with CRVO, and again, would be the most clinically useful condition to study.

Finally, with regards to Călugărus' comment using higher doses of bevacizumab, our study was not designed to determine treatment, prevention, or cure of NVG, and thus, we could not draw definitive conclusions about this topic. However, we did cite the results of the RAVE (Rubeosis Anti-VEGF) trial,[7] in which the investigators injected acute ischemic CRVO with 9 treatments of monthly anti-vascular endothelial growth factor (VEGF) therapy. In this trial, 50% of patients developed neovascularization after anti-VEGF injections were discontinued. The investigators of the RAVE trial previously responded to Călugăru regarding these differences in a published reply.[8] Although our study was not designed to answer the question of whether a series of anti-VEGF injections could prevent long-term development of NVG, we did not see a protective effect in patients who received an anti-VEGF injection on presentation compared with those who did not. We also noted, as did the RAVE trial, that those patients who suspended anti-VEGF therapy had a delayed onset of NVG compared with timelines set by previous natural history studies. Again, our study was not designed to look at prevention of NVG. However, we caution any readers who believe that anti-VEGF therapy will prevent or eliminate NVG risk to take into consideration our results as well as those of the RAVE trial.

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Amniotic Membrane Transplantation in Acute Severe Ocular Chemical Injury: A Randomized Clinical Trial

WE READ WITH GREAT INTEREST THE ARTICLE WRITTEN BY Elsani et al. on "Amniotic membrane transplantation in acute severe ocular chemical injury: a randomized clinical trial."[1] The investigators conducted a well-designed study to assess the role of amniotic membrane transplantation (AMT) in severe cases of acute chemical injury (Roper Hall grade 4). However, there are few concerns that we would like to highlight. The grading system used to describe severe chemical injury in this study is the Roper Hall system. It is well known that the Roper Hall grade 4 consists of patients who may markedly differ in the extent of ocular damage. To highlight, the Roper Hall grade 4 includes Dua's grade 4 (conjunctival involvement: >50%-75%; limbal involvement: 6-9 clock hours), grade 5 (conjunctival involvement: >75%-<100%; limbal involvement: 9-<12 clock hours), and grade 6 (conjunctival involvement: 100%; limbal involvement: 12 clock hours) with corresponding prognoses of good to guarded, guarded to poor, and very poor, respectively.[2] Thus, we believe, that if a subgroup analysis of the cases after subclassifying them in accordance with the Dua's grading system is done, the results may differ.

Although, Table 1 suggests that 2 groups were comparable in terms of age, sex, and type of chemical injury, were the 2 groups comparable at baseline in terms of clock hours of limbal involvement?

The investigators state that the remnants of AMT were manually removed at 3 weeks. What was the rationale behind doing the same and how many cases underwent this? Could this have affected the time to healing of epithelial defect? Also, it will be interesting to see if primary AMT affected the final outcome of ocular surface stem cell transplantation done at a later stage. Did the investigators note any difference?

The investigators used central corneal neovascularization as an outcome measure while ignoring the assessment of peripheral corneal neovascularization in the analysis, which is an important parameter for success of any future corneal transplantation that the patient may require. It would be interesting to know the impact of AMT on peripheral corneal neovascularization.

Previous studies reported a beneficial role of AMT in symptomatic relief in patients with chemical injury.[3] However, the investigators did not assess subjective scores (eg, pain) in this study, which they highlighted as a limitation of their study. Therefore, are they justified in concluding that AMT is not useful in these cases and would they recommend AMT if its use results in symptomatic improvement?

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Amniotic Membrane Transplantation in Acute Severe Ocular Chemical Injury: A Randomized Clinical Trial

WE THANK SAHAY AND ASSOCIATES FOR THEIR INTEREST IN our recently published article.

We chose the Roper-Hall system for patient recruitment because of its simplicity and practicality. Considering the incidence of severe chemical injury, it is hard to recruit enough patients with severe chemical injury, who are categorized based on Dua's system, to reach an 80% statistical power for detection of a meaningful difference of corneal epithelial healing (our primary outcome measure).[1] Most similar studies used the Roper-Hall system; thus, using this system allowed us to draw comparisons to these studies in the literature. In our study, all patients had >9 clock hours of limbal involvement, which is categorized as Dua's grades 5 and 6.

Most studies in support of amniotic membrane transplantation (AMT) in severe cases of acute chemical injury are nonrandomized or noncomparative case series. However, as we demonstrated in this trial, which was in line with other clinical trials (Table 4),[1] AMT did not have any added benefits to standard medical therapy in these patients.

We used 2 layers of amniotic membrane (AM); the first layer covered the entire cornea and the second was fixated to the entire ocular surface to decrease inflammation and symblepharon formation. Although the AM spontaneously sloughed off in most cases, there were remnants of AM from the superficial layer in a few cases after 3 weeks. Because of the therapeutic effects of AM have already been delivered to the ocular surface, the remnants are more of a foreign body at this point and need to be removed manually to prevent inducing extra inflammation.

We chose the central 5-mm of corneal neovascularization (NV) as a secondary outcome measure. It is well-known that all patients with severe chemical injury will develop peripheral corneal NV,[2-4] as all of our cases did. Therefore, measuring peripheral corneal NV would not be as valuable or accurate an outcome measure to compare in a randomized clinical trial.

The results of other studies are not conclusive on the effect of AMT for the subjective symptomatic relief in patients with severe chemical injury. We did not specifically include any subjective measures in our trial, as was discussed in our Limitations section. Although our study and other trials provided evidence on the lack of added benefits of AMT to medical therapy in terms of epithelial healing, visual acuity, and corneal NV in patients with severe chemical injury, perhaps future trials may shed more light on other outcome measures (eg, pain).

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