

Systemic contraindications for laser vision correction – an overview

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HIGHLIGHTS

Laser vision correction (LVC) is currently the most common ophthalmic surgery for treatment of refractive error. There are however some systemic patient conditions that constitute an absolute or relative contraindications for LVC.

ABSTRACT

Laser vision correction (LCV) is a common corneal surgery for the treatment of refractive errors. The rapid development of LVC techniques make this procedures safe and efficient. Despite the high safety profile of corneal refractive surgery, there are however some clinical conditions that constitute absolute or relative contraindication for this procedures. The aim of the paper was to overview and summarise the currently known systemic contraindications for LVC.

Key words: laser vision correction, systemic contraindications, autoimmune inflammatory disorders, diabetes, pregnancy, breastfeeding, systemic medication

INTRODUCTION

Laser vision correction is a group of refractive surgery procedures for the correction of refractive errors. The corneal surgery methods such as laser-assisted in situ keratomileusis (LASIK), small incision lenticule extraction and surface ablation (LASEK or PRK) are characterised by a high safety and efficacy profile, providing good visual outcomes. Although the procedures are the most commonly performed ophthalmic surgeries worldwide, there are some systemic clinical factors that constitute the contraindications for LVC due to the increased risk of postoperative corneal complications. The aim of the study is to summarise the systemic contraindications for LVC.

AUTOIMMUNE INFLAMMATORY DISORDERS (COLLAGEN VASCULAR DISEASES)

According to the recommendations of the Food and Drug Administration (FDA) and the American Academy of Ophthalmology (AAO), the well-controlled autoimmune diseases are currently considered as a relative contraindication for laser vision correction (LVC). In turn, uncontrolled autoimmune diseases constitute an absolute contraindication to refractive surgery [1–7]. The reason for that is potentially increased risk of an excessive inflammatory reaction in the eye tissues, resulting in vision-threatening corneal complications such as: severe dry eye disease, corneal opacities (haze), perforating ulcers, inflammatory infiltration or keratomalacia (corneal melting) [1, 3, 5, 7]. Recent studies have attempted to verify whether and which collagen vascular diseases (CVD) pose an increased risk of corneal postoperative complications [5].

Ocular manifestations of selected CVD

Rheumatoid arthritis (RA) is the most common entity in the spectrum of CVD. The autoimmune process in RA affects the joints of the peripheral skeleton, also having an extra-articular manifestation, including the eye. The ocular symptoms of RA include episcleritis and scleritis, which affect 5–10% of patients with RA. The acute keratitis occurs in 30–70% of cases with RA-related episcleritis or scleritis [5]. The pathophysiology of scleritis in RA patients comprise the immune complex deposition in scleral vessels, fibrinoid necrosis and thrombotic occlusion of blood vessels which results in a fulminant inflammatory response with severe pain of the eye [5].

Systemic lupus erythematosus (SLE) is characterized by autoimmune inflammatory affection of multiple organ systems. There are some ocular complications of SLE including: secondary Sjögren's syndrome with keratoconjunctivitis sicca or lupus retinitis. The corneal complications of SLE are the consequence of basement membrane tissue impair-

ment due to the immune complex, which are stimulated by the chronically activated complement system [5].

Seronegative spondyloarthropathies (SpA) is a group of autoimmune entities commonly affecting the spinal cord and peripheral joints. The SpA, including psoriatic arthritis, ankylosing spondylitis, and reactive arthritis (Reiter's syndrome) are associated with human leukocyte antigen B27 (HLA-B27) and negative rheumatoid factor (RF). The common ocular manifestations of SpA are acute anterior uveitis, iritis and conjunctivitis and their complications including band keratopathy, posterior synechiae, and cataracts. The pathophysiology of the ocular complications comprise the infiltration of the eye tissues by activated T lymphocytes reactive to autoantigens, which release proinflammatory mediators [5].

Sjögren's syndrome (SS) is an autoimmune inflammatory disease causing severe dry eye (keratoconjunctivitis sicca, KCS) and dry mouth (xerostomia) due to affection of the salivary and lacrimal glands. Decreased production of tear film results in severe dryness, discomfort, irritation, burning, foreign body sensation and photophobia. The epithelial erosions and superficial punctate keratopathy predispose to bacterial keratitis and ocular infections, which are not uncommon in SS [5].

