Title

Laser Refractive Surgery in Pregnancy or Breastfeeding Patients: A Systematic Review

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Abstract

This systematic review reported the outcomes of laser corneal refractive surgery in pregnant or breastfeeding patients. This study was carried out by searching in PubMed, Web of Science and Scopus databases, on June 15th, 2020. This review included 128 eyes from a total of 64 patients, mean maximum follow-up was 39.2 ± 36.14 months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of 23.42 ± 22.23 months. PRK and LASIK surgery appear to be stable procedures which are not modified during pregnancy, and safe to complete during breastfeeding. Nevertheless, the lack of weight prospective research avoids having a greater certainty on this matter and. Due to transitory nature of pregnancy and breastfeeding, we could still contemplate surgery risk outweigh the benefits. Additional investigation will be necessary to clarify these issues.

Introduction

The prevalence of refractive errors, mainly myopia, has noticeably increased over the past years, and those who suffer from it seek for its correction.[1] Moreover, ages between 20 and 30 years old represent the most common age range amongst the female gender population that seek refractive surgery, coinciding with the period in which they are most prone to getting pregnant.[1] Currently, Laser-assisted in-situ keratomileusis (LASIK) is one of the most common laser refractive surgery technique, with excellent visual outcomes and safety profile.[2] The introduction of the femtosecond laser has made LASIK even safer, with reduced intraoperative flap-related complications.[3] Small incision lenticule extraction (SMILE) is a flapless minimally invasive technique where femtosecond laser is used during the entire procedure. Similarly, SMILE has demonstrated good refractive outcomes.[3] Other procedures such as laser photorefractive keratectomy (PRK) or Laser assisted sub-epithelial keratomileusis (LASEK)[4] are accepted as effective techniques in treating refractive errors, especially for the correction of low to moderate myopia, hyperopia and astigmatism.[5] Post laser ectasia (PLE) was defined as a progressive weakening and bulging of the cornea that leads to corneal steepening and thinning, associated with a loss of visual acuity.[6] Although uncommon, with an approximate incidence between 0.04% and 0.9%, PLE remains one of the major fearsome complications after refractive surgery.[7] It has been reported that LASIK induces a higher PLE risk than PRK,[6] especially when the procedure is performed with a mechanical microkeratome instead of using femtosecond laser.[8] PLE has also been reported after SMILE procedure.[9]

Risk factors for PLE include abnormal preoperative tomography, patients' age at the surgery moment, an elevated refraction, central corneal thickness (CCT) less than 500 microns, or residual stromal bed thickness (RSBT) less than 300 microns.[10–13] Santhiago et al.[14] introduced the percent tissue altered (PTA) formula as a risk factor for PLE, when PTA is > 40%. Recently, it has been found that similar to the development of keratoconus, a vigorous eye rubbing could also result in chronic biomechanical failure, hence leading to PLE.[15] Currently, there is still an ongoing debate in the scientific community whether it is possible to correct refractive defects during pregnancy and/or breastfeeding due to possible refractive changes, particularly myopia progression. The latter may be caused by hormonal induced-changes inherent to pregnancy or breastfeeding, altering the biomechanical stability of the body's connective tissues, hence an increased risk of PLE.[16,17] In fact, it has been reported that it may be advisable to postpone any changes in eyeglass prescriptions until several weeks postpartum.[18] Traditionally, pregnancy has been considered as a contraindication for refractive surgery, and recommending female patients to avoid pregnancy one year post-surgery.[19,20] Modern studies have reported favorable results of refractive surgery in pregnancy[21], and in breastfeeding patients.[22] Conversely, in a well-designed and large-longitudinal cohort study, Fernández-Montero et al.[1] recently reported that pregnancy is inversely associated with myopia development or its progression.

Therefore, the aim of this systematic review is to report the outcomes of laser corneal refractive surgery in pregnant or breastfeeding patients, currently available in the scientific literature, seeking to establish a scientific consensus.

Methods

This systematic review study was carried out by searching in PubMed, Web of Science and Scopus databases, on June 15th, 2020. The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement recommendations.[23] An initial search was conducted, focused on obtaining case studies of outcomes of laser corneal refractive surgery in pregnancy or breastfeeding patients. The keywords used were (pregnancy OR breastfeeding) AND (photorefractive keratectomy OR laser in-situ keratomileusis OR PRK OR LASIK OR SMILE OR Small incision lenticule extraction OR Laser assisted sub-epithelial keratomileusis OR LASEK). Among the results, a total of 150 articles were identified, which were evaluated and selected according to the inclusion and exclusion criteria. Inclusion criteria were: (1) experimental studies, original articles, case reports and cases series studies. The exclusion criteria were: (1) narrative reviews; (2) animal studies; (3) non-English publications; (4) Studies that excluded pregnant or breastfeeding patients.

Subsequently, the following data was summarized in tables; (1) authors and year of publication, (2) study design, (3) follow-up, (4) number of patients, (5) number of eyes, (6) age, (7) time between surgery and complication expressed in months, (8) pregnant or breastfeeding period expressed in months, (9) type of refractive surgery, (10) best corrected visual acuity before surgery, (11) refraction expressed in spherical equivalent (SE) before surgery, (12) uncorrected distance visual acuity after surgery, (13) refraction expressed in SE after surgery, (14) recurrence expressed in months, (15) slit-lamp findings, (16) complementary diagnostic test, (17) complications, (18) treatments, (19) favor or against.

To assess risk of bias of the included studies, a summary table was created (Table 1) based on the Quality Assessment Tool for Case Series Studies from the National Heart, Lung, and Blood Institute.[24] Questions included in the tool were: (1) Is the study oriented to a clear question?; (2) Were all the patients results taken into account?; (3) Was the follow-up complete?; (4) Were the same conditions used in surgical treatment?; (5) Was the intervention clearly described?; (6) Was the duration of follow-up adequate?; (7) Were the results described correctly? This analysis did not result in the elimination of any article. However, articles with a higher risk of bias had a lower weight for the data synthesis. Risk of bias was assessed by C-RL and JM.SG. No disagreement was encountered among the authors.

Results

The selection process of this systematic review was presented with a flow chart diagram in Figure 1. A total of ten articles,[21,25–33] published between 1996 and 2020, were included. All of them were case series, case reports or cohort studies. We included pregnant and breastfeeding patients between 25 and 38 years old, with a preoperative manifest refractive spherical equivalent between -0.87 D and -11.75 D. The mean previous spherical equivalent was -5.27 ± 2.66 D. Best spectacle corrected distance visual acuity was 20/20 (Snellen scale). Patients' and surgeries' characteristics of the selected articles were reported in Table 2. This systematic review included 128 eyes from a total of 64 patients, and a maximum postoperative follow-up that ranged from 3 to 108 months, with the mean maximum follow-up of 39.2 ± 36.14 months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of 23.42 ± 22.23 months. Pregnant or breastfeeding surgery period ranged from 1 to 7 months, and mean value was 4.60 ± 2.57 months. Regarding the surgical technique, four articles[25–27,33] used PRK, and seven studies [21,28–33] used LASIK.

