

# Laser refractive surgery in pregnant or breastfeeding patients



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This systematic review reported the outcomes of laser corneal refractive surgery in pregnant or breastfeeding patients. This study was performed by searching in PubMed, Web of Science, and Scopus databases, on June 15, 2020. Included were 128 eyes from a total of 64 patients, with the mean maximum follow-up was  $39.2 \pm 36.14$  months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of  $23.42 \pm 22.23$  months. Photorefractive keratectomy and laser in situ keratomileusis surgery seem to be stable procedures that 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 because of transitory nature of pregnancy and breastfeeding, it could still be contemplated that surgery risk outweigh the benefits. Additional investigation will be necessary to clarify these issues.

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The prevalence of refractive errors, mainly myopia, has noticeably increased over the past years, and those who experience it seek for its correction.<sup>1</sup> Moreover, ages between 20 and 30 years represent the most common age range among the female population that seeks refractive surgery, coinciding with the period in which they are most prone to getting pregnant.<sup>1</sup> Currently, laser in situ keratomileusis (LASIK) is one of the most common laser refractive surgery techniques, with excellent visual outcomes and safety profile.<sup>2</sup> The introduction of the femtosecond laser has made LASIK even safer, with reduced intraoperative flap-related complications.<sup>2</sup> 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.<sup>2</sup> Other procedures such as laser photorefractive keratectomy (PRK) or laser-assisted sub-epithelial keratomileusis (LASEK) are accepted as effective techniques in treating refractive errors, especially for the correction of low to moderate myopia, hyperopia, and astigmatism.<sup>3,4</sup> Postlaser 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.<sup>5</sup> Although uncommon, with an approximate incidence between 0.04% and 0.9%, PLE remains one of the major fearsome complications after refractive surgery.<sup>6</sup> It has been reported that LASIK induces a higher PLE risk than PRK, especially when the procedure is performed with a mechanical microkeratome instead of using femtosecond laser.<sup>5,7</sup> PLE has also been reported after SMILE procedure.<sup>8</sup>

Risk factors for PLE include abnormal preoperative tomography, patients' age at the surgery moment, an elevated refraction, central corneal thickness (CCT) less than 500  $\mu\text{m}$ , or residual stromal bed thickness (RSBT) less than 300  $\mu\text{m}$ .<sup>9–12</sup> Santhiago et al. introduced the percentage tissue altered (PTA) formula as a risk factor for PLE, when PTA is more than 40%.<sup>13</sup> 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.<sup>14</sup> Currently, there is still an ongoing debate in the scientific community whether it is possible to correct refractive defects during pregnancy and/or breastfeeding because of possible refractive changes, particularly myopia progression. The latter may be caused by hormonal induced-changes inherent to pregnancy or breastfeeding,

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altering the biomechanical stability of the body's connective tissues, hence an increased risk for PLE.<sup>15,16</sup> In fact, it has been reported that it may be advisable to postpone any changes in spectacles prescriptions until several weeks postpartum.<sup>17</sup> Traditionally, pregnancy has been considered as a contraindication for refractive surgery, recommending female patients to avoid pregnancy 1 year postsurgery.<sup>18,19</sup> Modern studies have reported favorable results of refractive surgery in pregnancy and in breastfeeding patients.<sup>20,21</sup> Conversely, in a well-designed and large-longitudinal cohort study, Fernández-Montero et al. recently reported that pregnancy is inversely associated with myopia development or its progression.<sup>1</sup> Therefore, the aim of this systematic review was 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 performed 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 statement recommendations.<sup>22</sup> An initial search was conducted, focusing 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 experimental studies, original articles, case reports, and cases series studies. The exclusion criteria were as follows: (1) narrative reviews; (2) animal studies; (3) non-English publications; and (4) studies that excluded pregnant or breastfeeding patients.

