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Risk Factors for Developing Dry Eye after Lasik

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Abstract

Dry eye results in ocular surface damage & ocular discomfort symptoms that are related to visual disturbances. Assessing risk factors for the development of dry eye post laser-assisted in situ keratomileusis (Lasik). Our literature search process retrieved 400 records. 272 duplicated records were excluded using Endnote. After evaluating the titles & abstracts, sixteen articles met the criteria for full-text screening. Five of these studies have been involved into the meta-analysis. A manual search was conducted in the references of the investigations that were included, & no additional articles were involved. Our pooled analysis showed no significant difference regarding the mean ablation depth between cases with dry eye and no dry eye with pooled MD and 95% CI= 1.16[-5.85, 8.18], p-value=0.7. Our pooled analysis estimated no significant results regarding development of dry eye in women cases to greater than males. No significant results regarding development of dry eye in female patients greater than males with pooled MD and 95% CI= 2.52[0.26, 24.26], p-value = 0.43. Our pooled studies for this outcome were heterogenous with chi-p 0.00001 and I^2 98%. Our pooled analysis estimated no significant results regarding development of dry eye in female patients more than males with pooled RR and 95% CI= 6.09 [1.98, 10.21]. We can conclude that female gender, older age, LASIK treatment & decrease prior surgery refractive error, are correlated with an enhanced risk of dry eye illness at six months after surgery.

Keywords: Dry eye after Lasik, Risk factors, visual disturbances, pooled analysis.

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1. Introduction

Laser-assisted in situ keratomileusis has become the most prevalent corneal refractive operation in the US, with approximately one million procedures performed annually, over the past two decades [1]. Despite reports of high satisfaction, dry eye continues to be the most prevalent adverse effect associated with laser-assisted in situ keratomileusis. A considerable number of cases who had LASIK reported mild to moderate dry eye symptoms for several months. Although these symptoms can be adequately decreased with conventional tear substitutes, cases kept suffering from dry eye over an extended period of time. At least six months after the procedure, the incidence of chronic dry eye disorder ranged from twenty to forty percent [2]. Ocular surface damage & symptoms of ocular discomfort related to visual disturbance are the results of dry eye. These complications not just have a negative impact on the visual outcomes, but they also have a negative impact on the entire quality of life [3-5]. Consequently, it is viable to hypothesize that annually, hundreds of thousands of LASIK cases will develop chronic dry eye disease, thus worsening the health concerns of this younger & physically active population. A possible etiology of post- laser-assisted in situ keratomileusis dry eye is the combined influence of excimer photoablation and complete disruption of corneal nerves during flap creation. In the first few months following LASIK, there have been reports of a ninety percent reduction in central nerve fiber density, which persists for years until the density reaches preoperative levels again [6]. Consequently, LASIK decrease epithelial wound healing, tear secretion, tear film quality, & blinking rates—all of which are recognized to play a role in the development of dry eye disease. For LASIK, the femtosecond laser was created to enhance flap creation & permit custom. despite this, the management and optimization of flap characteristics yielded small improvement in post- laser-assisted in situ keratomileusis dry eye, showing the necessity to devise new techniques that enhance ocular surface protection following to refractive surgery. A recent technique, small incision lenticule extraction (SMILE), generates an intrastromal lenticule via femtosecond laser & removes it via a small Cornea incision [7-9]. The femtosecond refractive operation described here is all-in-one, excimer laser photoablation and a complete flap incision are not necessary for this procedure, in contrast to LASIK's requirements.

Consequently, by necessitating only a narrow passage, SMILE may serve as a minimally invasive technique for corneal refractive operation, thereby conferring extra

protection against iatrogenic dry eye disorders & potentially minimizing the impact on corneal innervation. While refractive outcomes, corneal sensitivity, & clinical dryness have been documented in clinical studies following SMILE, an assessment of the disease's overall severity is unclear. This would necessitate a combination of subjective & objective symptom evaluation, as suggested by Delphi, as well as an investigation into the disease's precise correlation with functional & morphologic alterations in corneal innervation [10]. Thus, long-term ocular surface recovery & subsequent case health status following SMILE remain uncertain; provided its theoretical benefits are demonstrated, SMILE could become the new gold standard for corneal refractive operation.

