Refractive Laser-Assisted Cataract Surgery versus Conventional Manual Surgery: Comparing Efficacy and Safety in 3144 Eyes

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• PURPOSE: To report on outcomes of the efficacy and safety in 1 of the largest series of eyes undergoing either conventional manual cataract surgery (MCS) or refractive femtosecond laser-assisted cataract surgery (ReLACS).

• DESIGN: Retrospective, consecutive, interventional comparative case series.

• METHODS: This study included 3144 consecutive eyes, of which 1580 were treated via MCS, and 1564 were treated via ReLACS at Uptown Surgical Centre in Vaughan, Ontario, Canada. Preoperative characteristics, best corrected visual acuity (BCVA), mean absolute spherical error (MAE), rates of intraoperative posterior capsular rupture, and postoperative complications were evaluated.

• RESULTS: Across all eyes, ReLACS was superior to MCS for reducing surgical time (MCS: 7.7 ± 0.1 min vs ReLACS: 6.8 ± 0.1 min, $P < 0.001$); was less commonly associated with postoperative cystoid macular edema (OR = 0.36, 95% CI: 0.14–0.91, $P = 0.031$) and more commonly reduced MAE (MCS: 0.60 ± 0.02 diopters (D) vs ReLACS: 0.54 ± 0.02 D, $P = 0.02$). There were no differences in rates of posterior capsular rupture ($P = 0.918$), overall postoperative complications ($P = 0.088$) or final BCVA ($P = 0.881$). When analyzing a subgroup of more difficult cases (n = 833), ReLACS was superior to MCS for: 1) being more likely to yield an improvement of more than 0.1 logarithm of the minimum angle of resolution BCVA (OR = 1.80, 95% CI: 1.15–2.74, $P = 0.01$); 2) reducing MAE (MCS: 0.73 ± 0.3 D vs ReLACS: 0.60 ± 0.27 D, $P = 0.04$); and 3) being more likely to yield an MAE within 0.5 D (OR = 1.61, 95% CI: 1.11–2.33, $P = 0.012$).

• CONCLUSIONS: Across all eyes, our results support that ReLACS and MCS yield similar outcomes. However, our results show trends toward a more pronounced benefit of ReLACS compared to MCS when treating more difficult eyes. (Am J Ophthalmol 2019;206:32–39. © 2019 Elsevier Inc. All rights reserved.)

PHACOEMULSIFICATION IS CONSIDERED THE STANdard of care for cataract extraction in the modern world, and it yields controlled lens removal in most patients with excellent results.[1,2] Critical steps of this surgery include the creation of clear corneal incisions, performing the anterior capsulorhexis and fragmenting and removing the lens with minimal ultrasonic energy expenditure and fluid turbulence exposure. These steps influence a number of visual, refractive and safety outcomes postoperatively and are technically challenging to master by physicians-in-training.[3,4]

Femtosecond lasers deliver ultrashort (10^{-15} seconds) pulses of energy at near infrared wavelengths, which can be focused at precise depths in the anterior segment of the eye.[5] This technology has been utilized by the ophthalmic community for many years, most commonly to create corneal flaps for refractive surgery.[6] With the integration of high-resolution anterior segment imaging and precise computer guidance, this laser allows the capability to perform main, side-port and astigmatic corneal incisions, anterior capsulotomy and nuclear fragmentation with minimal damage to surrounding tissue.[1,7–9] Since 2009, there has been tremendous interest in the integration of this technology into phacoemulsification surgery because it has the potential to improve many of the critical steps of the conventional procedure.[10,11] Specifically, this technology has the theoretic benefits of 1) reducing the magnitude of ultrasound energy delivery[12]; 2) reducing the potential of trauma to surrounding structures during lens extraction; and 3) improving the circularity and centration of the anterior capsulotomy and, thus, the effective intraocular lens position.[13] A number of large studies and meta-analyses have compared femtosecond refractive laser-assisted cataract surgery (ReLACS) and conventional phacoemulsification manual cataract surgery (MCS) and have found the safety and efficacy of both methods to be comparable when treating the average cataract.[10,12,14–18]

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Having established comparable outcomes in standard eyes, one must consider whether either method yields superior results in more difficult cases. This served as a point of further investigation, as many of the larger published cohorts excluded difficult cataracts in their analyses.[18,19] A number of studies have been published concerning factors to consider when evaluating the difficulty of a cataract.[20,21] Large cohorts are required to identify these less common difficult cases to allow for a meaningfully powered analysis. The present study reports on 1 of the largest single-center cohort of patients undergoing either ReLACS or MCS. Our aim was to add to the growing body of evidence by 1) reporting on the overall visual, refractive and safety outcomes in both methods of cataract surgery and 2) determining whether difficult cases are better treated by 1 of these modalities.

