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CLINICAL SCIENCE

Corneal endothelial cell loss after endo- and supracapsular phacoemulsification: the PERCEPOLIS randomized clinical trial

Jean-Marc Perone MD, FEBO[1], Cedric Ghetemme MD, FEBO[1], Yinka Zevering PhD[1], Mohamed Zaidi MD, FEBO[1], Nadia Ouamara[2], Christophe Goetz MD[2], Louis Lhuillier MD, FEBO[1]

[1] Department of Ophthalmology, Metz-Thionville Regional Hospital Centre, Mercy Hospital, 1 Allée du chateau, CS 45,001, 57,085 Metz-Cedex 03, France.

[2] Clinical Research Support Unit, Metz-Thionville Regional Hospital Centre, Mercy Hospital, 1 Allée du chateau, CS 45,001, 57,085 Metz-Cedex 03, France.

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Corresponding author:
Jean-Marc Perone, MD, FEBO

Department of Ophthalmology, Metz-Thionville Regional Hospital Centre, Mercy Hospital, 1 Allée du chateau, CS 45,001, 57,085 Metz-Cedex 03, France.

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

Telephone Number: +33 3 87 55 34 26

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Keywords

cataract, phacoemulsification, corneal endothelial cell loss, subluxation technique, divide-and-conquer

Abstract

Purpose: Subluxation techniques are superior to divide-and-conquer in terms of procedure duration, pain, and ultrasound quantity but their safety in terms of ECL is unclear. This randomized single-blind non-inferiority clinical trial aimed to determine whether subluxation supracapsular phacoemulsification techniques are inferior to a reference endocapsular technique (divide-and-conquer) with regard to postoperative corneal endothelial-cell loss (ECL).

Methods: Patients (≥18-years-old) with >+0.2 logMAR best spectacle-corrected visual acuity and normal–severe density cataract were randomized to subluxation or divide-and-conquer phacoemulsification in 2015–2016. Follow-up with ophthalmic tests was conducted on day 4 and months 1, 3, and 12. Primary study outcome was ECL at all timepoints. Secondary study endpoints were operative variables, including effective phaco time and procedure duration. A clinically relevant noninferiority ECL limit was established on the basis of the literature.

Results: In total, 292 patients (mean age, 73 years; 59% female) were randomized and underwent subluxation (*n*=148) or divide-and-conquer (*n*=144). Day-4 and month-1, -3, and -12 data were available for 243, 270, 275, and 198 patients, respectively. The unexpectedly high dropout at 12 months meant that the 12-month ECL data could only be assessed qualitatively. Surgery was successful in all patients. Subluxation was non-inferior to divide-and-conquer in terms of ECL. Effective phaco times were similar but subluxation associated with shorter procedure duration.

Conclusions: The subluxation technique was non-inferior to divide-and-conquer with regard to postoperative ECL, at least in the first 3 months, and associated with reduced intervention time. Subluxation techniques may be suitable alternatives to endocapsular techniques.

Trial registration: ClinicalTrials.gov Identifier: NCT02535819.

INTRODUCTION

Multiple studies have reported modifications to phacoemulsification surgery that aim to optimize its efficiency while minimizing corneal endothelial cell loss (ECL) and other complications [1–6]. Consequently, the phacoemulsification modalities can be subdivided into two types, namely, endocapsular [7–9] and supracapsular techniques [10–12].

The endocapsular modalities involve emulsification of the lens within the capsular bag. This approach was pioneered by Gimbel *et al*. [13], who reported the divide-and-conquer (DaC) technique: this is a systematic way of fracturing the nucleus into two or four quadrants. By contrast, supracapsular phacoemulsification employs nuclear fragmentation at the iris plane or above. Thus, these techniques totally or partially transpose the nucleus into the anterior chamber [11,14,15]. One of these supracapsular modalities is the Garde-à-vous ("stand at attention") subluxation technique that we described recently [11,16]: this is based on the tilt-and-tumble method [17]. It is distinguished by gentle and precise double-wave hydrodissection that is performed in micro-coaxial mode and achieves tilting of the nucleus in a vertical/oblique position [11,16].

