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Retinal Perfusion, Sensitivity, and Function in DR

Barton Blackorby:
Welcome to the New Retina Radio Journal Club with VBS. My name is Barton Blackorby from the Retina Institute in St. Louis. I'm joined today by Kat Talcott from the Cleveland Clinic.

Katherine Talcott:
Thanks so much for having me.

Barton Blackorby:
And Hong-Uyen Hua from the University of Miami.

Hong-Uyen Hua:
Hi there, thanks for having me.

Barton Blackorby:
And today we're going to be discussing a paper titled Retinal Sensitivity and Retinal Perfusion in Diabetic Retinopathy, is authored by Jennifer Hamilton-Pares and colleagues, and is published online in the JAMA Ophthalmology Journal on October 2025. So Dr. Hua, do you want to give us a quick summary of this paper?

Hong-Uyen Hua:
Absolutely. So this was an interesting paper, which was a prospective longitudinal cohort study looking at association between retinal sensitivity of about 110 degrees in projection perimetry and retinal perfusion with ultra widefield angiography at baseline and changes at one and two years in the study eye.
A little bit about the background and rationale of the study. So the functional relationship between nonperfusion and retinal sensitivity across the retina and how it evolves over time remains poorly understood. So these researchers sought to further characterize the association between retinal capillary nonperfusion and retinal sensitivity in eyes with moderate to severe diabetic retinopathy over up to two years of follow-up.
To do so, they designed a prospective longitudinal cohort study at a single center in the United Kingdom. And these participants were followed up to two years with a massed outcome assessors. The participants in this study included adults with moderate nonproliferative diabetic retinopathy, severe NPDR, very severe NPDR, and proliferative diabetic retinopathy with less than high risk characteristics. And at least one eye had to be naive to treatment. And they had to also have no other retinal issues.
The primary outcomes in this study included an association between retinal sensitivity, measured by 110 degrees projection perimetry, and retinal perfusion status assessed with ultra-widefield angiography at baseline and changes over one and two years. Secondary outcomes included rates of change and sensitivity deficits over time in perfused versus nonperfused retinal areas. And also looked at demographic and clinical correlates.
The findings in the study with 44 patients with at least one parametric exam included the mean age of 52.1 years, 29% of these patients were female, and the median hemoglobin A1c was about 9.1%. The mean best corrected visual acuity in the study was 20/20.
At baseline, sensitivity deficits were larger in nonperfused areas, about 11.8 decibels, versus perfused areas, 6.6 decibels. The age was the only factor positively correlated with greater sensitivity deficit in this study, interestingly. So A1c trended but was not significant. Diabetic retinopathy duration and diabetic retinopathy severity were not positively correlated.
A significant portion of perfused areas showed greater than five decibel deficit. And the notable fraction of nonperfused areas had normal sensitivity, which indicated imperfect structure-function correspondence. Over one year, sensitivity deficits decreased at similar rates in perfused and nonperfused regions. Over two years, sensitivity deficits decreases were more pronounced in nonperfused areas

compared with perfused areas.
So in conclusion, retinal capillary nonperfusion is associated with larger baseline retinal sensitivity deficits. But functional loss may be present in perfused regions and preserved in some nonperfused areas. Sensitivity deficits tended to improve over time despite poor glycemic control and advanced diabetic retinopathy. These dynamics should inform clinical management in the design of interventions targeting capillary nonperfusion in diabetic retinopathy. Retina ischemia and retinal function within areas of perfusion in ischemia and diabetic retinopathy is multifactorial and complex. The impact of retinal ischemia on function isn't uniform.

Barton Blackorby:
Thank you so much, Dr. Hua. That was a great summary of the paper. I'm going to just pass it over to Dr. Talcott here for a quick reaction. How do these findings align with how you currently think about nonperfusion as a driver for maybe functional vision loss in diabetic retinopathy?

Katherine Talcott:
Yeah, I think this is a really interesting paper. And Dr. Hua, I think did a great job summarizing it. I applaud the authors for doing such a great job organizing the study and testing sensitivity of the retina. Because I don't think that's something we can test normally in our clinic. And to be honest, I don't really think about it every day in clinic as much. Because when I think about my diabetic patients and them losing vision, I think about it due to complications like diabetic macular edema or bleeding or detachment. But to be honest, I don't think about functional peripheral vision loss as much as I maybe should.
And I think reading this paper and discussing this paper makes me think that maybe we should spend more time thinking about it. I think about central nonperfusion impacting visual acuity, but for me, thinking about peripheral functional vision loss is not something that I always think necessarily drives my treatment or management of these patients. But I'm really curious to hear what you guys think about this paper.

Barton Blackorby:
Right. I'm in your camp. The only time that I've typically thought about the peripheral functional field is after I did a PRP and my patient came back and said, "Hey, I got a little bit of a tunnel vision here." But it is important to them.
I do think it's an argument that is played out now within retina conversations where people are saying, "Well, we've got these great anti-VEGF drugs with PDR, maybe I don't need to do PRP with good follow-up." Versus the camps that says, "No, we need to do PRP." So I think we're going to look at that peripheral perfusion and that functional level a lot more to help drive the right treatments for these patients. What do you think, Dr. Hua?

Hong-Uyen Hua:
Yeah, I definitely agree with both of you with regards to, I guess, the clinical application of this study. I think more of, okay, how much of nonperfusion is present? And how at risk are these patients of advancing to proliferative diabetic retinopathy more? That's typically how I think of the periphery as compared to the functional sensitivity of these areas.

Barton Blackorby:
When we get back from the break, we're going to talk about some of these changes we saw in perfused areas and how they may or may not correlate with the function that Dr. Hua summarized with this paper. So stay tuned, in a few minutes we'll be diving deep into these details.