Subsequently, the following data were 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) preoperatively, (11) refraction expressed in spherical equivalent (SE) preoperatively, (12) uncorrected distance visual acuity (UDVA) postoperatively, (13) refraction expressed in SE postoperatively, (14) recurrence expressed in months, (15) slitlamp findings, (16) complementary diagnostic test, (17) complications, (18) treatments, and (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.<sup>30</sup> The following questions were included in the tool: (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 is presented with a flowchart diagram in Figure 1. A total of 10 articles,

published between 1996 and 2020, were included.<sup>16,20,21,23–29</sup> All of them were case series, case reports, or cohort studies. Pregnant and breastfeeding patients aged between 25 and 38 years, with a preoperative manifest refractive SE between  $-0.87$  diopters (D) and  $-11.75$  D, were included. The mean previous SE was  $-5.27 \pm 2.66$  D. Spectacle CDVA was 20/20 (Snellen scale). Patient and surgery characteristics of the selected articles are 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  $39.2 \pm 36.14$  months. Time from surgery to complication ranged from 1 to 67 months, with a mean value of  $23.42 \pm 22.23$  months. Pregnant or breastfeeding surgery period ranged from 1 to 7 months, and mean value was  $4.60 \pm 2.57$  months. Regarding the surgical technique, 4 articles used PRK, and 7 studies used LASIK.<sup>16,20,21,23–29</sup>

The results after all refractive surgeries available in the scientific literature are presented in Table 3. In the postoperative period, UDVA changed to  $20/32 \pm 16.81$ . SE refraction changed to  $-1.62 \pm 2.11$  D. Recurrence time from surgery to the first evident clinical sign ranged from 1 to 67 months, with a mean value of  $26.5 \pm 22.60$  months. The RSBT mean value was  $332.75 \pm 52.06$   $\mu\text{m}$ . Within the complications, myopic regression was present in 2 studies, haze in 2 studies, overcorrection in only 1 study, visual acuity decrease and halos in 2 studies, and finally ectasia in 4 studies.<sup>16,23–26,28</sup> Retreatment was performed in 3 studies.<sup>16,24,26</sup> Sharif retreated with PRK, whereas Hafezi et al. reported ectasia treatment with corneal crosslinking.<sup>16,24,26</sup>

In summary, only 3 studies were in favor, whereas the other 7 studies were against refractive surgery procedures on pregnant or breastfeeding patients.<sup>16,20,21,23–29</sup> Finally, the studies were grouped into 3 degrees, based on the risk of bias assessment tool: low evidence (yeyes = 0 to 2); medium evidence (yeyes = 3 to 5); and high evidence (yeyes = 6 to 7). Hefetz et al. and Hafezi et al. obtained a low evidence level.<sup>16,23</sup> Starr, Padmanabhan et al., and López-Prats et al. achieved medium evidence level.<sup>25,27,29</sup> Finally, Sharif, Hafezi and Iseli, Said et al., Alonso-Santander et al., and Kanellopoulos and Vingopoulos obtained high evidence level.<sup>20,21,24,26,28</sup>

## 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.<sup>31</sup> Morphological changes in the cornea may occur because of the development of corneal edema during pregnancy, therefore increasing the corneal curvature by 1.00 D and increasing the CCT between 1 and 16  $\mu\text{m}$ . Furthermore, the curvature of the lens seems to increase, leading to a loss of transient accommodation.<sup>31</sup> However, these changes usually reverse after delivery or lactation, and some authors have proposed that these changes do not involve

