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Efficacy and Safety of Femtosecond Laser-Assisted Cataract Surgery Compared with Manual Cataract Surgery

A Meta-Analysis of 14 567 Eyes

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Topic: To investigate the efficacy and safety of femtosecond laser-assisted cataract surgery (FLACS) relative to manual cataract surgery (MCS).

Clinical Relevance: It is unclear whether FLACS is more efficacious and safe relative to MCS.

Methods: A literature search of MEDLINE, EMBASE, and Scopus from 2007 to March 2016 was conducted. Studies containing both FLACS and MCS arms that reported on relevant efficacy and/or safety parameters were included. Weighted mean differences (WMDs) and risk ratios (RRs) with 95% confidence intervals (CIs) were calculated.

Results: From 2802 screened articles, 14 567 eyes from 15 randomized controlled trials and 22 observational cohort studies were included. For primary visual and refractive outcomes, no statistically significant difference was detected between FLACS and MCS in uncorrected distance visual acuity (WMD, −0.02; 95% CI, −0.04 to 0.01; $P = 0.19$), corrected distance visual acuity (WMD, −0.01; 95% CI, −0.02 to 0.01; $P = 0.26$), and mean absolute error (WMD, −0.02; 95% CI, −0.07 to 0.04; $P = 0.57$). In terms of secondary surgical end points, there was a statistically significant difference in favor of FLACS over MCS for effective phacoemulsification time (WMD, −3.03; 95% CI, −3.80 to −2.25; $P < 0.001$), capsulotomy circularity (WMD, 0.16; 95% CI, 0.11–0.21; $P < 0.001$), postoperative central corneal thickness (WMD, −6.37; 95% CI, −11.88 to −0.86; $P = 0.02$), and corneal endothelial cell reduction (WMD, −55.43; 95% CI, −95.18 to −15.69; $P = 0.006$). There was no statistically significant difference between FLACS and MCS for total surgery time (WMD, 1.25; 95% CI, −0.08 to 2.59; $P = 0.07$), capsulotomy circularity using a second formula (WMD, 0.05; 95% CI, −0.01 to 0.12; $P = 0.10$), and corneal endothelial cell count (WMD, 73.39; 95% CI, −6.28 to 153.07; $P = 0.07$). As well, there was a significantly higher concentration of prostaglandins after FLACS relative to MCS (WMD, 198.34; 95% CI, 129.99–266.69; $P < 0.001$). Analysis of safety parameters revealed that there were no statistically significant differences in the incidence of overall complications between FLACS and MCS (RR, 2.15; 95% CI, 0.74 to 6.23; $P = 0.16$); however, posterior capsular tears were significantly more common in FLACS versus MCS (RR, 3.73; 95% CI, 1.50–9.25; $P = 0.005$).

Conclusions: There were no statistically significant differences detected between FLACS and MCS in terms of patient-important visual and refractive outcomes and overall complications. Although FLACS did show a statistically significant difference for several secondary surgical outcomes, it was associated with higher prostaglandin concentrations and higher rates of posterior capsular tears. *Ophthalmology 2016;■:1–14 © 2016 by the American Academy of Ophthalmology.*

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Today, more than 9.5 million cataract surgeries are performed each year worldwide.[1] Advances in measurement technology, emergence of phacoemulsification, and invention of foldable lens designs have lead to increasingly safer and more predictable results. These technologies also have allowed cataract surgery to become a refractive procedure with increasingly precise postoperative refractive results.[2]

Manual cataract surgery (MCS) involves the creation of corneal incisions with a keratome blade, a continuous curvilinear capsulorrhexis using forceps or a cystotome, and manual splitting or cracking of the nucleus followed by phacoemulsification and cortical aspiration. Although the current standard of care procedure confers a favorable efficacy and safety profile, complication rates vary by surgeon

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and setting after MCS, suggesting that a more automated procedure may achieve more reproducible results.[3,4]

Femtosecond laser-assisted cataract surgery (FLACS) is a technology that uses a laser to replace several of the manual steps of cataract surgery with the goal of improving accuracy, safety, and refractive outcomes. Femtosecond laser-assisted cataract surgery uses a femtosecond laser to generate free electrons and ionized molecules, which in turn produce photodisruption and photoionization of optically transparent tissue through an acoustic shock wave.[5] The femtosecond laser is unique because of its shorter pulse time relative to other ophthalmic lasers.[6] Theoretically, lasers with shorter pulse times are able to reduce energy output significantly for a given effect, thereby reducing collateral damage to ocular tissues.

