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<https://reachmd.com/programs/cme/finding-the-patient-with-ph-among-us-how-we-optimize-treatment-based-on-patient-type/26442/>

Released: 07/22/2024

Valid until: 07/22/2025

Time needed to complete: 1h 03m

### ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

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## Finding the Patient With PH Among Us: How We Optimize Treatment Based on Patient Type

### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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### Dr. Channick:

We will now discuss risk stratification refinements with inclusion of hemodynamic variables at follow-up in patients with PH. Do you know what it's telling us about the evidence for alternative approaches to risk?

This is CME on ReachMD, and I'm Dr. Rich Channick.

So as with a lot of diseases, pulmonary arterial hypertension is not one condition, and all patients don't have the same prognosis. There are many, many factors that go into what is predicted outcomes for these patients.

Of course, now, with the advent of multiple effective therapies, it becomes really critical not just to prognosticate for the patients, but to really guide therapy based on how a patient is doing in the very broad sense.

And just again, by way of background, how a patient is doing can be measured in a lot of different ways. There's subjective parameters, how a patient is functioning or feeling, what their symptoms are like. There's more objective parameters, like 6-minute walk test or exercise capacity. And then there's the more objective parameters, such as blood tests, let's say, a BNP level, or even right heart catheterization to look at hemodynamics, echocardiography looking at right ventricular function. So all of these ways we have now to measure how a patient is doing and risk stratify that patient are really at our disposal.

With that in mind, it becomes very important to develop a system for stratifying these patients beyond just a very gestalt type of system. And so many investigators over the last several years have, using large registries of patients with pulmonary artery hypertension, developed different ways to risk stratify these patients. There's the Swedish registry. There's something called the COMPERA registry. There's the REVEAL risk score, which is a commonly used one. There's the French approach to risk stratification.

And these have been very useful in helping us determine how a patient is doing before they start therapy and on therapy, to help us determine what to do next and to give us some ability to prognosticate for these very heterogeneous patients.

More recently, this has been refined more. One of the observations was that many patients on treatment improve but remain in what we call intermediate risk. So they're not in the low-risk category, which I think consistently shows a very good prognosis, and they're not in the high-risk category, which suggests a poor prognosis and may require more aggressive treatment or even lung transplantation. But that intermediate group is a pretty large group, and it turns out that about 60% of patients remain in intermediate risk after initial therapy. And that therapy is often combination therapy, not the topic for this talk. But because that large group remains, there's been even further efforts to try to stratify those patients in the intermediate risk a little bit further.

And several years ago a group, a European group, looked at that intermediate risk and found you could stratify it into low- and high-

intermediate, so that you could sort of split the difference. And for patients who were in that intermediate-risk group, there was low-intermediate, and they had a somewhat better prognosis, and high-intermediate had a worse. And in fact, I can say that for the most recent treatment guidelines from the European Respiratory Society and ESC, intermediate-low and intermediate-high are separated.

Basically, what that tells you is that we've gone from a 3 strata model, which is low, intermediate, and high, to a 4 strata model, which is low, intermediate-low, intermediate-high, and high. And that allows us to, again, better discriminate how patients are doing.

So with that in mind, the investigators in the large French group said, "Well, what about hemodynamics?" We've been pushing, and I think rightfully so, that many patients can be followed just with noninvasive parameters, as the things I've mentioned, and do not necessarily require invasive follow-up testing in all cases. But what these investigators wanted to do was to determine, were there some patients in whom the hemodynamic measurements with right heart catheterization were useful to them and better discriminated how those patients were going to do?

And so what they did was they looked at the large registry over several years, over a decade really, and evaluated transplant-free survival and looked at the 4 strata model first, so where these patients fell into on treatment, and it was an average of about 5 months after starting treatment, and did they fall into the low, intermediate-low, intermediate-high, or high? So the 4 strata model. And then they went and applied hemodynamic measurements that had been done in many of those patients to see, did the hemodynamic measurements better separate out a transplant-free survival?

As you know, when we do invasive hemodynamic measurements, there are a lot of different things that we can measure: the right atrial pressure, pulmonary artery pressure, right ventricular pressure, wedge pressure, pulmonary vascular resistance. We can measure mixed venous oxygen saturation. We can calculate things like stroke volume, cardiac output. And so they looked at all of these various parameters to see, did any of them help discriminate outcomes in the patients who fell with whatever strata they were in? So that's the baseline of the French study.

It turns out, when you look at the patients who were in a low-risk status on treatment, the hemodynamic measurements didn't really seem to help that much. They remained low risk. They had similar survival if they were in low risk based on the 4 strata model. At the other end of the spectrum, patients who are in the high-risk category, so on treatment they remained high risk based on the 4 strata model using noninvasive parameters, the hemodynamics also didn't seem to make a difference. So if the patient was deemed to be high risk based on the noninvasive parameters, their survival was similarly poor, regardless of the hemodynamics. So that actually is useful by itself because it tells us that the noninvasive evaluation tools work, work well in helping us determine is a patient in low risk or high risk.

Now, if you look at the rest of them, and again, it was about 60% or so were intermediate risk. And that's where, again, the group that we have to pay a lot of attention to. Because we have a lot of options, we don't always know which way to go with those patients who are intermediate risk.

Well, here's where it got interesting, because they found that certain hemodynamic measurements actually were very strong in helping separate out transplant-free survival in both intermediate-low- and intermediate-high-risk patients. And they applied a lot of statistics and modeling to look at this and multivariable analyses. At the end of the day, they found 2 parameters. Stroke volume index, so that's obviously stroke volume corrected for body surface area of over  $37 \text{ mL/m}^2$  correlated with a better outcome than a lower stroke volume index in the intermediate risk. The second parameter, mixed venous oxygen saturation. So a mixed venous oxygen saturation above 65% correlated quite well with how a patient was going to do in that intermediate risk. And it fell out very nicely, because if they had both of those present, the adequate stroke volume index and the adequate mixed venous oxygen saturation, they did better than if they only had one of those or had none of those parameters.

So it really demonstrated that hemodynamics, in fact, do have an importance in evaluating how patients are doing on treatment, but specifically in that big intermediate-risk group.

How does that affect our overall approach to risk stratification for practitioners?

Well this really helps, I think, structure it, because now we have some pretty strong data suggesting that if that patient falls into that intermediate-risk category on treatment, and, you know, you're not sure, and you have other options before transplant to treat this patient, then I think it's better to get more data and refine our predictions. And that's where right heart catheterization comes in.

So now we have the 3 strata model for initial evaluation. We have the 4 strata model for initial follow-up. And then depending on what that looks like, if they're in intermediate risk, potentially going to the so-called 6 strata model, where there's 2 invasive hemodynamic parameters, stroke volume index and mixed venous oxygen saturation, can be used to help further risk stratify and to really help us guide our patients and guide our therapies.

Thank you.

**Announcer:**

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