METHODS

• **STUDY DESIGN:** This retrospective, consecutive, interventional comparative case series included eyes that underwent ReLACS or MCS with interocular lens (IOL) insertion as the solo procedure at a private cataract surgery center (Vaughan, Ontario, Canada). All patients were offered both modalities of surgery, and written informed consent was obtained based on their decision to proceed with either MCS or ReLACS. Five ophthalmologists performed the cataract surgeries between January 2015 and March 2017. The majority (90%) of all cases were performed by authors SS and EST, who performed both MCS and ReLACS. The remaining 10% of cases were performed by authors RM, FN and TL, who performed only MCS cases. This study was approved by the Research Ethics Board of the William Osler Health System in a retrospective manner and was conducted in accordance with the tenets of the Declaration of Helsinki.

• **INTERVENTIONS AND ASSESSMENTS:** Patients underwent baseline anterior and posterior segment examinations and optical biometry measurements preoperatively. The IOLMaster 500 (Carl Zeiss, Oberkochen, Germany) was used for biometry measurement in all patients, with the IOL power calculation and postoperative refractive target calculated using the Haigis formula for all eyes.[22] For eyes with axial length greater than 25 mm, a manual adjustment using the Wang-Koch formula was performed.[23] Eyes were retrospectively graded on their surgical degree of difficulty (DoD) using the criteria illustrated in Figure 1, based on their preoperative examinations. These criteria were adapted from previously published studies of cataract-difficulty grading.[20,21] Namely, the medical chart of each eye was reviewed to identify how many criteria outlined in Figure 1 were present prior to surgery. Lens Opacities Classification System III (LOCS III) grade 4, mature, brunescent or white cataracts were assigned a value of 2, while all other criteria in Figure 1 were assigned a value of 1. The final DoD score for each eye was then calculated by adding the assigned scores for each criterion in Figure 1 that was present preoperatively. Total scores were tabulated for each eye, with a minimum possible score of 0. Two days prior to surgery, all eyes were prescribed topical bromfenac, 1 drop daily; topical besifloxacin, 1 drop 3 times daily; and loteprednol gel, applied 3 times daily.

If an eye was undergoing MCS with a toric IOL, the cornea was marked on the steep meridian prior to the procedure. All MCS eyes were draped using a sterile technique, and topical anesthesia was administered. A metal keratome was used to create the 2.5 mm main clear corneal incision followed by the injection of cohesive (Healon GV, Johnson & Johnson Surgical Vision, Santa Ana, California, USA) and/or dispersive (Healon EndoCoat, Johnson

Surgical Difficulty Variable	Score
Lens Opacities Classification System III (LOCS III) = 3+	1
LOCS III = 4+ OR Mature/Brunescent/White	2
Axial Length > 27mm or Axial Length <20mm	1
Anterior Chamber Depth <2.5mm or Clinically Narrow	1
Previous Angle Closure Glaucoma	1
Previous Vitrectomy	1
Corneal Pathology	1
Small Pupil	1
Posterior Synechiae	1
Pseudoexfoliation	1
Phacodinesis/Zonular Weakness/Dehiscence/Flomax	1
Age > 88 Years	1
Posterior Capsular/Posterior Polar Cataract	1
Capsular Fibrosis/Plaque	1

FIGURE 1. Grading criteria used to measure surgical degree of difficulty (DoD) across all eyes that underwent refractive laser-assisted cataract surgery (ReLACS) or conventional manual cataract surgery (MCS).

