Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/on-the-frontlines-of-attr-cm/real-world-testing-attr-cm/49043/

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

Understanding Real-World Testing Patterns in ATTR-CM

Announcer:
You're listening to *On the Frontlines of ATTR-CM* on ReachMD. Here's your host, Dr. Steve Jackson.

Dr. Jackson:
As awareness of transthyretin amyloid cardiomyopathy, or ATTR-CM, continues to grow, so does urgency around accurate diagnosis. But new Medicare claims data suggest that many patients aren't undergoing the full consensus recommended testing pathway.

Welcome to *On the Frontlines of ATTR-CM* on ReachMD. I'm Dr. Steve Jackson, and joining me to discuss his recent research on diagnostic testing patterns in patients with wild-type ATTR-CM is Dr. Ronald Witteles. He's a Professor of Cardiovascular Medicine at Stanford Medicine, as well as the Co-Director of the Stanford Amyloid Center and the Stanford Multidisciplinary Sarcoidosis Program.

Dr. Witteles, thanks for being here today.

Dr. Witteles:
Thanks so much for having me.

Dr. Jackson:
Before we dive into the study itself, Dr. Witteles, can you give us some background on how ATTR-CM is currently diagnosed and why it's so important to evaluate how this actually looks in real-world practice?

Dr. Witteles:
Yes, absolutely. There's been an explosion in diagnoses in the last few years, and I'd say that's for two reasons. One has been the development of therapies, but the other has been that it's a lot easier to diagnose now than it used to be.

The big advance was what's called bone scintigraphy. In the United States, that's usually also referred to as a PYP scan, which stands for technetium pyrophosphate, the nuclear tracer. And basically, this takes advantage of the rather interesting and somewhat bizarre fact that amyloid deposits in the heart like to take up bone tracers. The bone tracers were developed originally for bone scans, of course, but they have been modified to be used to make the diagnosis of this disease.

The key is that the other main form of amyloidosis, AL amyloidosis, which is a completely different disease with completely different treatments, can also take up bone tracers, but it also doesn't reliably take up bone tracers. And so what that means is bone scintigraphy, or a PYP scan, can only be used to make the diagnosis of ATTR cardiomyopathy once AL amyloidosis has been ruled out. And that is done by ruling out the precursor protein for AL amyloidosis, a light chain, from being present.

And to do that, we need to rule out monoclonal protein production by the bone marrow, which is with three tests: a serum and urine protein electrophoresis with immunofixation and the serum free light chain ratio. And so if you combine a negative monoclonal protein evaluation with a positive PYP scan, you have now made the diagnosis of ATTR cardiomyopathy in an entirely non-invasive fashion. So that really helped increase the diagnoses of this disease, which used to have to be made by biopsy—typically an endomyocardial biopsy.

Dr. Jackson:
You analyzed Medicare Fee-for-Service claims from 2018 to 2022. Can you walk us through the methodology and explain what you were hoping to better understand through this analysis?

Dr. Witteles:

Absolutely. The concern that I and many others have, just as a clinician who cares for a lot of these patients, is that a lot of patients are not being diagnosed based on the actual proper algorithm. So how could they be diagnosed otherwise? Well, it could be that they just didn't get the monoclonal protein evaluation, for example. Or maybe they didn't get any of the testing at all, and somebody just had an echo or an MRI that looked suspicious for amyloid and felt that was enough, which it certainly isn't.

So what we wanted to try to understand is, in the Medicare population, which is the main population of this disease because it's a disease of mainly of older adults, what testing happens? And theoretically, for almost every patient, we should have access to testing based on claims data. So we looked at the Medicare population from 2018 to 2022 and who had the diagnosis based on ICD 10 code of wild-type ATTR cardiomyopathy, which is a very specific code, and then saw what series of testing was performed that led somebody there. We looked at things like, did they have those three components of the monoclonal protein testing performed? Did they have bone scintigraphy performed? Did they have endomyocardial biopsy performed?

We got into the weeds a little bit more to try to exclude things that might have been falsely coded as ATTR cardiomyopathy. But for all practical purposes, that's what we were looking at with the question, how many people are being diagnosed according to what the guideline recommendations are?

Dr. Jackson:
For those just joining us, this is *On the Frontlines of ATTR-CM* on ReachMD. I'm Dr. Steve Jackson, and I'm speaking with Dr. Ronald Witteles about diagnostic patterns among patients with wild-type ATTR-CM.

So, Dr. Witteles, when you evaluated how these patients were being diagnosed, what findings stood out to you the most?

