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Outcomes for PDR Patients LTFU for at Least 1 Year

Kyle Kovacs:
Welcome to the New Retina Radio Journal Club with VBS. My name is Kyle Kovacs. I'm from Weill Cornell Medical College in New York. And I'm joined today by Matt Starr from Mayo Clinic.

Matt Starr:
Thanks, Kyle. Happy to be here.

Kyle Kovacs:
And also with us is Nita Valikodath from the University of Michigan.

Nita Valikodath:
Hi. Thanks for having me.

Kyle Kovacs:
Today, we're going to be discussing an interesting paper on outcomes of patients with proliferative diabetic retinopathy treated with anti-VEGF therapy and/or panretinal photocoagulation in the United States who were lost to follow-up. And this was published recently by Rahul Karana in Ophthalmology Retina in December 2025. Matt, would you mind summarizing the paper for us?

Matt Starr:
Yeah. Thanks, Kyle. This was a retrospective cohort which utilized the American Academy of Ophthalmology's IRIS Registry dataset, and it was essentially a follow-up paper to a couple of previous papers. And just a plug, it's always fun to cite several papers in your intro and methods and then you got to go read them again as a new timer. It was a few papers, if you really want to understand it, you have to take into account the first one being their first paper that they published. The same group of authors published an initial IRIS Registry dataset just looking at the rates of loss to follow-up in proliferative diabetic retinopathy patients and what were the rates and then what were potential risk factors. And so they cited previous reports of anywhere from 15%, 17%, to 60% of PDR patients being lost to follow-up. However, within their previous IRIS Registry dataset is about 10% to 12%, depending on the previous treatment modality. Risk factors were certainly socioeconomic, as you would expect. Unilateral eye involvement, baseline vision of 20/40 or worse, and then private insurance.

And so just based on that, they wanted to then take it a step further and assess how did loss of follow-up affect treatment outcome... Or affect visual and anatomic outcomes. And so this was a really much larger dataset in a real world setting rather than a single institution setting. And they wanted to answer the question, how do patients do after being lost to follow-up after previously undergoing some sort of treatment for their PDR? In the first paper, they tell you how many eyes that they had. And so they had about 300,000 unique eyes that popped up with a diagnosis code of PDR in the IRIS dataset. However, you have to exclude quite a bit for having other diagnoses that they didn't want to include such as AMD, RVO, myopic degeneration, idiopathic CMV. And ultimately, it led to about 73,000 eyes with a diagnosis of PDR, just a simple CPT code who had some sort of treatment on the same day or thereafter the diagnosis of PDR with either anti-VEGF therapy, PRP, or a combination of both, again, based on coding.

Of that 73,000 eyes, they ended up with about 8,600 unique eyes that ended up being lost to follow-up. And they identified loss to follow-up as 12 months without clinic visits after treatment. Of those 8,600 eyes that met the inclusion criteria for loss of follow-up, 2,600 of those eventually came back. You had 74,000 eyes with PDR that were treated in the IRIS Database, about 12%, 8,600 are lost of follow-up, and then about 31% of the loss of follow-up eyes came back. When you looked at the eyes that were then lost to follow-up, about 36% had PRP only before, 29% received anti-VEGF only before, and then about 35% had a combination of PRP and anti-VEGF

prior to being lost to follow-up.

When they looked at the outcome measures of those eyes, between those three cohorts, they were looking at this visual acuity and then they looked at complications of proliferative diabetic retinopathy being diabetic macular edema, vitreous hemorrhage, and tractional detachment, as well as neovascular glaucoma. When you looked at the mean overall vision before loss of follow-up, it was about 20/55. However, at presentation after loss of follow-up, that visual acuity was significantly worse but it was only 20/60, and then the VA did return back to a baseline of about 20/55 12 months after the return visit. When you looked at the multi-variable regression analysis for risk factors for VA, worse than 200 had return visits, treatment with anti-VEGF monotherapy prior to loss of follow-up compared to PRP monotherapy was a risk factor for having worse vision at the return visit, as well as worse baseline vision. Risk factors for visual acuity worse than 2,200 at the final visit after 12 months included, again, anti-VEGF monotherapy compared to PRP therapy, worse baseline vision, and then female sex.

When you looked at the complications upon returning, about 15% of eyes had DME at the return visit, 8% had vitreous hemorrhage, 3% had neovascular glaucoma, and 0.5% had a tractional retinal detachment. PRP monotherapy, again, was associated with a lower complication risk profile compared to the other cohorts and then lower risk of final VA worse than 2,200. This paper concluded that loss of follow-up in PDR did lead to significant vision loss and vision-threatening complications. However, restoration is possible with treatment in some patients.

Kyle Kovacs:
Thank you, Matt, for that excellent background and thorough summary of the material.

Nina, I wonder if you have any initial reactions to either the different complication profiles or the outcomes or anything that caught your eye on the granularity of the data from this IRIS Registry study?