& Johnson Surgical Vision) viscoelastic agents into the anterior chamber. The majority of surgeons employed the soft-shell technique,[24] but in some cases used only a single ophthalmic viscosurgical device of their choice, depending upon the individual case. The single-plane side-port incision was made at approximately 3 clock hours from the main incision by using a 2.5 mm metal keratome. Following ophthalmic viscosurgical device injection, an intended 5.0 mm diameter continuous curvilinear capsulorhexis was initiated with a 27-gauge cystotome and completed with capsulorhexis forceps. Thorough hydrodissection was completed using balanced salt solution through a 27-gauge cannula in a 3 mL syringe. Cataract extraction was conducted using the WhiteStar Signature Phacoemulsification System (Advanced Medical Optics, Santa Ana, California, USA). The technique of nuclear removal was left to the discretion of the surgeon. Residual cortex was aspirated by coaxial irrigation/aspiration, and an IOL was implanted into the capsular bag by a wound-assisted technique. The irrigation/aspiration handpiece was used to remove any remaining viscoelastic. Incisions were hydrated with a balanced salt solution, and the operated eye was covered with a plastic shield.

The ReLACS cases were completed using the Catalys Precision Laser System with Liquid Optics Interface (Abbott Medical Optics, Santa Ana, California, USA). The femtosecond laser was employed for the creation of a 2.5 mm main corneal incision, a 1.2 mm side-port incision, a 5.0 mm diameter anterior capsulotomy, steep meridian corneal markings (for toric IOL implantations), 4.5 mm diameter lens fragmentation with grid softening, and limbal relaxing incisions on the steep meridian, as appropriate for each case. Following laser administration, patients proceeded with cataract surgery as described for the MCS group. There were no medical contraindications for ReLACS in this study.

During the 1-month postoperative period, all eyes were prescribed topical bromfenac, 1 drop daily, topical besifloxacin 1 drop 3 times daily and loteprednol gel applied 3 times daily. Patients were reviewed within 24 hours and at 1 and/or more weeks postoperatively. The mean maximum follow-up across all eyes was 22 days (range 7–60 days). At these follow-up visits, a complete slit-lamp examination, tonometry and measurements of visual acuity and refraction were completed.

• **OUTCOME MEASURES:** Intraoperative outcomes of interest were: 1) odds ratio (OR) of ReLACS having an intraoperative posterior capsular rupture or tear (PCR) relative to MCS; 2) differences in duration of cataract surgery; and 3) differences in effective phacoemulsification time (EPT). Surgical time was measured as the time between the application and the removal of sterile draping used for phacoemulsification. Visual outcomes included: 1) the difference in the logarithm of the minimum angle of resolution (LogMAR) best corrected visual acuity (BCVA) at last follow-up between groups; 2) the OR of ReLACS achieving an improvement of at least 0.1 LogMAR BCVA at last follow-up relative to MCS; and 3) the OR of ReLACS achieving BCVA 20/40 or better relative to MCS. Refractive outcome measures included: 1) difference in mean absolute refractive error (MAE) (calculated by finding the absolute difference between the final refractive spherical equivalent and the refractive target predicted as per preoperative biometry); 2) the OR of ReLACS achieving a MAE within 0.5 diopters (D) relative to MCS; and 3) the OR of ReLACS having a postoperative refractive surprise (MAE $>$ 2.0 D) relative to MCS. The OR of having postoperative complications (defined as a composite of developing corneal edema, intraocular pressure spike, anterior chamber reaction, lens complication, iritis, vitreous loss, cystoid macular edema, dysphotopsia, or posterior capsular opacification at any postoperative time point within 3 months) was computed. These analyses were repeated in a subgroup of cases with surgical DoD $>$ 0.

• **STATISTICAL ANALYSIS:** Baseline categorical parameters were reported as proportions, with differences compared using the Fisher exact test, and continuous variables were reported as means ± standard deviation (SD) with differences compared using the *t* test. For the purpose of data analysis, Snellen visual acuity measurements were converted to the logMAR equivalents. OR and estimated means are presented after adjusting for baseline characteristics, such as age, visual acuity, keratometry, spherical equivalent, and surgical DoD. Adjusted estimates were computed using generalized linear models for mean differences and logistic regression for adjusted OR. A 2-tailed $P < 0.05$ was considered statistically significant throughout the study. All data were extracted and stored in Microsoft Excel software (Microsoft, Redmond, Washington, USA). Statistical analysis was performed using SPSS version 22 (IBM, Armonk, New York, USA).

