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Editorial

Ophthalmology Retina Enters Year 4

Some Comments on Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema

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Welcome to the fourth year of *Ophthalmology Retina*. The journal is now indexed in PubMed/MEDLINE, and the few years' process is underway to apply for and obtain our initial impact factor.[1] Based on current volumes, I anticipate that the journal will have received approximately 550 submissions for 2019, and our acceptance rate for direct submissions to the journal will be approximately 20%, likely falling as the number of submissions increases. Again, I thank the authors, reviewers, editorial board members, and journal staff for their tireless efforts and support.

This issue contains a number of important articles with excellent teaching value. I would like to comment briefly on 4 of them, 3 of which deal with neovascular, or wet, AMD and one that deals with diabetic macular edema (DME) management. Two were funded by the National Eye Institute, one was supported by industry, and one is a real-world study from an academic medical center and large practice consortium.

The Age-Related Eye Disease Study 2 report number 19 speaks to visual acuity outcomes for patients who demonstrated wet AMD and received at least 1 anti−vascular endothelial growth factor treatment (see pg. 3).[2] Although refracted visual acuities were obtained in a clinical trial environment, treatment was not protocol driven, but rather was community based. So, this is a partial real-world report, but benefits from refracted best-corrected visual acuity (BCVA) testing, something often missing in real-world reports. Data exist on approximately 1100 eyes from approximately 1000 participants. At the outset, mean BCVA was 68 letters (Snellen equivalent, approximately 20/40). Loss of approximately 1.5 to 2 letters per year to 61.5 letters (Snellen equivalent, approximately 20/60) at year 5 was observed. The mean number of injections per year was 2.9, 3.9, 3.3, 3.1, and 3.0, respectively. I suspect that this injection frequency represents undertreatment. At 5 years, half of eyes achieved BCVA of 20/40 or better, and approximately one sixth of eyes showed 20/200 BCVA or worse. In comparison, the Comparison of Age-Related Macular Degeneration Treatments Trials participants lost fewer letters at 5 years, approximately 3.3.[3] A large Australian and New Zealand registry experience showed somewhat better outcomes, with a 0.7-letter loss at 5 years.[4] The inclusion and exclusion criteria vary across the studies, so baseline case-mix differences likely impact the 5-year outcomes. However, a general sense exists that more treatment is associated with better outcomes; for example, Comparison of Age-Related Macular Degeneration Treatments Trials participants received a mean of 4 to 5 injections per year compared with approximately 3 injections in the Age-Related Eye Disease Study report.

Ciulla et al[5] have a larger population, almost 50 000 eyes, but shorter follow-up, 1 year, for their real-world report (see pg. 19). Unlike the Age-Related Eye Disease Study 2 report, visual acuity determinations were not standardized. A similar theme relating to likely undertreatment emerged. At 1 year after a mean of 7.3 injections, a mean gain of 1 letter was observed, but a linear relationship was found between mean letters gained over 1 year and mean number of injections, which numbered between 4 and 10 injections per year. Of course, the registration trials relied on monthly injections per the study protocol, so typically, eyes would receive 11 or slightly more injections per year in those studies. Table 1 in the Ciulla et al report summarizes these study outcomes, which shows an average of 8.5 letters of improvement at year 1. As a rule, for each injection for neovascular AMD in year 1, expect approximately a 1-letter improvement.

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Khurana et al[6] report on the value of prior response to anti−vascular endothelial growth factor for wet AMD in a subanalysis of the HARBOR study (see pg. 13). Their objective was to examine whether disease activity-free intervals and duration of the response to treatment inform future disease activity and need for subsequent injections. Recall that the HARBOR study included participants receiving as-needed pro re nata ranibizumab injections as well as those receiving monthly injections. Although longer treatment-free intervals seemed to indicate longer future treatment-free intervals, the relationship is unpredictable. We still need to follow up patients closely. My take on these 3 reports is that I often undertreat and that close follow-up is good. Many of us undertreat, likely because patients prefer a reduced treatment burden, that is, fewer visits and fewer injections. Various sustained-release and longer treatment-interval anti−vascular endothelial growth factor options are coming soon and may help reduce undertreatment. For example, brolucizumab was just approved by the United States Food and Drug Administration, and after 3 initial monthly doses, fully 50% of patients remain dry with every-12-week injections.[7]

Finally, turning to DME, VanderBeek et al[8] report on the initial treatment choice for this condition by studying an administrative medical claims database from a large, national insurer (see pg. 41). Newly diagnosed patients

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from 2013 through 2016 were included. Diabetic macular edema was defined by the first date of an International Classification of Diseases, Ninth or Tenth Edition, DME diagnosis code. Among those who underwent follow-up, initial treatment was observation in approximately half (48%), approximately 20% received bevacizumab, approximately 6% received ranibizumab or aflibercept, 19% received focal laser therapy, approximately 1% received steroid injections, and approximately 2% received an unspecified drug. Importantly, having a copay lowered the odds of receiving any treatment and of receiving each treatment individually. Patient choices such as copays were an important factor for initiation of treatment. Although not a focus of the article, the study has some important implications on the importance of patient choice beyond willingness to undertake treatment. For example, as insurance companies roll out risk models for reimbursement, they should consider that physician choice is not the only thing that impacts costs or outcomes. Patient insurance (e.g., existence of a substantial copay) clearly has an influence on the probability of receiving treatment. So, placing full risk on the physician may not be logical or financially appropriate. An additional complexity relating to the impact of a high deductible on access to treatment is that physicians may not know that the patient has not reached their deductible at the time treatment is recommended.

For our articles published in 2017 and 2018 (it is too soon to have mature or stable 2019 citation data), 8 of our top 10 most cited manuscripts are imaging (OCT) related. Our most downloaded articles, however, relate more to disease management (retinal detachment, endophthalmitis, injections, etc.) than imaging (diagnosis). The journal homepage (https://www.ophthalmologyretina.org/) has tabs for articles in press, most read articles, and most cited articles. The information updates regularly. Please explore it.

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