



Major approaches and clinical findings of cataract surgery using the femtosecond laser: a systematic review

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Abstract

Introduction: In the scenario of eye problems, cataract is a disease characterized by the opacification of the lens, which leads to a decrease in visual acuity, due to a change in the refractive index. A cataract is the leading cause of blindness worldwide and surgery for its correction is the most performed surgical procedure in the world, with an estimated 19 million surgeries per year. The Femtosecond laser was approved for ophthalmic surgery in 2000, having been recently developed to integrate cataract surgery. **Objective:** It was to highlight the main clinical and scientific considerations related to the application of the Femtosecond laser in cataract surgery, highlighting its efficacy and safety to the conventional phacoemulsification technique. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from August to October 2022 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases, using articles from the last 15 years. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 229 articles were found, of which only 55 were part of this systematic review, after an eligibility analysis. Femtosecond laser-assisted cataract surgery appears to be beneficial in some patient groups, ie those with low baseline endothelial cell counts, or those planning to receive multifocal intraocular lenses. However, considering that the advantages of femtosecond laser-assisted cataract surgery may not be clear in all routine cases, it cannot be considered cost-effective. The adoption of the Femtosecond laser in cataract surgery has divided opinions as it results from the adaptation of a technology already used in other

areas to a surgical procedure that, at the time, was already successful.

Keywords: Cataract. Femtosecond laser. Phacoemulsification. Ophthalmic surgery. Cataract surgery. Clinical studies.

Introduction

In the scenario of eye problems, cataract is a disease characterized by the opacification of the lens, which leads to a decrease in visual acuity, due to a change in the refractive index [1]. The lens undergoes alterations in the majority of the population over 65 years of age, with advanced age being the main cause of cataracts [2].

Also, cataract is the main cause of blindness worldwide and surgery for its correction is the most performed surgical procedure in the world, with some an estimated 19 million surgeries per year [3]. However, this number is expected to come increasing, as a result of the increasing size of the population, the increase in average life expectancy, the increase in chronic diseases associated with aging, such as diabetes mellitus, and the development of expectations regarding health [4-7].

In this context, the current gold standard in the treatment of cataracts is phacoemulsification, which since 1967 has allowed for a smaller surgical incision, without the need for sutures, less induction of astigmatism, less postoperative inflammation, and the conversion of this surgical procedure to an outpatient procedure [8-11].

In this sense, the Femtosecond laser assisted cataract surgery (FLACS) was approved for ophthalmic surgery in 2000, having been recently developed to integrate cataract surgery [12]. The application of the

Femtosecond laser allows a more accurate capsulotomy, less loss of endothelial cells, and a reduction in the energy used by phacoemulsification, decreasing the trauma of adjacent structures [13]. However, the cost-effectiveness of its use is still controversial.

Furthermore, the mission of the Femtosecond laser is complex because the standard technique (Phacoemulsification) currently has low complication rates and high patient satisfaction rates, challenging the Femtosecond laser to prove its effectiveness and benefit in its implementation [14-18].

Therefore, the present study aimed to highlight the main clinical and scientific considerations related to the application of the Femtosecond laser in cataract surgery, highlighting its efficacy and safety concerning the conventional phacoemulsification technique.

Methods

Study Design

The rules of a systematic review of the PRISMA Platform (Transparent reporting of systematic review and meta-analysis (www.prisma-statement.org/)) were followed.

Data Sources And Research Strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): "*Cataract. Femtosecond laser. Phacoemulsification. Ophthalmic surgery. Cataract surgery. Clinical studies*". The research was carried out from August to October 2022 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. Scientific articles from the last 15 years were selected. In addition, a combination of keywords with the Booleans "OR", "AND" and the "NOT" operator were used to target scientific articles of interest.

Study Quality And Risk Of Bias

The quality of the studies was based on the GRADE instrument. The highest rankings were for randomized controlled trials, prospective or retrospective observational trials, meta-analysis studies, and statistically significant sample sizes ($n > 30$ patients). The risk of bias was analyzed using the Cochrane instrument, based on the effect size of each study versus the sample size.