RESULTS

A TOTAL OF 3144 CONSECUTIVE EYES WERE INCLUDED IN THIS study; 1580 eyes were in the MCS group, and 1564 eyes were in the ReLACS group. Table 1 outlines the demographics and preoperative characteristics of both groups. All cases planned for ReLACS were successfully completed. Patients in the ReLACS group were slightly younger ($P < 0.001$), had greater mean preoperative spherical equivalents ($P < 0.001$), IOPs ($P = 0.008$), axial lengths ($P < 0.001$), anterior chamber depths (ACD) ($P < 0.001$), and DoDs ($P = 0.014$) when compared to the MCS group. ReLACS was associated with 64% greater odds of treating eyes with a DoD score greater than 1 when compared to MCS ($P = 0.008$). The refractive target was slightly more myopic

TABLE 1. Baseline Characteristics of Eyes That Underwent Refractive Laser-Assisted Cataract Surgery or Conventional Manual Cataract Surgery

	MCS (N = 1580)	ReLACS (N = 1564)	*P* Value
Age at surgery (years)	70.6 ± 9.7	68.6 ± 9.5	<0.001
Age <70 years	44.1%	52.0%	<0.001
Age >70 years	55.9%	48.0%	
Female	56.1	55.2	NS
BCVA LogMAR	0.50 ± 0.4	0.52 ± 0.4	NS
BCVA ≤0.2 LogMAR	19.7%	19.4%	0.816
BCVA >0.2 LogMAR	80.3%	80.6%	
Mean keratometry (D)	43.9 ± 1.7	43.8 ± 1.7	NS
Spherical equivalent (D)	2.3 ± 2.4	2.8 ± 3.4	<0.001
Cylinder (D)	1.25 ± 0.90	1.24 ± 0.96	0.784
IOP (mmHg)	14.7 ± 3.4	15.1 ± 3.7	0.008
Refractive target (D)	−0.24 ± 0.5	−0.36 ± 0.7	<0.001
Targeted for distance (>−0.5 D)	92.2%	87.3%	<0.001
Not targeted for distance (<−0.5 D)	7.8%	12.7%	
Axial length (mm)	23.6 ± 1.3	23.9 ± 1.6	<0.001
Axial myope (≥24.8 mm AL)	14.9%	24.8%	<0.001
Nonaxial myope (<24.8 mm AL)	84.1%	75.2%	
Axial hyperope (≤22 mm AL)	6.8%	4.2%	0.002
Nonaxial hyperope (>22 mm AL)	93.2%	95.8%	
ACD (mm)	3.0 ± 0.4	3.1 ± 0.4	<0.001
Deep AC (≥3.5 mm)	14.6%	22.3%	<0.001
Nondeep AC (<3.5 mm)	85.4%	77.7%	
Shallow AC (≤2.5 mm)	8.4%	5.7%	0.003
Nonshallow AC (>2.5 mm)	91.6%	94.3%	
LOCS III Grade 0–2+	90.4%	87.0%	0.003
LOCS III Grade ≥3+	9.6%	13.0%	
IOL power (D)	21.1 ± 3.5	20.4 ± 4.3	<0.001
Surgical DoD	0.29 ± 0.5	0.34 ± 0.6	0.014
Surgical DoD >0	25.3%	27.7%	0.115
Surgical DoD >1	3.1%	5%	0.008
Follow-up length (days)	22.3 ± 28	22.4 ± 28	NS

ACD = anterior chamber depth; AL = axial length; BCVA = best corrected visual acuity; DoD = degree of difficulty; IOP = intraocular pressure; LOCS = Lens Opacities Classification System III; LogMAR = logarithm of the minimum angle of resolution.

Data are mean ± standard deviation unless otherwise indicated.

in the ReLACS group ($P < 0.001$), and the power of the implanted IOL was slightly greater in the MCS group ($P < 0.001$). The mean length of maximum follow-up was similar in both groups ($P = 0.90$).

