

BroadcastMed | Right Ventricular Dysfunction in HFpEF: No Innocent Bystander

DR. JEFFREY GESKE: Greetings I'm Dr. Jeffrey Geske, assistant professor of medicine at Mayo Clinic. Today we will be convening a roundtable review discussing two recent publications. Right ventricular function and heart failure with preserved ejection fraction, a community based study which was recently published in circulation in December of 2014, as well as right heart dysfunction in heart failure with preserved ejection fraction, which was published in the European Heart Journal in December 2014. I'm joined today by my colleagues Dr. Barry Borlaug, Dr. Margaret Redfield, and Dr. Selma Mohammed. Thank you so much for joining us.

DR. SELMA MOHAMMED: Thank you for having us.

DR. JEFFREY GESKE: For someone who might not have read one or both of these articles, can you tell us a little bit about what the study objectives were and how the studies differed?

DR. SELMA MOHAMMED: Our study included heart failure community cohort from All State County, Minnesota and this is a very well characterized cohort of heart failure with preserved EF. We've used two highly feasible measures of right ventricular function, namely tricuspid annular plane systolic excursion which is a quantitative measure as well as semi quantitative assessment to assess right ventricular function. We also had longer term outcome on these patients with follow up up to 10 years for heart failure hospitalizations all causing cardiovascular mortality.

DR. JEFFREY GESKE: And tell me a bit about the other study.

DR. BARRY BORLAUG: Jeff, so our study was a bit smaller in a cath lab based study, so not as sort of representative of the community in general. But by having the invasive data, it gave us a little bit more mechanistic insight into the load dependence of right ventricular dysfunction, the impact of pulmonary hypertension, and to kind of explore some of the reasons why these patients develop that. We also have outcome data, but again, with the caveat of being a referral population. So I think the two studies really complement one another.

DR. JEFFREY GESKE: Now, I know that right ventricular dysfunction is common in patients with heart failure with reduced ejection fraction. What do we know about it in patients with preserved ejection fraction and why look at that?

DR. MARGARET REDFIELD: Well I think it's important to look at it for several reasons, but first and foremost is just to assist in clinicians recognizing hfpef when they see it. So when they see a patient with symptoms of heart failure, EF is normal but the RV is bad, they need to put hfpef in the differential as they're thinking about pulmonary hypertension and RV infarction-- other things that can be associated with a normal EF and RV dysfunction. So I think that's very important to help people recognize hfpef. I think by starting to understand the right ventricle and hfpef, you get some insights into the pathophysiology. And Barry and Selma will talk a little bit more about that-- why do they get RV dysfunction. And then, as you mentioned, we know RV dysfunction in hfpef is a poor prognostic marker. So understanding the implications of RV dysfunction and hfpef is important to help people recognize potentially a high risk hfpef patient.

DR. JEFFREY GESKE: How do we go about defining what right ventricular dysfunction is and how often do we see it in these patients with preserved ejection fraction?

DR. SELMA MOHAMMED: Assessing right ventricular function is very challenging and this is well known. In the community, we have utilized two measures of right ventricular dysfunction and prevalence does vary depending on which measure we use. When using TAPSE or quantitative assessment, right ventricular dysfunction was present in as much as about 1/3 of the hfpef population, whereas when we use semi quantitative assessment, the prevalence is less common, but still about 1/5 of subjects was hfpef had evidence of right ventricular dysfunction.

DR. JEFFREY GESKE: Knowing that it's that common, do you think we're just seeing a bad right ventricle-- that this is intrinsic to the myocardium and the ventricle itself? Or are we seeing a reactive process to pulmonary hypertension.

DR. BARRY BORLAUG: Well, it's probably a little bit of both, Jeff, and that was one of the keys behind our doing the invasive study. Because if you think about it, the relative after load mismatch that the right ventricle sees in patients with pulmonary hypertension is staggering. Normal PA systolic pressure would be about 25, and these patients with pulmonary hypertension it's about threefold higher than that. Contrast that to the left ventricle, which maybe sees hypertension which is about 180 versus 130 millimeters of mercury.

So this would be like a left ventricle seeing a pressure of 300 400 millimeters of mercury. So in patients with pulmonary arterial hypertension-- or group 1 pulmonary hypertension-- they actually have enhanced right ventricular contractility. So if you measure with a conductance catheter, they have their ventricles-- their right ventricles are stronger than ours. But they have low RV fractional area change or TAPSE or some of these other markers because of after load mismatch because they're trying to eject against such a high pressure.

So we measured both the fractional shortening-- or the RV fractional area change-- and we scaled that to the pressure that we saw in the hfpef patients. And when we do that, we see that they're not only as after load mismatch, but there is intrinsic myocardial dysfunction. So to state it differently, for any PA pressure, the extent of shortening of the right ventricle is significantly shifted downward indicating it's a bad RV, unlike the PHH type patients where it's more of an after load mismatch. The other thing that we saw is that when you plot the fractional area change of the right ventricle versus the pressure load, there's a steeper drop off, indicating that there's heightened after load sensitivity which could have some important implications for treatment. Unloading the right ventricle might be more beneficial in these patients.

DR. JEFFREY GESKE: What other things do we know looking at patients who have right ventricular dysfunction and heart failure with preserved ejection fraction versus those that don't? What do we know about differences in those cohorts?