Results after all refractive surgeries available in the scientific literature were presented in Table 3. In the postoperative period, uncorrected distance visual acuity changed to 20/32 ± 16.81. SE refraction changed to -1.62 ± 2.11 D. Recurrence time from surgery to the first evident clinical sign ranged from 1 to 67 months, with a mean value of 26.5 ± 22.60 months. RSBT mean value was 332.75 ± 52.06 µm. Within the complications, we observed that myopic regression was present in two studies,[25,26] haze was present in two studies,[26,27] overcorrection in only one study,[27] visual acuity decrease and halos in two studies,[27,28] and finally ectasia in four studies.[27,28,30,31] Retreatment was performed in three studies.[26,28,31] Sharif [26] retreated with PRK, while Hafezi et al.[28,31] reported ectasia treatment with corneal crosslinking.

In summary, only three studies[21,25,33] were in favor, while the other seven studies[26–32] were against refractive surgery procedures on pregnant or breastfeeding patients. Finally, the studies were grouped into three degrees, based on the risk of bias assessment tool: low evidence (yeses = 0 to 2); medium evidence (yeses = 3 to 5); high evidence (yeses = 6 to 7). Hefetz et al.[25] and Hafezi et al.[31] obtained a low evidence level. Starr[27], Padmanabhan et al.[29] and, López-Prats et al.[32] achieved medium evidence level. Finally, Sharif[26], Hafezi & Iseli[28], Said et al.[30], Alonso-Santander et al.[33] and, Kanellopoulos & Vingopoulos[21] obtained high evidence level.

Discussion

Refractive changes

Ocular changes associated with pregnancy, such as the variation in tear production, intraocular pressure, and corneal and lens topographic alterations have been studied with inconclusive results in recent years. The role of estrogen receptors in corneal and lens modifications during pregnancy has been proposed.[34] Morphological changes in the cornea may occur due to the development of corneal edema during pregnancy, therefore increasing the corneal curvature by one diopter (D) and increasing the central corneal thickness between 1 to 16 μm. Furthermore, the curvature of the lens appears to increase, leading to a loss of transient accommodation.[34] However, these changes usually reverse after delivery or lactation, and some authors have proposed that these changes do not involve significant variations in visual acuity or refractive error during pregnancy.[35,36]

The effect of pregnancy on the progression of myopia has been studied in a recent publication[1]. A cohort of 10,401 women between 20 and 50 years old was prospectively evaluated since 1999. Pregnancies and myopia were repeatedly assessed in each biennial follow-up questionnaire during 14 years of follow-up. Authors conclude that pregnancy was inversely associated with the risk of myopia development or progression during each of the two-year periods. Complications of corneal refractive surgery associated with pregnancy, such as myopic regression, PLE, and haze, have been reported. It has been proposed that these complications may be a result of pregnancy physiological variations in underlying biomechanically weakened corneas.[35,37–39]

PRK

Hefetz et al.[40] were the first to assess the effect of pregnancy on PRK. They studied 11 eyes of 8 women who became pregnant 1 to 5 months after surgery. Out of these, one woman experienced myopic regression in both eyes when she became pregnant 5 months after surgery. However, this study did not report whether these changes remained permanent after delivery. Subsequently, Sharif [41] studied the same effect in 18 eyes of 9 women who became pregnant in the first 12 months after PRK. Preoperative myopia ranged from -1.25 to -6 D, and the follow-up was from 12 to 24 months. He observed that twelve eyes underwent myopic regression, of which ten also developed corneal haze. All of them became pregnant in the first 5 months after surgery. Both complications improved after delivery in 50% of the eyes and the other 50% required retreatment with PRK. Furthermore, they observed that these complications were more frequent the more complex the pregnancy was. However, this study did not report the degree of preoperative myopia of all patients, which some authors related with corneal haze development.[42] There is also no reference to the degree of myopic regression and its clinical implication for the patient, although we presume it was substantial as a new surgery was required. The results of this study seem to indicate that there is a risk of myopic regression and haze development in patients who become pregnant in the first 5 months after PRK.

In the same way, Starr[43] reported a case of a woman who experienced a +3 D overcorrection and corneal haze during pregnancy after myopic PRK in her right eye (RE). Preoperative myopia was -5 D, and it was estimated that she became pregnant one week after surgery. The patient suffered an abortion in the third month of pregnancy and the overcorrection suffered a regression. In the tenth month after surgery, she had an uncorrected distance visual acuity (UDVA) of 20/20, a refraction of +0.25 D and the haze had disappeared. Although this study refers to an isolated case, the results are striking given the overcorrection in the short period of time between surgery and the beginning of pregnancy, as well as for the complete regression of the overcorrection after the abortion. It also seems to point out the risk of corneal haze and refractive changes in patients who become pregnant in a short period of time after PRK. We can conclude that, although there are no weight studies that assess the effect of pregnancy in patients with PRK surgery, it seems reasonable to delay gestation between 6 and 12 months after the intervention. Likewise, the few published studies suggest that it is important to point out that refractive changes and corneal haze revert after the end of pregnancy in most patients, including those who become pregnant in the first 6 months after surgery. Therefore, it is recommended to wait several months before considering the possibility of retreatment in patients who continue with sequelae after delivery.

LASIK

LASIK can alter corneal biomechanics, which seems to suppose a greater risk of PLE than other refractive surgery corrections, such as PRK or SMILE.[3] Hafezi and Iseli [37] reported a case of bilateral PLE in the third trimester of a woman's first pregnancy, 26 months after LASIK correction of -5.5 D in the RE and -5.25 D in the left eye (LE). According to the presurgical examination, the cornea had no pre-existing signs of disease, and 68 µm were ablated in the RE and 62 µm in the LE. After LASIK, the UDVA was 20/20 with normal topographies, and central corneal thickness was 410 µm in the RE and 400 µm in the LE. These parameters remained stable for two years. During the third trimester of the first pregnancy, PLE was developed, and the patient had a minimum corneal thickness of 370 µm in the RE and 360 µm in the LE. Two years later, during the second pregnancy, the patient suffered a sudden vision deterioration in her RE due to PLE progression. This case is distinctive due to the late onset of PLE, happening and progressing both times in the second trimester of pregnancy, and due to its stable behavior out of the pregnancy period. Changes in estrogen levels could play a role in LASIK-induced ectasia as they had been proposed to reduce corneal biomechanical stability in experimental studies.[37]

In the same way, Padmanabhan et al. reported another case of bilateral PLE in the first trimester of gestation, 18 months after myopic LASIK surgery. Similarly, the preoperative and tomographic clinical examinations did not suggest a presumable forme fruste or subclinical keratoconus in any eye. In this case, the patient had a 20/20 BCVA with a refractive error of -10.50 -2 x 10 in the RE, and -11.50 -1 x 160 in the LE. After the intervention, there was a RSBT of 305 µm in the RE and 282 µm in the LE, and a UDVA of 20/20. Eighteen months after surgery, during the first month of gestation, the patient was diagnosed with progressive PLE. Likewise, this article suggested the action of estrogens as a factor that modifies corneal biomechanics, and proposed that we should be cautious with arbitrary cut-off values, recalling that preoperative corneal thickness and RSBT are not absolute predictive values for the development of ectasia. This case report and the previous one referred to the fact that there were no pre-existing factors of ectasia; however, the anterior and posterior elevation curvature values prior to the intervention were not reported, so it cannot be ruled out that there was any anomaly. Topographic features, such as asymmetry between the two eyes, skewed radial axis, inferior/superior ratio greater than 1.4, and young patients with against-the-rule astigmatism could indicate a subclinical risk for ectasia due to intrinsic biomechanical instability.[44] Moreover, this case did not collected a complete history, that includes smoking, allergies and eye rubbing, which are known risk factors for PLE.[10]