Table 2 outlines intraoperative and postoperative outcomes. After correcting for patient age and DoD, ReLACS eyes were associated with faster surgical times ($P < 0.001$), and there was a trend toward lower EPT in the ReLACS eyes, but this was not found to be statistically significant ($P = 0.217$). In eyes with LOCS III Grade 0–2+ cataracts, surgical time was significantly less when treated via ReLACS (ReLACS, 6.38 ± 2.75 minutes, vs MCS, 7.14 ± 4.82 minutes; $P < 0.001$). In eyes with LOCS III Grade ≥ 3+ cataracts, surgical time was, again, significantly less when treated via ReLACS (ReLACS, 7.80 ± 3.63 minutes vs MCS, 10.02 ± 10.42 minutes; $P = 0.02$). The rates of PCR were comparable ($P = 0.92$). The odds of having any postoperative complication were similar in both groups ($P = 0.09$) after adjusting for patient age and surgical DoD. A total of 23 eyes developed postoperative cystoid macular edema (CME). The odds of developing CME were significantly less in eyes from the ReLACS group (OR = 0.36, 95% CI: 0.14–0.91, $P = 0.03$).

Table 3 outlines visual and refractive outcomes. Final adjusted LogMAR BCVA was similar in both groups ($P = 0.88$). The odds of improving LogMAR BCVA by more than 0.1 was similar in both groups ($P = 0.14$). The odds of achieving a BCVA of 20/40 or better was similar in both groups ($P = 0.48$) but was more likely in eyes with DoD = 0 (OR = 1.45, 95% CI: 1.15–1.82, $P = 0.002$). The MAE was significantly less in the ReLACS group ($P = 0.02$), and the odds of being within 0.5 D of MAE was similar in both groups ($P = 0.43$). The odds of having a refractive surprise were similar in both groups ($P = 0.59$).

• **SUBGROUP ANALYSIS OF DIFFICULT EYES:** A total of 833 eyes had a DoD > 0; 399 eyes were treated via MCS, and 434 eyes were treated via ReLACS. After adjusting for confounders, ReLACS eyes had faster surgery times than MCS eyes ($P < 0.001$). There was a trend toward lower EPT in the ReLACS eyes, but this was not found to be statistically significant ($P = 0.50$). The odds of PCR were not different in the groups ($P = 0.55$). The odds of having any postoperative complications were similar in both groups ($P = 0.91$).

The final adjusted LogMAR BCVA was superior in the ReLACS group when compared to the MCS group ($P = 0.028$). Similarly, the ReLACS group showed an increased magnitude of LogMAR BCVA improvement compared to MCS (ReLACS −0.25 ± 0.1 vs MCS −0.20 ± 0.1, $P = 0.03$), and the odds of improving LogMAR BCVA by more than 0.1 was significantly more likely in the ReLACS group (OR = 1.80, 95% CI: 1.15–2.74, $P = 0.01$). The odds of achieving a BCVA of 20/40 or better was similar in both groups ($P = 0.33$). The MAE was significantly less in the ReLACS group ($P = 0.04$), and the odds of MAE being within 0.5 D was more likely in the ReLACS group (OR = 1.61, 95% CI: 1.11–2.33, $P = 0.012$). The odds of having a refractive surprise were similar in both groups ($P = 0.95$).

TABLE 2. Intraoperative and postoperative Outcomes Across All Eyes That Underwent ReLACS or MCS and across Eyes With Surgical Degree of Difficulty Greater Than 0

	All Eyes (N = 3144)[a]			DoD >0 Subgroup (N = 833)[b]		
	MCS	ReLACS	*P* Value	MCS	ReLACS	*P* Value
ST (min)	7.7 ± 0.1	6.8 ± 0.1	<0.001	10.0 ± 2.0	8.6 ± 2.0	<0.001
EPT (sec)	33.4 ± 1.1	31.8 ± 0.8	NS	40.4 ± 13	38.3 ± 13	NS
% PCR	0.7	0.6	NS	1.3	0.7	NS
% CC	7.2	7.3	NS	9.0	8.1	NS
% CME	1.1	0.4	0.03	NR	NR	NR

CC = 3-month complication composite; CME = cystoid macular edema; DoD = degree of difficulty; EPT = effective phacoemulsification time; MCS = manual cataract surgery; NR = not reported due to small cell size; PCR = posterior capsular rupture; ReLACS = refractive laser-assisted cataract surgery; ST = surgical time.

