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Comparing the Changing Trends in the Treatment of Diabetic Macular Edema

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Dear Editor,

I read with great interest the article by Jusufbegovic *et al.* titled, “Changing Trends in the Management of Diabetic Macular Edema at a Single Institution Over the Past Decade.” [1] Although the study has several interesting results, the finding that stood out most was the 2013 cohort's 0.3 logMar (equivalent of 2 Snellen lines) improvement in visual acuity particularly when compared to the near zero (0.01 logMar) improvement in the 2003 cohort. Having a visual acuity outcome in a “real-world” population that compares as closely as the 2013 cohort's does to DME clinical trial results represents a tremendous accomplishment for the ophthalmologists who treated these patients. This study uses a large sample size that alone suggests a certain degree of validity to the results; however confirming this through replication in other populations will be difficult due to the omission of several important details from the original manuscript.

Certainly one question is whether the apparent magnitude of improvement between the 2003 and 2013 cohorts is due to differences in the composition of the two cohorts. With the multitude of clinical trials demonstrating the superior visual results from anti-VEGF agents relative to focal laser for DME, few would disagree that injections are the new standard of care for the majority of DME patients. The majority, however, does not mean all, and currently, little guidance exists on the benefit of treating patients with DME not involving the fovea or DME involving the fovea with very good vision (better than 20/40) with anti-VEGF agents. This becomes an important point when reviewing this study, and may explain part of the visual acuity differences seen between the 2003 cohort and the 2013 cohort. Given the study requires a patient to have received at least 1 treatment for inclusion, the 2003 cohort likely had more patients with a better starting visual acuity. This would be due to the classical guidelines for treating clinical significant macular edema including edema

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adjacent to the fovea, but not necessarily involving the fovea, with focal laser therapy. It is unclear what percent of these patients were included in the 2003 cohort or how these patients were dealt with in the 2013 cohort. If non-fovea involving DME was treated by this practice with bevacizumab, then attaining a 0.3logMAR visual improvement is even more impressive since most of these patients are not able to improve by 2 Snellen lines of acuity. Although determining percentages of patients with fovea-involving DME would be difficult, this issue could be partially clarified by reporting results based on 2-3 categories of starting vision, or at the very least, the initial and end visual acuities of each cohort.

Other important population characteristics that affect change in vision after treatment are also not specified. For example, could DME patients be carried over from one year's cohort to another, or were only new patients included? If the patients were new, did they have to be treatment naïve or just new to the practice? Given the 2013 cohort's visual acuity results, it is most likely these were treatment naïve patients (bevacizumab treated patients would not be expected to average a 2 Snellen line improvement in the middle of a therapeutic course), but these characteristics are never explicitly stated. Nor were the follow-up requirements for inclusion in the study provided. Presumably each patient had to have at least 2 visits in the cohort period for beginning and end comparisons. Alternatively, it is unclear if a DME patient first seen in September 2013 would be followed for a full calendar year for pre-and post comparisons or only until the last visit prior to the stated end of the study, November 2013. This has direct implications for interpreting the average number of office visits (if all data is cut-off in November 2013, then the visit number is likely an underestimation) and may also inform why the visual change seen in the 2003 cohort (0.01 LogMar improvement) was so little. In the protocol I DRCRnet trial, the focal laser only arm had gradual visual improvement throughout the last 6 months of the first year of treatment, which if the author's 2003 cohort had an arbitrary cutoff of December 31, then many treated patients would not have the potential for full improvement.[2]

Lastly, new studies are most beneficial when they are placed within the context of other previous reports. This represents the first “real-world” experience that mirrors the results seen in clinical trials for DME. Prior to this, one “real-world” DME study using administrative claims data showed an average of 3.6 injections over 5.3 office visits[3] and another practice based study demonstrated 2.6 injections in the first year of treatment with a mean 3.7 letter increase in vision.[4] These results led Kiss *et al.* to speculate that the difference between clinical trial and real world visual acuity results is likely due to a lower rate of injections received.[4] The current study demonstrates that an average of 9 visits (compared to 13 per year in most clinical trials) can obtain clinical trial level visual acuity results, but without injection frequency data, the reader is unable to fully determine how the ophthalmologists in the practice accomplished this.

The study by Jusufbegovic *et al.* has set a high mark for visual outcomes in a typical clinic setting that the rest of the DME treating community will have to try and match. However, comparisons between this population and others have been greatly limited by the report's omission of important features of the study cohorts and methods for calculating change in visual acuity. Inclusion of these study characteristics would greatly aid the replication of this study in other populations.

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