Also Furthermore, Said et al.[39] reported an association between late onset of PLE after LASIK surgery and pregnancy. They collected a series of 19 patients and 29 eyes that developed this complication. Of these, they studied five eyes of three were women, who became pregnant between 2 and 5 years after surgery, with a SE between -5 and -9 D, and with an average RSBT of 277 µm. This article attributed this fact to the effect of the relaxing hormone, which increases during pregnancy and inhibits collagen remodeling. Furthermore, they affirmed that ectasia may occur after successful LASIK procedures, even in the absence of apparent preoperative risk factors. Once again, they did not report data about corneal curvature or elevation map values before the intervention, therefore such preoperative risk factors cannot be ruled out. In the same year, Hafezi et al.[17] performed a review of five patients who experienced visual impairment during pregnancy, and who had undergone LASIK surgery averagely 67 months before gestation. All patients, except one, were primiparous, and all presented a progressive PLE. They only reported the complete data of one patient, who was operated for -5 D in the RE and -4.5 D in the LE. The patients' BCVA and UDVA was 20/20, and the minimum corneal thickness was 359 µm. This study provides the least information about the patients compared to the previous reports; therefore, its results should be carefully assessed. Furthermore, the authors emphasize "we cannot rule out that some of the cases could have had a pre-existing minimal corneal thickness at the lower end of the normal distribution (i.e., 505 µm), a minor asymmetry and elevation at the posterior pole (i.e., 12 µm at a reference sphere of 8 mm), or even keratoconus".

Subsequently, López-Prats et al.[35] conducted a prospective study comparing a group consisting of 18 eyes from pregnant women who underwent LASIK prior to pregnancy, and a control group with 18 eyes from pregnant women with non-corrected refractive errors. No statistically significant differences were found in the mean BVCA, or in the sphere of both groups between the first and second trimester of gestation. Regarding the cylinder refraction, in the LASIK group they observed an average increase of 0.3 D on average, and 0.01 D in the control group, both with significant differences. SE experienced an average increase of 0.5 D in the LASIK group and 0.11 D in the control group, being both results statistically significant. The main issue of this study is that most of the parameters studied did not change in a statistically significant way, and those that did, did not suppose a relevant variation. On the other hand, it was not studied whether these changes returned to baseline after delivery. For all these reasons, we would say that, although there could be tomographic changes during pregnancy and these could be greater in women who underwent LASIK, these changes are not clinically relevant.

Conversely, Kanellopoulos & Vingopoulos[21] have recently published a prospective study with 64 pregnant women and 128 eyes who underwent bilateral myopic LASIK before pregnancy. They studied the UDVA, SE, sphere, cylinder, flattest keratometry values and corneal and central epithelial thickness before LASIK, twelve months after LASIK, during the third trimester of pregnancy and one year postpartum. Refractive error before intervention ranged from -1.00 D to -11.00 D, with an average of 6.72D. None of the comparisons revealed statistically significant differences. Therefore, the authors concluded that corneal and refractive stability after LASIK appears to be unaffected by pregnancy. Despite the lack of consensus in the literature, most authors agree on the transient nature of these changes, which may vary during pregnancy and return to baseline after delivery.[21,36] These changes have been associated with the role of estrogens in corneal biomechanics. However, due to the small sample of studies that reported PLE, the fact that none of them have correctly reported preoperative predisposing factors, and according to the results of the recent research,[21,35] there seems to be no evidence to support the existence of tomographic, refractive or clinically relevant changes during pregnancy in patients who underwent LASIK surgery. Even so, an additional risk of PLE in these patients cannot be completely ruled out. As it has been proposed[17], women younger than 40 years old could be considered as an additional risk factor to be added in Randleman's Ectasia Risk Score System (ERSS). Patients undergoing refractive surgery with undetected abnormal tomographies, such as pre-existing subclinical keratoconus, thin RSBT, high PTA, eye rubbing, young age or other unknown factors, pregnancy may be a trigger factor for PLE.[6] Even so, further quality prospective studies will be needed to clarify the relationship between PLE and pregnancy.

Breastfeeding

A retrospective case series has been recently published by Alonso-Santander et al.[22] in which they compare the refractive changes between women who underwent PRK and LASIK during lactation, and women who stopped breastfeeding a minimum of 3 months before the intervention. They studied a total of 237 eyes from 168 women. In the breastfeeding group, there were 142 women, of which 131 underwent LASIK and 11 PRK. In the non-breastfeeding group, there were 95 women, of which 85 underwent LASIK and 10 PRK. They studied UDVA, SE, sphere, cylinder, predictability, safety and retreatments in both groups, and there were no significant differences between them in any of the parameters. No infants experienced adverse effects. The study is limited by its retrospective nature and it is based on databases. Despite this, it is the first and only study that analyses this group of patients. According to the results, we would conclude that there appears to be no differences in effectivity and safety in LASIK and PRK in breastfeeding women. However, more prospective studies will be necessary in the future.

Strength and limitations and future research

According to the latest guidelines, refractive laser surgery is contraindicated in pregnancy and lactation, advising to postpone any intervention until 1 year after cessation of breastfeeding.[6] This is based on the alleged refractive and tomographic changes that occur in the cornea during this period.[45] Nevertheless, there are no major studies that assess the effect of pregnancy in patients with refractive laser surgery, and most authors agree on the transient nature of these changes, which may vary during pregnancy and return to the state baseline after delivery.[21,36] The few studies that exist on the effect of pregnancy in patients operated for PRK seem to indicate that refractive changes and corneal haze revert after the end of pregnancy in most patients, even in those who become pregnant in the first 6 months after surgery. There is also no evidence to support the existence of tomographic, refractive, or clinically relevant changes during pregnancy in LASIK patients. Nevertheless, we cannot rule out that pregnancy could trigger PLE in predisposed patients. According to this systematic review, being a woman younger than 40 years old should be considered as an additional risk factor for PLE. During this review, we have not found any study that assesses the effect of pregnancy and lactation with other corneal refractive surgeries, such as LASEK or SMILE, among others, neither phakic intraocular lens surgeries. There does not seem to be any difference in effectiveness or safety in performing LASIK and PRK in lactating women either. Future biomechanical studies in pregnant and lactating women with biomechanical data assessed with new devices, such as the Corvis-ST Placido dual-Scheimpflug analyzer or artificial intelligence could be especially interesting in these patients.[44,46–48]

In conclusion, PRK and LASIK surgery seem to be stable procedures which are not modified during pregnancy, and safe to perform during breastfeeding. However, the lack of weight prospective studies prevents having a greater certainty on this matter and, considering the transitory nature of pregnancy and lactation, we could still ponder whether the possible risks of these surgeries outweigh the benefits. Further research will be necessary to clarify these questions.