Several studies have shown that compared to endocapsular techniques, subluxation techniques such as tilt-and-tumble, Garde-à-vous, and others decrease total procedural time, pain, and energy [11,14,18–21]. However, it has been suggested that the supracapsular methods may be limited by the fact that the ultrasound is used closer to the endothelial cells, which could increase damage to the corneal endothelium [12,22]. This was not borne out by small (n=96 and 160 eyes) non-randomized prospective studies comparing DaC to the tilt-and-tumble or Garde-à-vous subluxation techniques, which showed that the two methods did not differ in corneal edema 1–2 hours or 4 days after cataract surgery [16,23]. Since early (2 hours–5 days) increase in corneal edema correlates strongly with greater ECL at 1 and 6 months [11,24], these studies suggest that subluxation methods do not increase ECL.

However, these studies addressed the question indirectly and had study design limitations. To directly and more rigorously test the safety of subluxation phacoemulsification, we conducted the PERCEPOLIS (PERte Cellulaire Endotheliale après PhacOemuLsification Intra ou Supracapsulaire/endothelial cell loss after endo- or supracapsular phacoemulsification) study. This randomized controlled trial determined whether Garde-à-vous subluxation phacoemulsification was non-inferior to DaC technique in terms of ECL over 1 postoperative year. We hypothesized that subluxation phacoemulsification is non-inferior to endocapsular phacoemulsification in terms of ECL.

METHODS

Study Design and Ethics

PERCEPOLIS was a single-centre randomized noninferiority trial (ClinicalTrials.gov Identifier: NCT02535819, IDRCB 2015-A00789-49) that determined whether Garde-à-vous was non-inferior to DaC in terms of average central ECL percentage at Day 4 and Months 1, 3, and 12. It was approved by the CPP Est-III Ethics Committee and the Ethics Committee of the French Society of Ophthalmology (IRB 00008855 Société Française d'Ophtalmologie IRB#1). It adhered to the Declaration of Helsinki. All subjects provided signed informed consent before randomization.

Patient Screening and Randomisation

In June 2015–April 2016, a convenience series of patients was examined for study eligibility during screening visits (baseline visit) in the Ophthalmology Department of Metz-Thionville Regional Hospital Centre (Metz, France) that involved a complete ophthalmic examination (see below). Patients were eligible for inclusion at screening if: they were ≥18

years old; their best spectacle-corrected visual acuity (BSCVA) was >+0.2 logMAR; they had a posterior nuclear (NO1–NO4; NC1–NC4), cortical (C1–C5), or subcapsular (P1–P5) cataract of normal–severe density, as determined by LOCSIII classification [25]; and they consented to participate in the study. Exclusion criteria were: white/brown cataracts; diabetes with insulin dependence/retinal complications; preexisting cornea, ocular tone, or posterior segment pathology; preoperative endothelial-cell density <1500 cells/mm^2; pregnancy; and history of retinal detachment, ocular trauma, or anterior/posterior segment surgery. Patients undergoing additional procedures apart from cataract removal and intraocular-lens implantation were also excluded.

Eligible patients were scheduled for phacoemulsification surgery 4–6 weeks after screening. On arrival, they were randomly assigned 1:1 to undergo subluxation or DaC phacoemulsification by employing computerized random numbers that were given to the surgeon (JMP) by the research methodologist (CG) in the form of sequentially numbered, opaque, sealed, and stapled envelopes. The patients were blinded to the allocation. The allocated surgical procedure was performed unless intraoperative issues caused the surgeon to convert to the other procedure.

The patients were followed up by full ophthalmic examinations (see below) 4 days and 1, 3, and 12 months after surgery.

Pre-and Postoperative Assessments

Complete ophthalmic examinations were conducted at screening and on postoperative Day 4 and Months 1, 3, and 12. They consisted of: intraocular-pressure measurement (Goldmann applanation tonometry); macular OCT (RS 3000, OCT RetinaScan Advance, NIDEK Co, LTD); non-contact central-corneal pachymetry to measure corneal edema and endothelial cell density (specular microscopy; CEM-530, Nidek Co., Ltd.); slit-lamp/fundus

examination; and BSCVA measurement by using the Monoyer chart, after which the values were converted into logMAR. Intra- or postoperative complications (posterior capsular rupture, corneal trauma, possible infections, cystoid macular edema, and visual acuity loss) were recorded.