2. Methods

The reporting of this systematic review and meta-analysis was carried out in accordance with the principles as defined in the PRISMA statement. The study was conducted in strict compliance to the guidelines outlined in the Cochrane Handbook of Systematic Reviews & Meta-analyses of Interventions. The study was conducted in Nour Al-Haya Eye Center.

2.1. Eligibility criteria

For inclusion in our assessment, studies had to meet the subsequent criteria: The inclusion criteria for this study comprised the following: myopia falling within the range of –2.00 to 10.00 diopters (D), absence of intraocular or prior ocular surgery, stable refraction for a minimum of twelve months prior to laser-assisted in situ keratomileusis, & no indications or symptoms of dry eye. One surgeon conducted every LASIK operation.

2.2. Study design

Retrospective cohort studies and clinical trials either controlled or single arm that investigate.

2.3. Information sources and search strategy

From the beginning of the study to the 22nd of February 2024, we conducted an exhaustive search of four electronic databases, namely PubMed, Google scholar, Web of Science, & the Cochrane Central Register of Controlled Trials, utilizing the terms as follows: “refractive surgery,” “dry eye disease,” “keratoconjunctivitis sicca,” “keratitis sicca,” & “dry eye syndrome” & “laser-assisted in situ keratomileusis” and “LASIK” were employed in the search strategy. Additionally, potential eligible research was identified by manually searching the references of the investigations involved.

2.4. Selection process

The references obtained from Endnote (Clarivate Analytics, PA, USA) were subjected to a two-step screening process. Initially, the titles/abstracts of all identified articles were examined independently by all authors to identify their relevance to the meta-analysis. Subsequently, the full-text articles corresponding to those with identifiable abstracts were assessed to identify their final eligibility for the meta-analysis.

2.5. Data collection process and data items

The extracted data was standardized on a data extraction sheet. The extracted data comprised the following:

- Features of the studies that were involved.
- Features of the included studies' population.
- Domains associated with the risk of bias.
- Outcome measurements.

2.6. Assessing the risk of bias in the individual studies

Based on the information provided in the Cochrane Handbook of Systematic Reviews of Interventions 5.1.0 (which was most recently updated in March 2011), the quality of the retrieved RCTs was assessed according to the Cochrane ROB1 tool and for single-arm clinical trials, and we used the NIH tool for pre- and post-clinical trials.

2.7. Data synthesis

Our meta-analysis involved combining the mean changes (M.C.s) and their corresponding ninety-five percent confidence intervals (C.I.s) for our continuously measured outcomes. Ratios of categorical outcomes were combined using ninety-five percent confidence intervals. If the effect measure was derived from a collection of homogeneous investigations, the fixed effect model was initially utilized. If not, the random effect model was applied. Using the I2 statistics chi2 test, we examined the statistical heterogeneity between studies; outcomes with chi2-p > 0.1 were deemed heterogeneous, whereas I2≥50% indicated high heterogeneity. Open Meta-Analyzer software was utilized for single-arm meta-analyses of dichotomous outcomes, whereas Review Manager Software (RevMan) version 5.4 was employed for single-arm analyses of continuous outcomes.

3. Results and Discussion

3.1. Literature search results

The literature search yielded a total of four hundred documents. Using Endnote, 272 duplicate records were eliminated. After evaluating the abstracts and titles, we determined that sixteen articles met the criteria for full-text screening. Five of these studies were involved into the meta-analysis. A manual search was conducted in the references of the investigations that were involved, and no additional articles were involved. Figure 1 demonstrates the PRISMA flow diagram, which depicts the process of selecting studies. Dry eye is frequently observed as a postoperative complication, and refractive surgery has been associated with the development or worsening of preexisting dry eye via multiple mechanisms [2]. Dry eye is, in fact, the most common complication following laser-assisted in situ keratomileusis, according to refractive surgeons [3]. As demonstrated by utility evaluation, dry eye following refractive surgery is not only extremely common but also has the potential to significantly impair a person's standard of life. The utility scores reported by cases undergoing hospital dialysis or moderate–severe dry eye is comparable to those of cases with moderate–severe angina [4-5]. Significant morbidity correlates with even mild dry eye, with utility scores comparable to those of severe migraines [6-7].