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Figure Captions

Figure 1 – Systematic review flowchart

Laser Refractive Surgery in Pregnant or Breastfeeding Patients

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Abstract

This systematic review reported the outcomes of laser corneal refractive surgery in pregnant or breastfeeding patients. This study was carried out by searching in PubMed, Web of Science and Scopus

databases, on June 15, 2020. Included were 128 eyes from a total of 64 patients, mean maximum follow-up was 39.2 ± 36.14 months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of 23.42 ± 22.23 months. Photorefractive keratectomy and laser in situ keratomileusis surgery appear to be stable procedures which are not modified during pregnancy, and safe to complete during breastfeeding. Nevertheless, the lack of weight prospective research avoids having a greater certainty on this matter and. Due to transitory nature of pregnancy and breastfeeding, we could still contemplate surgery risk outweigh the benefits. Additional investigation will be necessary to clarify these issues.

Introduction

The prevalence of refractive errors, mainly myopia, has noticeably increased over the past years, and those who suffer from it seek for its correction.[1] Moreover, ages between 20 and 30 years old represent the most common age range amongst the female gender population that seek refractive surgery, coinciding with the period in which they are most prone to getting pregnant.[1] Currently, Laser-assisted in-situ keratomileusis (LASIK) is one of the most common laser refractive surgery technique, with excellent visual outcomes and safety profile.[2] The introduction of the femtosecond laser has made LASIK even safer, with reduced intraoperative flap-related complications.[3] Small incision lenticule extraction (SMILE) is a flapless minimally invasive technique where femtosecond laser is used during the entire procedure. Similarly, SMILE has demonstrated good refractive outcomes.[3] Other procedures such as laser photorefractive keratectomy (PRK) or Laser assisted sub-epithelial keratomileusis (LASEK)[4] are accepted as effective techniques in treating refractive errors, especially for the correction of low to moderate myopia, hyperopia and astigmatism.[5] Post-laser ectasia (PLE) was defined as a progressive weakening and bulging of the cornea that leads to corneal steepening and thinning, associated with a loss of visual acuity.[6] Although uncommon, with an approximate incidence between 0.04% and 0.9%, PLE remains one of the major fearsome complications after refractive surgery.[7] It has been reported that LASIK induces a higher PLE risk than PRK,[6] especially when the procedure is performed with a mechanical microkeratome instead of using femtosecond laser.[8] PLE has also been reported after SMILE procedure.[9]

Risk factors for PLE include abnormal preoperative tomography, patients' age at the surgery moment, an elevated refraction, central corneal thickness (CCT) less than 500 microns, or residual stromal bed thickness (RSBT) less than 300 microns.[10–13] Santhiago et al.[14] introduced the percent tissue altered (PTA) formula as a risk factor for PLE, when PTA is > 40%. Recently, it has been found that similar to the development of keratoconus, a vigorous eye rubbing could also result in chronic biomechanical failure, hence leading to PLE.[15] Currently, there is still an ongoing debate in the scientific community whether it is possible to correct refractive defects during pregnancy and/or breastfeeding due to possible refractive changes, particularly myopia progression. The latter may be caused by hormonal induced-changes inherent to pregnancy or breastfeeding, altering the biomechanical stability of the body's connective tissues, hence an increased risk of PLE.[16,17] In fact, it has been reported that it may be advisable to postpone any changes in eyeglass prescriptions until several weeks postpartum.[18] Traditionally, pregnancy has been considered as a contraindication for refractive surgery, and recommending female patients to avoid pregnancy one year post-surgery.[19,20] Modern studies have reported favorable results of refractive surgery in pregnancy[21], and in breastfeeding patients.[22] Conversely, in a well-designed and large-longitudinal cohort study, Fernández-Montero et al.[1] recently reported that pregnancy is inversely associated with myopia development or its progression.

Therefore, the aim of this systematic review is to report the outcomes of laser corneal refractive surgery in pregnant or breastfeeding patients, currently available in the scientific literature, seeking to establish a scientific consensus.

Methods

This systematic review study was carried out by searching in PubMed, Web of Science and Scopus databases, on June 15, 2020. The study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement recommendations.[23] An initial search was conducted, focused on obtaining case studies of outcomes of laser corneal refractive surgery in pregnancy or breastfeeding patients. The keywords used were (pregnancy OR breastfeeding) AND (photorefractive keratectomy OR laser in-situ keratomileusis OR PRK OR LASIK OR SMILE OR Small incision lenticule extraction OR Laser assisted sub-epithelial keratomileusis OR LASEK). Among the results, a total of 150 articles were identified, which were evaluated and selected according to the inclusion and exclusion criteria. Inclusion criteria were: (1) experimental studies, original articles, case reports and cases series studies. The exclusion criteria were: (1) narrative reviews; (2) animal studies; (3) non-English publications; (4) Studies that excluded pregnant or breastfeeding patients.

Subsequently, the following data was summarized in tables; (1) authors and year of publication, (2) study design, (3) follow-up, (4) number of patients, (5) number of eyes, (6) age, (7) time between surgery and complication expressed in months, (8) pregnant or breastfeeding period expressed in months, (9) type of refractive surgery, (10) corrected distance visual acuity (CDVA) before surgery, (11) refraction expressed in spherical equivalent (SE) before surgery, (12) uncorrected distance visual acuity after surgery, (13) refraction expressed in spherical equivalent (SE) after surgery, (14) recurrence expressed in months, (15) slitlamp findings, (16) complementary diagnostic test, (17) complications, (18) treatments, (19) favor or against.

To assess risk of bias of the included studies, a summary table was created (Table 1) based on the Quality Assessment Tool for Case Series Studies from the National Heart, Lung, and Blood Institute.[24] Questions included in the tool were: (1) Is the study oriented to a clear question?; (2) Were all the patients results taken into account?; (3) Was the follow-up complete?; (4) Were the same conditions used in surgical treatment?; (5) Was the intervention clearly described?; (6) Was the duration of follow-up adequate?; (7) Were the results described correctly? This analysis did not result in the elimination of any article. However, articles with a higher risk of bias had a lower weight for the data synthesis. Risk of bias was assessed by C.R.L. and J.-M.S.-G. No disagreement was encountered among the authors.

Results

The selection process of this systematic review was presented with a flow chart diagram in Figure 1. A total of 10 articles,[21,25–33] published between 1996 and 2020, were included. All of them were case series, case reports or cohort studies. We included pregnant and breastfeeding patients between 25 and 38 years old, with a preoperative manifest refractive spherical equivalent between -0.87 diopter (D) and -11.75 D. The mean previous spherical equivalent was -5.27 ± 2.66 D. Spectacle CDVA was 20/20 (Snellen scale). Patient and surgery characteristics of the selected articles were reported in Table 2. This systematic review included 128 eyes from a total of 64 patients, and a maximum postoperative follow-up that ranged from 3 to 108 months, with the mean maximum follow-up of 39.2 ± 36.14 months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of 23.42 ± 22.23 months. Pregnant or breastfeeding surgery period ranged from 1 to 7 months, and mean value was 4.60 ± 2.57 months. Regarding the surgical technique, four articles[25–27,33] used PRK, and seven studies [21,28–33] used LASIK.