Surgical Techniques and Operative Variables

The phacoemulsification technique was either the DaC [13] or the subluxation (Garde-à-vous) [11,16] technique. All phacoemulsification procedures were performed under topical anesthesia with 1.6 mg/0.4 mL oxybuprocaine chlorhydrate (Laboratoires Théa, France). Pupillary dilation was achieved with an ophthalmic insert that was saturated with sustained-release 0.28/5.4-mg tropicamide/phenylephrine hydrochloride (Mydriasert; Laboratoires Théa, France), placed under the lower eyelid 1 hour before surgery, and removed just before starting surgery. The surgical steps were as follows: positioning of a blepharostat; creation of a coaxial 2.2-mm corneal mini-incision; injection of dispersive viscoelastic into the anterior chamber (DuoVisc; Alcon Laboratories, Switzerland); creation of a second incision (90° to the first incision) with a 20-gauge needle; circular capsulorhexis; and lens-nucleus hydrodissection.

All phacoemulsifications were performed with the same machine (Stellaris; Bausch & Lomb, Inc., Canada). Surgery was completed with a corneal stitch if required. All patients were given 0.1-mL intracameral injection of cefuroxime (1 mg/0.1 mL, Aprokam; Laboratoires Théa, France) at the end of surgery.

The following operative variables were collected: % ultrasonic power, average phaco time (APT), effective phaco time (EPT), and total procedure time.

Study Endpoints

The primary study endpoint was average percentage of central ECL at day 4 and month 1, 3, and 12 relative to presurgical central endothelial-cell density. The secondary study endpoints were operative variables and surgical success (defined as lack of serious complications and BSCVA of <0.1 logMAR at 3 months). Safety was also assessed by recording intraoperative, immediate, and late (up to 12 months) postoperative complications.

Sample Size

The literature [26–28] indicates that the ECL 1 month after any type of phacoemulsification surgery varies from 5% to 12% with an average standard deviation of 8%. Given a 5% non-inferiority margin, a 95% two-sided significance level, and 90% statistical power, 122 participants per intervention arm were needed (244 in total). Assuming a 20% loss to follow-up rate at 12 months, the target recruitment number was 294 participants.

Statistical Analysis

Patients Excluded From Analysis

Between 0% and 18% of patients did not attend the planned follow-up visit at day 4 and month 1, 3, and 12. These patients were excluded from the analysis at the relevant timepoint. In addition, 28% of the enrolled patients dropped out at some point during the 1-year study, either because they were lost to follow-up, withdrew consent, died, or their implant was changed. These patients were excluded from the analyses at all timepoints after dropout.

Dealing With Patients Who Did Not Undergo the Procedure to Which They Had Been Randomized

In total, 15 (5%) of enrolled patients did not undergo the phacoemulsification procedure specified by the sealed envelope; instead, for clinical reasons, they underwent the other procedure. These patients were included in all data analyses. The Results section largely focuses on analyses that were conducted according to the treatment that was received (per-protocol analysis). However, all analyses were also conducted according to the treatment to which the patients had been randomized (intention-to-treat analysis).

Comparative Statistical Analyses

Baseline and operative variables and ECL at various timepoints were expressed as mean±standard deviation or *n* (%). The patients who underwent DaC and subluxation phacoemulsification were compared in terms of baseline and operative variables by using Fisher's exact test, Student's *t*-test, or Wilcoxon's test. The same analysis was conducted to compare the patients who were randomized to DaC or subluxation. The five subluxation-randomized patients who underwent DaC were compared to the remaining patients who underwent subluxation in terms of baseline and operative variables and ECL at each timepoint by Wilcoxon's or Fischer's exact tests. The same analysis was conducted to compare the 10 DaC-randomized patients who underwent subluxation to the remaining patients who underwent DaC. P values were considered significant when they were <0.05.

Non-inferiority in terms of ECL was assessed with a one-sided *t*-test with the margin added to the null value. Thus, in terms of change in central ECL relative to baseline, the null hypothesis (subluxation is inferior to DaC) was rejected if the upper limit of the two-sided 95% confidence intervals (CI) that were obtained by comparing the interventions in terms of change in ECL was <5%.

All statistical analyses were performed in SAS (version 9.3, SAS Inst., Cary, NC, USA).

Results

Patient Selection and Surgery

In total, 314 patients were considered for inclusion into the study. Of these, seven did not fulfill an eligibility criterion: four had visual acuity <+0.2 logMAR and three had white/brown cataracts. Another 15 failed screening just before randomization and surgery because the protocol had not been/could not be followed: in 12 cases, a check of the patient's case report form showed that the baseline specular microscopy measurements were either missing or inadequate. In another three cases, the protocol-approved surgeon was not available and the surgery had to be conducted by another surgeon. None of these 15 patients were randomized (Figure 1).

