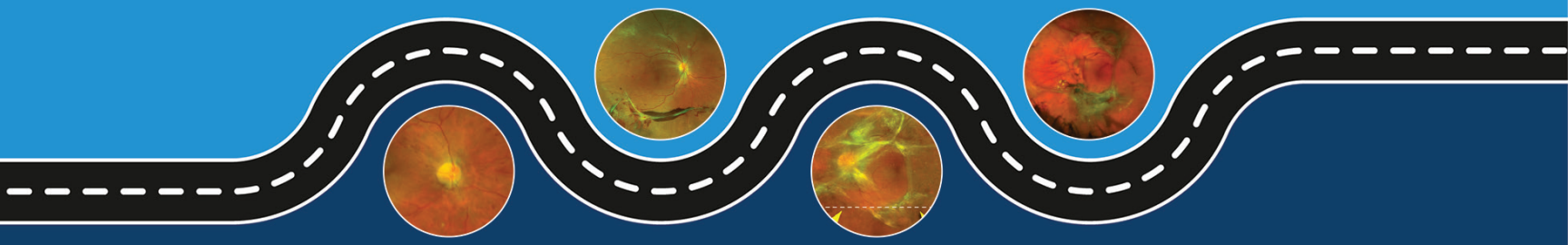

STRATEGIES FOR COMBATTING LTFU

Experts share why follow-up is crucial for patients with diabetes and how you can keep patients on the schedule.

BY RAHUL N. KHURANA, MD, FASRS; KATHERINE TALCOTT, MD; AND JASON HSU, MD

RETINA TODAY: HOW DOES LOSS TO FOLLOW-UP (LTFU) AFFECT THE DIABETES PATIENT POPULATION?

Jason Hsu, MD: The issue of LTFU is huge in the diabetic population. Unfortunately, to develop more severe diabetic retinopathy (DR), there is often some element of noncompliance with physician recommendations and nonadherence to treatment regimens.

I have seen too many patients who have unforeseen circumstances, such as an extended hospitalization, loss of insurance, or problems getting transportation, that lead them to delay returning for eye care. As expected, the prognosis for some of these patients can be abysmal.

Patients who are LTFU generally have worse visual outcomes. However, some of this depends on past treatments. For example, patients with proliferative DR (PDR) who were treated with panretinal photocoagulation (PRP) and were then LTFU had a lower rate of long-term adverse outcomes compared with patients who were treated only with anti-VEGF injections.[1] More recently, we found that patients who had been receiving anti-VEGF injections for diabetic macular edema (DME) were, on average, able to recover vision after a period of LTFU.[2] While this is reassuring, it does not address the fact that these patients may have gained even more vision had they stayed on regular treatments, rather than missing appointments.

Katherine Talcott, MD: Even in clinical trials where patients have the support of research coordinators and are often compensated for transportation, long lapses in care are common, as was demonstrated in the Diabetic Retinopathy Clinical Research Retina Network's Protocol S.[3] There are visual consequences associated with these lapses, especially in patients undergoing treatment for PDR, where the goal of treatment is often to slow vision loss.

When DR patients are LTFU, they are at an increases risk of disease progression or experiencing a vision-threatening complication. In the case of PDR, it can mean that neovascularization or fibrovascular proliferation worsens and leads to vitreous hemorrhage, neovascular glaucoma, or a tractional retinal detachment (Figures 1 and 2). These complications require more interventions for the patient, including more intravitreal injections or PRP, but can also mean retina or glaucoma surgery. Additionally, it may increase the risk of further and permanent vision loss. This obviously affects patients' vision but can also impact their ability to work or take care of themselves or their families.

RT: WHAT DO WE KNOW ABOUT THE PREVALENCE OF LTFU FROM THE LITERATURE?

