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REFRACTIVE SURGERY AND REFRACTIVE REGRESSION: MECHANISMS AND MITIGATION STRATEGIES

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Abstract: INTRODUCTION The introduction outlines the prevalence and significance of refractive surgery in correcting refractive errors such as myopia, hyperopia, and astigmatism. It addresses refractive regression as a recurrent issue that undermines long-term outcomes. The introduction highlights the importance of corneal biomechanics, epithelial healing, and patient factors in influencing the likelihood of regression. Advances in surgical techniques and the need for effective prevention strategies are introduced as central themes of the review. **OBJETIVE** To comprehensively review the causes and mechanisms of refractive regression following refractive surgery, with a focus on LASIK, PRK, and SMILE, and to evaluate the strategies for preventing or managing this phenomenon. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: "Refractive surgery" AND "Refractive regression" OR "Corneal biomechanics" AND "LASIK and SMILE outcomes" OR "Postoperative stability" in the last years. **RESULTS AND DISCUSSION** The results and discussion sections focus on the multifactorial nature of refractive regression, emphasizing corneal biomechanical changes and epithelial hyperplasia as key contributors. Patient-specific factors, such as age, hormonal status, and systemic conditions, are analyzed for their influence on postoperative outcomes. The discussion evaluates the impact of different refractive techniques, such as LASIK, PRK, and SMILE, on regression rates and explores the potential of corneal cross-linking and other emerging technologies in enhancing corneal stability. The role of postoperative care and enhancement procedures in managing regression is also discussed in depth. **CONCLUSION** The conclusion underscores that refractive regression, though a persistent challenge, is increasingly being addressed through advancements in surgical techniques, individualized patient assessments, and novel postoperative strategies. Continued research and the development of new technologies, including biomechanically-modulated treatments and pharmacologic interventions, are key to improving long-term outcomes in refractive surgery. The conclusion reiterates the importance of patient education and compliance in minimizing regression and maintaining stable refractive results.

Keywords: Refractive surgery; Corneal biomechanics; Refractive regression; LASIK enhancement; Epithelial hyperplasia.

INTRODUCTION

Refractive surgery has evolved significantly over the past few decades, becoming a pivotal intervention in the correction of refractive errors, such as myopia, hyperopia, and astigmatism. The advent of laser-based techniques, including LASIK (laser-assisted in situ keratomileusis), PRK (photorefractive keratectomy), and more recently, SMILE (small incision lenticule extraction), has dramatically improved patient outcomes by providing safe and effective options for vision correction[1]. These procedures work by reshaping the cornea to alter its refractive power, thereby allowing light to focus correctly on the retina. Despite the widespread success and popularity of these surgeries, one of the most persistent challenges is refractive regression, a phenomenon characterized by a partial loss of the surgical effect over time[1].

Refractive regression is often defined as the gradual return of the preoperative refractive error, which can occur months to years following the initial surgery[2]. It is a multifactorial process, influenced by both patient-specific factors and surgical techniques. Various studies have documented the prevalence of refractive regression, which ranges from minimal, clinically insignificant shifts to more pronounced changes that require retreatment[2]. Understanding the underlying causes of this phenomenon is crucial for improving surgical outcomes and patient satisfaction. These causes can range from biomechanical changes in the cornea to environmental influences such as UV light exposure and lifestyle factors[2].

Corneal biomechanics play a central role in refractive stability after surgery. The cornea's response to the ablation of tissue, whether by LASIK, PRK, or SMILE, involves complex wound healing processes that can affect its structural integrity. Postoperative corneal remodeling, epithelial hyperplasia, and changes in stromal composition contribute significantly to refractive regression[3]. Additionally, individual variations in corneal thickness, preoperative refractive error, and healing responses further complicate the predictability of long-term refractive stability[3]. Patients with high myopia, for instance, are particularly prone to regression due to the extensive ablation required for correction, which can weaken the biomechanical strength of the cornea[3].