The remaining 292 patients were enrolled in the study. Of these, 143 and 149 were randomized to undergo subluxation and DaC phacoemulsification, respectively. However, during surgery, 10 patients who were randomized to receive DaC were converted to the subluxation technique due to the presence of an overly soft core. In addition, five cases who were randomized to receive subluxation surgery were converted to DaC due to poor pharmacologically-induced pupillary dilation (n=2), significant anterior chamber narrowness (n=2), and severely hard crystalline lens (n=1). Thus, 148 and 144 patients actually underwent subluxation and DaC surgery, respectively (Figure 1). All sections below discuss per-protocol analyses except for the last section, which discusses intention-to-treat analyses.

Patient Dropouts and Non-attendance at Follow-up Visits

Of the 148 subluxation and 144 DaC patients, none dropped out before day 4. However, before the month-1 visit, one subluxation patient and four DaC patients were lost to follow-up and were excluded from further analyses. In addition, two subluxation and nine DaC patients dropped out before the month-3 visit due to an implant change, withdrawal of consent, or loss to follow-up. Thus, of the 148 and 144 patients who respectively underwent subluxation and DaC surgery, three (2%) and 13 (9%) dropped out by 3 months. The drop-out rate was much higher at 12 months: 28 subluxation and 40 DaC patients dropped out of the study before the 12-month visit due to withdrawal of consent, loss to follow-up, or death. Thus, of the 148 and 144 patients who respectively underwent subluxation and DaC surgery, 31 (21%) and 53 (37%) dropped out by 12 months (Fig. 1).

Since 0–18% of patients did not attend the planned follow-up visit at day 4 and month 1, 3, and 12, the data of 243, 270, 275, and 198 patients were available for analysis at the day-4, and month-1, -3, and -12 timepoints, respectively. The non-visit rates at the various timepoints were similar for the subluxation and DaC groups (Figure 1).

Since the drop-out/visit non-attendance rate at 12 months exceeded the anticipated rate of 20%, we discussed the month-12 ECL data below in qualitative terms only.

Comparison of Subluxation- and DaC-treated Groups in Terms of Baseline Characteristics

The 148 subluxation-treated patients were significantly younger than the 144 DaC-treated patients (72 *vs.* 75 years, p=0.01) but did not differ in sex or baseline ophthalmic characteristics or, importantly, in preoperative endothelial cell density (p=0.88) (Table 1).

Comparison of Subluxation- and DaC-treated Groups in Terms of Operative Variables and Surgical Success

Table 2 shows that as expected [11], subluxation associated with significantly greater ultrasonic power (17% *vs.* 13%, p<0.001), shorter APT (34 *vs.* 46 sec, p<0.001), and shorter total procedure time (5.09 *vs.* 6.31 min, p<0.001). Most importantly, however, there was no difference in EPT (6 *vs*. 7 sec, p=0.18). Surgery was successful in 100% of patients.

Non-inferiority of Subluxation Surgery Relative to DaC in Terms of ECL Change

The subluxation- and DaC-treated groups had similar baseline endothelial cell densities (2393 *vs.* 2385 cells/mm^2). In both, ECL rose to 7.9–8.5% on postoperative day 4 and then plateaued at 12.7–14.0% around month 1. Compared to DaC, subluxation associated with less ECL relative to baseline at the day-4 (7.9% *vs.* 8.5%), month-1 (12.7% *vs.* 14.0%), and month-3 (12.9% *vs.* 13.4%) visits. At all three timepoints, the upper 95% CIs for the difference between the two groups in ECL were below the non-inferiority limit of 5% (all p≤0.01). Thus, subluxation was not inferior to DaC in ECL in the first 3 months (Table 3). With regard to the 12-month timepoint, subluxation associated with more ECL at the 12-month visit (13.1±11.7% *vs.* 12.5±14.6%) but the delta (95% CIs) was +0.6 (-2.6 – +3.8) (*i.e.* the upper 95% CI was below 5%). It should be emphasized, however, that the study was not sufficiently powered at 12 months for us to definitively conclude that subluxation non-inferiority extends to 12 months as well.

Safety

The DaC-treated group had 11 postoperative complications (mainly superficial epithelial lesions) whereas the subluxation-treated group had six. This difference did not achieve statistical significance. One patient in the subluxation group experienced minor intraoperative capsule rupture that had no effect on lens placement, postoperative course, or final visual outcome (Table 4).