Nita Valikodath:
I think one overarching thing to consider is that this is an IRIS Registry study so there will be limitations related to EHR-derived data, it could be incomplete, inconsistent documentation. Disease severity may not be captured accurately here and may not incorporate imaging that we often rely on as well. And then in terms of ICD and CPT coding, that's another factor that could introduce misclassification. When looking at the outcomes and looking at how things were included, you do have to keep these limitations in mind as well.

Kyle Kovacs:
And Matt, what do you think about those points with the irises or anything else specific about some of the more granular details of the study that caught your eye in thinking about this?

Matt Starr:
I think with any big database study, it's great that it's going to give you some real world implications but you're so limited based on coding, you can't get the nuances of treatment. And diabetic patients, each one is unique. With EMB, it's inject, inject, inject. With diabetes, if there's certain variables, certain nuances, you're going to have some diabetic macular edema in the center of the fovea, some outside the fovea, maybe it's a lot, maybe it's little, and you're just going to have to then quantify the amount of DME. And that's going to affect how you're going to treat a lot of these PDR patients too, whether it's a little bit of an injection here and there, it's steroids, which they didn't even include potentially in the study analysis, as well as laser and early vitrectomy for some patients. I think that these are such a nuanced set of patients, it's hard to really get down and box them into an ICD-10 code.

Kyle Kovacs:
And yet that's where the IRIS Registry can be incredibly powerful with the range of its capture, and yet it's limited really, I think, to these big questions and we're really stuck when we try to get into the granularity of treating the individual patients sometimes with some of this as we're all expressing.

We have a very interesting IRIS Registry study, long definition of loss to follow-up of 12 months, very differing profiles of our cohorts in terms of who got combined therapy, PRP, anti-VEGF, and then significant outcome data that showed some differences amongst them, however, maybe not the differences we were all expecting. What do you think about just the overall rates of loss to follow-up, Nita? Does that reflect your own clinical practice?

Nita Valikodath:
Yeah, this was a really interesting paper and the loss to follow-up of 12 months is definitely very different than in a lot of patients what I would consider lost to follow-up, especially in these sick PDR patients. I tend to see more loss to follow-up patients. I think with being at a tertiary care center, we get a lot of referrals for very sick diabetic patients with very advanced PDR, with other comorbidities, and

they're oftentimes balancing their eye appointment with their dialysis, with endocrinology, and all these other appointments. And I have several patients who have consistently missed appointments because they're hospitalized for a wound infection or other complications from their diabetes, or they have transportation issues because they have VKAs, they can't drive themselves, they need to rely on transport, we're in Michigan so the weather is horrible. All these factors that, to me, it seems like the loss to follow-up rate is higher. And I tend to be more stringent on that loss to follow-up time, I'm not thinking 12 months but actually a shorter duration I would consider loss to follow-up in some of these patients.

Kyle Kovacs:
Would we be expecting there to be a higher complication rate than in these then eventually severe complications like TRD, vitreous hemorrhage, neovascular glaucoma compared to what they found in the study with their definition though, especially with our anecdotal experience thinking that this was a fairly low loss of follow-up rate? What do you think, Matt?

Matt Starr:
Yeah. I didn't touch on it too much in the initial summary but we see all the complications, which they defined as DME, VH, all that kind of stuff. And it was fairly low and really the only significant one was DME, but you did see things like low rates of neovascular glaucoma, not a very low rate of TRD in these patients. And given the length of time, they're not there. A lot of times for high-risk PDR patients, the ones that we anecdotally are really worried about, they don't look good to present on. And if they missed a year, I know what they're coming back at and it's not great, and it's a pressure of 50 and a vision of hand motion and it's not a good eye. And they didn't have too many of those, and it's interesting.

Again, that's also the beauty of the IRS database. In the real world, there's maybe not that many eyes but we only think about the really bad ones. And I think maybe being lost to follow-up for a year is not as bad as we think about it, we just can envision only the really, really bad ones, we don't remember the good eyes. And so it's interesting. I think they had... It's 3% around or so of these patients having TRDs and no NVG in the PRP groups, it' just it's not what we expect.

Kyle Kovacs:
Yeah. Not all ICD-based diagnoses of PDR are the same, that's a really great point. And some of them, I think we're always anecdotally following some of the worst cases that we see and treating those in our mind. And I think this study is capturing a lot of not those cases, obviously. There's some really big differences in the loss to follow-up rates between the different treatment arms. Do you think that was selection bias or how did you interpret that, Nita?

Nita Valikodath:
Yeah, that was really interesting as well. I think this is another limitation of IRIS Registry or any retrospective data looking at treatment, especially for PRP. It's hard to capture how the PRP was done and it can be very variable in different patients, you can get denser burns, you can get moderate PRP, light PRP, depending on what was covered and how active they were, and they don't mention fluorescein data going along with PDR activity. The treatment could have been variable in terms of how dense the PRP was. And then also there could be selection bias in terms of who is getting anti-VEGF therapy. For example, in my patients, if there's coexistent DME or vithim, I may tend towards doing anti-VEGF in addition to PRP if there's a view in those vithim patients, for example.