Continuous variables are expressed as estimated means ± standard error. All estimates included patient age as a covariate.

[a]Estimate model adjusted by DoD.

[b]Estimate model included surgical DoD characteristics from Figure 1 as factors.

TABLE 3. Visual and Refractive Outcomes at Final Follow-up Across All Eyes That Underwent Relacs or MCS and Across Eyes With Surgical Degree of Difficulty Greater Than 0

	All Eyes (N = 3144)[a]			DoD >0 subgroup (N = 833)[b]		
	MCS	ReLACS	*P* Value	MCS	ReLACS	*P* Value
Final BCVA	0.26 ± 0.01	0.25 ± 0.01	NS	0.41 ± 0.1	0.36 ± 0.1	0.028
% ΔBCVA >0.1	66.0	69.1	NS	67.8	75.3	0.01
% BCVA >20/40	77.2	77.9	NS	68.0	70.0	NS
MAE	0.60 ± 0.02	0.54 ± 0.02	0.02	0.73 ± 0.3	0.60 ± 0.27	0.04
% MAE ± 0.5 D	57.0	58.3	NS	51.4	58.0	0.012
% MAE >2.0 D	2.9	2.4	NS	2.8	2.9	NS
Cylinder	0.91 ± 0.22	0.67 ± 0.23	<0.001	1.00 ± 0.05	0.76 ± 0.05	0.002

BCVA = best corrected visual acuity; ΔBCVA >0.1 = improvement in LogMAR BCVA >0.1; BCVA >20/40 = achieved BCVA 20/40 or better; D = diopter; DoD = degree of difficulty; MAE = mean absolute spherical error; MAE ± 0.5 D = mean absolute spherical equivalent achieved within 0.5 D of refractive target; LogMAR = logarithm of the minimum angle of resolution; MAE >2.0 D = refractive surprise.

Continuous variables expressed as estimated means ± standard error.

All estimates included patient age, preoperative LogMAR BCVA, preoperative spherical equivalent and mean keratometry as covariates.

[a]Estimate model adjusted by DoD.

[b]Estimate model included surgical DoD characteristics from Figure 1 as factors.

DISCUSSION

THIS STUDY REPORTS ON 1 OF THE LARGEST CONSECUtive cohort of patients undergoing either MCS or ReLACS. Consequently, it provided the opportunity to analyze a large subgroup of patients with eyes more difficult to treat. Across all eyes, our results corroborate previously published studies demonstrating a similarity of visual and refractive outcomes of ReLACS vs MCS. However, upon further investigation, our results show trends toward a more pronounced benefit of ReLACS compared to MCS when treating more difficult eyes.

The noninferiority of ReLACS relative to MCS with regard to visual and refractive outcomes has been reported by a number of studies. In their large prospective, consecutive series of patients undergoing either modality of cataract extraction, Ewe and associates (2016) found marginally better BCVA in their laser-assisted cases; however, patients treated with MCS showed greater improvement in LogMAR visual acuity.[17] More recently, Berk and associates (2018) did not detect a difference between MCS and ReLACS in the proportion of patients achieving favorable uncorrected visual acuity.[18] Furthermore, results from the European Registry of Quality Outcomes for Cataract and Refractive Surgery (EUREQUO) similarly indicated

comparable visual outcomes in both groups; however, this study discussed the difficulty associated with matching their cases, thus compromising the ability to compare consecutively entered patients.[16] Regarding refraction, studies have reported better[25] and poorer outcomes in eyes treated with ReLACS,[17] whereas other studies have shown no difference between the groups.[18,26] Interestingly, in the present study, across all eyes, there was a marginal refractive benefit of pursuing ReLACS.