Results after all refractive surgeries available in the scientific literature were presented in Table 3. In the postoperative period, uncorrected distance visual acuity changed to 20/32 ± 16.81. SE refraction changed to -1.62 ± 2.11 D. Recurrence time from surgery to the first evident clinical sign ranged from 1 to 67 months, with a mean value of 26.5 ± 22.60 months. RSBT mean value was 332.75 ± 52.06 µm. Within the complications, we observed that myopic regression was present in two studies,[25,26] haze was present in two studies,[26,27] overcorrection in only one study,[27] visual acuity decrease and halos in two studies,[27,28] and finally ectasia in four studies.[27,28,30,31] Retreatment was performed in three studies.[26,28,31] Sharif [26] retreated with PRK, while Hafezi et al.[28,31] reported ectasia treatment with corneal crosslinking.

In summary, only three studies[21,25,33] were in favor, while the other seven studies[26–32] were against refractive surgery procedures on pregnant or breastfeeding patients. Finally, the studies were grouped into three degrees, based on the risk of bias assessment tool: low evidence (yeses = 0 to 2); medium evidence (yeses = 3 to 5); high evidence (yeses = 6 to 7). Hefetz et al.[25] and Hafezi et al.[31] obtained a low evidence level. Starr[27], Padmanabhan et al.[29] and, López-Prats et al.[32] achieved medium evidence level. Finally, Sharif[26], Hafezi & Iseli[28], Said et al.[30], Alonso-Santander et al.[33] and, Kanellopoulos & Vingopoulos[21] obtained high evidence level.

Discussion

Refractive changes

Ocular changes associated with pregnancy, such as the variation in tear production, intraocular pressure, and corneal and lens topographic alterations have been studied with inconclusive results in recent years. The role of estrogen receptors in corneal and lens modifications during pregnancy has been proposed.[34] Morphological changes in the cornea may occur due to the development of corneal edema during pregnancy, therefore increasing the corneal curvature by 1 D and increasing the central corneal thickness between 1 to 16 µm. Furthermore, the curvature of the lens appears to increase, leading to a loss of transient accommodation.[34] However, these changes usually reverse after delivery or lactation, and some authors have proposed that these changes do not involve significant variations in visual acuity or refractive error during pregnancy.[35,36]

The effect of pregnancy on the progression of myopia has been studied in a recent publication[1]. A cohort of 10,401 women between 20 and 50 years old was prospectively evaluated since 1999. Pregnancies and myopia were repeatedly assessed in each biennial follow-up questionnaire during 14 years of follow-up. Authors conclude that pregnancy was inversely associated with the risk of myopia development or progression during each of the two-year periods. Complications of corneal refractive surgery associated with pregnancy, such as myopic regression, PLE, and haze, have been reported. It has been proposed that these complications may be a result of pregnancy physiological variations in underlying biomechanically weakened corneas.[35,37–39]

PRK

Hefetz et al.[40] were the first to assess the effect of pregnancy on PRK. They studied 11 eyes of 8 women who became pregnant 1 to 5 months after surgery. Out of these, one woman experienced myopic regression in both eyes when she became pregnant 5 months after surgery. However, this study did not report whether these changes remained permanent after delivery. Subsequently, Sharif [41] studied the same effect in 18 eyes of 9 women who became pregnant in the first 12 months after PRK. Preoperative myopia ranged from -1.25 to -6 D, and the follow-up was from 12 to 24 months. He observed that twelve eyes underwent myopic regression, of which ten also developed corneal haze. All of them became pregnant in the first 5 months after surgery. Both complications improved after delivery in 50% of the eyes and the other 50% required retreatment with PRK. Furthermore, they observed that these complications were more frequent the more complex the pregnancy was. However, this study did not report the degree of preoperative myopia of all patients, which some authors related with corneal haze development.[42] There is also no reference to the degree of myopic regression and its clinical implication for the patient, although we presume it was substantial as a new surgery was required. The results of this study seem to indicate that there is a risk of myopic regression and haze development in patients who become pregnant in the first 5 months after PRK.

In the same way, Starr[43] reported a case of a woman who experienced a +3 D overcorrection and corneal haze during pregnancy after myopic PRK in her right eye (RE). Preoperative myopia was -5 D, and it was estimated that she became pregnant one week after surgery. The patient suffered an abortion in the third month of pregnancy and the overcorrection suffered a regression. In the tenth month after surgery, she had an uncorrected distance visual acuity (UDVA) of 20/20, a refraction of +0.25 D and the haze had disappeared. Although this study refers to an isolated case, the results are striking given the overcorrection in the short period of time between surgery and the beginning of pregnancy, as well as for the complete regression of the overcorrection after the abortion. It also seems to point out the risk of corneal haze and refractive changes in patients who become pregnant in a short period of time after PRK. We can conclude that, although there are no weight studies that assess the effect of pregnancy in patients with PRK surgery, it seems reasonable to delay gestation between 6 and 12 months after the intervention. Likewise, the few published studies suggest that it is important to point out that refractive changes and corneal haze revert after the end of pregnancy in most patients, including those who become pregnant in the first 6 months after surgery. Therefore, it is recommended to wait several months before considering the possibility of retreatment in patients who continue with sequelae after delivery.

LASIK

LASIK can alter corneal biomechanics, which seems to suppose a greater risk of PLE than other refractive surgery corrections, such as PRK or SMILE.[3] Hafezi and Iseli [37] reported a case of bilateral PLE in the third trimester of a woman's first pregnancy, 26 months after LASIK correction of -5.5 D in the RE and -5.25 D in the left eye (LE). According to the presurgical examination, the cornea had no pre-existing signs of disease, and 68 µm were ablated in the RE and 62 µm in the LE. After LASIK, the UDVA was 20/20 with normal topographies, and central corneal thickness was 410 µm in the RE and 400 µm in the LE. These parameters remained stable for two years. During the third trimester of the first pregnancy, PLE was developed, and the patient had a minimum corneal thickness of 370 µm in the RE and 360 µm in the LE. Two years later, during the second pregnancy, the patient suffered a sudden vision deterioration in her RE due to PLE progression. This case is distinctive due to the late onset of PLE, happening and progressing both times in the second trimester of pregnancy, and due to its stable behavior out of the pregnancy period. Changes in estrogen levels could play a role in LASIK-induced ectasia as they had been proposed to reduce corneal biomechanical stability in experimental studies.[37]

