points of view in this unique medical education setting, exploring best practices in the treatment of PAH patients.

Dr. Elwing:
Welcome members of the jury. Today we have a case for you to try. Should all adult Fontan patients be placed on PAH Group 1 therapy? As a member of the jury, you'll be asked to listen and vote for the best result to the cases mentioned. And now, ladies and gentlemen, please welcome the Honorable Judge, Dr. Richard Krasuski of Duke University.

Dr. Krasuski:
Pulmonary Hypertension Court is now in session. Welcome, ladies and gentlemen to Holding Court in PAH. Fontan palliation has revolutionized the care of single-ventricle patients by creating a stable passive circulation that can last for decades, but it is the expectation that failure is an inevitability. In the absence of an effective right ventricle, even a slight increase in the pulmonary vascular resistance could result in low cardiac output with extravascular fluid accumulation, protein-losing enteropathy, hepatic congestion, and cyanosis. All of which are associated with increased mortality. Recent data indicate a unique pattern of adverse pulmonary vascular remodeling in long-term Fontan circulation that may be contributory to these hemodynamic changes and adverse outcomes.

Staged single-ventricle palliation and the Fontan operation have undergone many iterations over the past five decades. It was originally thought that the atrial systole was essential to propel blood forward. Thus, the entire right atrium was incorporated into the circuit with the appendage and astemos to most of the pulmonary artery, the so-called atrial pulmonary connection or APC Fontan. This is now known not to be necessary, and that incorporating the right atrium results in increased risk for rhythm abnormalities and for blood clots. Instead, blood is routed through the atrium via lateral tunnel or connected via tube from the inferior vena cava directly to the pulmonary arteries.

Pulmonary arterial hypertension is commonly associated with congenital heart disease and relates to the type of underlying cardiac defects and repair history. Patients with a Fontan circulation, despite not strictly fulfilling criteria for PAH, may develop elevated pulmonary vascular resistance. There is some recent evidence suggesting that these patients may benefit from targeted vasodilator therapy, but more data are required before general recommendations can be made. This then forms the crux of the court argument here today. Given the high-risk nature of vascular and cardiac aberrations in Fontan patients and their risk for hepatic and other complications, should these patients routinely be prescribed Group 1 vasodilator therapy to offset potential changes in PVR? This will be decided by you, the jury. To argue today's case, we have two very accomplished attorneys. Dr. Jamil Aboulhosn, Director of the

Ahmanson/UCLA Adult Congenital Heart Disease Program in Los Angeles, California will be arguing the pro-side that all adult Fontans should be receiving Group 1 PAH medications. Dr. Joseph Kay, Professor of Pediatrics and Internal Medicine and the Program Director of the Colorado Adult and Teen Congenital Heart Disease Program at the Children's Hospital in Colorado will be arguing the concept that Fontan patients should not all be receiving Group 1 PAH medications. Both attorneys will be calling witnesses to support their arguments. Dr. Aboulhosn, you may begin with your opening statement.

Dr. Aboulhosn:
Thank you, your Honor. Ladies and gentlemen of the jury, there is no question that single ventricle patients who have undergone Fontan corrective surgery remain at risk for developing pulmonary arterial hypertension. Nowadays, most patients undergoing a Fontan procedure will survive into adulthood. We know this, but mortality is still estimated to increase by about 10% per decade. Based on physiologic considerations, there's a linear relationship between central venous pressure and pulmonary arterial resistance which also has been supported with clinical data. As a consequence, a mild increase in pulmonary arterial resistance needs to result in a marked increase in central venous pressure to maintain cardiac output. Consequently, low pulmonary arterial resistance is necessary to sustain adequate pulmonary blood flow at a low central venous pressure. However, central venous pressure is invariably elevated even in a well-functioning Fontan patient with an inherent risk of complications related to this chronic venous hypertension and circulatory failure. Now, let's go back a little bit. Before a cavopulmonary connection is established in patients with a univentricular heart, the single ventricle is commonly exposed to abnormal loading conditions. Therefore, the Fontan circulation is prone to fail. There is some evidence suggesting that chronic pulmonary vascular processes lead to progressive elevation of pulmonary arterial resistance, systolic and or diastolic ventricular dysfunction, obstruction of the Fontan pathway, elevated pulmonary arterial resistance. All of these can aggravate chronic systemic venous hypertension and lead to symptoms of heart failure such as ascites, peripheral edema, hepatomegaly, splenomegaly. Or they can result in specific complications related to the lymphatic system such as plastic bronchitis or protein-losing enteropathy. Now, what can be done to palliate this progressive loss of pulmonary vascular function and the normal regulatory processes that control vascular tone and reactivity in the pulmonary arterial tree? Should we do nothing? No, I don't think so. As pulmonary arterial resistance modulates pulmonary blood flow and systemic ventricular preload in Fontan patients, pulmonary vasodilators obviously should improve cardiac output. Now, you pick the way you want to look at exercise capacity. Okay, six-minute walk test, anaerobic threshold on cardiopulmonary exercise testing, peak VO2, oxygen pulp, time on exercise testing spent on the treadmill or on the bike, or an increase in cardiac index with exercise. All of those have indeed been shown to improve in a number of small trials. Now we're talking about Fontans here. You're not going to have a trial of a thousand patients. So please let's you know have appropriate expectations for these trials. Thank you, Judge.

Dr. Krasuski:
We have heard the opening statement from the prosecuting attorney. Dr. Kay, would you care to make an opening remark?

Dr. Kay:
Thank you, Your Honor. What is clear is that the pulmonary hypertension observed in Fontan-corrected univentricular patients, especially in adulthood, is not your mother's pulmonary hypertension. In the absence of a right ventricle and with pulmonary blood flow being driven by passive central venous flow, the usual pulsatile influences of cardiac output on the pulmonary vasculature and endothelium are largely absent. To examine the merits of using Group 1 PAH medications in Fontan patients, we need to look carefully at the available clinical trial evidence to determine if this is indeed a valid approach to managing these patients. In point of fact, there is only one randomized controlled trial showing efficacy on the primary endpoint for a therapy was sentin in adults with Fontans. Other trials have really failed to show efficacy in reaching the primary endpoints of the study. It is even likely that some Group 1 vasodilators may make patients worse. If these are used in the wrong type of Fontan patient, there may be a drop of systemic vascular resistance. And because of this, careful assessment is needed before considering initiating a therapy. PVR is one of the main determinants of cardiac output in the Fontan patients. The degree of elevated transpulmonary gradient in which PAH therapy would help in Fontans has really not been identified to date. Moreover, what combination of pulmonary vascular resistance, mean PA pressure or transpulmonary gradient is indicative of the patient who will likely benefit from these medications still is not clear. In summary, there are pathophysiologic situations that may support the use of pulmonary vascular dilators in patients with Fontan failure and elevated PVR, but scientific evidence is quite scarce. To date, although safe and well tolerated, there is no evidence that prophylactic pulmonary vasodilator therapy has an impact on prognosis of the entire group of Fontan patients. We intend to show that current published experience does not support proactive pulmonary vasodilator therapy in well-functioning Fontan patients with low pulmonary artery pressures in low PVR. Thank you, Your Honor.

Dr. Krasuski:
Thank you both for your opening remarks. We will now proceed to the evidentiary portion of the trial.

Announcer:

You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.