**Table 1. Quality Assessment of Articles.**

| Author (yr)  | Q1  | Q2  | Q3  | Q4  | Q5  | Q6  | Q7  |
|--|-----|-----|-----|-----|-----|-----|-----|
| Hefetz et al. <sup>23</sup> (1996)                 | Yes | No  | No  | Yes | No  | No  | No  |
| Sharif <sup>24</sup> (1997)                        | Yes | Yes | Yes | Yes | Yes | Yes | No  |
| Starr <sup>25</sup> (1998)                         | Yes | Yes | No  | Yes | Yes | No  | No  |
| Hafezi and Iseli <sup>26</sup> (2008)              | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Padmanabhan et al. <sup>27</sup> (2010)            | Yes | Yes | No  | Yes | Yes | No  | No  |
| Said et al. <sup>28</sup> (2011)                   | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Hafezi et al. <sup>16</sup> (2012)                 | Yes | No  | No  | No  | No  | No  | No  |
| López-Prats et al. <sup>29</sup> (2012)            | Yes | Yes | No  | Yes | Yes | No  | Yes |
| Alonso-Santander et al. <sup>21</sup> (2020)       | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Kanellopoulos and Vingopoulos <sup>20</sup> (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?

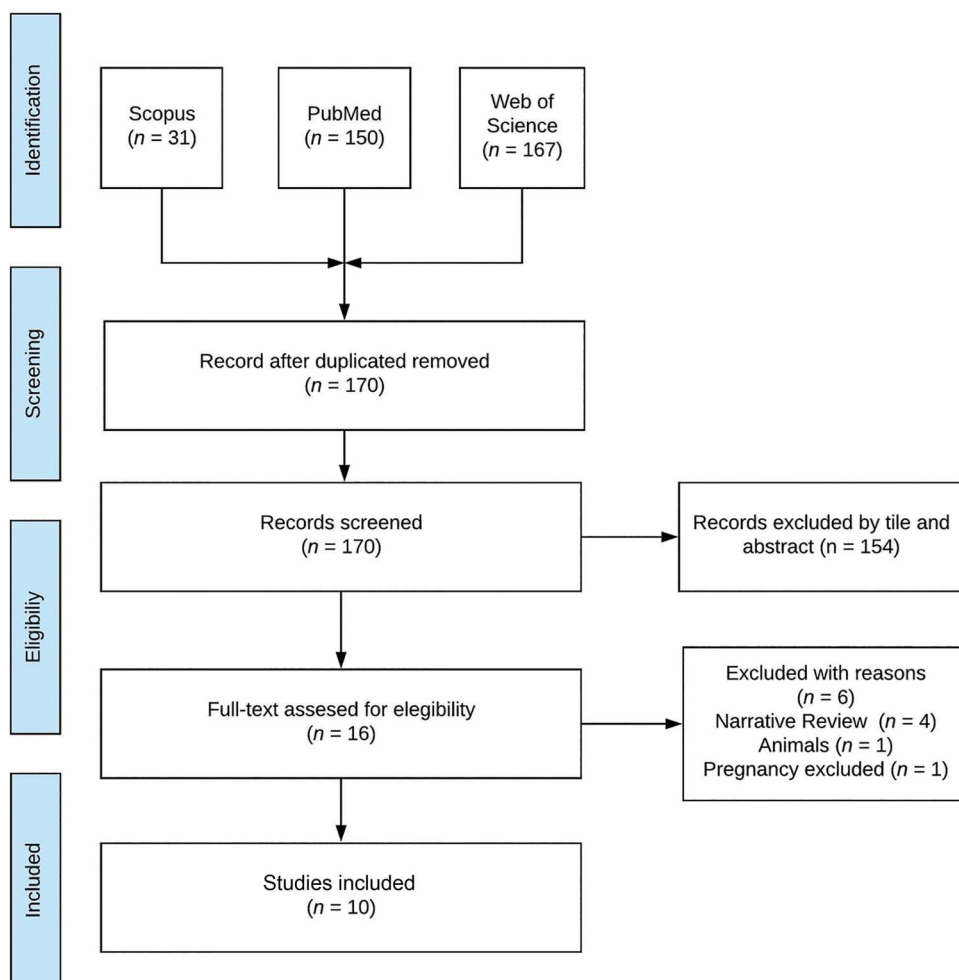
significant variations in visual acuity or refractive error during pregnancy.<sup>29,32</sup>