Analysis of the patients according to the randomized treatment

Comparison of DaC-randomized subluxation-treated patients to DaC-randomized/treated patients

The data analyses above all relate to the actual treatment that the patients received. However, 10 DaC-randomized patients underwent subluxation because of an overly soft core. Compared to the DaC-randomized/treated patients, these patients were younger (57±9 *vs.* 75±9 years, $p<0.0001$), more often female (100% *vs.* 55%, $p=0.005$), and associated with shorter EPT (2±1 *vs.* 7±2 sec, $p<0.0001$). However, their baseline endothelial cell density and ECL at the four postoperative timepoints were similar (data not shown).

Comparison of subluxation-randomized DaC-treated patients to subluxation-randomized/treated patients

Five subluxation-randomized patients underwent DaC due to poor pupillary dilation, narrow anterior chamber, or very hard crystalline lens. Compared to the subluxation-randomized/treated patients, these five patients were older (83±3 *vs.* 75±9 years, $p=0.03$) and associated with longer EPT (13±5 *vs.* 7±3 sec, $p=0.04$). Most importantly, despite their similar baseline endothelial cell density (2436 *vs.* 2393 cells/mm^2), their average ECL was three-fold higher than the average ECL of the other subluxation-randomized patients at the month-1

(43.3±21.4 *vs.* 13.2±14.5%, p<0.0001), month-3 (37.0±17.1 *vs.* 13.3±15.8%, p=0.001), and month-12 (32.4±16.2 *vs.* 13.2±11.9%, p=0.01) visits. This is because four of these patients had extremely high ECL after surgery: the mean ECL of these patients at month-1 (3/4 patients attended this visit), month-3 (4/4 patients attended this visit), and month-12 (3/4 patients attended this visit) was 54%, 44%, and 39%, respectively. The subluxation-randomized DaC-treated patients did not differ in ECL from the other subluxation-randomized patients on day 4 because three of the four patients with high ECL did not attend the day-4 visit.

Comparison of subluxation-randomized patients to DaC-randomized patients in terms of baseline and operative variables

Intention-to-treat analysis showed that unlike in the per-protocol analysis, subluxation no longer associated significantly with a younger age (73±10 *vs.* 74±9 years, p=0.69). This is because the 10 DaC-randomized-subluxation-treated patients were younger than the DaC-randomized/treated patients (57 *vs.* 75 years) whereas the five subluxation-randomized patients who converted to DaC were older than the subluxation-randomized/treated patients (83 *vs.* 75 years).

As with the per-protocol analyses, differences were not observed between the subluxation-randomized and DaC-randomized groups in sex, baseline ophthalmic variables, or EPT (data not shown). Thus, it appears that the shorter EPT of the 10 DaC-randomized-subluxation-treated patients annulled the longer EPT of the five subluxation-randomized-DaC-treated patients. Importantly, the two groups did not differ in terms of baseline endothelial cell density and ECL at all timepoints (data not shown).

Non-inferiority of subluxation to DaC in the intention-to-treat analysis

Per-protocol analysis showed that subluxation was not inferior to DaC in ECL at all timepoints (Table 3). However, intention-to-treat analyses showed that although subluxation non-inferiority was again observed at the day-4 and month-1 timepoints (p=0.001 and 0.03, respectively), this was no longer true at 3 and 12 months (p=0.05 and 0.08, respectively). This pattern reflects the high ECL of four of the five subluxation-randomized-DaC-treated patients and the fact that three and one of these patients did not attend the day 4 and month-1 visits, respectively.

Significantly, when these four patients were excluded from intention-to-treat analysis, subluxation was again non-inferior to DaC at all timepoints in terms of ECL (data not shown). However, it should be emphasized again that the study was insufficiently powered at 12 months to definitively conclude that subluxation was non-inferior to DaC at that timepoint.

Discussion

Randomized and prospective studies have shown that compared to endocapsular modalities, supracapsular techniques associate with reduced surgical time [11,20,21] and pain [11] and require lower energy levels during phacoemulsification [11,20,21]. However, there are concerns that subluxation techniques induce higher ECL because of the proximity of the ultrasound to the endothelial cells [12,22].

ECL in the Treatment-received and Randomized-treatment Cohorts

To rigorously address this concern, the PERCEPOLIS randomized controlled trial compared ECL after subluxation and endocapsular phacoemulsification. Our study showed that subluxation is non-inferior to DaC in terms of central ECL, at least during the first 3 months.

