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# How Should Cardiopulmonary Comorbidities Influence PH Treatment Strategy?

**Announcer:**
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**Dr. Channick:**
Hello, my name is Richard Channick from UCLA. And today we're going to be discussing the impact of comorbidities on our treatment choices for pulmonary arterial hypertension. I'm delighted to be joined by two colleagues, Dr. Jean Elwing from University of Cincinnati, and Dr. Richard Krasuski from Duke University. Welcome.

**Dr. Elwing:**
Thank you.

**Dr. Krasuski:**
It's great to be here.

**Dr. Channick:**
So let's get right into it. As I'm sure you know, there's some revised guidelines out of the European Society of Cardiology and European Respiratory Society that specifically talk about patients who have pulmonary arterial hypertension, with concomitant comorbidities. And the suggestion in this evidence-based treatment algorithm is possibly those patients should be considered for monotherapy, rather than combination therapy, which we use for most patients with pulmonary arterial hypertension. I want to get your sort of overall opinion of that, especially let's say for our patients of intermediate, or even intermediate-high risk pulmonary hypertension, Jean.

**Dr. Elwing:**
Well, I was actually taken aback when I read that, thinking, how is this going to impact our patients, right? Like, how is this going to affect how patients come to us? And how are they started on therapy? So I do believe that complex patients

require complex management. But I don't think we should necessarily withhold therapies that are indicated for them. I think we have to take our medicine hat and put it on and say, 'Hey, this person has a little bit of this, a little bit of that, but a lot of pulmonary arterial hypertension, and we think this is driving their symptomatology,' and then they're going to go in the regular algorithm, for me, at least. Those patients that I don't believe have a lot of pre-capillary pulmonary hypertension, I might even approach them differently, work on their other comorbidities before I even think about assessing and providing therapy.

But what do you think?

**Dr. Channick:**
Yeah, no, I think that that's - you said it perfectly, that, you know, all comorbidities are not created equal. And I think that, you know, each patient, as you said, should be looked at individually. I mean, Rich, you're a cardiologist, you know, many of your patients have cardiovascular comorbidities. And, you know, do you think this, you know, is a problem, to be very frank, this new recommendation?

**Dr. Krasuski:**
Well, you know, I think you have to step back a little bit and recognize what the data so far has shown. If you actually go back and look at the AMBITION trial, for instance, early on in the AMBITION trial, they realized when they had looked at the 6-month data, that there was, you know, different groups coming out. And there was clearly a group that was benefiting more from treatment, and another group that was potentially not getting the same benefit, and maybe even achieving more harm. And they realized that that group that had underlying group 2 disease that probably had been underdiagnosed, and so they actually changed the screening criteria in terms of lowering the wedge threshold that was allowed, and then looking for concomitant risk factors. And they look specifically at things like obesity, you know, BMI over 30, diabetes, hypertension, coronary disease, that kind of thing, which all increased the risk of diastolic heart failure. And when they did that, you know, they suddenly saw a population, and in fact, got greater benefits. So, I think that it's something that we're continuously assessing when we're in clinic, and trying to differentiate the groups we think are going to benefit from treatment versus those that aren't.

**Dr. Channick:**
Absolutely. And I think even in the AMBITION trial, you know, there was still a benefit from those patients who were sort of in that borderline category. But I think we would agree there's a group of patients where monotherapy may be reasonable. And certainly, in my practice, there are some of those patients that were, quote, more cautious with and don't follow the so-called AMBITION algorithm. I mean, give us an example of a typical patient that you would really consider monotherapy in, and with what.

**Dr. Elwing:**
That's all hard, you know, you see patients that especially in the region I'm in with a lot of emphysema, and, you know –

**Dr. Channick:**
Give me an example.

**Dr. Elwing:**
Okay, okay, you're going to make me –

**Dr. Channick:**
A patient where you would use monotherapy.

**Dr. Elwing:**
A patient who comes with more mild pulmonary hypertension, maybe they have a history of methamphetamine use or cocaine use in the past, but they have a lot of emphysema per se. And I might cautiously start them and see their response, watch them, see if they have significant side effects and see what their oxygenation does. Because at that point, I don't know if they're early meth-induced or cocaine-associated pulmonary arterial hypertension, or are they really pulmonary hypertension associated with their underlying lung disease? That would be one example.

**Dr. Channick:**
Yeah. And I'll say the same to you in the heart world.

**Dr. Krasuski:**
Well, I think if you saw an older patient, let's say 75 years old, and they've got some cardiovascular risk factors, they're a little overweight, but they have an elevated, you know, RVSP on the echo, and you cath them, and, you know, their wedge at that point is, let's say 14 and their mean PA pressure is 35. So you're - clearly meets criteria for elevated PVR and - but it's in that kind of like gray window where you really don't know, maybe you didn't do a fluid challenge. Maybe you didn't do anything else in the cath lab. And maybe they've got more diastolic heart failure than you think. And so I think that's somebody that I would start on treatment with a single agent. And I would make sure I bring them back and I reassess how they do. And I probably would recath them at 3 months just to see whether or not - you know, what their hemodynamic response is.

**Dr. Channick:**
Yeah. And I think that raises a really important point of risk assessment and follow-up risk assessment, not just for efficacy, but for side effects and tolerability in that patient population. I mean, certainly the, you know, anecdotes, for instance, that, you know, endothelin receptor antagonists in older patients with that - what you're describing as – the Europeans describe as a left heart phenotype, you know, is a very high incidence of edema and just intolerance for that whole class of drugs. I don't know if you guys have –

**Dr. Elwing:**
Definitely have seen that happen in our older patients, or our patients that are high - have higher BMIs. So taken with caution then.

**Dr. Channick:**

So I suppose you would - maybe would start a PDE5 inhibitor, reassess, and then add on. I think that's really, really a critically important part of this.

**Dr. Krasuski:**
Just to put the other side, though, Rich, you know, sometimes we have those patients, and we're remarkably impressed that they actually respond well to treatment. I've been surprised pleasantly by some that I thought, 'No, this guy definitely is not going to do well with this, but let's do it.' And then they come back and they feel better, and their numbers look better. So I think that, you know, it's not all doom and gloom in those patients.

**Dr. Channick:**
Yeah. And that's, you know, where the expertise and close follow-up comes in there. You're 100% correct. And that's been my experience. And I think that was a nice thing about the European, if you read the text of it, not just the algorithm, they talk about this left heart phenotype, this cardiopulmonary phenotype being pretty distinct and requiring a lot more attention I think than we've previously given to them.

Well, that's about all the time we have. Thank you very much for your insightful comments.

**Dr. Elwing:**
Well, thank you for having us.

**Dr. Krasuski:**
Thanks, Rich, it was great.

**Announcer:**
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