The decision on LVC surgery in patients with CVD is always challenging. Current retrospective analyses and some prospective reports suggest that patients with well-controlled CVD without a history of ocular manifestations may be suitable candidates for LVC. No severe sight-threatening complications have been reported in those patients. Although there were some complications of laser refractive surgery in patients with controlled CVD, the risk to them was similar to those observed in patients without autoimmune diseases [3, 8–10]. On this condition, many authors concluded that LVC in patients with well controlled RA, SLE, or SpA may be beneficial and not burdened with an increased risk of corneal complications [1, 5, 10]. However, the symptomatic dry eye disease due to either primary or secondary SS is considered an absolute contraindication to LVC, as the postoperative complications may be significant resulting in poor refractive outcomes [1, 5, 8].

KELOIDS

A history of cutaneous keloid formation is an absolute contraindication to surface procedures such as PRK. It is believed that in patients with keloids there is a risk of excessive corneal scarring and resulting visual acuity compromise [9]. The LASIK or SMILE procedure may be considered in these patients as the deep corneal refractive surgery procedures in patients with cutaneous keloids are relatively contraindicated [9].

PSORIATIC ARTHROPATHY

Psoriatic arthropathy is an absolute contraindication to surface procedures of LVC (PRK, LASEK) [9]. Psoriasis in turn does not constitute the contraindication to LVC. There is little research on the impact of psoriasis or psoriatic arthropathy on ocular complications after LVC. In those reports, however, the frequency of intra- or postoperative epithelial defects ranged from 2% to 4% [9].

LICHEN PLANUS

Lichen planus is a chronic, autoimmune inflammatory disease affecting mucocutaneous membranes of the skin, oral cavity or vagina. The ocular manifestation is extremely rare and includes cicatrizing conjunctivitis, subepithelial fibrosis, blepharitis, Meibomian glands dysfunction, dry eye and lacrimal duct obstruction [11]. The mechanism of autoimmune inflammation is hypothesized as a T-cell mediated response that stimulate dendritic cells into layers of the epithelium. First-line treatments for cutaneous and oral lichen planus are acitretin (a retinoid) and topical corticosteroids respectively. Acitretin intake constitutes a contraindication to LVC as many patients develop dry eyes and rarely corneal ulceration and keratitis. Therefore, the Schirmer test and TBUT test should be performed. LASIK surgery may be considered only when the tear film parameters are normal in both of the above tests [11]. Frequent post-operative lubrication should be advised and any epithelial insults should be managed intensively and immediately to avoid severe dry eye, keratitis, corneal melt and perforation [11].

OCULAR ALLERGY AND MASTOCYTOSIS

According to the AAO guidelines, an uncontrolled ocular allergy is an absolute contraindication to LASIK procedure while well drug-controlled ocular allergy is considered as a relative contraindication.

Mastocytosis is a rare condition caused by an excessive accumulation of mast cells in the tissues.

Some reports described a diffuse lamellar keratitis (DLK) 5 days after the LASIK surgery in patient with mastocytosis [6]. The DLK was successfully treated in this patient with prednisolone acetate with the final visual outcome of 20/20 in each eye [12]. In any suspicion of mastocytosis or active ocular allergy, the use of an antihistaminic and mast cell stabilizers can protect the patient against postoperative complications [6].

DIABETES

Currently, the FDA considers diabetes as a relative contraindication to LVC especially in patients with poor HbA_{1c}

control and insulin-dependent disease. Ocular complications of diabetes include vitreoretinal complications, diabetic retinopathy, cataract and instable refractive error. There are also many abnormalities within the corneal layers that predispose to corneal complications in patients with diabetes such as impaired corneal sensation, decrease in epithelial cell number, superficial debris, thickening and rupture of epithelium basement membrane, epithelial barrier dysfunction, structural changes in the corneal stroma, Descemet's membrane, and endothelium [9]. As the result the clinical manifestation of diabetic keratopathy comprise superficial punctate keratopathy, recurrent corneal erosions, poor epithelial healing, high risk of corneal surface infection, tear film deficiency and neurotrophic keratopathy [9, 13, 14]. The abovementioned factors may affect safety and refractive outcomes of LVC in patients with diabetes and the enhancement procedure may often be required [9, 12, 13]. However, several studies indicate that LASIK may be safe in diabetic patients with no ocular and systemic complications and tight glycaemic control defined as HbA_{1c} levels remaining below 7.5% [12, 15].

INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease (IBD) is a group of inflammatory autoimmune diseases affecting the gastrointestinal (GI) tract. The entities included in IBD are Crohn's disease (CD) and ulcerative colitis (UC). The common ocular manifestations of IBD are anterior uveitis, scleromalacia perforans, and optic neuritis. Dry eye symptoms are also not uncommon in these patients due to fat-soluble vitamin deficiencies. The LVC is relatively contraindicated in IBD [3, 9, 16]. The LASIK surgery is relatively possible in well controlled stage of the disease, while in exacerbation of the IBD, the immune response may result in unfortunate complications such as necrotizing keratitis [16, 17]. Immunomodulating medication use, in the management of IBD, such as azathioprine, tacrolimus and methotrexate does not constitute a contraindication for LVC. However, immunosuppression poses the risk of post-surgical herpes simplex virus or Varicella-Zoster virus infections, therefore acyclovir should be considered in perioperative prophylaxis. As it has been reported that the IBD have a strong association with keratoconus, the corneal topography should be carefully analysed in planning the LVS surgery in those patients [9, 16].

HERITABLE DISORDERS OF CONNECTIVE TISSUE

Heritable disorders of connective tissue (HDCTs) are a group of diseases that compromise the connective tissue integrity. Many HDCTs, including: osteogenesis imperfecta (OI), Ehlers-Danlos syndrome (EDS), Marfan syndrome (MFS), Loeys-Dietz syndrome (LDS), epidermolysis

bullosa (EB), Stickler syndrome (STL), Wagner syndrome and pseudoxanthoma elasticum (PXE) cause ocular manifestations such as high myopia [18]. According to the FDA requirements, EDS constitutes an absolute contraindication for LASIK. Abnormal collagen structure in HDCTs is a risk factor of post-LASIK ectasia, poor wound healing, poor refractive predictability, and even rupture of the globe. The corneal hysteresis (CH), central corneal thickness (CCT) and overall corneal biomechanics is decreased in HDCTs. Moreover, the keratoconus and increased eye rupture rate are commonly associated with this group of diseases [18]. The assessment of LVC complications in patients with HDCTs is difficult due to the limited number of treated patients. Some authors reported a safe radial keratotomy, PRK, LASIK, or LASEK in patients with EDS or MFS [18]. Currently, the screening of refractive surgery candidates to avoid corneal ectasia is very thorough. Although all HDCTs are currently an absolute contraindications for LVC, the diagnostic tools, including corneal biomechanics may be the future chance for determining the possibility of refractive surgery options in selected cases [18].

PREGNANCY AND BREASTFEEDING

According to the most recent reports, pregnancy and breastfeeding constitute a relative contraindication for LVC [1]. However some authors as well as the FDA claim pregnancy as an absolute contraindication [2, 19]. In pregnancy, there is a significant increase in progesterone and oestrogen levels in a woman's body [19]. The human cornea has oestrogen, progesterone, and androgen-hormone receptors. The hormonal changes influence the eye of pregnant women causing an increase in corneal pachymetry, weakening of corneal biomechanics, excessive water accumulation in the cornea and lens leading to temporal myopic shift, increase in keratometry values, decreased corneal sensitivity and tear film production [1]. Not all pregnant women notice the changes in visual acuity, however the stability of the refractive error in this period is questionable [19]. LASIK surgery performed during pregnancy carries a risk of keratectasia due to reduced corneal biomechanics. Therefore, LVC is not recommended during pregnancy [1, 20]. A few days after delivery, the levels of oestrogen and progesterone return to pre-pregnancy values, while the prolactin level increase promoting the lactation process [19]. Although refractive error fluctuations are not as prominent in breastfeeding as during pregnancy, the changes in keratometry seem to persist throughout the lactation period [1, 19]. K-reading differences suggests that prolactin may play a role in changes of corneal morphology, although no prolactin receptors have yet been identified in the human cornea [19]. In conclusion, the risk of corneal complications of LVC during pregnancy and breastfeeding outweighs a potential bene-

fits. Therefore, many authors recommend postponing the LVC procedure for a period of several months from the delivery and/or termination of breastfeeding.