The effect of pregnancy on the progression of myopia has been studied in a recent publication.<sup>1</sup> A cohort of 10 401 women aged between 20 and 50 years was prospectively evaluated since 1999. Pregnancies and myopia were repeatedly assessed in each biennial follow-up questionnaire during 14 years of follow-up. The authors concluded that pregnancy was inversely associated with the risk for myopia development or progression during each of the 2-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 because of pregnancy-related physiological variations in underlying biomechanically weakened corneas.<sup>26–29</sup>

### PRK

Hefetz et al.<sup>23</sup> 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 postoperatively. Of these, 1 woman



**Figure 1.** Systematic review flowchart.

Table 2. Study Characteristics.

| Author (date)                                      | Design | Follow-up (mo) | Patients | Eyes | Age (y) | Surgery to complication time | POB period | Refractive surgery   |
|--|--------|----------------|----------|------|---------|------------------------------|------------|----------------------|
| Hefetz et al. <sup>23</sup> (1996)                 | CS     | 12             | 8        | 11   | NR      | 5                            | NR         | PRK                  |
| Sharif <sup>24</sup> (1997)                        | CS     | 12             | 9        | 18   | 25      | 5                            | NR         | PRK                  |
| Starr <sup>25</sup> (1998)                         | CR     | 14             | 1        | 1    | 38      | 1                            | 1          | PRK                  |
| Hafezi and Iseli <sup>26</sup> (2008)              | CR     | 90             | 1        | 2    | 33      | 26                           | 7          | LASIK                |
| Padmanabhan et al. <sup>27</sup> (2010)            | CR     | 25             | 1        | 2    | 20      | 18                           | 2          | LASIK                |
| Said et al. <sup>28</sup> (2011)                   | SC     | 108            | 3        | 5    | 32      | 42                           | NR         | LASIK                |
| Hafezi et al. <sup>16</sup> (2012)                 | SC     | 67             | 5        | 10   | 31      | 67                           | 7          | LASIK                |
| López-Prats et al. <sup>29</sup> (2012)            | Cohort | 6              | 9        | 18   | 27      | NR                           | 6          | LASIK                |
| Alonso-Santander et al. <sup>21</sup> (2020)       | SC     | 3              | 71       | 142  | 33      | NR                           | NR         | LASIK (131)/PRK (11) |
| Kanellopoulos and Vingopoulos <sup>20</sup> (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

experienced myopic regression in both eyes when she became pregnant 5 months postoperatively. However, this study did not report whether these changes remained permanent after delivery. Subsequently, Sharif studied the same effect in 18 eyes of 9 women who became pregnant in the first 12 months after PRK.<sup>24</sup> Preoperative myopia ranged from  $-1.25$  to  $-6.00$  D, and the follow-up was from 12 to 24 months. He observed that 12 eyes underwent myopic regression, of which 10 also developed corneal haze. All of them became pregnant in the first 5 months postoperatively. 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.<sup>33</sup> 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 for myopic regression and haze development in patients who become pregnant in the first 5 months after PRK.

In the same way, Starr reported a case of a woman who experienced a  $+3.00$  D overcorrection and corneal haze during pregnancy after myopic PRK in her right eye (RE).<sup>34</sup> Preoperative myopia was  $-5.00$  D, and it was estimated that she became pregnant 1 week postoperatively. The patient had an abortion in the third month of pregnancy and the overcorrection a regression. In the tenth month postoperatively, she had an UDVA of 20/20 and 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 and for the complete regression of the overcorrection after the abortion. It also seems to point out the risk for 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 months and 12 months after the intervention. Similarly, 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,