The current study showed that there were females were common affected as mentioned in Albietz et al., (2004), Denoyer et al., (2015), Paiva et al., (2006) [11,12,14]. As similar, Albietz et al., (2005) established that post-refractive operation dry eye is associated with the known risk factor of female gender, which is also associated with more severe

symptoms & impaired tear function [18]. On the contrary, Mashor et al., (2019) documented that males were prevalent [13]. There has been a lack of gender-relative reference in multiple investigations [16-17]. Our results demonstrated that the age of cases in the involved researches varied from 27 to 36 years. This study showed regarding visual acuity ranged from -2 to 10 D as in Paiva et al., (2006), Shoja and Besharati (2007) and -4 (2.26) D in Albietz et al., (2004) [11, 14, 15]. According to Toda et al., (2001) dry eye syndrome is the most common complication following laser-assisted in situ keratomileusis [19]. In uncommon cases, it may result in significant visual impairment, although it is typically harmless. Paiva et al., (2006) and Ang et al., (2001) [14,20]. Dry eye can cause a temporary deterioration in the cornea's optical quality, which can persist for a maximum of one year. Contrary to our findings, Smith's study (2004) found no sex-related variations in the development of dry eye following laser-assisted in situ keratomileusis [21]. The potential correlation between ablation depth & dry eye risk could be attributed to the comparatively higher prevalence of dry eye symptoms & diagnosed dry eye in the general population of Asian nations compared to other regions. According to Australian & Danish investigations, the prevalence of dry eye was eleven percent and eight percent, respectively [22-23]. Shehadeh-Mashor et al., (2019) who demonstrated that at six months following LASIK surgery, there is a higher chance of developing dry eye disease in cases who are older, female, have a reduce prior surgery refractive error, & have had the procedure [13]. Understanding the risk factors for dry eye following refractive operation is essential for identifying at-risk cases & preventing this complication, which has a substantial negative impact on patient satisfaction. Depending on the risk, some candidates may choose not to have surgery, while others may choose to take preventive perioperative assesses to stabilize the ocular surface. Besharati and Shoja (2007) intended to identify risk factors & incidence of dry eye following myopic laser-assisted in situ keratomileusis [15]. A retrospective case series was conducted to evaluate 190 eyes that had undergone LASIK for the presence of dry eye syndrome. At least six months after laser-assisted in situ keratomileusis for myopia, cases develop dry eye and impaired tear function, the researchers concluded. cases who require greater refractive correction & women are at an elevated risk of developing dry eye. Toda (2008) provided evidence that dry eye is a common complication that typically resolves within six to nine months following Kerat refractive surgery [24]. Achieving symptoms & signs of dry eye following LASIK was observed in fifty percent, forty percent, and twenty percent to forty percent of cases one week, one month, & six months after the procedure, respectively. At least six months after LASIK, the incidence of dry eye, as determined by symptomatic and/or objective observations, varied among 8.3 percent & forty-eight percent in various investigations [14,20,22-23].

3.2. Study results

3.2.1. Characteristics of included studies

This meta-analysis and systematic review comprised five studies. In Table 1, a summary of the attributes of the investigations that were involved is presented.

3.2.2. Risk of bias assessment

Our two RCTs had a low risk of bias corresponding to the Cochrane ROB tool 1 and the other included three retrospective cohort studies were of good quality regarding the NIH tool. To see for Comprehensive Summary of our ROB assessment tools see (Table 2). Q1: Was there a clear statement of the research objective or question? Q2: Was the population under investigation clearly defined & specified? Q3: Did at least fifty percent of eligible individuals participate? Q 4: Were all of the subjects recruited or chosen from populations that were identical or comparable in nature, involving period of time? Were the criteria for inclusion & exclusion in the research predetermined & consistently applied to all participants? Question 5: Were there any reasons for the sample size, descriptions of power, or estimations of variance & effect included? Q6: In the analyses presented in this paper, were the exposures under investigation measured prior to the outcomes were evaluated? Question 7: Was the duration of the study adequate to reasonably predict the presence of a correlation among the exposure & the outcome, should one exist?, Question 8: Did the investigation examine the relationship between various levels of exposure & the outcome, specifically for exposures that may vary in amount or level (e.g., exposure categories or exposure measured as a continuous variable)?, Q9: Were the exposure measures, which constituted the clearly defined, independent variables, valid, & reliable, & were they consistently applied to all research participants?, Question 10: Did the exposures undergo multiple assessments over a period of time?, Q11: Were the outcome measurements, which constituted the dependent variables, clearly defined, valid, and reliable, & were they applied uniformly to all participants in the research? Q12: Were the outcome assessors not informed of the participants' exposure status? Q13: When was the loss to follow-up percentage or less after baseline? Q14: Were critical potential confounding variables assessed & statistically adjusted to determine their influence on the association among outcomes & exposures? For ROB graph and summary see (Figure 2).

