



## Ocular Manifestations of Patients Receiving Heart Transplants: A Single-Center Experience of 311 Consecutive Cases

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### ABSTRACT

**Purpose.** The purpose of this study was to investigate ocular manifestations of patients undergoing heart transplantations.

**Method.** We retrospectively reviewed the clinical data of 311 patients who underwent orthotopic heart transplantations from January 1989 to December 2007, including the demographic data, general conditions, medications, as well as the basic ophthalmic examinations, ophthalmic diagnosis, and management.

**Results.** Of the 311 heart transplant recipients, common diagnoses included cataract (96 cases; 30.87%), dry eye syndrome (24 cases; 7.72%), allergic conjunctivitis (78 cases; 25.08%), and glaucoma (19 cases; 6.11%). The patients after heart transplantation had much lower incidences of severe opportunistic infections than patients undergoing the same procedure one decade ago. However, autoimmune-related endocrinopathy such as diabetes and Graves' disease became more prevalent. Diabetes-related complications were unexpectedly frequent, including nonproliferative diabetic retinopathy (6 cases; 1.93%), proliferative diabetic retinopathy (6 cases; 1.93%), retinal vein occlusion (6 cases; 1.93%), and neovascular glaucoma (4 cases; 1.29%). The occurrence of cataract formation and steroid glaucoma was often due to post-transplantation steroid use.

**Conclusion.** Ophthalmologists and cardiac surgeons should collaborate and perform regular ophthalmic examinations, especially for those who have new-onset diabetes and difficulty tapering off steroids.

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**E**FFECTIVE immunosuppression is important in the prevention of rejection after solid organ transplantation. Its adequacy highly influences the immune status and infection rate after transplantation. The transplant recipients were subjected to various opportunistic ocular infections, including cytomegalovirus (CMV) retinitis, acute retinal necrosis, and infectious chorioretinitis [1]. The opportunistic infections have been reported as the most serious retinal complications, which might cause significant visual consequence after bone marrow transplantation and solid organ transplantation [2].

New-onset diabetes after transplantation (NODAT) has been reported in 2%–53% of patients receiving solid organ transplantation [3]. Both glucocorticoid and nonsteroid immunosuppressants, such as calcineurin inhibitor and sirolimus, participate in the pathogenesis of NODAT [4]. Post-transplantation diabetes can adversely affect the graft outcome and cause diabetes-related complications. The long-term adverse effects of systemic glucocorticoid are well known, including hypertension, diabetes, hyperlipidemia,

and osteoporosis. It may also cause several ocular complications, such as cataract, glaucoma, and central serous chorioretinopathy [5].

The patients with long-lasting immunosuppressive agents after organ transplantation may develop autolymphocytotoxicity [6]. Graves' disease followed by endocrine ophthalmopathy has been found in a patient under continuous immunosuppressive therapy after heart transplantation. The arisen Graves' ophthalmopathy was poorly responsive to conventional corticosteroid treatment [7]. In consequence

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of the lasting immunotherapy of transplant recipients, these subjects were vulnerable to certain ocular manifestations, comprising ocular opportunistic infection, autoimmune-related endocrinopathy and ophthalmopathy, and steroid-induced ocular complications. This retrospective audit aims to investigate the long-term ocular manifestations following heart transplantation in a single center.

## METHODS

From January 1989 to December 2007, we retrospectively reviewed the medical records of 311 consecutive patients undergoing heart transplantation. Demographic and clinical findings of each case were recorded including the following: age, gender, systemic diseases, involved eye, best corrected visual acuity, intraocular pressure, and crystalline lens status. Data associated with cataract, vitreoretinal, and glaucoma surgery were also compiled. The medications, such as immunosuppressive and antiglycemic agents, were recorded. This research protocol was approved by the National Taiwan University Hospital ethics committee.

## RESULTS

From January 1989 to December 2007, we enrolled 311 patients who received heart transplants. Of them, 257 patients were male (82.64%) and 54 patients were female (17.36%). The mean age of patients receiving heart transplants was 44.9 years. The ocular manifestations of all cases are listed in Table 1. The mean follow-up time was 12.1 years. Figure 1 is a timeline of first diagnosis of various ocular complications after heart transplantation in the earlier and later eras.