Kyle Kovacs:
Matt, we're going to put our cards on the table here. What's your initial preference for PDR in the absence of DME, and how does this paper make you feel about your choices or considerations for future practice?

Matt Starr:
Yeah, it's interesting. I think it's not going to change a lot of what I do right now. We were talking offline, I like to laser a lot of my patients right away. I'm not going to sugarcoat it. I've got a great primary care network, I've got a great endocrinology network, I'm surrounded by a lot of other great doctors and we all do a good job taking care of these diabetic patients from a team-based setting. And so if they're missing eye appointments and things like that, their PCP is hounding them and I'm lucky and unfortunate to be in that environment. I don't have too much worry if I'm going to do a really aggressive initial laser that may be uncomfortable for patients. And a lot of it is a discussion but it's just we put a lot of emphasis on eye health and I'm very fortunate to be able to do some of these things and not have to be too worried about some of these loss of follow-up issues.

Kyle Kovacs:
And what about you, Nita, your initial practice and how are we doing things differently, if at all, after this?

Nita Valikodath:
Yeah, I agree with Matt. I tend to do PRP as soon as possible in these patients, almost for the opposite reason that I am afraid that they could be lost to follow-up, especially if they're sicker so I try to do the laser as soon as possible, both eyes complete treatment if I can. In

a lot of patients, it is uncomfortable and we do have to do it in sessions but we tend to schedule them as soon as we can, or we'll bring them back later that week however we can with their schedules to get the PRP in sooner. I don't know how much it changes my practice right now but it's definitely something to think about in terms of who is being lost to follow up and what this paper was reporting in terms of who and what types of treatments were being performed.

Kyle Kovacs:
I wonder, Matt, also you mentioned something I just wanted to go back to, the network of care that you're integrated with that helps facilitate and as a safety net capturing these patients so they aren't lost to follow up. Are there any other practices besides just the well-embedded endocrinologists, primary cares that are helping to mitigate loss of follow-up? Are there things that your practice may do otherwise or that you may personally do to help make sure that retention rates are high?

Matt Starr:
In fellowship, they hired a full-time staff to essentially always keep an eye on these kind of things and that was a luxury that the practice could help and afford. We don't do that here. It is nice to have a good support staff and always keeping an eye on our patient orders that are placed and when they're not completed. We've had a couple other really good retina surgeons, retina docs who have made it a primary point of emphasis that when orders are not followed through our patients are not coming in their timeline to make a bigger deal of that. And those are now an Epic build and a flag in the system that when someone is outside of the return window that it's a flag and we're going to try to get them back in ASAP.

And so again, we're fortunate enough to have that built in and it's becoming a bigger priority. We realize that these patients who were lost to follow-up have poor outcomes, come back in shapes that they may not have not been in if they had received treatment. And this paper, again, sheds light into that. I think it reinforces the [inaudible 00:17:34] paper on a bigger scale. And in reality, it'd be nice to come up with better ways how can we mitigate these loss of follow-up rates? And we may never do that for diabetics, as you were pointing out, Nita, with strokes and wound care and all the other things. It's a hard population but there's definitely ways we can try to mitigate that as a field.

Kyle Kovacs:

It's so multifactorial. It's so hard. There's human-human interactions, there's the treatments that aren't so nice, there's other systemic comorbidities, there's movement, there's too many appointments are different, there are so many a myriad of factors that are impediments at so many different levels of healthcare. Any last thoughts, Nita, also on retention for your high-risk PDR patients?

Nita Valikodath:
Yeah. Those are great points, Matt. I think you alluded to the biggest issue that this paper touches on, which is loss to follow-up and needing to have better systems to be able to retain these patients. At Michigan, there are multiple ways that we try to contact the patients, they get a message through the portal, they get a letter, their offices reach out but oftentimes the patients are not next to their phone, they don't have the portal set up or they may not be checking it or they're hospitalized and they're not getting these messages. It's very complex and I think more work should be done on how to individualize towards certain patients of how to retain them.

Matt Starr:
I'll be remiss if we didn't talk about it in a loss of follow-up paper but again, this paper points out to the... It just supports [inaudible 00:19:11] paper and the utility of still doing good PRP in our patients. But there's only 2018, the study, and I'd love telling the residents, ret is the best field, there are so many good therapies coming out, there's just such long duration of treatment strategies. And with the newer drugs, maybe that's going to be another play to it with the TKIs and gene therapy and suprachoroidal delivery. We're looking at maybe even not discussing this several years down the road.

Kyle Kovacs:
Not discussing laser, Matt? You will pry the laser from my cold, dead hands.

Matt Starr:
Lost to follow up, lost to follow-up. Maybe we won't even have to... They're just always going to get treatment. Treatment is always on.

Kyle Kovacs:
Well, on that note, I want to thank both of you for joining me for this discussion. And I want to thank the listeners here for listening to our new Retina Radio Journal Club with VBS. Stay tuned for further episodes. Thank you.