Femtosecond lasers have been used in several different stages of cataract surgery, including clear corneal incisions, capsulotomy, and lens fragmentation. Femtosecond laser-assisted cataract surgery was approved for cataract surgery by the United States Food and Drug Administration in 2010.[7] By 2013, more than 120 000 eyes globally had undergone FLACS.[8] A 2014 survey of new FLACS adopters in the United States showed that 30% of cataract patients choose FLACS over conventional MCS.[9]

Given the increasing interest in FLACS, evidence of safety and efficacy of this technology is needed urgently. In 2013, the Department of Veterans Affairs published a systematic review in the gray literature that concluded that there was no current benefit in the safety and effectiveness of FLACS relative to MCS.[10] Furthermore, they noted that there were significant methodologic concerns in the included studies, including low sample sizes, unclear study methods, few randomized controlled trials, issues with patient selection, and financial conflicts of interest. More recently, the first published meta-analysis of FLACS compared with MCS was conducted in 2015 by Chen et al.[11] Analyzing a total of 989 eyes and 9 randomized controlled trials, the authors found a statistically significant improvement for FLACS over MCS in terms of mean phacoemulsification energy and effective phacoemulsification time; however, there was no difference for surgical complications. There were conflicting results for visual outcomes, central corneal thickness, and endothelial cell count depending on the length of follow-up at which outcomes were compared.

An updated and comprehensive meta-analysis of peer-reviewed clinical studies comparing FLACS with MCS is needed. This synthesis would be useful to clinicians, policy makers, and researchers who are interested in identifying the role of FLACS. Thus, we performed a meta-analysis to investigate the comparative efficacy and safety of FLACS relative to MCS in published clinical studies.

Methods

Search Strategy

Using Ovid MEDLINE (2007−March 2016, week 2), MEDLINE In-Process and Other Non-Indexed Citations (up to March 18, 2016), EMBASE (2007−2016, week 12), and Scopus (2007−March 2016), a systematic search of the literature was performed (Appendix 1A−C, available at www.aaojournal.org). Reference lists of included articles and pertinent reviews also were searched.

Eligibility Criteria

Studies were included if they met the following criteria: (1) randomized controlled trials or prospective or retrospective observational cohort studies; (2) studies that included only patients who underwent cataract surgery; (3) studies that provided safety or efficacy data, or both, for both FLACS and MCS study arms; and (4) studies that accrued more than 5 eyes to each study arm. The following exclusion criteria were used in the selection of included studies: (1) nonpublished articles (e.g., abstracts and conference proceedings); (2) articles not published in English; (3) articles with repeat data; (4) case reports or small ($\leq$5 eyes per study arm) case series; and (5) literature reviews, letters to the editor, correspondence, notes, editorials, and forthcoming journal articles. Given that existing studies in the published literature were used for this meta-analysis, institutional review board approval was not necessary. Nonetheless, the study adhered fully to the Declaration of Helsinki.

Study Selection, Data Collection, and Outcome Measures

Two authors (M.P. and X.C.-M.) examined search results to select pertinent articles for inclusion, first by title and abstract screening and then by screening full text articles. Uncertainty in inclusion was resolved through consultation with a third author (M.B.S.). The same 2 authors (M.P. and X.C.-M.) extracted the following baseline demographic and clinical data from each study arm: study design, country of origin, femtosecond laser type, date of intervention, number of included eyes, mean cohort age, gender distribution, mean corrected distance visual acuity (CDVA), and mean axial length. In addition, a comprehensive list of intraoperative and postoperative outcomes were extracted from included studies and were reported using the following headings:

1. Primary visual and refractive outcomes: uncorrected distance visual acuity (UDVA), CDVA, mean absolute error (MAE) of manifest refraction spherical equivalent.
2. Secondary surgical end points, effective phacoemulsification time, surgery time, balanced salt solution volume, cumulative dissipated energy (CDE), circularity of capsulotomy or capsulorrhexis, capsule opening diameter, absolute mean deviation from intended capsule diameter, intraocular lens (IOL) horizontal and vertical decentration, central corneal thickness, corneal endothelial cell count and preoperative to postoperative reduction, total prostaglandin concentration, and mean aqueous flare.
3. Safety parameters: overall complications, capsular complications, corneal complications, and pupillary complications.

In the extraction of data, continuous variables were recorded as means $\pm$ standard deviations, whereas categorical variables were reported as percentages of the total sample. If any included study provided acceptable measures of variation that could be converted to a standard deviation (e.g., standard error), these data also were extracted. To facilitate the meta-analysis design, complications were grouped by anatomic site (Table 1, available at www.aaojournal.org). Data for all postoperative outcomes were collected at last follow-up. To ensure balance in the average length of follow-up between comparators, outcomes were extracted from each included study at the same follow-up period for both FLACS and MCS eyes. If outcome data were repeated in 2 or more