While non-inferiority was also observed at 12 postoperative months, the drop-out/visit non-attendance rate decreased the sample size below that needed to identify statistically significant noninferiority (*n*=198; 244 patients needed). Therefore, we cannot conclude that subluxation is non-inferior to DaC at 12 months as well. Nonetheless, these findings suggest that supracapsular techniques are not more prone to more severe ECL. This is the first study that directly tests this question.

It is important to discuss here the analyses that focused on the randomized treatments rather than the treatment that was actually performed: 15 patients did not undergo the surgery to which they were randomized. On intention-to-treat analysis, subluxation was no longer non-inferior to DaC in ECL at month 3 (and month 12, although again, these data must be interpreted with caution due to the high dropout rate at this timepoint). This reflects the high ECL of four of the five subluxation-randomized-DaC-treated patients. This in turn reflected the fact that the lens nucleus in these patients was particularly hard, as demonstrated by their long EPT (13 sec): by contrast, the other subluxation-randomized patients had an EPT of 7 sec (p=0.04). This relationship between EPT, hard cataract, and ECL is confirmed by O'Brien *et al.*: they initially showed on univariate analysis that longer EPT and harder cataracts associated significantly with greater ECL at month 1 (p=0.003 and 0.024, respectively). However, on multivariate analysis, only hard cataract associated with ECL (p=0.048), which indicates that hard cataract accounted for the univariate association between EPT and ECL [49].

In relation to this, it is important to note that the subluxation and DaC groups did not differ in terms of EPT regardless of whether the data were analyzed according to treatment randomized or received: this reflects the small number of subluxation-randomized-but-DaC-treated patients with high ECL. Most importantly, when we removed the four subluxation-randomized-but-DaC-treated patients with high ECL from the analyses, subluxation was again non-inferior to DaC in terms of ECL at all postoperative timepoints.

Other Subluxation and DaC Operative Variables

Subluxation associated with significantly shorter overall procedure time than DaC. This is consistent with previous studies [11,20,21]. This difference reflects the fact that in DaC, the crystalline lens must be fragmented into four or two parts, after which each fragment must then be disintegrated or aspirated: this is time-consuming and prolongs the intervention. By contrast, supracapsular techniques do not require nucleus fragmentation.

Study Limitations

This study has some limitations. First, it was performed in a single center. Further trials in other centers with different surgeons are needed to validate our findings.

Second, the number of patients lost to follow-up increased over time from 6% at 3 months to 29% at 12 months. This was higher than expected: we had anticipated a maximum drop-out rate of 20% when determining the sample size needed for the primary endpoint. The marked drop-out at 12 months may reflect the fact that the study follow-up visits were in the hospital rather than at the usual ophthalmologist; patients who felt well may have been less motivated to travel the extra distance at 12 months. Moreover, compared to subluxation, DaC associated with more drop-out at 3 months (9% *vs.* 3%) and particularly at 12 months (37% *vs.* 21%). This may reflect the fact that the DaC-treated patients were significantly older than the subluxation-treated patients and thus may have been more prone to forgetting the later visits or less able to make the trip to the hospital. While the baseline and 12-month study populations did not differ significantly in terms of baseline variables (data not shown), the 12-month results have been described qualitatively only and should be interpreted with caution.

Third, we did not record the amount of fluid used during the two phacoemulsification techniques. Since subluxation phacoemulsification associates with shorter intervention times

than DaC, and fluid amounts correlate with intervention time [50,51], it is possible that subluxation associates with less fluid use than DaC. This may be significant because the use of large amounts of fluid can promote ECL [50,52,53]. Further studies are needed to determine whether subluxation also has the advantage of employing less fluid.

Conclusions

The subluxation technique was as safe as the DaC method in terms of ECL, at least in the first 3 months. Supracapsular techniques also associate with several advantages compared to the reference endocapsular technique. First, they are easier: they only require two steps that are performed in a continuous and uninterrupted manner. This makes these procedures particularly suitable for novice practitioners. Second, they reduce the risk of capsular rupture because they move the phacoemulsification probe away from the posterior capsular plane. Thus, these procedures may be particularly indicated for younger patients with soft nuclei and myopic patients with large anterior chambers. Third, they lower the APT and EPT and therefore the total procedural time. This saves the surgeon time and money and reduces postoperative pain in patients [11]. Thus, subluxation techniques may be a suitable alternative to endocapsular techniques.