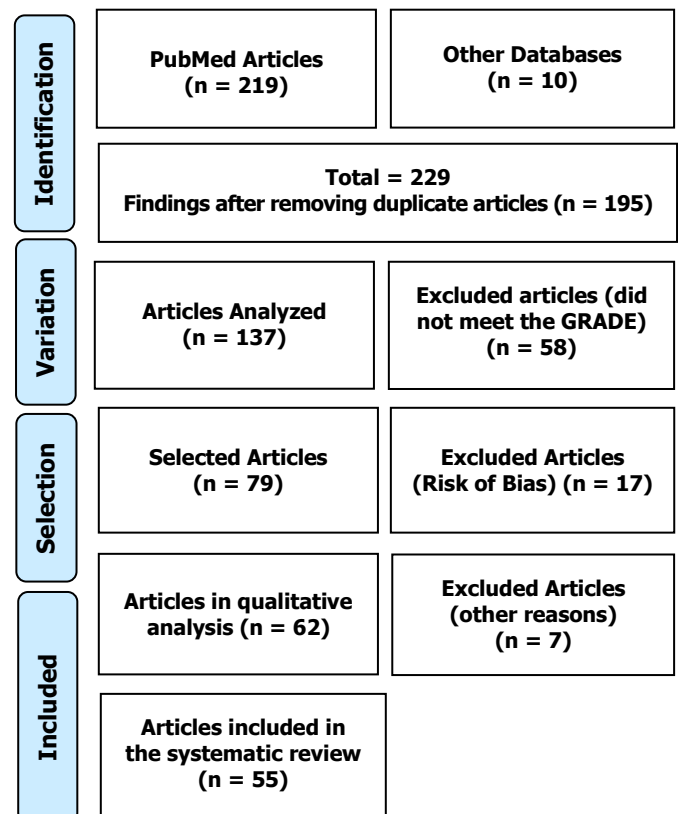
Results and Discussion

Summary Of Literary Findings

A total of 229 articles were found. Initially, article duplication was excluded. After this process, the

abstracts were evaluated and a new exclusion was performed, removing articles that did not include the topic of this article, resulting in 137 articles. A total of 62 articles were fully evaluated and 55 articles were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 17 studies at high risk of bias and 58 studies that did not meet the GRADE.

Figure 1. Flowchart showing the article selection process.



Cataract - Incidence, Prevalence, and Pathophysiology

Cataracts are the leading cause of blindness worldwide 9, and it is estimated to affect around 95 million people globally [8]. A study carried out estimated that in 2000, in the United States of America there were 20.5 million people, 40 years of age or older, with cataracts and who, with increased hope life expectancy, the prevalence in 2020 would increase to 30.1 million patients affected by this pathology [19]. In the United States of America, cataracts are the leading cause of vision loss, with an estimated onethird of the population will need cataract surgery during their lifetime [20].

This pathology has a relevant impact in social, physical, and economic terms [17], being responsible for an important percentage of health-related expenditures with vision [19]. It is estimated that in the United States of America 50% of the population with aged between

65 and 74 years and 70% of people over 75 years old have cataracts [21].

Still, about 90% of the described cataract cases are found in developing countries, manifesting itself as a public health problem of high importance dimension in these countries [22], particularly among females, higher rates of vision loss due to cataracts are reported in women, worldwide [16,19]. Treatment was one of the main goals set by the

WHO and the International Agency for the Prevention of Blindness when presenting the VISION 2020: The Right to Sight project in 1999, whose main objective is to eliminate avoidable blindness by 2020 [22].

Furthermore, the WHO estimates that non-surgically corrected cataracts are responsible for 35% of cases of blindness [23]. Studies have shown an increase in the prevalence of cataracts with aging, as well as a higher prevalence in females than males [17,19]. A study carried out with a specific population, the Latino population residing in Los Angeles, corroborated the significant increase in the prevalence of all types of cataracts in older patients and a predominance of cortical cataracts in this population, because of the comparatively increased prevalence of cataracts. nuclear power in Caucasians [21]. A higher prevalence of nuclear cataracts was also detected in female subjects.