Dr. Hsu: At Wills Eye Hospital, we performed many of the early studies exploring risk factors for LTFU in patients with diabetes receiving intravitreal anti-VEGF injections. In our offices, the major risk factors included younger age;

AT A GLANCE

- New research suggests approximately 10% of patients with proliferative diabetic retinopathy are lost to follow-up.
- Risk factors for loss to follow-up include older age, male sex, Black or Latinx race/ethnicity, unilateral disease, and having private insurance.
- Retinal imaging can be helpful to explain–and show–the concerning findings and improve patient engagement.

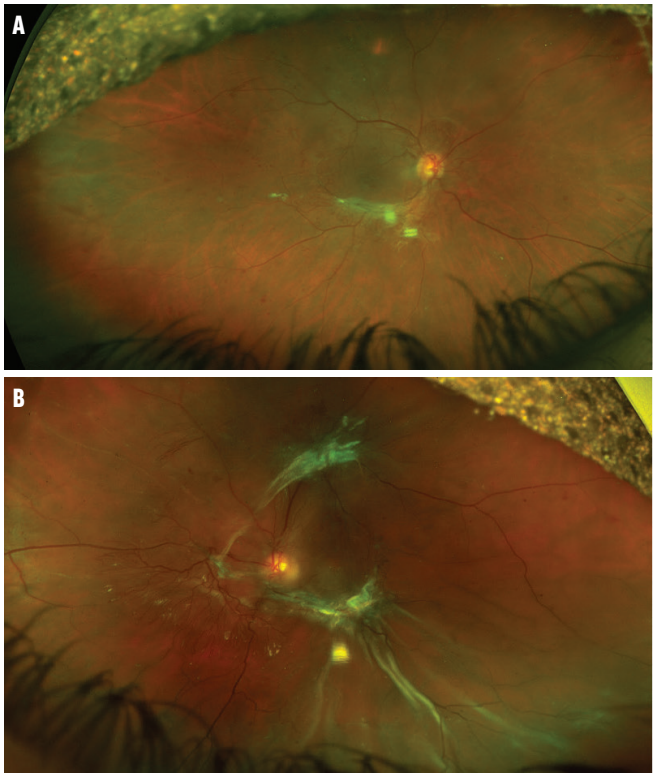

Figure 1. This 58-year-old woman with diabetes was LTFU for 4 years. When she returned to the office, she had developed PDR in each eye. Note the traction and a full-thickness macular hole in the right eye (A) and a tractional retinal detachment in the left eye (B).

identifying as Black, Hispanic, or not reporting race; having worse baseline visual acuity; and living in a zip code with a lower average adjusted gross income.[1,4]

Risk factors in other studies include older age (unlike what we found), poor mobility, need for transportation assistance, insurance status, and having multiple comorbidities. However, what I've learned is that you can never be certain who is going to be LTFU, as patients don't follow a manual.

Rahul N. Khurana, MD, FASRS: A few single-institution studies have shown that anywhere from 25% to 51% of patients with PDR are LTFU after their first treatment.[4,5] These rates of LTFU vary for each institution and clinic, so my group wanted to see what was true on a national level for patients with PDR treated with only anti-VEGF therapy, only PRP, or a combination of both.[6] We used the IRIS Registry from the American Academy of Ophthalmology, which offers access to a huge number of patients to help eliminate bias introduced by single-site studies (ie, single sites may list patients as LTFU if they are seeing another clinician and not truly lost).[6]

We found nearly 300,000 patients who were newly diagnosed with PDR between 2013 and 2015. After applying various exclusion criteria, we separated them into three treatment groups: anti-VEGF therapy alone (approximately 40,000 patients), PRP alone (approximately 32,000 patients),