Dr. Witteles:
A couple things. There were the things to be expected; over the period we were looking at, 2018 to 2022, there was a progressive decrease in the percentage of patients getting cardiac biopsy. That makes sense because, again, there was now this non-invasive way to make the diagnosis, and there was overall a modest increase in the use of bone scintigraphy. Again, it became more established and more well-known. That all makes sense.

I expected to see that a lot of patients were getting diagnosed without undergoing the proper assessment, just knowing the patients I see in clinic. But the degree of that was still surprising to me. 14 percent of those who had a diagnosis of ATTR wild-type cardiomyopathy had the proper testing. 14 percent. So really shockingly low, and it makes you wonder what exactly is going on to get to these diagnoses, or supposed diagnoses, in other patients.

It really ran the gamut. Sometimes it was just the laboratory testing being done but not complete. So maybe they did it, but they didn't do the free light chains, and they only did the serum and urine protein electrophoresis, for example. Or maybe they did the rule-outs of the monoclonal protein, but they never did a PYP scan. And we can only ask, how did they get to the diagnosis? Again, maybe it was the appearance on an echo or MRI, for example, but that is not one of the accepted ways of getting to the diagnosis.

Now, like anything, this is an administrative claims database. It's theoretically possible some people had some of this testing with outside insurance, and I'm sure for small numbers that's the case. But not for most of these, and it doesn't clearly account for the fact that only 14 percent seem to have had the complete testing.

Dr. Jackson:
So as you just said, one of the most striking findings was that only 14 percent of patients underwent the recommended combination. Why do you think that gap persists, and why is comprehensive testing such a critical part of this diagnostic pathway?

Dr. Witteles:
Great question. Let me start with the second part first. Why is it such an important part of the diagnostic pathway? Because it's critical to get the diagnosis right. The worst thing in this disease is to give somebody the diagnosis of ATTR cardiomyopathy when they actually have AL amyloidosis. As I said, the treatment is completely different. The treatment for AL amyloidosis in particular is very time-sensitive, and it can truly be a matter of life or death to get that diagnosis right. And so, as an example, if the diagnosis is made with scintigraphy and there's no monoclonal protein assessments, there's going to be some patients who have AL amyloidosis who just get misdiagnosed and frankly end up succumbing to the disease because of that. So it's really critical.

Why do I think the gap persists? I think it's a couple of things. The truth is the algorithm of the testing is really simple. The problem is these aren't tests that most cardiologists are used to ordering. Cardiologists know echoes, they know MRIs, they know CTs, et cetera. Bone scintigraphy is a newer thing, and monoclonal protein testing, again, is just not testing that cardiologists will often do.

It can also get a little bit more complicated. There's some ways to get caught in unintentional mistakes. So for example, with free light chain testing, the test to order is serum free light chains. But you can mistakenly order urine free light chains or serum total light chains.

And so if you're not used to exactly what to order and you haven't done it before, you can easily make mistakes on it, even if you're trying to do the right thing. So again, it's actually pretty straightforward to do, but not until you learn it.

Dr. Jackson:
Given those findings, what kinds of system-level changes could help close that gap between guideline recommendations and everyday clinical practice?

Dr. Witteles:
I think it's two things. One is more education for healthcare providers who might see these patients of the tests to order. And there's also a question of who you should suspect the disease in, which is separate. But once you've suspected the disease, these are the tests to order. Again, it's not hard, but you just have to learn it.

The other thing is just systems-level change. And some electronic health records have this—instead of forcing the cardiologist who's not used to ordering these tests, simply have a monoclonal protein panel—one order that you could put in your electronic health record that just gets the right tests. There's also some places where you can order an ATTR amyloid evaluation, and the lab tests will be right there just to check. and then the PYP scanner bone scintigraphy will be right there to check.

Dr. Jackson:
Before we wrap up, Dr. Witteles, what key takeaways do you hope clinicians remember from this study when they evaluate patients with suspected wild-type ATTR-CM?

Dr. Witteles:
There's a right way and a wrong way to do this, and it's critically important to get this diagnosis right. We want to diagnose people who have this disease, hopefully efficiently, and get them started on treatments that can make a huge difference.

Dr. Jackson:
And with those key takeaways in mind, I want to thank my guest, Dr. Ronald Witteles, for joining me to discuss how we can improve our approach to diagnosing ATTR-CM.

Dr. Witteles, it was great having you on the program.

Dr. Witteles:
Thank you very much. Great to be here.

Announcer:
You've been listening to *On the Frontlines of ATTR-CM* on ReachMD. To access this and other episodes in our series, visit *On the Frontlines of ATTR-CM* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!