The main manifestations of cornea and conjunctiva included keratoconjunctivitis sicca (24 cases; 7.72%), allergic conjunctivitis (78 cases; 25.08%), and herpes zoster ophthalmicus (12 cases; 3.86%). One case had vertex keratopathy due to long-term Amiodarone (Cordarone, Wyeth, United States) use. One case showed band keratopathy owing to chronic renal failure. Cataracts were found in 96 cases (30.87%). Nuclear sclerosis, posterior subcapsular opacity, and cortical opacity were also found.

Of all of the heart transplant cases, retinal disorder was found in 24 cases (7.72%) and was responsible for the main causes of visual loss in our study population. They included diabetic retinopathy (12 cases; 3.86%), rhegmatogenous retinal detachment (4 cases; 1.29%), epiretinal membrane (4 cases; 1.29%), and retinal vascular occlusive disorders (6 cases; 1.93%). One patient showed central serous chorioretinopathy due to steroid use after transplantation. Vitreoretinal surgery was performed in 11 cases after heart transplantation. The surgical indications consisted of diabetic retinopathy with nonclearing vitreous hemorrhage and tractional retinal detachment (6 cases), rhegmatogenous retinal detachment (4 cases), and epiretinal membrane (1 case). All of these cases showed poor visual prognosis during follow-up.

Glaucoma were found in 19 cases (6.11%) and could be classified into steroid responder (6 cases), primary open angle glaucoma (7 cases), primary angle closure glaucoma (2 cases), and neovascular glaucoma (4 cases). Of the 4

**Table 1. Ocular Findings of Patients With Heart Transplants**

Ocular Findings	No. of Patients
<b>Eyelid</b>	
Hordeolum, chalazion	5 (1.61%)
Preseptal cellulitis	1 (0.32%)
Dacryocystitis	1 (0.32%)
<b>Cornea and Conjunctiva</b>	
Dry eye syndrome	24 (7.72%)
Allergic conjunctivitis	78 (25.08%)
Herpes zoster ophthalmicus	12 (3.86%)
Vertex keratopathy	1 (0.32%)
Band keratopathy	1 (0.32%)
<b>Lens</b>	
Cataract	96 (30.87%)
<b>Retina</b>	
Nonproliferative diabetic retinopathy	6 (1.93%)
Proliferative diabetic retinopathy	6 (1.93%)
Macular lesion	
Epiretinal membrane	4 (1.29%)
Age-related macular degeneration	1 (0.32%)
Central serous chorioretinopathy	1 (0.32%)
Vascular occlusive disorders	
Central retinal vein occlusion	3 (0.96%)
Branch retinal vein occlusion	3 (0.96%)
<b>Optic nerve</b>	
Glaucomatous optic neuropathy	19 (6.11%)
Optic nerve atrophy	1 (0.32%)
<b>Systemic associations</b>	
Marfan syndrome (lens subluxations, RRD)	1 (0.32%)
Graves' ophthalmopathy	3 (0.96%)

Abbreviation: RRD, rhegmatogenous retinal detachment.

cases with neovascular glaucoma, all cases were associated with proliferative diabetic retinopathy. Two cases without light perception were arranged for cyclocryotherapy surgery after failure of medical treatment.

Three cases developed Graves' disease after heart transplantation. Two cases were male and 1 was female. All of these cases showed mild Graves' ophthalmopathy and presented as eyelid edema, retraction, and proptosis. No case experienced acute inflammation of orbit and could be treated with medications without further surgery. One case of Marfan syndrome with aorta dissection and congestive heart failure underwent heart transplantation. Crystalline lens subluxation and myopic maculopathy was found in this patient.

Regarding ocular opportunistic infection, no case experienced CMV retinitis, acute retinitis necrosis, progressive outer retinal necrosis, or fungal chorioretinitis. Herpes zoster ophthalmicus was the most frequent opportunistic infection in our patients.

## DISCUSSION

The ocular complications of patients after heart transplantation could be briefly divided into 3e groups: opportunistic infections, autoimmune-related endocrinopathy, and immunosuppressant-associated side effects. In our study,

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