3.2.3. The mean ablation depth as a risk factor for dry eye

Our pooled analysis showed no significant distinction regarding the mean ablation depth between cases with dry eye & no dry eye with pooled MD and 95% CI= 1.16 [-5.85, 8.18], p-value=0.7. Our pooled studies for this outcome were heterogenous with chi-p 0.006 and I^2 80%. Figure 3 depicts the forest plot for this outcome.

3.2.4. Female sex as a risk factor for dry eye

Our pooled analysis estimated no significant results regarding development of dry eye in female patients more than males with pooled MD and 95% CI= 2.52[0.26, 24.26], p-value = 0.43. Our pooled studies for this outcome were heterogenous with chi-p 0.00001 and I^2 98%. Figure 4 depicts the forest plot for Female sex.

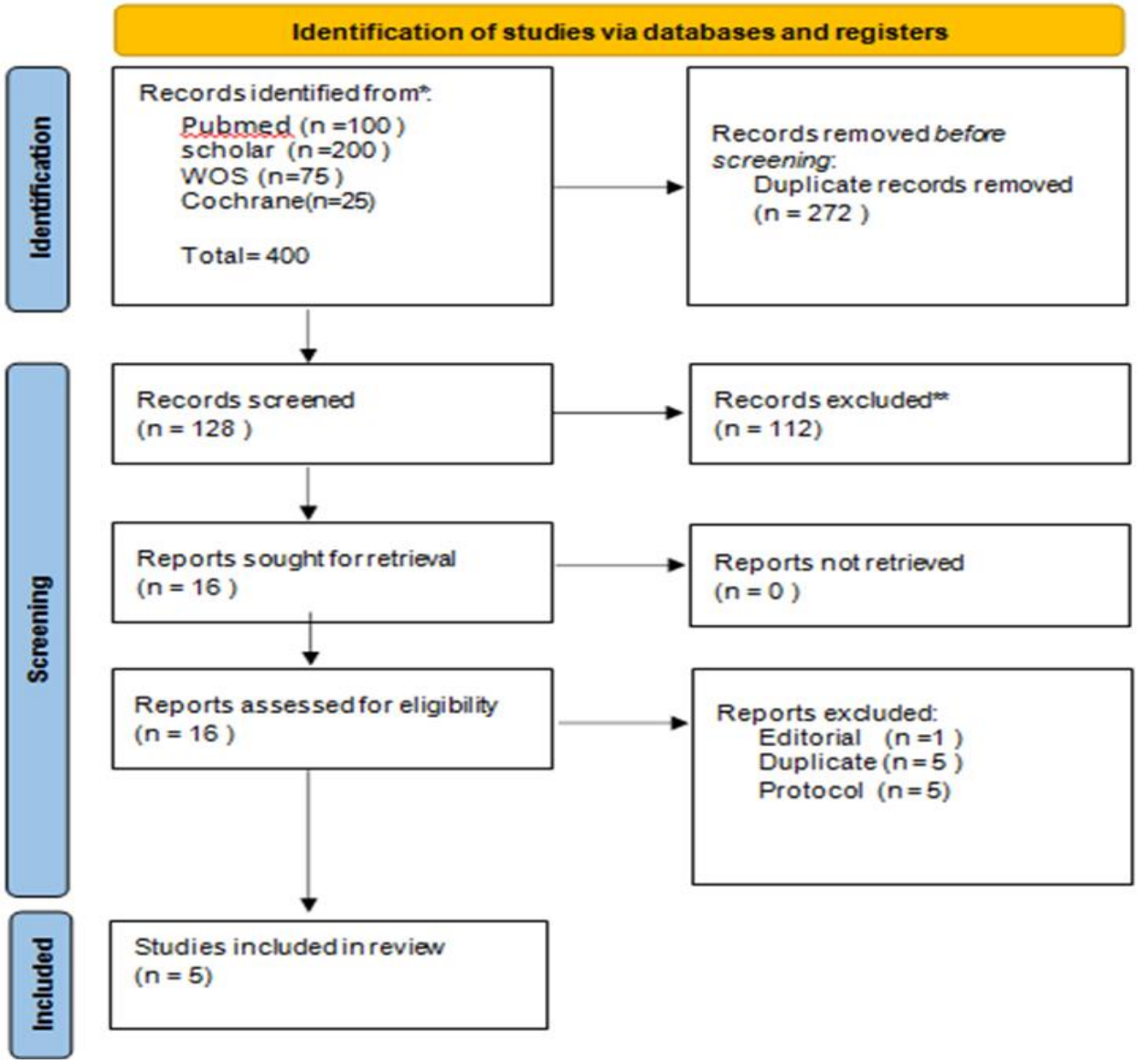

Figure 1: Demonstrates the PRISMA flow diagram, which depicts the process of selecting studies

Table 1: Characteristics of the included studies.

Study ID	Study design	Number of patients and eyes	Mean age	Sex (M)	Visual acuity	Duration of follow up
Albietz et al., [11]	Retrospective	565	36	44%	-4 (2.26) D	12 months
Denoyer et al., [12]	RCT	30	32.2	47%	NR	6 months
Mashor et al., [13]	Retrospective	25,317	27	55%	NR	6months
Paiva et al., [14]	RCT	18	35	10	- 2 to 10 D	6months
Shoja and Besharati [15]	Retrospective	190	31	NR	-2 to 10 D	6 months

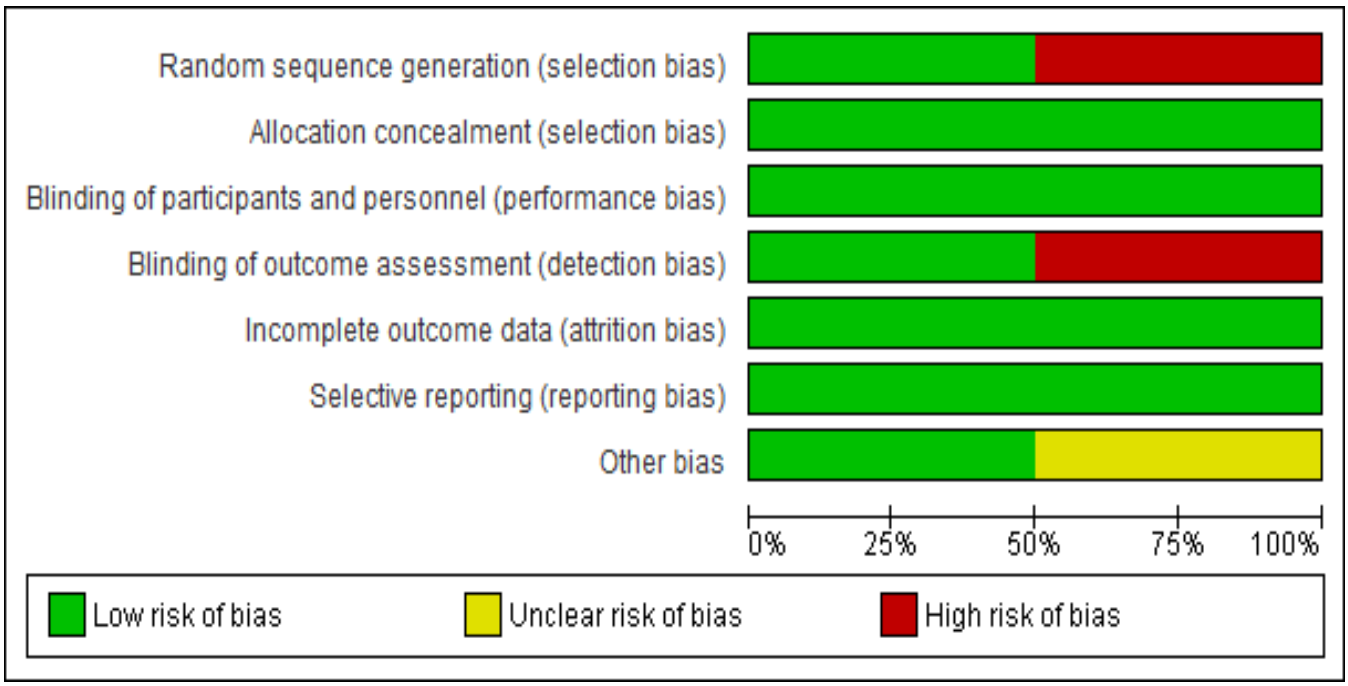

Figure 2: Risk of bias assessment.