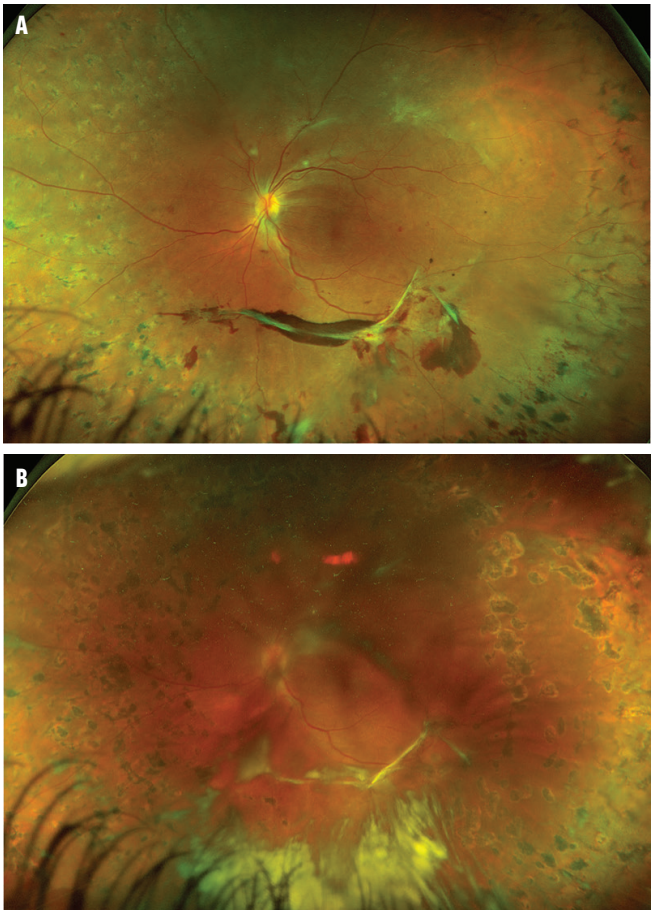

Figure 2. This 32-year-old woman with PDR presented with a vitreous hemorrhage (A). She was LTFU for 6 months and eventually returned with worsening traction and vitreous hemorrhage (B).

and combined anti-VEGF therapy and PRP (approximately 33,000 patients).[6]

We found that 10.7% of patients treated with anti-VEGF therapy alone were LTFU (defined as a visit more than 12 months after the last treatment), 9.5% of patients treated with PRP alone were LTFU, and 9.8% of patients treated with combination therapy were LTFU. The difference between the anti-VEGF therapy and both PRP and the combination therapy arms was statistically significant.[6]

When we initiated this study, I thought that the LTFU number would be higher because the LTFU rates were so high for other institutions, but that's one of the issues with determining this rate from a single site or even a single system. Patients move and see other providers, and they aren't really LTFU, but they are counted as such in a single-institution study. The national registry provides a much more accurate number, even though it still doesn't capture all ophthalmologists. Regardless, the 10% number we found is still an unacceptably high number.

As for demographics, patients who were older were more likely to be LTFU when they were treated with anti-VEGF

therapy alone. We also found that women were less likely to be LTFU in both the anti-VEGF and the PRP arms. We noticed that Black and Latinx patients were more likely to be LTFU in each of the three treatment groups compared with White patients. We also noted that patients who had unilateral disease had a nearly twofold higher rate of LTFU compared with those with bilateral disease. Finally, when we looked at insurance, we found that patients with private insurance were more likely to be LTFU compared with patients who had Medicare.[6]

RT: HOW DOES THIS DATA AFFECT CLINICAL PRACTICE?

Dr. Khurana: One of the most important findings in our study was the demographics at risk for LTFU. We need to emphasize the importance of following up for all patients, but for certain groups that are at a higher riskf for LTFU, it makes sense to spend even more time explaining why treatment is important and why coming back is a must.

Dr. Hsu: It would be great if we had a formula to calculate each patient's risk for LTFU. We could then tailor an intervention to each individual. For example, if a patient has PDR and is calculated to have a high risk of LTFU, then PRP would be the go-to treatment. On the flip side, if they have a low risk of LTFU, then anti-VEGF therapy might be better, which requires ongoing treatments to ensure optimal outcomes. However, we cannot create a formula that has any degree of certainty in predicting who is going to be LTFU. While certain risk factors are evident, they do not hold true across the board. Therefore, just using those factors to tailor treatment is risky. As a result, I basically assume that everyone is equally at risk of LTFU and treat them with that in mind.