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

| Author (yr)  | Previous |          | Posterior |         |
|--|----------|----------|-----------|---------|
|  | CDVA     | Rx (SE)  | UDVA      | Rx (SE) |
| Hefetz et al. <sup>23</sup> (1996)                 | NR       | $-4.80$  | NR        | $-0.80$ |
| Sharif <sup>24</sup> (1997)                        | NR       | $-3.50$  | NR        | NR      |
| Starr <sup>25</sup> (1998)                         | 20/20    | $-5.00$  | 20/20     | $+0.25$ |
| Hafezi and Iseli <sup>26</sup> (2008)              | 20/20    | $-5.75$  | 20/63     | $-6.00$ |
| Padmanabhan et al. <sup>27</sup> (2010)            | 20/20    | $-11.75$ | NR        | NR      |
| Said et al. <sup>28</sup> (2011)                   | NR       | $-7.00$  | NR        | NR      |
| Hafezi et al. <sup>16</sup> (2012)                 | 20/20    | $-5.00$  | NR        | NR      |
| López-Prats et al. <sup>29</sup> (2012)            | 20/20    | $-0.87$  | 20/25     | $-1.37$ |
| Alonso-Santander et al. <sup>21</sup> (2020)       | 20/20    | $-3.80$  | 20/20     | $-0.20$ |
| Kanellopoulos and Vingopoulos <sup>20</sup> (2020) | 20/20    | $-6.05$  | 20/20     | $-0.37$ |

CXL = corneal crosslinking; NR = not reported; PRK = photorefractive keratectomy; Rx = refraction; SE = spherical equivalent<sup>a</sup>After LASIK

Table 3. Continued

| Recurrence (mo) | Slitlamp findings | Complementary diagnostic tests | Complication                    | Treatment | Favor/against |
|-----------------|-------------------|--------------------------------|---------------------------------|-----------|---------------|
| NR              | NR                | NR                             | Myopic regression               | NR        | Favor         |
| 5               | Haze              | NR                             | Myopic regression and haze      | PRK       | Against       |
| 1               | Haze              | NR                             | Overcorrection and haze         | NR        | Against       |
| 26              | NR                | 405 $\mu\text{m}^a$            | VA decrease, halos, and ectasia | CCL       | Against       |
| 18              | NR                | 290 $\mu\text{m}^a$            | VA decrease, halos, and ectasia | NR        | Against       |
| 42              | NR                | 277 $\mu\text{m}^a$            | Ectasia                         | NR        | Against       |
| 67              | NR                | 359 $\mu\text{m}^a$            | Ectasia                         | CCL       | Against       |
| NR              | NR                | NR                             | NR                              | NR        | Against       |
| NR              | NR                | NR                             | NR                              | NR        | Favor         |
| NR              | NR                | NR                             | NR                              | NR        | Favor         |

including those who become pregnant in the first 6 months postoperatively. 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 for PLE than other refractive surgery corrections, such as PRK or SMILE.<sup>2</sup> Hafezi and Iseli reported a case of bilateral PLE in the third trimester of a woman's first pregnancy, 26 months after LASIK correction of  $-5.50$  D in the RE and  $-5.25$  D in the left eye (LE).<sup>26</sup> According to the presurgical examination, the cornea had no preexisting signs of disease, and  $68 \mu\text{m}$  were ablated in the RE and  $62 \mu\text{m}$  in the LE. After LASIK, the UDVA was 20/20 with normal topographies, and CCT was  $410 \mu\text{m}$  in the RE and  $400 \mu\text{m}$  in the LE. These parameters remained stable for 2 years. During the third trimester of the first pregnancy, PLE was developed, and the patient had a minimum corneal thickness of  $370 \mu\text{m}$  in the RE and  $360 \mu\text{m}$  in the LE. Two years later, during the second pregnancy, the patient experienced sudden vision deterioration in her RE due to PLE progression. This case is distinctive because of the late onset of PLE, happening and progressing both times in the second trimester of pregnancy, and because of 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.<sup>26</sup>