The overall results of our study are consistent with previously published studies, but it is important to note subtle differences in patient selection. Namely, previous studies excluded patients with coexisting ocular conditions and/or extremes of optical parameters.[18,19] However, the present study analyzed patients consecutively, which increases the generalizability of our results. It was, therefore, found that in this cohort, ReLACS seemed to be the technique used in more difficult cases. Despite this difference, the overall visual and refractive outcomes were similar when the 2 groups were compared. Furthermore, the inclusion of all cases allowed us to perform a subgroup analysis of more difficult eyes so as to delineate whether either modality yields superior results in such cases. These potential differences may have been masked in previously published studies investigating mostly routine cataracts.

When looking only at eyes more difficult to treat, our results indicated that ReLACS improves vision by roughly one-half a line of BCVA (0.05 LogMAR) more than MCS, on average, and eyes that improved by at least 0.1 LogMAR BCVA were associated with 80% higher odds of being treated by ReLACS. MAE was lower in ReLACS compared to MCS by an order of magnitude of 0.13 D in difficult eyes (DoD > 0). Furthermore, difficult eyes within 0.5 D of refractive target were associated with 61% higher odds of having been treated by ReLACS. The effect sizes present in the subgroup of difficult-to-treat eyes were not only statistically significant but were also larger in magnitude when compared to the overall sample. Although the clinical meaningfulness of these differences is debatable, these results highlight the importance of investigating these modalities in a wider context of patients, especially in those presenting with eyes more challenging to treat.

Martin and associates (2013) published a review of the potential of femtosecond-laser-assisted cataract surgery in challenging cases and encouraged future studies to explore the broader clinical indications and possible benefits of this expanding technology.[27] Previous studies have considered surgical difficulty as a modifier variable in their analyses. In their analysis of the EUREQUO, Manning and associates carefully matched both groups of patients by the prevalence of surgical difficulty variables.[16] However, eyes in their laser-assisted group were more likely to have had previous refractive surgery and pseudoexfoliation, while white cataracts and small pupils were more likely in the MCS group. Nonetheless, the study reported on overall outcomes and did not stratify their analyses by level of surgical difficulty. In their large retrospective analysis, Berk and associates identified a number of factors in which laser-assisted surgery was more likely to be within an absolute refractive error of 0.5 D: 1) eyes with axial length > 22.0 mm; 2) deep anterior chamber and nonshallow anterior chamber; 3) nuclear sclerosis grade 0–2+; 4) eyes receiving a monofocal IOL; and 5) patients without diabetes mellitus.[18] Furthermore, the usefulness of ReLACS with regard to the creation of the anterior capsulotomy has also been reported in mature cataracts and in eyes with zonulopathy.[28] ReLACS has also been reported to significantly reduce EPT when compared to MCS in brunescent cataracts.[29] Although our results did not identify a difference in EPT between groups, we found surgical time to be significantly less in the ReLACS procedure eyes across all eyes. Among the subgroup analysis in eyes with DoD greater than 1, a greater benefit of ReLACS in reducing surgical time was noted. This is likely to be due to the time saved from having completed laser-induced lens fragmentation and capsulotomy formation.

With regard to the lens capsule integrity, one would expect that the benefits of a femtosecond laser capsulotomy (consistency of capsulotomy size,[28] less lens manipulation and less ultrasound energy delivery to the eye[29]) would help to reduce the risk of PCR. However, the tensile strength of the lens capsule following femtosecond laser-induced capsulotomy may be debatable.[30] A meaningful comparison of PCR rates is difficult, given the small number of events, even in large studies. In their meta-analysis, Popovic and associates pooled data from 4 prospective studies and 1 retrospective study, which yielded a weighted overall risk ratio of 3.73 (95% CI: 1.50–9.25, $P = 0.005$) in favor of MCS being less associated with PCR.[10] Since then, a number of large studies have published their PCR data, which did not show a clear difference in PCR risk.[16,18] Berk and associates indicated a PCR rate of 4 of 883 eyes in the MCS group and 9 of 955 eyes in the laser-assisted group,[18] and Manning and associates reported PCR in 15 of 4987 MCS-operated eyes and 8 of 2814 laser-assisted operated eyes.[16] Our data showed PCR rates of 11 of 1580 eyes treated in the MCS group and 9 of 1564 eyes treated with ReLACS. By pooling the data from these large series of patients with the studies pooled in Popovic and associates, using Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark), we recalculated a smaller meta-estimated risk ratio of 2.09 (95% CI: 1.04–4.20, $P = 0.04$) in favor of MCS being less closely associated with PCR (Figure 2). Interestingly, across the 8 studies from which data were pooled, the largest 2 (the present study and Manning and associates) were the only ones to yield a risk ratio in favor of ReLACS, although these results were not statistically significant. The variability of the relative PCR rates from these studies probably depends on surgeons' experience and the surgical difficulty of the cases treated.[15]