Table 2: Comprehensive Summary of our ROB assessment tools.

Study ID	Quality assessment for Single-arm observational studies according to the NIH tool															
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Overall Score	Overall quality
Albietz et al., [11]	Y	Y	Y	Y	CD	Y	Y	N	Y	N	Y	N	Y	CD	9	Good
Mashor et al., [13]	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	CD	Y	N	11	Good
Shoja and Besharati [15]	Y	Y	Y	Y	N	Y	N	Y	CD	Y	Y	CD	N	Y	9	Good

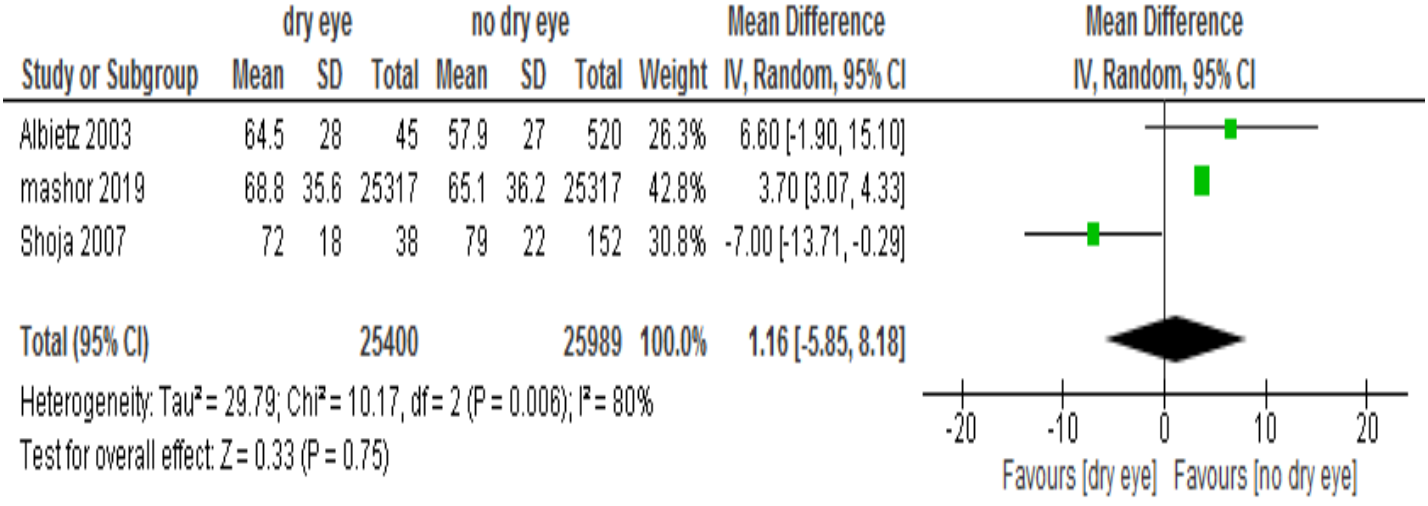

Figure 3: Forest plot for mean ablation depth as a risk factor for dry eye.