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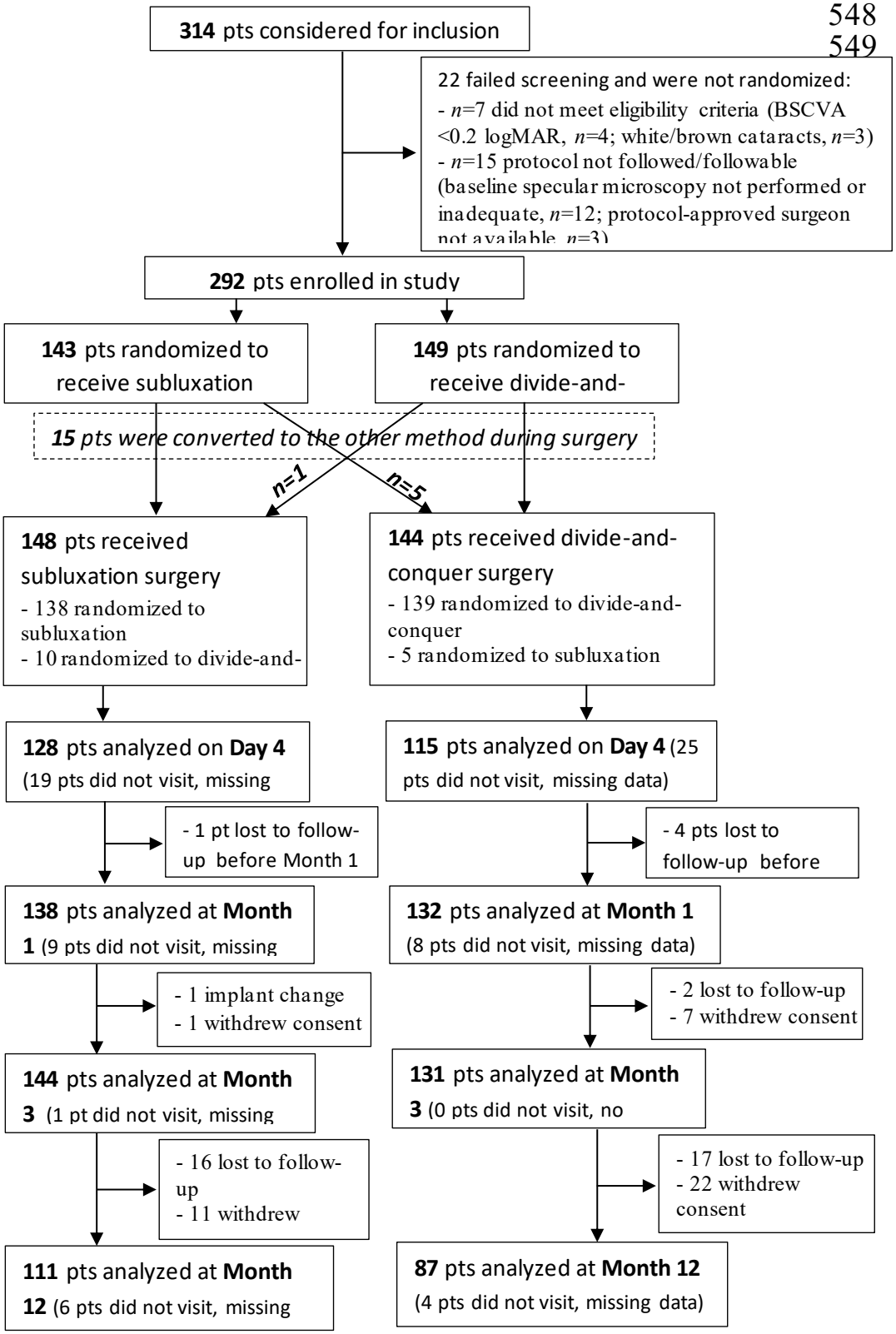
FIGURE

FIGURE 1 Flow diagram depicting patient inclusion and follow-up. BSCVA, best spectacle-corrected visual acuity; pt, patient.



