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ECG Markers as Predictors of Adverse Outcomes in COPD: Insights from the IMPACT Trial

ReachMD Announcer:

You're listening to *On the Frontlines of COPD* on ReachMD. And now, here's your host, Ryan Quigley.

Ryan:

This is *On Frontlines of COPD* on ReachMD, and I'm Ryan Quigley. Here with me today is Dr. Chad Wade, who is an Assistant Professor at the University of Alabama at Birmingham, School of Medicine. Together, we'll be exploring insights from a post hoc analysis of the IMPACT trial, where two electrocardiographic markers—CIIS and P pulmonale—emerged as potential predictors of adverse outcomes in patients with COPD. Dr. Wade, welcome to the program.

Dr. Wade:

Glad to be here. Appreciate you having me.

Ryan:

It's a pleasure to have you. So, Dr. Wade, to start, can you briefly walk us through how the IMPACT trial's study design and existing data shaped your analysis?

Dr. Wade:

Yeah. So IMPACT was a very large, randomized trial comparing once-daily triple inhaler therapy with umecclidinium/vilanterol/fluticasone, otherwise known by its brand name TRELEGY, to dual inhaler therapy with either a LABA/LAMA, which in this case was umecclidinium/vilanterol, or a LABA/ICS, which in this case was vilanterol/fluticasone. So the study enrolled over 10,000 patients with moderate to severe COPD and a history of exacerbations. Due to the study's large size and phenotype population as well as the rigorous capture of adverse events, IMPACT contains a wealth of information to understand the COPD population at large beyond what the original study even demonstrated.

Ryan:

And now, what led you to investigate CIIS and P pulmonale specifically as prognostic indicators in this population, and what methods did you use to assess them?

Dr. Wade:

Cardiac injury infarction score, or CIIS, is a well-established ECG biomarker. It was originally used in cardiology to measure the extent of myocardial injury after a myocardial infarction. It has also been found to be predictive of mortality when the score is greater than 20, which was in a Scandinavian study of COPD patients. So that was the reason we chose CIIS as well as the score greater than or equal to 20. It was based upon this prior data in COPD.

P pulmonale is a marker of right atrial enlargement, which is prevalent in patients with underlying pulmonary hypertension. Pulmonary hypertension has been shown to be a risk factor for increased disease, morbidity, exacerbations, and mortality in COPD, and so we chose to use P pulmonale due to its increased sensitivity in this population.

The goal of the study was to really see if we could validate these markers using data from IMPACT since the study is so much larger than our typical COPD studies, and we hypothesized that these ECG biomarkers could be used as a sort of noninvasive evaluation for underlying ischemic heart disease in pulmonary hypertension. We also wanted to explore relationships—not just with the biomarkers and outcomes, but also with these biomarkers in COPD treatment overall.

Ryan:

That's interesting. Now, with all that in mind, Dr. Wade, let's zero in on the findings. What did the study reveal about the risk of death, hospitalizations, and exacerbations in relation to CIIS and P pulmonale?

Dr. Wade:

By analyzing these ECG biomarkers in nearly 10,000 patients from IMPACT, we found that a CIIS greater than or equal to 20 was associated with an increased risk of all-cause mortality, a composite outcome of hospitalization or death, cardiovascular adverse events, and exacerbations, both moderate and severe—which in this case, severe were exacerbations requiring hospitalization. For P pulmonale, the presence of this biomarker was, again, associated with increased risk of death, the composite outcome of hospitalization or death, and exacerbations, both moderate and severe.

Ryan:

For those just tuning in, you're listening to *On the Frontlines of COPD* on ReachMD. I'm Ryan Quigley, and I'm joined by Dr. Chad Wade about his recent study on two electrocardiographic markers that could be predictors of adverse outcomes in COPD patients.

Now, as I understand it, Dr. Wade, the study also looked at treatment response to different triple versus dual therapy combinations, so can you walk us through those results?

Dr. Wade:

It's one of the more interesting aspects of our study. Because of IMPACT's large size and the fact that it was comparing inhaler combinations we commonly use in practice, we were able to investigate associations between these ECG biomarkers and outcomes in each treatment group in IMPACT. We found that the single inhaler triple therapy TRELEGY—or fluticasone/umeclidinium/vilanterol—was associated with a reduced risk of cardiovascular adverse events as compared to umeclidinium/vilanterol, which was the inhaler not containing ICS. The other findings we saw that favored the single inhaler triple therapy were similar to those in the IMPACT trial overall: that a closed triple inhaler reduced the risk of exacerbation and hospitalization or death as compared to either dual inhaler.

Ryan:

Given all of these findings, Dr. Wade, how might they influence clinical risk stratification or decision-making in COPD care?

Dr. Wade:

Findings from the study suggest that these ECG biomarkers are important to identify patients at an increased risk of cardiovascular disease from either ischemic heart disease, which is what CIIS is assessing, or pulmonary hypertension, which is what P pulmonale is assessing. Both of these conditions are prevalent and detrimental in COPD patients, but we don't have a widely available consensus method to screen for them in COPD. Also, our findings of a closed triple inhaler therapy reducing cardiovascular risk is very interesting and suggest that these agents could be evaluated further in COPD patients who are at increased cardiovascular risk.

Ryan:

These are certainly encouraging findings. Now, to end our discussion, Dr. Wade, what future prospective research would you prioritize to validate or expand on the findings from this post hoc analysis?

Dr. Wade:

Even with the number of treatments for COPD, we as a field haven't made a meaningful IMPACT on the mortality in this disease. Cardiovascular disease kills nearly as many COPD patients as respiratory issues, but we don't have any specific way, like I mentioned, to evaluate for this, nor do we have any specific treatments for it. So I think focusing on identifying COPD patients who are at increased cardiovascular risk and exploring treatments targeting this population should really be prioritized in future research to try and improve this mortality in COPD.

Ryan:

Well, as those forward-looking thoughts bring us to the end of today's program, I want to thank my guest, Dr. Chad Wade, for joining me to share these findings on an emerging area of cardiopulmonary care. Dr. Wade, it was great having you on the program today.

Dr. Wade:

Thank you, Ryan, I enjoyed the opportunity.

ReachMD Announcer:

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