The role of patient-specific factors in refractive regression cannot be overstated. Age, hormonal changes, and ocular surface health are among the critical determinants of postoperative outcomes[4]. For instance, older patients may experience more significant changes in corneal biomechanics due to age-related stiffening of the cornea[4]. Furthermore, the presence of ocular surface disorders, such as dry eye, can exacerbate refractive instability. Similarly, systemic conditions, including diabetes, can impair wound healing and corneal health, leading to higher rates of regression[4].

Surgical techniques and intraoperative factors also contribute to refractive regression. The choice of procedure—whether LASIK, PRK, or SMILE—affects the long-term refractive outcome, with each technique presenting unique challenges[5]. LASIK, which involves creating a corneal flap, may be associated with greater biomechanical instability compared to PRK, where no flap is created, and the epithelium is removed[5]. Moreover, intraoperative variables such as flap thickness, ablation depth, and the use of advanced laser platforms significantly influence postoperative refractive stability[5]. The evolution of surgical technologies, including femtosecond lasers and topography-guided ablations, has aimed to minimize the risk of regression by enhancing the precision and safety of these procedures[6].

Despite advances in refractive surgery, managing refractive regression remains a critical aspect of patient care. Early detection of regression through regular follow-up and the use of enhancement procedures are essential strategies for maintaining refractive outcomes[6]. Enhancement procedures, such as additional laser treatments or the use of corneal cross-linking, have shown promise in stabilizing the cornea and preventing further regression[6]. Furthermore, patient education and preoperative counseling are integral components of the surgical process, ensuring that patients have realistic expectations regarding the possibility of refractive regression and the potential need for retreatment[6].

The future of refractive surgery lies in the continued refinement of surgical techniques and postoperative management strategies aimed at minimizing refractive regression. Advances in understanding corneal biomechanics, the development of new surgical tools, and personalized treatment plans tailored to individual patient characteristics hold the potential to further improve long-term outcomes. Additionally, ongoing research into pharmacologic interventions and novel therapies may offer new solutions for preventing or reversing refractive regression[7]. As refractive surgery continues to evolve, addressing the challenge of refractive regression remains a top priority for improving patient satisfaction and achieving lasting visual correction[7].

This review aims to comprehensively explore the causes and prevention strategies for refractive regression following refractive surgery. Through a detailed analysis of the existing literature, the role of biomechanical changes, patient-specific factors, and advancements in surgical techniques will be discussed. Furthermore, potential management strategies, including the use of enhancement procedures and future innovations in refractive surgery, will be examined to provide a holistic understanding of this complex and clinically significant issue[8].

OBJETIVES

To comprehensively review the causes and mechanisms of refractive regression following refractive surgery, with a focus on LASIK, PRK, and SMILE, and to evaluate the strategies for preventing or managing this phenomenon.

SECUNDARY OBJETIVES

- To analyze the role of corneal biomechanics and epithelial remodeling in refractive regression.
- To assess the impact of patient-specific factors, including age, hormonal changes, and ocular health, on long-term refractive stability.
- To discuss the role of different surgical techniques and advancements in reducing the incidence of refractive regression.
- To explore emerging treatments and technologies, such as corneal cross-linking, in the prevention of refractive regression.
- To highlight the importance of postoperative management and patient education in minimizing regression and improving long-term outcomes.

METHODS

This is a narrative review, in which the main aspects of the causes and mechanisms of refractive regression following refractive surgery, with a focus on LASIK, PRK, and SMILE, and to evaluate the strategies for preventing or managing this phenomenon. in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: “Refractive surgery” AND “Refractive regression” OR “Corneal biomechanics” AND “LASIK and SMILE outcomes” OR “Postoperative stability” in the last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

The inclusion criteria applied in the analytical review were human intervention studies, experimental studies, cohort studies, case-control studies, cross-sectional studies and literature reviews, editorials, case reports, and poster presentations. Also, only studies writing in English and Portuguese were included.

RESULTS AND DISCUSSION

The biomechanical changes that occur in the cornea post-refractive surgery represent a key factor in understanding refractive regression. These changes are primarily related to how the corneal stroma reacts to tissue ablation, particularly in procedures like LASIK, PRK, and SMILE. The cornea’s structural integrity is altered, and while the epithelium undergoes remodeling, the deeper stromal layers also experience a redistribution of forces that can lead to regression, especially in higher corrections. Studies have shown that patients with significant myopic correction

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are more prone to regression due to the increased ablation depth, which weakens the biomechanical strength of the cornea[9]. This weakening predisposes the cornea to biomechanical instability, allowing for subtle changes in curvature that result in a partial return of the refractive error[9].