In the same way, Padmanabhan et al. reported another case of bilateral PLE in the first trimester of gestation, 18 months after myopic LASIK surgery. Similarly, the preoperative and tomographic clinical examinations did not suggest a presumable forme fruste or subclinical keratoconus in any eye. In this case, the patient had a 20/20 CDVA with a refractive error of -10.50 -2 x 10 in the RE, and -11.50 -1 x 160 in the LE. After the intervention, there was a RSBT of 305 µm in the RE and 282 µm in the LE, and a UDVA of 20/20. Eighteen months after surgery, during the first month of gestation, the patient was diagnosed with progressive PLE. Likewise, this article suggested the action of estrogens as a factor that modifies corneal biomechanics, and proposed that we should be cautious with arbitrary cut-off values, recalling that preoperative corneal thickness and RSBT are not absolute predictive values for the development of ectasia. This case report and the previous one referred to the fact that there were no pre-existing factors of ectasia; however, the anterior and posterior elevation curvature values prior to the intervention were not reported, so it cannot be ruled out that there was any anomaly. Topographic features, such as asymmetry between the two eyes, skewed radial axis, inferior/superior ratio greater than 1.4, and young patients with against-the-rule astigmatism could indicate a subclinical risk for ectasia due to intrinsic biomechanical instability.[44] Moreover, this case did not collected a complete history, that includes smoking, allergies and eye rubbing, which are known risk factors for PLE.[10]

Also Furthermore, Said et al.[39] reported an association between late onset of PLE after LASIK surgery and pregnancy. They collected a series of 19 patients and 29 eyes that developed this complication. Of these, they studied 5 eyes of 3 were women, who became pregnant between 2 and 5 years after surgery, with a SE between -5 and -9 D, and with an average RSBT of 277 µm. This article attributed this fact to the effect of the relaxing hormone, which increases during pregnancy and inhibits collagen remodeling. Furthermore, they affirmed that ectasia may occur after successful LASIK procedures, even in the absence of apparent preoperative risk factors. Once again, they did not report data about corneal curvature or elevation map values before the intervention, therefore such preoperative risk factors cannot be ruled out.

In the same year, Hafezi et al.[17] performed a review of 5 patients who experienced visual impairment during pregnancy, and who had undergone LASIK surgery averagely 67 months before gestation. All patients except one were primiparous, and all presented a progressive PLE. They only reported the complete data of one patient, who was operated for -5 D in the RE and -4.5 D in the LE. The patients' CDVA and UDVA was 20/20, and the minimum corneal thickness was 359 µm. This study provides the least information about the patients compared to the previous reports; therefore, its results should be carefully assessed. Furthermore, the authors emphasize "we cannot rule out that some of the cases could have had a preexisting minimal corneal thickness at the lower end of the normal distribution (i.e., 505 µm), a minor asymmetry and elevation at the posterior pole (i.e., 12 µm at a reference sphere of 8 mm), or even keratoconus".

Subsequently, López-Prats et al.[35] conducted a prospective study comparing a group consisting of 18 eyes from pregnant women who underwent LASIK prior to pregnancy, and a control group with 18 eyes from pregnant women with noncorrected refractive errors. No statistically significant differences were found in the mean CDVA, or in the sphere of both groups between the first and second trimester of gestation. Regarding the cylinder refraction, in the LASIK group they observed an average increase of 0.3 D on average, and 0.01 D in the control group, both with significant differences. SE experienced an average increase of 0.5 D in the LASIK group and 0.11 D in the control group, being both results statistically significant. The main issue of this study is that most of the parameters studied did not change in a statistically significant way, and those that did, did not suppose a relevant variation. On the other hand, it was not studied whether these changes returned to baseline after delivery. For all these reasons, we would say that, although there could be tomographic changes during pregnancy and these could be greater in women who underwent LASIK, these changes are not clinically relevant.

Conversely, Kanellopoulos and Vingopoulos[21] have recently published a prospective study with 64 pregnant women and 128 eyes who underwent bilateral myopic LASIK before pregnancy. They studied the UDVA, SE, sphere, cylinder, flattest keratometry values and corneal and central epithelial thickness before LASIK, twelve months after LASIK, during the third trimester of pregnancy and one year postpartum. Refractive error before intervention ranged from -1.00 D to -11.00 D, with an average of 6.72D. None of the comparisons revealed statistically significant differences. Therefore, the authors concluded that corneal and refractive stability after LASIK appears to be unaffected by pregnancy. Despite the lack of consensus in the literature, most authors agree on the transient nature of these changes, which may vary during pregnancy and return to baseline after delivery.[21,36] These changes have been associated with the role of estrogens in corneal biomechanics. However, due to the small sample of studies that reported PLE, the fact that none of them have correctly reported preoperative predisposing factors, and according to the results of the recent research,[21,35] there seems to be no evidence to support the existence of tomographic, refractive or clinically relevant changes during pregnancy in patients who underwent LASIK surgery. Even so, an additional risk of PLE in these patients cannot be completely ruled out. As it has been proposed[17], women younger than 40 years old could be considered as an additional risk factor to be added in Randleman's Ectasia Risk Score System (ERSS). Patients undergoing refractive surgery with undetected abnormal tomographies, such as preexisting subclinical keratoconus, thin RSBT, high PTA, eye rubbing, young age or other unknown factors, pregnancy may be a trigger factor for PLE.[6] Even so, further quality prospective studies will be needed to clarify the relationship between PLE and pregnancy.

Breastfeeding

A retrospective case series has been recently published by Alonso-Santander et al.[22] in which they compare the refractive changes between women who underwent PRK and LASIK during lactation, and women who stopped breastfeeding a minimum of 3 months before the intervention. They studied a total of 237 eyes from 168 women. In the breastfeeding group, there were 142 women, of which 131 underwent LASIK and 11 PRK. In the non-breastfeeding group, there were 95 women, of which 85 underwent LASIK and 10 PRK. They studied UDVA, SE, sphere, cylinder, predictability, safety and retreatments in both groups, and there were no significant differences between them in any of the parameters. No infants experienced adverse effects. The study is limited by its retrospective nature and it is based on databases. Despite this, it is the first and only study that analyses this group of patients. According to the results, we would conclude that there appears to be no differences in effectivity and safety in LASIK and PRK in breastfeeding women. However, more prospective studies will be necessary in the future.

Strength and limitations and future research

According to the latest guidelines, refractive laser surgery is contraindicated in pregnancy and lactation, advising to postpone any intervention until 1 year after cessation of breastfeeding.[6] This is based on the alleged refractive and tomographic changes that occur in the cornea during this period.[45] Nevertheless, there are no major studies that assess the effect of pregnancy in patients with refractive laser surgery, and most authors agree on the transient nature of these changes, which may vary during pregnancy and return to the state baseline after delivery.[21,36] The few studies that exist on the effect of pregnancy in patients operated for PRK seem to indicate that refractive changes and corneal haze revert after the end of pregnancy in most patients, even in those who become pregnant in the first 6 months after surgery. There is also no evidence to support the existence of tomographic, refractive, or clinically relevant changes during pregnancy in LASIK patients. Nevertheless, we cannot rule out that pregnancy could trigger PLE in predisposed patients. According to this systematic review, being a woman younger than 40 years old should be considered as an additional risk factor for PLE. During this review, we have not found any study that assesses the effect of pregnancy and lactation with other corneal refractive surgeries, such as LASEK or SMILE, among others, neither phakic intraocular lens surgeries. There does not seem to be any difference in effectiveness or safety in performing LASIK and PRK in lactating women either. Future biomechanical studies in pregnant and lactating women with biomechanical data assessed with new devices, such as the Corvis-ST Placido dual-Scheimpflug analyzer or artificial intelligence could be especially interesting in these patients.[44,46–48]

In conclusion, PRK and LASIK surgery seem to be stable procedures which are not modified during pregnancy, and safe to perform during breastfeeding. However, the lack of weight prospective studies prevents having a greater certainty on this matter and, considering the transitory nature of pregnancy and lactation, we could still ponder whether the possible risks of these surgeries outweigh the benefits. Further research will be necessary to clarify these questions.