Physioanatomopathological

The cataract corresponds to the loss of transparency of the lens due to its opacification. The lens is an avascular, non-innervated, biconvex structure, composed of fibers generated by its epithelium, which migrate from the periphery to the center. This migratory process causes the lens nucleus to be formed by older fibers and the periphery (cortex) by newly formed cells. The lens fibers are surrounded by a thin capsule. The function of this biconvex structure is to refract and focus the light beams on the retina and promote accommodation [8,11].

Age-related cataracts can be differentiated into nuclear, cortical, and posterior subcapsular, the different types may exist simultaneously, varying their geographical distribution and etiological factors depending on the different types morphological. Most cataract patients have more than one type morphological at the same time [16,17]. It is a common disease in the elderly and is especially prevalent in people over 65 years of age. This pathology manifests with gradual deterioration of visual acuity, alteration of color perception, decreased contrast sensitivity, hemeralopia, and occasionally monocular diplopia [9].

Changes in visual acuity resulting from cataracts have negative effects on the patient's quality of life.

In the early stages of pathology development, decreased visual acuity and associated symptoms can be alleviated through proper refractive correction and chromatic/polarized filters. The surgical approach is usually proposed when the loss of vision acquires a significant magnitude, affecting the patient's activities of daily living; when the surgery is expected to contribute to the improvement of the symptoms that may be associated with it; or when the cataract, due to its volume, causes a reduction in the iridocorneal angle and significantly increases the risk of developing narrow-angle glaucoma [8].

Based on this, a randomized clinical trial compared Femtosecond laser with phacoemulsification in two parallel groups (permuted block randomization stratified into centers via a centralized web-based application, allocation ratio 1:1, a block size of 2 or 4 for unilateral cases and 2 or 6 for bilateral cases). Of the 907 patients (1476 eyes) randomly assigned, 870 (704 eyes in the Femtosecond group and 685 eyes in the phacoemulsification group) were analyzed. No significant differences were identified in the success rate of surgery between the Femtosecond and phacoemulsification groups.

The incremental cost-benefit ratio was €10,703 saved per additional patient who was successful with phacoemulsification treatment compared to Femtosecond. No serious adverse events were observed during the femtosecond laser procedure [24].

In this regard, age is the main etiological factor for cataract 1, with multiple risk factors for cataractogenesis described, such as diabetes mellitus, chronic exposure to ultraviolet radiation, steroids, and smoking. Other factors with lower relative risk or still under study include hormone therapy and exogenous estrogens, myopia, fat consumption, and overweight, among others [16,17]. Cataracts can also be hereditary or congenital. A pediatric cataract is one of the leading causes of treatable blindness in children. Genetic factors, metabolic diseases, multisystem syndromes, intrauterine infections, trauma, toxic effects, or idiopathic causes are its main etiological factors [8,18].

In the presence of a patient with visual complaints, the initial assessment involves determining visual acuity using the Snellen visual acuity chart, which has been widely used in clinical practice. However, this assessment alone does not reveal the eye changes in their entirety, nor is the diagnosis based solely on the change in visual acuity. In primary care, using the pupillary moonlight test, the reflex that would normally be bright red, in the presence of a cataract (particularly visible with posterior cortical or subcapsular types), will

appear with dark areas, inducing a suspicion of the diagnosis. Ophthalmological evaluation with a biomicroscope allows for confirming the diagnosis, as well as characterizing the type and density of the cataract [11].

Cataract Surgery - Femtosecond Laser

With technological advances in the field of intraocular lenses, it is currently possible to combine cataract treatment with the elimination of refractive errors and even the compensation of presbyopia [1-3]. Since their introduction, intraocular lenses have changed in terms of shape, constituent material, location, sphericity, toxicity, and some focal points, which have allowed rapid visual recovery and important surgical advances. Most intraocular lenses currently used are made of acrylic or silicone polymers [4,5].

Furthermore, the application of LASERs in cataract surgery began to be investigated in the seventies [6,7,25-28]. The argon laser, whose wavelength lies in the visible light spectrum, was the first laser to be used clinically in Ophthalmology [7]. This works through molecular vibration, causing localized thermal effects, and having a photocoagulation effect on tissues [12,27].