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  $-10.50 - 2 \times 10$  in the RE and  $-11.50 - 1 \times 160$  in the LE. After the intervention, there was an RSBT of  $305 \mu\text{m}$  in the RE and  $282 \mu\text{m}$  in the LE and a UDVA of 20/20. Eighteen months postoperatively, during the first month of gestation, the patient was diagnosed with progressive PLE. Similarly, this article suggested the action of estrogens as a factor that

modifies corneal biomechanics and proposed that we should be cautious with arbitrary cutoff 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 preexisting 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 2 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.<sup>25</sup> Moreover, this case did not collect a complete history that includes smoking, allergies, and eye rubbing, which are known risk factors for PLE.<sup>9</sup>

Furthermore, Said et al. reported an association between late onset of PLE after LASIK surgery and pregnancy.<sup>28</sup> They collected a series of 19 patients and 29 eyes that developed this complication. Of these, they studied 5 eyes of 3 women who became pregnant between 2 years and 5 years postoperatively, with an SE between  $-5.00$  D and  $-9.00$  D, and with a mean RSBT of  $277 \mu\text{m}$ . 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. performed a review of 5 patients who experienced visual impairment during pregnancy and who had undergone LASIK surgery, on average, 67 months before gestation.<sup>16</sup> All patients except one were primiparous, and all presented a progressive PLE. They reported the complete data of only 1 patient who was operated on for  $-5.00$  D in the RE and  $-4.50$  D in the LE. The patients' CDVA and UDVA were 20/20, and the minimum corneal thickness was  $359 \mu\text{m}$ . This study provided the least information about the patients compared with those of the previous reports; therefore, its results should be carefully assessed. Furthermore, the authors emphasized, "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 (ie, 505  $\mu\text{m}$ ), a minor asymmetry and elevation at the posterior pole (ie, 12  $\mu\text{m}$  at a reference sphere of 8 mm), or even keratoconus.”

Subsequently, López-Prats et al. 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.<sup>29</sup> 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 a mean increase of 0.30 D and 0.01 D in the control group, both with statistically significant differences. SE experienced a mean increase of 0.50 D in the LASIK group and 0.11 D in the control group, both results being 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 have recently published a prospective study with 128 eyes of 64 pregnant women who underwent bilateral myopic LASIK before pregnancy.<sup>20</sup> They studied UDVA, SE, sphere, cylinder, flattest keratometry values, and corneal and central epithelial thickness before LASIK, 12 months after LASIK, during the third trimester of pregnancy, and 1 year postpartum. Refractive error before intervention ranged from  $-1.00$  to  $-11.00$  D, with a mean of 6.72 D. None of the comparisons revealed statistically significant differences. Therefore, the authors concluded that corneal and refractive stability after LASIK seems 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.<sup>20,32</sup> These changes have been associated with the role of estrogens in corneal biomechanics. However, because of 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, 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.<sup>20,29</sup> Even so, an additional risk for PLE in these patients cannot be completely ruled out. As it has been proposed, women younger than 40 years could be considered as an additional risk factor to be added in Randleman Ectasia Risk Score System (ERSS).<sup>16</sup> 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.<sup>5</sup> 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. in which they compared 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.<sup>21</sup> 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 nonbreastfeeding 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 statistically 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, to our knowledge, it is the first and only study that analyzes this group of patients. According to the results, we would conclude that there seems to be no statistically significant differences in effectiveness 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.<sup>5</sup> This is based on the alleged refractive and tomographic changes that occur in the cornea during this period.<sup>35</sup> 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.<sup>20,32</sup> The few studies that exist on the effect of pregnancy in patients operated on 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 postoperatively. 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 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, nor phakic intraocular lens surgeries. There does not seem to be any statistically significant 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 disk–dual Scheimpflug analyzer

or artificial intelligence could be especially interesting in these patients.<sup>25,36–38</sup>

In conclusion, PRK and LASIK surgery seem to be stable procedures that 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 for these surgeries outweigh the benefits. Further research will be necessary to clarify these questions.

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