Dr. Talcott: If I'm worried that a patient may be at risk for a lapse in care, I make management decisions that may help lessen the burden of follow-up or could help to maintain vision if they have a lapse in care, whether that's treating DME with longer-acting agents or opting for PRP for patients with PDR. This may require taking them to the OR for PRP or working with my ophthalmology colleagues to do PRP in the OR in conjunction with another procedure.

RT: ANY TIPS FOR IMPROVING ADHERENCE TO FOLLOW-UP?

Dr. Khurana: All clinics have a variety of tools to help, whether it's a phone call or reminder cards. Furthermore, monitoring patients who miss treatment follow-up visits is even more crucial; having programs in place to do that is important in the clinical system. These simple measures are helpful, but when we look at other chronic diseases and conditions, those physicians usually have other people on the team whose sole job is to educate and motivate patients. We as a community are going to have to think about adding those components in our retina practices as we deal with these chronic conditions in the future.

Dr. Hsu: Patient education is paramount. Helping them understand the nature of their disease and the benefits of ongoing follow-up and treatment is critical. The availability of digital imaging, including OCT and fundus photography, has allowed us to show patients what is going on in their eyes, which helps augment the educational discussions.

Tracking these high-risk patients is also important. Our practice instituted a call-back system where patients who have received treatment are carefully tracked. If they miss a visit, a staff member contacts them immediately. If they continue to miss visits or cannot be reached, we send them a certified letter explaining our concern and the risks they may face by not being seen and treated.

Dr. Talcott: This is the biggest challenge. It's one thing to understand why a patient might be LTFU or the visual consequences associated with it, but it's an entirely different issue to prevent it. Patients with diabetes face a lot of issues that put them at risk for LTFU. Compared with most of our retina patients, they tend to be younger and are often balancing retina appointments with work and family responsibilities. Patients with diabetes with retina pathology often have concomitant end-organ damage and have multiple medical appointments with other specialties or even frequent hospital admissions.

I stress the importance of regular follow-up with all my patients with DR and any family members who accompany them. I try to get a sense of a patient's social support because involved family members can be critical to help the patient get to their appointments. I try to engage the patient and their caregiver (if appropriate) from our first visit by carefully explaining their disease and what could happen if it progresses. Imaging, including wide-angle fundus photography or fluorescein angiography at baseline, can be helpful to explain and show the concerning findings. Additionally, the treatment approach is important because PRP may help prevent vision-threatening complications if patients are LTFU.

RT: WHAT ARE SOME CHANGES THAT MIGHT HELP MITIGATE THESE RISKS FOR LTFU?

Dr. Hsu: There are two avenues that need to be developed. The first is improving communication and patient education. Our clinics are busier than ever as more therapies are becoming available to treat retinal diseases. Better integrating patient education in a way that helps patients understand their condition and treatment plan will likely help to improve patient adherence. More innovative educational experiences, both office-based and mobile, may be one route. Smartphone applications that assist with education, help detect visual issues, and even remind patients that they are overdue for an appointment may be useful tools.

The second is extended-duration therapies, which I believe will ultimately play the largest role in improving outcomes.

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Less frequent treatments that still provide long-lasting benefit is the Holy Grail of attenuating the risk of LTFU.

Dr. Talcott: I'm excited about the new wave of diabetes medications that are easier for patients to use, and I've seen patients achieve better control of their diabetes, which then helps slow or prevent DR progression. In addition, I practice in an academic center with a plethora of resources, but I wonder if having social workers associated with our ophthalmology department could help with these issues as well.

Dr. Khurana: We know that diabetes is a challenging disease. These patients are under a lot of stress, and it's not easy to make all the visits. We are cognizant of that, but we must think about how to leverage technology and various tools to better educate and empower patients to follow-up. I also agree with Dr. Hsu that extended-duration therapies can minimize the treatment burden, which may help with LTFU.

Empowering our patients through better education of their disease process is crucial, and thinking outside the box on how to engage and motivate patients will help minimize LTFU in the future. Our field should look towards other specialties that manage chronic diseases with more providers to ensure our patients follow up for their sight-saving care. ■

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