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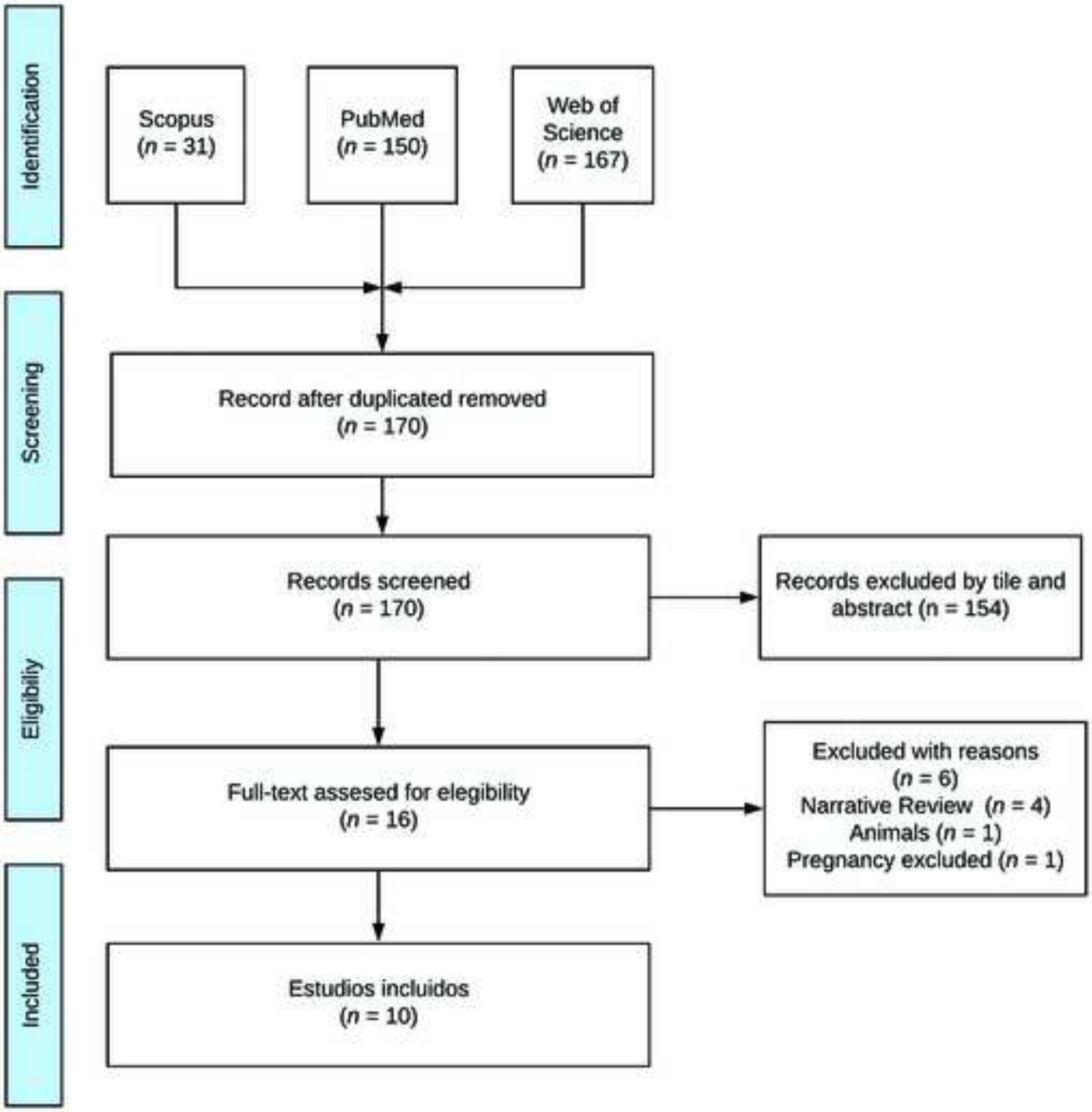
Figure Captions

Figure 1 – Systematic review flowchart

PRK and LASIK appear to be stable procedures which are not modified during pregnancy, and safe to perform during breastfeeding. However, the lack of weight studies prevents having greater certainty.

Figure 1


Identification
Screening
Eligibiliy
Included
Scopus
(n = 31)
PubMed
(n = 150)
Web of
Science
(n = 167)
Record after duplicated removed
(n = 170)
Records screened
(n = 170)
Records excluded by tile and
abstract (n = 154)
Full-text assesed for elegibility
(n = 16)
Excluded with reasons
(n = 6)
Narrative Review (n = 4)
Animals (n = 1)
Pregnancy excluded (n = 1)
Estudios incluidos
(n = 10)

Table

Table 1. Quality assessment of articles							
Author and Date	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**
Hefetz et al.[1] (1996)	Yes	No	No	Yes	No	No	No
Sharif[2] (1997)	Yes	Yes	Yes	Yes	Yes	Yes	No
Starr[3] (1998)	Yes	Yes	No	Yes	Yes	No	No
Hafezi & Iseli[4] (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Padmanabhan et al.[5] (2010)	Yes	Yes	No	Yes	Yes	No	No
Said et al.[6] (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hafezi et al.[7] (2012)	Yes	No	No	No	No	No	No
López-Prats et al.[8] (2012)	Yes	Yes	No	Yes	Yes	No	Yes
Alonso-Santander et al.[9] (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kanellopoulos & Vingopoulos[10] (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Q= Question; (Q1): Is the study oriented to a clear question?; (Q2): Were all the patients results taken into account?; (Q3): Was the follow-up complete?; (Q4): Were the same conditions used in surgical treatment?; (Q5): Was the intervention clearly described?; (Q6): Was the duration of follow-up adequate?; (Q7): Were the results described correctly?