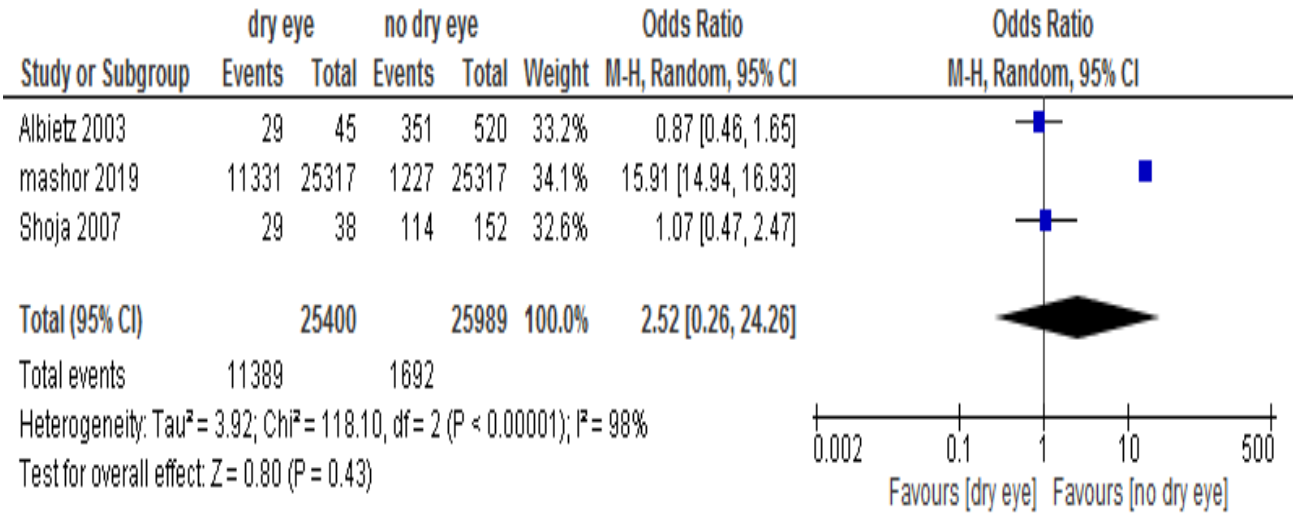

Figure 4: Forest plot for Female sex.

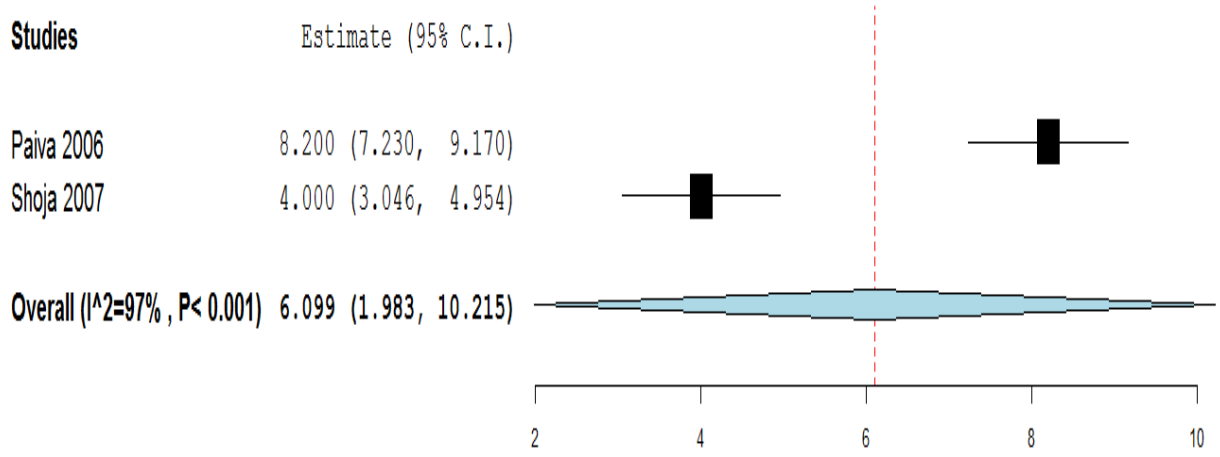

Figure 5: The forest plot for TBUT.