DR. BARRY BORLAUG: Well, in our study-- and I'll let Maggy and Selma comment what they found. But we observed that things like New York heart class were worse, kidney disease was worse, but some of the strongest predictors were coronary disease, the presence of atrial fibrillation-- which may have a causal relationship as well-- and evidence of what we call ventricular interaction. So as the left ventricular function-- both systolic function-- got worse, we saw more of a drop off in RV function. And part of that's probably related to the septum and how that contributes to RV shortening in these patients. So even a little bit of depressed LV function can really impair the RV function as well.

DR. SELMA MOHAMMED: We too have found strong association with atrial fibrillation and expected the association was pulmonary artery systolic pressure as well as frequency of right ventricle pacing in our community cohort. Our study was more cross-sectional so we cannot really establish causality, but it's very intriguing going forward to look at how these factors play into right ventricular dysfunction and failure in the hearts of population.

DR. MARGARET REDFIELD: And they also had worse diastolic dysfunction-- LV diastolic dysfunction-- the patients who had RV dysfunction as well. And a higher prevalence of RV pacing which is potentially another etiology contributing to their RV dysfunction.

DR. JEFFREY GESKE: Knowing those differences between the groups, did you find a difference in outcomes?

DR. MARGARET REDFIELD: Well in Selma's study, yes, we found that even adjusting for the level of pulmonary hypertension and pertinent co-morbidities, patients with RV dysfunction-- as espoused by semi quantitative assessment-- had worse survival and shorter time to first hospitalization and to all time hospitalization. And the same prognostic implications were seen when you use TAPSE to define LV dysfunction. But it wasn't as strong a predictor as actually the semi quantitative assessment and perhaps it's because not just the isolated longitudinal impairment in RV contractility, but also radial. Maybe more of akin to the RV fractional area change that you measured in yours. And you also found association with worse mortality.

DR. JEFFREY GESKE: Well, this brings up in my mind are we seeing the chicken or the egg here? Is right ventricular dysfunction just a marker of an adverse phenotype that's going to have worse prognosis, or do we think that the right ventricular dysfunction is driving that outcome?

DR. BARRY BORLAUG: Well, it's hard to say in a cross-sectional study like this obviously. We'd need more of a longitudinal study or we'd need to have some intervention to fix it and see if things get better to have more insight into that. But I think it's probably both. I think it's probably a marker of-- Maggy mentioned more severe LV diastolic dysfunction, more pulmonary hypertension. So all the things that lead to that are more severe. So it is kind of traveling with the other things that cause adverse outcome. But the fact that it is still predictive of higher mortality above and beyond that suggests it, along with just the biological plausibility-- that is your RV fails, you're going to get more systemic venous congestion, liver dysfunction, cardiorenos, all these other things that are sort of upstream of the right ventricle are going to be compromised.

DR. JEFFREY GESKE: Great. You know, sitting here next are heart failure experts, sometimes I just want the bottom line. So for the clinician out there who's watching, what is the take home point that they should be using in their day to day practice as far as reading both of these studies and using that data?

DR. SELMA MOHAMMED: First and foremost, I think I'd like to emphasize importance of right ventricular function and heart failure in general, and heart with preserved ejection fraction in particular. They right ventricle is critical to prognosis and the signify advanced heart failure phenotype, and therefore should not be considered an innocent bystander. Second measurement of right ventricular dysfunction should be an integral part of echocardiographic assessment of heart failure subjects.

And from our study, we found that even if quantitative measurements may not be feasible, semi quantitative-- or even visual assessment-- does provide significant prognostic information. And third, we don't really know if there is causality between what we have observed with high prevalence of atrial fibrillation and RV pacing, but attempts should be made to treat or prevent right ventricular dysfunction by attempting rhythm control in these subjects and minimizing right ventricular pacing. And obviously also unloading the right ventricle as Doctor Borlaug mentioned earlier.

DR. JEFFREY GESKE: And what are the next steps research wise? What are the questions that are looming in your mind that we still need to answer?

DR. MARGARET REDFIELD: Well I think Selma touched on some of those. In hfref we haven't had great luck with rhythm control as a strategy to improve outcomes. But I think in the hfpef population we need to think more than about outcomes. We need to think of how these patients feel. So I think exploring rhythm control in hfpef is still an important area that we need to look into. We've seen some anecdotal cases of dramatic improvement in their overall clinical status with rhythm control. Now we just need to figure out who those patients are and which ones will respond.

I think I'm very interested in what Barry alluded to-- is this all a reaction to the pulmonary hypertension. And group 2 pulmonary hypertension-- the type that comes from chronically elevated left atrial pressures-- may impose a unique load on the RV. And so looking at measures to reduce left atrial pressures may be a way to assess preservation of RV function. And I'm very intrigued about cardiomechs. That device monitors PA pressures as a surrogate for left atrial pressures. And the study showed that if you manage to keep those pressures down, you reduce heart failure hospitalizations in hfpef. And we'd be very interested in looking at the impact of managing to PA pressures on RV function as part of the mechanisms why patients did better when they were managed to pressures.

And then we're always looking for new drugs. Barry has a very interesting study he's completed that we hope will be published soon about a unique way to drop filling pressures and studies looking at that drug to preserve RV function and improve outcomes in hfpef will be important.

DR. JEFFREY GESKE: Well thank you so much for all these interesting insights with regards to right ventricular dysfunction and heart failure with preserved ejection fraction. And thank you to our viewers for joining us. We hope that you'll continue to follow the roundtable review series at theheart.org on Netscape.