This was followed by the Neodymium yttrium aluminum garnet (Nd: YAG), with a wavelength close to the infrared and with a photodisruption effect, which would cause tissue damage that could exceed 100 μm [12]. The Excimer laser emerged after the Nd:YAG, and has a spectrum wavelength close to the ultraviolet range, has a photoablation effect on tissues, and is absorbed by the anterior surface of the cornea, having excellent results in corneal ablation, but not in surgery of cataracts [12,28].

In the early nineties, Dr. Juhasz and his team built the prototype of the first Femtosecond laser ophthalmic system at the University of Michigan College of Engineering Center for Ultrafast Optical Sciences. Several members of this team created The IntraLase Corporation in 1997. In 2000 the FDA approved the IntraLase for corneal flap in LASIK surgery. Early Femtosecond laser systems were sensitive to environmental disturbances, requiring strict humidity and temperature conditions [12].

The first cataract surgery using the Femtosecond laser was carried out in August 2008, in Budapest, by Professor Nagy, using LenSx LASER. The Femtosecond laser gained FDA approval for application in cataract surgery in 2010 [29]. In February 2010, the a second procedure, in Houston (USA) by Dr. Slade [30]. The Femtosecond laser stands out from the rest due to the short duration of its pulses (1 femtosecond = 10-15 seconds), when compared to other lasers used in eye

surgery, which employ pulses with 10-9 seconds, such as Argon (photocoagulation), Excimer (photoablation) and Nd: YAG (photodisruption) [29].

Also, the Femtosecond laser delivers ultra-short pulses of energy with wavelengths near the infrared, 1053 nm [31-33]. These pulses create expanding plasma bubble micro cavitation on the order of 1.0 μm that separates tissue planes precisely with virtually no collateral damage to the surrounding zone, creating cut planes [30].

In this aspect, the incorporation of the Femtosecond laser in cataract surgery allows the creation of perfectly circular capsulotomies with diameter and centrality accurate, with minimal collateral damage, contributing to the fact that the length Femtosecond laser waveform not be absorbed by the cornea [31,34-36].

The described benefits of the use of the Femtosecond laser in the surgery of the cataracts include lower ultrasound energy required for phacoemulsification, improved surgical wound architecture reduced the potential for mechanical trauma to the surrounding structures and precision of capsular incisions less dependent on the a surgeon who performs it [31]. Consequently, it may help to minimize inflammation mediated by prostaglandins and cystoid macular edema. It can lead to greater security and precision, culminating in more predictable refractive results and fewer complications postoperative [37-39].

Besides, Femtosecond laser can also improve postoperative astigmatism. This procedure is performed by creating corneal incisions that minimize astigmatism, simultaneously with cataract treatment, allowing the creation of more precise incisions than the manual procedure [37].

Still, an important application of the Femtosecond laser is the creation of entry ports, with any location and size in the cornea [30]. These corneal incisions are selfsealing and provide a gateway to access the anterior chamber. The precision of the incision and the consistency of its Femtosecond laser architecture enable better postoperative healing, allowing for better control of postoperative infection [6,7].

Effect on Endothelial Cells

One of the main advantages proposed for the implementation of laser Femtosecond was the reduction of the effective time of phacoemulsification, reducing the damage of collateral tissues, particularly the corneal endothelium [37], as well as the reduction of the ultrasound energy received by the anterior chamber, decreasing postoperative inflammation, and resulting in lower rates of corneal edema and cell loss endothelial

[40-45].

In this sense, two of the studies analyzed showed the advantage of applying Femtosecond laser assisted cataract surgery (FLACS) in creating more precise, uniform, and predictable capsulotomies [31,46]. A study was also reviewed that did not find [29] a relevant influence of the difference in capsulotomy dimensions, achieved manually or with FLACS, on the results, 3 months after the procedure [44].

Analyzed studies found significant reductions in the effective time of phacoemulsification [31,33,40] and a shorter core removal time with FLACS [40]. There was a decrease in the cumulative energy dissipated, even in cataracts hard [31,33,40], except for one study, which did not demonstrate it [40]. Reducing the ultrasound energy required in FLACS decreased biomechanical damage to the cornea and resulted in lower rates of corneal edema and endothelial cell loss [47].