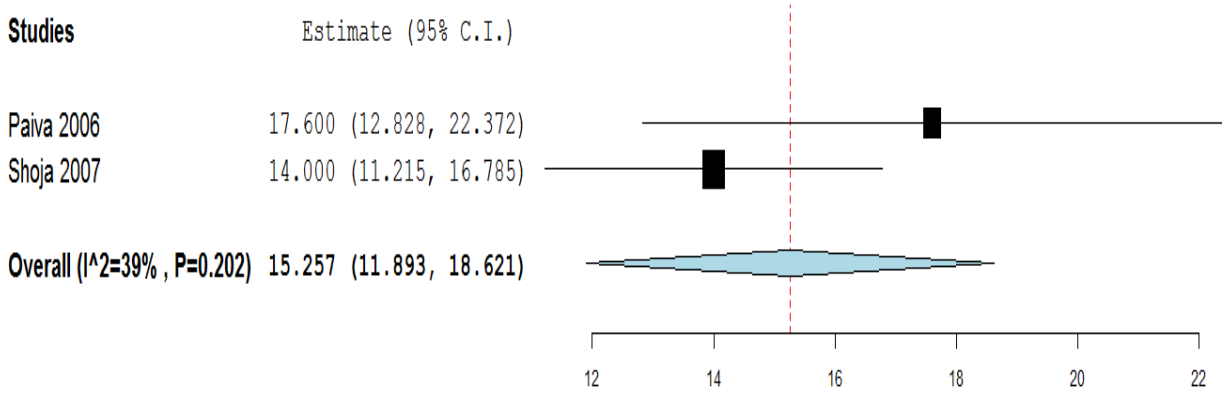

Figure 6: The forest plot for schirmer's test.

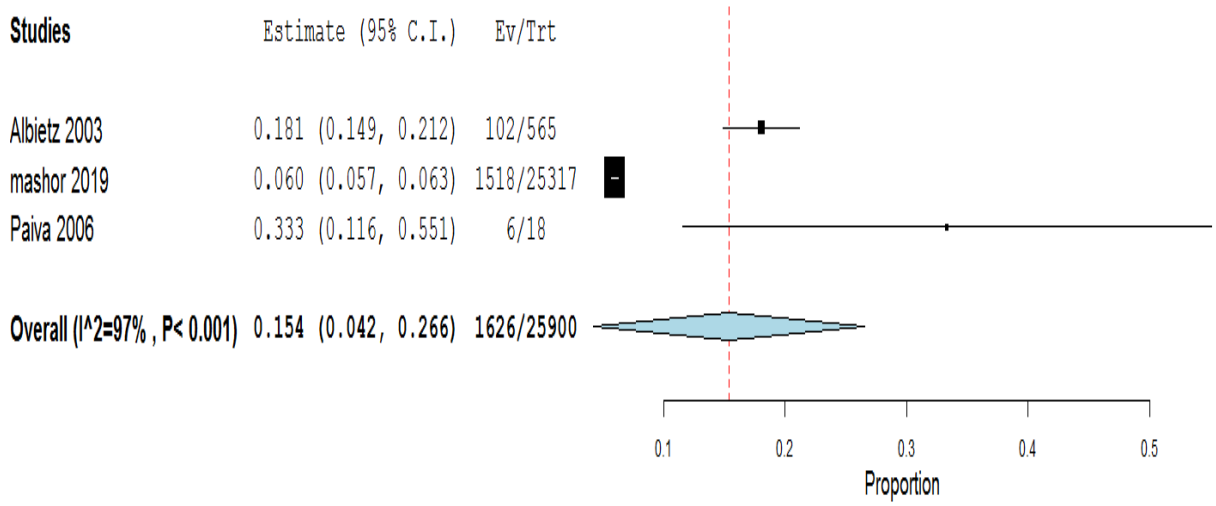

Figure 7: The forest plot for dry eye symptoms.

3.2.5. Tear break up time TBUT

Our pooled analysis estimated no significant results regarding development of dry eye in female patients more than males with pooled RR and 95% CI= 6.09 [1.98, 10.21], our pooled studies for this outcome were heterogenous with chi-p 0.001 and I^2 97%. Figure 5 depicts the forest plot for TBUT.

3.2.6. Schirmer's test

Our pooled analysis estimated pooled RR and 95% CI= 15.25 [11.89, 18.62], our pooled studies for this outcome were homogenous with chi-p 0.2 and I^2 39%. Figure 6 depicts the forest plot for schirmer's test.

3.2.7. Dry eye symptoms

Our pooled analysis estimated pooled RR and 95% CI= 0.15 [0.04, 0.26], our pooled studies for this outcome were heterogenous with chi-p 0.001 and I^2 97%. Figure 7 depicts the forest plot for dry eye symptoms.

4. Conclusions

There is a correlation between LASIK treatment, advanced age, female gender, & a reduced before surgery refractive error with an elevated likelihood of developing dry eye disease six months after the procedure. It is critical to know about the risk factors correlated with dry eye following refractive operation in order to identify cases who are at risk and to prevent this complication, which has a significant effect on case satisfaction. Depending on the level of risk, preventive perioperative assesses to stabilize the ocular surface may be necessary for some candidates or to avoid surgery completely.

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