

1 **LETTER TO THE EDITOR**

2 **Corneal Endothelial Cell Loss After Endocapsular and**
3 **Supracapsular Phacoemulsification: The PERCEPOLIS**
4 **Randomized Clinical Trial**

5 Jean-Marc Perone, MD, FEBO^{1*}, Christophe Goetz, MD², Yinka Zevering, PhD¹

6 ¹ Ophthalmology Department, Regional Hospital Center of Metz-Thionville, Metz, France

7 ² Clinical Research Support Unit, Regional Hospital Center of Metz-Thionville, Metz, France

8
9 *Corresponding author:

10 Jean-Marc PERONE, MD

11 Ophthalmology Department

12 Regional Hospital Center of Metz-Thionville

13 1 Allée du Chateau, 57530 Metz, France

14 Phone: +33 3 87 55 77 77

15 Email: jm.perone@chr-metz-thionville.fr

16
17
18 **Financial disclosures/conflicts of interest:** None reported.

19
20 **Key words:** Phacoemulsification surgery, endothelial cell loss, “garde à vous” subluxation
21 technique, divide-and-conquer, anterior chamber depth

To the Editor:

In the March 2023 issue of *Cornea* (Volume 42, Issue 3), Knutsson et al.¹ posed two pertinent questions regarding our prospective randomized clinical trial (designated PERCEPOLIS). This trial, which involved 292 patients with normal–severe density cataracts and no other ocular complications, compared our subluxation phacoemulsification technique (Garde-à-vous)² to a standard endocapsular phacoemulsification technique (Divide-and-Conquer [DAC])³ in terms of postoperative endothelial cell loss (ECL). The study concluded that the subluxation technique was non-inferior to the reference technique in ECL at 3 and 12 postoperative months. Secondary outcome analysis also showed that the effective phaco times were similar but subluxation associated with significantly shorter procedure duration⁴.

Knutsson et al. first noted that our analyses did not include the fluid volume used during the procedure, which is known to contribute to ECL⁵. We agree that this is a study limitation and are addressing it with a large prospective study that is currently underway in our department. This study, which is designated PREDICS (PREDictors of corneal endothelial cell loss in Cataract Surgery; ClinicalTrials.gov Identifier: NCT05265832), is examining the relationships between ECL and ten potential predictive factors, including phacoemulsification technique and amount of fluid used.

The second question posed by Knutsson et al. was whether subluxation and DAC differed in terms of the relationship between anterior chamber depth (ACD) and ECL. This is an excellent question because some studies suggest that shallow ACDs may associate with more phacoemulsification-induced ECL⁶. Since the subluxation technique involves fragmenting the lens in the anterior chamber rather than in the capsular bag, it is indeed possible that this technique induces more ECL in shallow eyes than DAC. To address this question, we conducted Spearman rank correlations. However, a relationship between preoperative ACD and ECL at 3 months was not observed for either the subluxation arm ($r=-0.02$; 95% confidence intervals=-

0.18–0.15; $p=0.83$) or the DAC arm ($r=0.06$; 95% confidence intervals= -0.12 – 0.22 ; $p=0.53$). It should be noted that the subluxation and DAC groups did not differ in preoperative ACD distribution (3.09 ± 0.38 vs. 3.06 ± 0.39 ; $p=0.33$ by Student's *t*-test).

The lack of relationship between ACD and ECL has also been observed by other studies⁷. The reason for this disparity in the literature is not known but Knutsson et al. suggested that it could reflect interactions between ACD and nuclear density, meaning that ECL may only become prominent when the operated eyes have both shallow ACD and a hard cataract. We agree that such risk-factor interactions (and others) may play key roles in ECL and are intending to test these possibilities in the PREDICS study. However, to directly address the possibility proposed by Knutsson et al., we conducted generalized linear model regression analysis with the per-protocol PERCEPOLIS database. The dependent variable was ECL at 3 months and the independent variables were 15 baseline patient factors: age; sex; operated eye side; surgeon experience; preoperative intraocular pressure, central corneal thickness, endothelial cell count, and best-corrected visual acuity; normal/abnormal eye background (e.g. abnormal fundus or associated macular damage); sphere; cylinder; lens thickness; axial length; ACD; and nuclear hardness as indicated by the LOCSIII classification. ACD did not overall predict ECL in the subluxation-arm patients (Beta= $+0.035$; $p=0.43$). Moreover, the interaction terms for ACD in mild (N1–2) or hard (N4–5) cataract hardness relative to the interaction term for ACD in moderate (N3) cataract hardness were negative (Beta= -0.02 ; $p=0.77$ and Beta= $+0.06$; $p=0.40$, respectively). Thus, the subluxation technique did not induce worse ECL when the eyes had both a shallow ACD and a hard nucleus.