TABLES

TABLE 1. Demographic and Ophthalmic Characteristics of the Enrolled Patients and Their Operated Eye

Characteristic	Subluxation-treated patients *n*=148	Divide-and-conquer-treated patients *n*=144	p value †
Age, years	72±10	75±9	0.01
Female sex	88 (59)	81 (56)	0.90
No. operated on the right eye	71 (48)	78 (54)	0.35
Intraocular pressure, mmHg	18±4	17±3	0.44
Central corneal thickness, μm	557	563	0.13
Endothelial cell density, cells/mm^2	2393	2385	0.88
Density of the cataract			0.15
N1/2	30 (20)	19 (13)	
N3	74 (50)	71 (49)	
N4/5	44 (30)	54 (38)	
Preoperative BSCVA, logMAR	0.41±0.21	0.44±0.18	0.14
Abnormal eye background	15 (10)	13 (9)	0.67
Sphere, D	-0.12±3.89	0.27±3.18	0.36
Cylinder, D	-0.67±0.86	-0.64±0.90	0.83
Anterior chamber depth, mm	3.09±0.38	3.06±0.39	0.33
Lens thickness, mm	4.65±0.33	4.64±0.37	0.90
Axial length, mm	23.32±0.71	23.17±0.77	0.10

The data are presented as average±standard deviation or number (%).
† P values were obtained by comparing the subluxation and divide-and-conquer groups by Fisher's exact test or Student's *t*-test.
BSCVA, best spectacle-corrected visual acuity.

560 **TABLE 2.** Operative Characteristics of the Subluxation and Divide-and-conquer
561 Interventions

Characteristics	**Subluxation *n*=148**	**Divide-and-conquer *n*=144**	**p value †**
Pharmacologically-induced dilation	5 (3)	5 (3)	0.99
Ultrasonic power, %	17±6	13±5	<0.001
Average phaco time (APT), sec	34±11	46±14	<0.001
Effective phaco time (EPT), sec	6±3	7±4	0.18
Overall procedure time, min	5:09±1:03	6:31±2:11	<0.001
Use of a corneal wire	0 (0)	1 (1)	0.49

562 The data are presented as average±standard deviation or number (%).
563 † P values were obtained by comparing the subluxation and divide-and-conquer groups by
564 Fisher's exact test or Student's *t*-test.
565
566

TABLE 3. Postoperative Central Endothelial Cell Loss in the Subluxation- and Divide-and-conquer-treated Eyes

Time point† and variable	Subluxation-treated eyes	Divide-and-conquer-treated eyes	Delta [95% CIs]	p value‡
Before the intervention				
No. of eyes	148	144		
No. of cells per mm²	2393±269	2385±300		
At postoperative day 4				
No. of eyes	128	115		
No. of cells per mm²	2205±337	2194±371		
% loss of cells relative to BL	7.9±12.6	8.5±11.8	-0.6 [-3.2 – +2.0]	<0.001
At postoperative month 1				
No. of eyes	138	132		
No. of cells per mm²	2077±398	2040±471		
% loss of cells relative to BL	12.7±14.4	14.0±16.3	-1.3 [-4.4 – +1.8]	<0.001
At postoperative month 3				
No. of eyes	144	131		
No. of cells per mm²	2078±407	2062±455		
% loss of cells relative to BL	12.9±14.3	13.4±15.6	-0.5 [-3.4 – +2.4]	0.001

The data are presented as number of eyes examined, average±standard deviation of cells/mm², or % endothelial cell loss.

BL, baseline; CI, confidence interval.

† The 12-month data are not shown because the sample size at that time point was insufficient for reliable analysis.

‡ P values were obtained by comparing the subluxation and divide-and-conquer groups by one-sided *t*-tests with the margin added to the null value. Subluxation was considered to be non-inferior to divide-and-conquer with regard to endothelial cell loss when p was <0.05, namely, the upper limit of the 95% confidence intervals that were obtained by comparing the interventions in terms of change in endothelial cell loss relative to baseline was below the non-inferiority margin of 5%.

582 **TABLE 4.** Intra- and Postoperative Complications of the Subluxation- and Divide-and-
583 conquer-treated Eyes

Complication†	**Subluxation-treated eyes *n*=148**	**Divide-and-conquer-treated eyes *n*=144**	**p value‡**
Intraoperative			
Capsule rupture	1 (0.7)	0 (0)	0.99
Postoperative			
Persistent lens masses	2 (1.4)	3 (2.1)	0.67
Macular edema	2 (1.4)	2 (1.4)	0.99
Superficial epith. lesion	2 (1.4)	6 (4.2)	0.16
Total	7 (4.7)	11 (7.6)	0.33

584 The data are presented as number (%).
585 †All complications were minor, including the intraoperative capsule rupture. Persistent lens
586 masses refer to residual masses that do not interfere with visual acuity or induce endothelial
587 cell loss.
588 ‡ P values were obtained by comparing the subluxation- and divide-and-conquer-treated
589 groups by Fisher's exact test.
590 Epith., epithelial
591