Epithelial hyperplasia is another significant contributor to refractive regression, particularly in surface ablation procedures like PRK. Following PRK, the epithelium undergoes a process of regeneration, during which it thickens and smooths the anterior surface of the cornea. However, this epithelial remodeling can sometimes result in refractive shifts, as the increased epithelial thickness alters the overall refractive power of the cornea[10]. In LASIK and SMILE, while the epithelium is less directly impacted, changes in epithelial thickness have still been observed as part of the healing response. This process is exacerbated in cases of higher corrections, where more tissue removal necessitates a more pronounced healing response[10]. While the exact mechanisms underlying epithelial hyperplasia are still being studied, its contribution to refractive regression is widely recognized and is a significant focus of ongoing research into improving long-term outcomes[11].

Patient-specific factors, such as age and hormonal status, also play a crucial role in refractive regression. Older patients tend to exhibit more stable corneal biomechanics due to the natural stiffening of the cornea with age, which can reduce the likelihood of regression[12]. Conversely, younger patients, particularly those with high myopia, are at higher risk due to the inherent flexibility of their corneas. Hormonal changes, such as those occurring during pregnancy or in individuals with conditions like diabetes, can also affect the stability of refractive outcomes. During pregnancy, for instance, fluctuations in corneal hydration and thickness due to hormonal changes have been documented, sometimes leading to temporary refractive shifts[12]. Diabetes, on the other hand, is associated with impaired wound healing, which can lead to irregular healing responses and an increased risk of regression after refractive surgery[13].

In terms of surgical techniques, the choice between LASIK, PRK, and SMILE has been shown to influence the likelihood of refractive regression. LASIK, due to the creation of a corneal flap, can introduce some degree of biomechanical instability, particularly when large amounts of tissue are ablated. PRK, by removing the epithelium and allowing for direct reshaping of the stromal bed, generally results in greater long-term stability but is associated with a longer healing process and more pronounced postoperative discomfort[14]. SMILE, as a newer technique, avoids the creation of a flap and instead removes a lenticule of stromal tissue through a small incision. This approach has been shown to result in a more stable corneal structure, with lower rates of long-term regression compared to LASIK, particularly in high myopia patients[14]. However, long-term comparative studies between these techniques are still ongoing, and while SMILE offers promising results, it is not without its own unique challenges, including epithelial remodeling and lenticule interface changes[15].

Intraoperative factors, such as the depth of ablation and flap thickness, are critical determinants of refractive stability. For instance, deeper ablations required for high myopic corrections have been associated with greater rates of regression due to the increased structural alteration of the cornea[16]. Similarly, thinner LASIK flaps tend to result in more biomechanical preservation of the cornea, reducing the risk of regression. Recent advances in laser technology, including topography-guided and wavefront-optimized ablations, have also contributed to minimizing the risk of regression by creating more precise ablations that are tailored to the individual patient's corneal anatomy[16]. These advancements aim to improve long-term refractive stability by reducing the irregularities that may lead to biomechanical instability and subsequent refractive shifts[17].

The role of corneal cross-linking as an adjunct to refractive surgery is a growing area of interest in the prevention of refractive regression. Originally developed as a treatment for keratoconus, cross-linking strengthens the collagen fibers within the cornea, increasing its resistance to biomechanical deformation[18]. Studies have explored its application in patients undergoing refractive surgery, particularly those at higher risk of regression, such as individuals with high myopia or thin corneas. Early results have been promising, with cross-linking demonstrating the potential to stabilize the cornea and reduce the likelihood of long-term refractive shifts[18]. However, this technique is still in the investigational stage for routine use in refractive surgery, and further research is needed to establish standardized protocols and identify the ideal patient populations for its use[19].