PSYCHOLOGICAL FACTORS

A patient's unrealistic expectations and periods of emotional instability constitute absolute contraindications to LVC [1]. As it was reported in the retrospective analysis, patients with bipolar disorder, schizophrenia and obsessive-compulsive disorder found their 6-months postoperative visual outcomes as good in 85.71%, 88.52% and 93.75% of cases respectively [1]. The psychiatrist opinion should be recorded prior the LASIK surgery, to confirm the stable psychological state of the patient [1].

AGE

According to the AAO, an age below 18 years is an absolute contraindication for LVC, while between 18 and 21 years constitutes a relative contraindication. Nevertheless, in some cases the LVC may be considered in ages below 18 for amblyopia, anisometropia or accommodative esotropia on the condition of stable refraction [1].

SYSTEMIC MEDICATION

Taking some systemic medication, such as isotretinoin, amiodarone, sumatriptan, colchicine and levonorgestrel implant constitute a relative contraindication to LASIK and surface ablation [1].

Isotretinoin, taken as a treatment of acne is considered as an absolute contraindication to LASIK or PRK [1, 2]. Isotretinoin alters gene expression in the meibomian glands epithelium, which inhibits meibocyte proliferation, promoting their apoptosis. As a consequence, ocular side effects such as dry eye, blepharitis and conjunctivitis may occur [1]. LVC is allowed after 6 months of the cessation of taking isotretinoin [1, 21]. However, some authors postulate the change in approach to LVC in patients with active isotretinoin treatment, as a results of refractive procedures conducted in these patients were safe and effective [1, 20].

Amiodarone is a class III antiarrhythmic drug. Taking amiodarone is considered as a relative contraindication to LVC [1, 2]. Corneal deposits known as cornea verticillata, vortex keratopathy or whorl keratopathy occur in over 90% of cases treated with amiodarone longer than 6 months [1, 22]. Other side effects of chronic amiodarone intake include blurred vision, dry eye, palpebral skin irritation, colour vision alterations, anterior subcapsular deposits, optic neuropathy and non-arteritic anterior ischemic optic neuropathy [22]. Contraindications to LASIK or PRK for patients treated with amiodarone were, however not sup-

ported in scientific studies as no significant complications in visual recovery or healing process were found [1, 22].

TRIPTANS

Triptans are drugs of the first choice in pharmacological treatment of migraines. It is believed that triptan use increases the incidence of epithelial defects and decreased TBUT post-LASIK surgery. The statement was however based on preclinical toxicological evaluation of high doses of sumatriptan used in dogs. Although no such effects have been reported in humans, the triptans are relatively contraindicated in LVC candidates [23].

IMMUNOSUPPRESSANTS AND BIOLOGIC THERAPY

The treatment with immunosuppressants such as azathioprine, tacrolimus and methotrexate as well as taking biologic drugs does not constitute an absolute contraindication for LVC, however surgeons should be aware of the increased risk of perioperative infections in treated patients [9]. Rituximab has been associated with HSV keratitis [11]. In turn, taking CsA is not related to increased risk of opportunistic infections [11].

Corticosteroids when used chronically in high doses (for at least 30 days at doses of 40 mg/24 h) may compromise the wound healing process. Therefore, LASIK procedure in patients on high doses of steroid drugs is contraindicated [11].

CONCLUSIONS

The current list of absolute contraindications for LVC include patient's conditions and systemic diseases such as SS, uncontrolled autoimmune inflammatory disorders (RA, SLE, SpA, IBD), psoriatic arthropathy, history of cutaneous keloid formation (for PRK or LASEK), uncontrolled ocular allergy, heritable disorders of connective tissue, uncontrolled diabetes (especially insulin-dependent diabetes), pregnancy, taking isotretinoin, age below 18 years, unrealistic patient's expectations and periods of emotional instability. The relative contraindications comprise well controlled autoimmune inflammatory disorders in the chronic remission stage, well-controlled ocular allergies, keloids formation (for SMILE or LASIK), lichen planus in remission stage, well controlled diabetes, amiodarone therapy, systemic steroids or taking immunosuppressants and biological therapy, age between 18 and 21 years, breastfeeding, controlled mental disorders such as bipolar disease, schizophrenia and obsessive-compulsive disorder. The decision process on eligibility for LVC in patients with relative contraindications is always challenging. In those cases, the clinical status should be considered individually based on the balance of benefits and potential risks related to refractive surgery procedures.

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