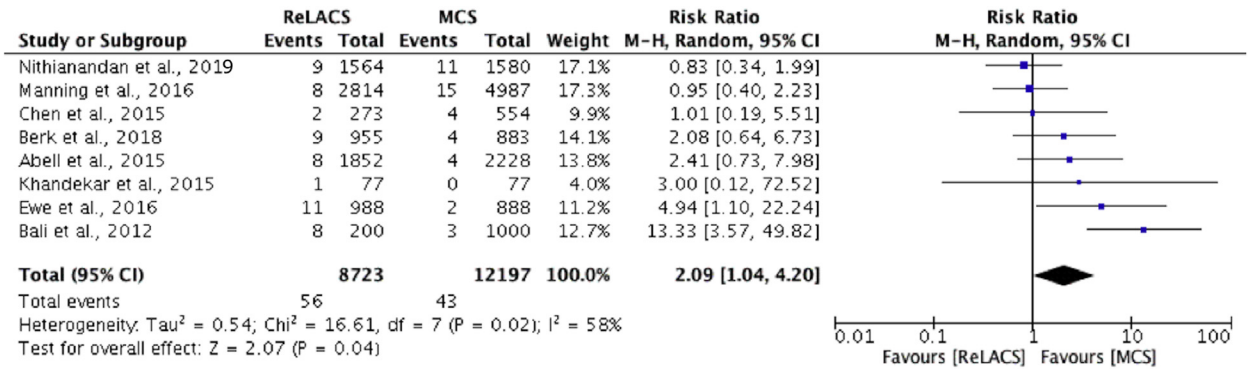

FIGURE 2. Meta-estimate of posterior capsular rupture rates in recent cohorts comparing femtosecond laser-assisted cataract surgery and conventional manual cataract surgery.

With regard to overall postoperative complications, our study did not detect significant differences in complication rates across all eyes or in the subgroup of difficult eyes. This finding is consistent with other studies.[10,14] However, in our series, CME was more prevalent in those treated by MCS. This is in contrast to the results reported by Ewe and associates, which demonstrated CME to develop in 0.8% and 0.1% in laser-assisted and conventional MCS cases, respectively.[17] The meta-analysis published by the Cochrane Review yielded inconclusive evidence concerning differences in CME rates in these groups.[31] Interestingly, increased levels of prostaglandins have been reported in laser-assisted procedures relative to MCS[32,33]; however, the perioperative use of topical NSAID eye drops may partially explain the lack of any difference in clinical CME rates in the 2 groups in our series.

Despite the strengths of this large consecutive series, it does follow a retrospective design, which has its own inherent limitations. First and foremost, our study design was not able to randomize patients preoperatively to either treatment group, which led to slightly different baseline characteristics between MCS and ReLACS in our study. To address these possible confounders, we employed the use of robust statistical methods and reported adjusted estimates of effect sizes based on factors that likely affected our outcomes. As with all nonrandomized studies in this area, it is likely that patients who elected to pursue ReLACS represented a different socioeconomic population than those undergoing MCS. Although the mean follow-up of 22 days in our series may not have captured all later-onset complications (eg, CME), nonetheless, these results may still be generalizable to most clinical practices where stable patients with good outcomes are discharged to a primary care provider sooner. Furthermore, we did not detect differences between our treatment groups with regard to their mean maximum length of follow-up.

Our study supports the well-established similarity between ReLACS and MCS with regard to visual and refractive outcomes in a very large, consecutive cohort. However, our results support the potential role for ReLACS in more difficult cases, although larger randomized studies in such cases are needed to further delineate this trend. Surgeon experience and comfort, patient preference and economic considerations remain critical factors of consideration for the choice of cataract surgery modality.

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