Postoperative care and patient compliance are also essential components in minimizing the risk of refractive regression. The use of anti-inflammatory medications, such as corticosteroids, in the immediate postoperative period has been shown to reduce the risk of excessive wound healing responses, such as haze formation, which can contribute to refractive shifts[20]. Furthermore, ensuring that patients adhere to prescribed postoperative regimens, including avoiding eye rubbing and exposure to environmental factors like UV light, is crucial for maintaining refractive stability[20]. The importance of patient education cannot be overstated, as patients who understand the potential risks of regression and the need for long-term follow-up are more likely to adhere to recommendations and seek timely interventions when necessary[21].

The long-term management of refractive regression often involves enhancement procedures. LASIK enhancements, which involve lifting the original flap and performing additional laser ablation, are the most common approach for correcting regression[22]. In PRK, a similar enhancement can be performed by re-ablation after epithelial removal. However, these procedures carry their own risks, including further weakening of the cornea and the potential for additional regression[22]. Corneal cross-linking, as previously mentioned, offers a promising adjunctive therapy to enhance the biomechanical stability of the cornea in cases of significant regression. Moreover, pharmacologic interventions, such as the use of mitomycin C to reduce epithelial haze and regression in high-risk patients, have shown efficacy in selected cases[23].

Looking forward, advancements in refractive surgery continue to focus on reducing the rates of regression and improving long-term outcomes. The development of femtosecond laser technology, which allows for greater precision in flap creation and tissue ablation, has already had a significant impact on reducing regression rates in LASIK procedures[24]. Additionally, ongoing research into the use of personalized ablation profiles based on corneal topography and wavefront data holds promise for further minimizing irregularities that could lead to regression[25]. Emerging technologies, such as biomechanically-modulated ablation, aim to tailor the ablation pattern not only to the patient's refractive error but also to the corneal biomechanical properties, thereby reducing the risk of long-term refractive instability[26].

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CONCLUSION

In conclusion, refractive regression remains a critical concern in refractive surgery, despite the significant advancements in surgical techniques and postoperative management. While procedures like LASIK, PRK, and SMILE have demonstrated remarkable success in correcting refractive errors, the phenomenon of regression continues to affect long-term outcomes for a subset of patients. The underlying causes of refractive regression are multifactorial, involving a complex interplay between biomechanical changes in the cornea, epithelial remodeling, and patient-specific factors such as age, hormonal influences, and pre-existing ocular conditions.

Corneal biomechanics play a pivotal role in determining the long-term stability of refractive outcomes. The structural alterations induced by tissue ablation can predispose the cornea to biomechanical instability, particularly in patients requiring higher refractive corrections or those with thinner corneas. This is further compounded by the variable healing response of the epithelium, which can contribute to shifts in corneal curvature and refractive power over time. Epithelial hyperplasia, especially following surface ablation procedures, has been recognized as a significant contributor to postoperative refractive shifts, emphasizing the need for further research into controlling epithelial healing responses.

Patient factors such as age and systemic conditions, including diabetes, introduce additional layers of complexity in the management of refractive regression. Hormonal fluctuations, particularly in women during pregnancy, and impaired wound healing in diabetic patients, highlight the importance of individualized patient assessments before selecting the appropriate surgical technique. These factors underscore the need for tailored surgical approaches and close postoperative monitoring in at-risk patient populations.

Technological advancements have played a crucial role in mitigating the risk of refractive regression. The introduction of femtosecond laser technology, topography-guided ablations, and wavefront-optimized procedures has significantly improved the precision of refractive corrections and reduced biomechanical complications. Furthermore, emerging adjunctive therapies such as corneal cross-linking offer promising avenues for enhancing the biomechanical stability of the cornea, particularly in patients with higher risk profiles. However, the integration of cross-linking into routine refractive surgical practice requires further clinical validation and the development of standardized protocols.

The role of postoperative management in reducing refractive regression cannot be overlooked. Effective anti-inflammatory regimens, patient compliance with postoperative instructions, and the judicious use of enhancement procedures are vital components in maintaining long-term refractive stability. Enhancements, while effective in correcting regression, carry inherent risks and must be considered carefully, particularly in patients with thinner corneas or those with pre-existing biomechanical weaknesses.

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