Table

Table 2. Study characteristics								
Autor (date)	**Design**	**Follow-up (months)**	**Patients**	**Eyes**	**Age**	**Surgery to complication time**	**POB Period**	**Refractive Surgery**
Hefetz et al.[1] (1996)	SC	12	8	11	NR	5	NR	PRK
Sharif[2] (1997)	SC	12	9	18	25	5	NR	PRK
Starr[3] (1998)	CR	14	1	1	38	1	1	PRK
Hafezi & Iseli[4] (2008)	CR	90	1	2	33	26	7	LASIK
Padmanabhan et al.[5] (2010)	CR	25	1	2	20	18	2	LASIK
Said et al.[6] (2011)	SC	108	3	5	32	42	NR	LASIK
Hafezi et al.[7] (2012)	SC	67	5	10	31	67	7	LASIK
López-Prats et al.[8] (2012)	Cohort	6	9	18	27	NR	6	LASIK
Alonso-Santander et al.[9] (2020)	SC	3	71	142	33	NR	NR	LASIK (131)/PRK (11)
Kanellopoulos & Vingopoulos[10] (2020)	SC	55	64	128	32.5	NR	No	LASIK
SC= Serie of Cases; LASIK: Laser assisted in-situ keratomileusis; PRK: Photorefractive keratectomy; CR: Case Report; POB: pregnant or breastfeeding; NR: not reported								

Table

Table 3. Evaluation of the visual results after the laser refractive surgery on pregnant of breastfeeding patients										
Autor (date)	**Previous**		**Posterior**		**Recurrence (months)**	**Slit-Lamp Findings**	**Complementary Diagnostic Tests**	**Complication**	**Treatment**	**Favor / Against**
	BCVA	**Rx***	**UDVA**	**Rx***						
Hefetz et al.[1] (1996)	NR	-4.80	NR	-0.80	NR	NR	NR	Myopic regression	NR	Favor
Sharif[2] (1997)	NR	-3.50	NR	NR	5	Haze	NR	Myopic regression, Haze	PRK	Against
Starr[3] (1998)	20/20	-5.00	20/20	+0.25	1	Haze	NR	Overcorrection, Haze	NR	Against
Hafezi & Iseli[4] (2008)	20/20	-5.75	20/63	-6.00	26	NR	405 µm	VA decrease, halos, ectasia	CCL	Against
Padmanabhan et al.[5] (2010)	20/20	-11.75	NR	NR	18	NR	290 µm	VA decrease, halos, ectasia	NR	Against
Said et al.[6] (2011)	NR	-7.00	NR	NR	42	NR	277 µm	Ectasia	NR	Against
Hafezi et al.[7] (2012)	20/20	-5.00	NR	NR	67	NR	359 µm	Ectasia	CCL	Against
López-Prats et al.[8] (2012)	20/20	-0.87	20/25	-1.37	NR	NR	NR	NR	NR	Against
Alonso-Santander et al.[9] (2020)	20/20	-3.80	20/20	-0.20	NR	NR	NR	NR	NR	Favor
Kanellopoulos & Vingopoulos[10] (2020)	20/20	-6.05	20/20	-0.37	NR	NR	NR	NR	NR	Favor

*BCVA: Best corrected visual acuity; Rx: Refraction (*expressed in spherical equivalent); NR: not reported; UDVA: Uncorrected distance visual acuity; CCL: Corneal collagen Crosslinking;* µm: *micra (thinnest point) after LASIK*

Table 2. Study characteristics								
Autor (date)	**Design**	**Follow-up (mo)**	**Patients**	**Eyes**	**Age (y)**	**Surgery to complication time**	**POB period**	**Refractive surgery**
Hefetz et al.[1] (1996)	CS	12	8	11	NR	5	NR	PRK
Sharif[2] (1997)	CS	12	9	18	25	5	NR	PRK
Starr[3] (1998)	CR	14	1	1	38	1	1	PRK
Hafezi and Iseli[4] (2008)	CR	90	1	2	33	26	7	LASIK
Padmanabhan et al.[5] (2010)	CR	25	1	2	20	18	2	LASIK
Said et al.[6] (2011)	SC	108	3	5	32	42	NR	LASIK
Hafezi et al.[7] (2012)	SC	67	5	10	31	67	7	LASIK
López-Prats et al.[8] (2012)	Cohort	6	9	18	27	NR	6	LASIK
Alonso-Santander et al.[9] (2020)	SC	3	71	142	33	NR	NR	LASIK (131)/PRK (11)
Kanellopoulos & Vingopoulos[10] (2020)	SC	55	64	128	32.5	NR	No	LASIK

CR = case report; CS = case series; NR = not reported; POB = pregnant or breastfeeding; PRK = photorefractive keratectomy

T1 EO

Table 1. Quality Assessment of Articles.

Author and Date	Q1	Q2	Q3	Q4	Q5	Q6	Q7
Hefetz et al.[1] (1996)	Yes	No	No	Yes	No	No	No
Sharif[2] (1997)	Yes	Yes	Yes	Yes	Yes	Yes	No
Starr[3] (1998)	Yes	Yes	No	Yes	Yes	No	No
Hafezi & Iseli[4] (2008)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Padmanabhan et al.[5] (2010)	Yes	Yes	No	Yes	Yes	No	No
Said et al.[6] (2011)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hafezi et al.[7] (2012)	Yes	No	No	No	No	No	No
López-Prats et al.[8] (2012)	Yes	Yes	No	Yes	Yes	No	Yes
Alonso-Santander et al.[9] (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kanellopoulos & Vingopoulos[10] (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Q1 = Is the study oriented to a clear question?; Q2 = Were all the patients results taken into account?; Q3 = Was the follow-up complete?; Q4 = Were the same conditions used in surgical treatment?; Q5 = Was the intervention clearly described?; Q6 = Was the duration of follow-up adequate?; Q7 = Were the results described correctly?

T3 EO

Table 3. Evaluation of Visual Results After Laser Refractive Surgery on Pregnant and Breastfeeding Patients.

Autor (date)	Previous		Posterior		Recurrence (mo)	Slitlamp findings	Complementary Diagnostic Tests	Complication	Treatment	Favor/Against
	CDVA	Rx (SE)	UDVA	Rx (SE)						
Hefetz et al.[1] (1996)	NR	-4.80	NR	-0.80	NR	NR	NR	Myopic regression	NR	Favor
Sharif[2] (1997)	NR	-3.50	NR	NR	5	Haze	NR	Myopic regression, Haze	PRK	Against
Starr[3] (1998)	20/20	-5.00	20/20	+0.25	1	Haze	NR	Overcorrection, Haze	NR	Against
Hafezi & Iseli[4] (2008)	20/20	-5.75	20/63	-6.00	26	NR	405 µm[a]	VA decrease, halos, ectasia	CCL	Against
Padmanabhan et al.[5] (2010)	20/20	-11.75	NR	NR	18	NR	290 µm[a]	VA decrease, halos, ectasia	NR	Against
Said et al.[6] (2011)	NR	-7.00	NR	NR	42	NR	277 µm[a]	Ectasia	NR	Against
Hafezi et al.[7] (2012)	20/20	-5.00	NR	NR	67	NR	359 µm[a]	Ectasia	CCL	Against
López-Prats et al.[8] (2012)	20/20	-0.87	20/25	-1.37	NR	NR	NR	NR	NR	Against
Alonso-Santander et al.[9] (2020)	20/20	-3.80	20/20	-0.20	NR	NR	NR	NR	NR	Favor
Kanellopoulos and Vingopoulos[10] (2020)	20/20	-6.05	20/20	-0.37	NR	NR	NR	NR	NR	Favor

CXL = corneal crosslinking; NR = not reported; Rx = refraction; SE = spherical equivalent;
[a]after LASIK