It was also highlighted that the ability of FLACS to create smaller fragments in phacoemulsification, results in lower requirements of time and energy applied to perform a complete removal of the cataract, increasing the efficiency of phacoemulsification [31,40]. The greater precision of the incisions produced by FLACS allows for to reduction of astigmatism and the creation of entrance doors with self-tight incisions, with better healing, greater stability, reproducibility, and less extravasation [48-50].

The learning curve inherent to the introduction of a new technique was evident in the evaluated studies, with a decrease in complications and complications with increasing cumulative experience [15,38,45]. It was also found that this technology, by creating more predictable and reproducible incisions, allows for the attenuation of discrepancies in parameters related to cumulative energy dissipated and core removal time, among professionals with different experiences [40].

Regarding the visual results, the studies did not reveal the benefits of clinically significant visuals arising from the use of FLACS technology [48-53]. In assessing the safety of FLACS, studies related to complications resulting from the surgical procedure are not consensual. A study with a large population sample (1876 eyes) recorded a higher incidence of rupture anterior or posterior capsular, Descemet's membrane trauma, and macular edema cystoid in the FLACS-treated group compared to the standard procedure 40.

A study with a smaller sample (826 eyes) detected a percentage significantly higher number of intraoperative complications in the group submitted to standard procedure, with FLACS being considered the safest procedure [39]. In the subjective criteria, there were no marked benefits of FLACS, there was even more pain and worse subjective global experience reported by

the patients treated with the new FLACS technique [54,55]. The high cost of FLACS technology is one of the most relevant obstacles to its implementation, having been shown that currently, the FLACS procedure does not present a positive cost-effectiveness relationship [52]. However, the cost is currently one of the parameters that can be mitigated [30] by technological development and the dissemination of the procedure and can be monetized by improvements in efficiency, in the number of cases treated, and/or if the price of the patient interface is reduced. considerably [14,25].

In this context, a retrospective study developed by Chen et al analyzed the complications recorded in procedures performed by experienced surgeons. In a sample of 273 eyes submitted to FLACS and in 553 submitted to manual phacoemulsification, a significantly higher percentage of intraoperative complications was detected in the group submitted to the standard procedure (1.8% vs. 5.8%) [39]. FLACS was considered the safest procedure.

Limitations and Complications

There is a lack of studies with a longer follow-up period, to evaluate long-term outcomes and possible complications or benefits in this period, and with larger populations, indicating the existence of few studies large-scale, with significant populations, and studies with randomization and double-blindness, factors capable of inducing bias in the results.

Also, corneal scars are a contraindication for laser Femtoseconds application are also contraindications regarding mature cataracts and the small, non-expandable, less than 6 mm in diameter [27]. Some complications may be associated with the Femtosecond laser procedure, namely pupillary constriction, anterior or posterior capsular rupture, corneal perforation, capsular block syndrome, large increases in intraocular pressure, incomplete capsulotomy, unstable pupil, reflex miosis, or subconjunctival hemorrhage [27,55]. Ewe et al reported a higher incidence of anterior or posterior capsular rupture, Descemet's membrane trauma, and cystoid macular edema in the Femtosecond lasertreated group compared to the standard procedure [48].

Conclusion

Femtosecond laser-assisted cataract surgery appears to be beneficial in some patient groups, ie those with low baseline endothelial cell counts, or those planning to receive multifocal intraocular lenses. However, considering that the advantages of femtosecond laser-assisted cataract surgery may not be clear in all routine cases, it cannot be considered cost-effective. The adoption of the Femtosecond laser in

cataract surgery has divided opinions as it results from the adaptation of a technology already used in other areas to a surgical procedure that, at the time, was already successful. The Femtosecond laser appears as a complement to the current technique, whose use aims to reduce the surgical risks and maximize the visual improvement obtained. The implementation of a new surgical technique, in an area where there is a very safe and effective gold standard, with very satisfactory results, with wide acceptance by professionals, and with lower defined and investments already made, implies the existence of evidence that prove significantly superior results in surgical procedures subject to improvement, so that there is a return on the monetary investment and the learning curve inherent to the new technology.

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Ethics approval

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Informed consent

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Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

Similarity check

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