Speaker 4:
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Barton Blackorby:
Welcome back to the New Retina Radio Journal Club with VBS. Let's get into a longer discussion about the paper Dr. Hua summarized in the first part of this episode. Talcott, I'll start with you first. What factors might explain why some nonperfused retinal areas retain a normal sensitivity while some perfused areas show a marked functional loss?

Katherine Talcott:
Yeah, I think that's a really good question. And something that I found curious as I was reading the paper. And I think the authors did a nice job thinking about that in their discussion. Even if there's technically blood flow in the retina, it doesn't necessarily mean that it's functioning well. We know that there can be inflammation going on. There's a lot of interest in that as it applies to diabetic retinopathy and diabetic macular edema, especially with a lot of discussion with new agents and IL-6, other mediators. There's also oxidative stress that's present as well. And so all those things can impact the way a retina is functioning, even if the perfusion doesn't look good. And so I think that might help to explain a little bit why we didn't see in this paper that there was perfect structure-function correspondence.

Barton Blackorby:
And Dr. Hua, you mentioned earlier about the role of OCTA and how that can play into looking at the ischemic nature of the peripheral retina, as well as the macula. It's actually one of the modalities they'll look for to see that fine detail for macular ischemia. What limitations do you see that potentially fluorescein angiography has on the assessment of perfusion that widefield OCTA might give us?

Hong-Uyen Hua:
Yeah, I would say that ultra widefield fluorescein is only able to give us more of a two-dimensional picture of perfusion. Whereas OCT angiography, we're able to look at different slabs and different layers of perfusion within the retina. So it would be interesting to see a parallel study of the effects of retinal perimetry using the ultra-widefield OCT angiography that's available in research studies as well.

Barton Blackorby:
Well, let's talk about some of those modalities we have available. Not all of us have a ultra-widefield OCTA. A lot of us have fluorescein angiography. And some of us have the ability to test peripheral visual field perimetry. But Dr. Hua, what challenges do you think clinics might face in integrating this widefield perimetry or a similar function testing into just a regular diabetic retinopathy exam?

Hong-Uyen Hua:
Yeah, I think real-world applications of retinal perimetry could certainly be challenging. If you think of a busy retina clinic, certainly the last thing I'm thinking about is using even a Humphrey visual field to look at how my patients are able to see in the periphery with diabetic retinopathy. And how their nonperfusion is affecting or even if patients have panretinal photocoagulation, I have never ever used a visual field to assess their function there. So I think it might be a challenge for retina specialists to apply retinal perimetry in the clinical setting.

Barton Blackorby:
How about you, Dr. Talcott in Cleveland, I think this is something that might be a challenge or usually integrated into your clinic?

Katherine Talcott:
I think it'd be really interesting to figure out how long it took to do all these tests on these patients. Because I can only imagine correlations from things like the MIA or microperimetry that are currently often used in trials for our AMD patients, I know those can be really cumbersome and really depend on a patient's fixation. So I can imagine that there's a lot of challenges here.
I know I am personally really excited to hear that visual fields are going away from the screening recommendations for Plaquenil for us. So to add back in the visual field component, it's challenging in a busy clinic, you have to feel like that test is giving you something that will allow you to change your management of these patients. And so I think that that piece is still out there and needs to be fleshed out if this is going to be integrated into busy clinical practices.

Barton Blackorby:
Right. And if I look back to my residency days, I think a visual field was 15 or 20 minutes, and it's definitely an exam burden and a patient burden. They're already going through a lot in terms of their testing.
As we see more of an interest in this peripheral visual field and function, it reminds me of a few years ago when I was at AAO, I tried out a device called a RETeval. And you use it in the clinic at the chair side and it gives you just a full field ERG of your retina. It was very easy to do. And they did provide a diabetic retinopathy score to look for intervention. Certainly something that I would need to look into more as well as this peripheral perimetry.
But I think as we get more tools available to look at the peripheral retina of diabetics, it's going to be the next frontier. I think we have macular disease well controlled. Now it's seeing that peripheral retina that may need the help a little bit more.
So we learned about the functional and perfusion of the peripheral retina and diabetics in this paper. Now let's see how that applies to our clinical judgment. Dr. Talcott, did this influence you in terms of applying PRP or anti-VEGF for patients with nonperfusion and potentially good function?

Katherine Talcott:
Yeah, I think that's a really good question. I used to really worry about adding PRP in for some of my PDR patients. That it can certainly limit their peripheral vision. But I feel like the protocol study actually taught us a lot in looking at those five-year outcomes. Because in those studies there was no difference in the visual fields between patients who got PRP versus patients who were continued on anti-VEGF injections for five years. So although that's something that I used to worry about a lot, now I don't because I think in a lot of ways, I mean, I think peripheral nonperfusion probably does impact patients' peripheral vision. And so even if we treat it with laser versus not, the underlying disease still impacts things.

Barton Blackorby:
What about you, Dr. Hua?

Hong-Uyen Hua:
Yeah, for me, it's more important to prevent progression of disease. So that's what I tell patients, it's more important for us to preserve your long-term central vision. And hardly any patients, it's a rare patient that really complains of their functional peripheral vision loss, so it hasn't really changed my clinical management.

Barton Blackorby:
Yeah, I'm a bit of a mix. I will give some patients the options of anti-VEGF versus PRP. But I tell them if you miss one appointment or you're late, there is no option, you just get laser after that.
Well, I do appreciate you guys discussing this paper with me. I think it was a great paper to dive into. It'll open up even more in the future.
For everyone listening at home, in your car or wherever you are, thank you for listening to the New Retina Radio Journal Club with VBS. Stay tuned for future episodes.