Notably, however, when the same analysis was conducted with the DAC-arm patients, shallower ACD tended overall to associate with more ECL (Beta= $+0.09$; $p=0.11$). Moreover, an ACD:cataract-grade interaction analysis tended to be significant (N1/2: Beta= -0.22 ; $p=0.09$). Subgroup analyses suggested that in soft cataracts, shallower ACDs associated with more ECL

(Beta=-0.29; p=0.18). This relationship was not seen for moderate and hard cataracts. We will examine these relationships further with our PREDICS study but nonetheless, these data support the notion that quite complex interactions between patient and surgical variables can lead to higher ECL. Defining those interactions is likely to reveal new avenues to further reducing phacoemulsification-induced ECL.

Knutsson et al. suggested that if the subluxation technique continues to perform robustly in even a potentially worst-case scenario (shallow ACD and hard cataract), it could be helpful for cases with reduced visibility due to corneal alterations. Given the PERCEPOLIS trial and our analyses above, we agree that subluxation would be useful in such cases. We also note that the subluxation technique is easy to learn and use, including for novice operators, and that it associates with significantly shorter total procedure times (5.06 vs. 6.31 min for DAC; p<0.001 on Student's t-test). Thus, we also recommend subluxation as a standard alternative to DAC.

REFERENCES

1. Knutsson KA, Paganoni G, Rama P. Corneal Endothelial Cell Loss After Endocapsular and Supracapsular Phacoemulsification: The PERCEPOLIS Randomized Clinical Trial. *Cornea*. 2023;42:e6. doi:10.1097/ICO.0000000000003224.
2. Perone J-M, Goetz C, Zaidi M, et al. Supracapsular phacoemulsification: Description of the “Garde à vous” technique and comparative clinical results. *J Fr Ophtalmol*. 2019;42:597-602. doi:10.1016/j.jfo.2019.03.002.
3. Coppola M, Marchese A, Rabiolo A, et al. Comparison of two popular nuclear disassembly techniques for cataract surgeons in training: divide and conquer versus stop and chop. *Int Ophthalmol*. 2019;39:2097-2102. doi:10.1007/s10792-018-1046-4.

- 97 4. Perone J-M, Ghetemme C, Zevering Y, et al. Corneal Endothelial Cell Loss After
98 Endocapsular and Supracapsular Phacoemulsification: The PERCEPOLIS Randomized
99 Clinical Trial. *Cornea*. 2022;41:714-721. doi:10.1097/ICO.0000000000002822.
- 100 5. Ungricht EL, Culp C, Qu P, et al. Effect of phacoemulsification fluid flow on the corneal
101 endothelium: experimental study in rabbit eyes. *J Cataract Refract Surg*. 2022;48:481-
102 486. doi:10.1097/j.jcrs.0000000000000768.
- 103 6. Hwang HB, Lyu B, Yim HB, et al. Endothelial Cell Loss after Phacoemulsification
104 according to Different Anterior Chamber Depths. *J Ophthalmol*. 2015;2015:210716.
105 doi:10.1155/2015/210716.
- 106 7. Reuschel A, Bogatsch H, Oertel N, et al. Influence of anterior chamber depth, anterior
107 chamber volume, axial length, and lens density on postoperative endothelial cell loss.
108 *Graefes Arch Clin Exp Ophthalmol*. 2015;253:745-752. doi:10.1007/s00417-015-2934-1.