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Detection Rate of Corneal Endothelial Lesions in Civil Aviation Flying Cadets

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Abstract: *This study focuses on the detection of corneal endothelial lesions among flight students at the Civil Aviation Flight Academy of China, aiming to delve into the principles of aviation medical identification for such lesions and assess whether flight students with these conditions pose safety risks in special aviation environments. Between March 2019 and March 2024, a cluster random sampling method was employed to select 24,810 flight trainees who underwent annual physical examinations at the Flight Personnel Physical Examination and Appraisal Center of the Civil Aviation Flight Academy Hospital of China. All the trainees received comprehensive ophthalmic examinations, encompassing assessments of naked - eye far vision, near vision, color vision, extraocular muscles, slit lamp microscopy, and direct ophthalmoscopy. The examination results were then subjected to statistical analysis. The findings revealed that a total of 55 flight trainees (80 eyes) were diagnosed with corneal endothelial lesions, yielding an overall detection rate of 0.22%. Specifically, 30 trainees (37 eyes) presented with corneal endothelial opacities accompanied by vesicular changes, with a detection rate of 0.12%, while 25 trainees (43 eyes) had simple corneal endothelial opacities, showing a detection rate of 0.10%. An analysis of corneal endothelial cell count in flight trainees with corneal endothelial lesions over the past three years indicated that as the years progressed, the corneal endothelial cell count gradually declined. However, this difference was not statistically significant ($P < 0.05$). In conclusion, the corneal endothelial lesions observed among the civil aviation flight students at our school are all in the early stages of the disease. These students exhibit good visual function status and meet the criteria for aviation medical identification. It is recommended to implement tracking and observation of these students, along with regular checks of their visual function and corneal physiological function indicators.*

Keywords: *Flight Cadet; Corneal Endotheliopathy; Detection Rate*

1. Introduction

Corneal tissue is an important refractive medium, and corneal endothelial cells play a crucial role in maintaining corneal transparency and dehydration [1]. Posterior polymorphous corneal dystrophy (PPCD/PPMD), also known as hereditary deep corneal dystrophy, hereditary corneal edema, inner bullous keratopathy, and Schnyder posterior vesicles [2] is a relatively rare hereditary corneal disease inherited in an autosomal dominant manner. It has been demonstrated that this condition is associated with mutations in four genes [3]. PPCD was first described by Koeppe [4] in 1916 and involves the Descemet membrane and endothelial layer of the cornea, exhibiting highly variable morphological features. PPCD often has an insidious onset, may be non-progressive or progress very slowly, and patients are frequently asymptomatic, often being diagnosed during routine health examinations, making it prone to clinical oversight. Pilots, as a special group, rely heavily on good visual function during aviation activities, making aeromedical examination and evaluation particularly important. This study aims to analyze the detection rate of corneal endothelial disorders among flight trainees during annual physical examinations and evaluate corneal physiological function indicators. The goal is to assess whether flight trainees with corneal endothelial disorders pose potential safety risks in the unique aviation environment, thereby enhancing the understanding of corneal endothelial disorders among medical examiners. This will provide a reference and basis for better aeromedical evaluation, ensuring flight operation safety. The report analysis is presented as follows:

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2. Object and Method

2.1 Object

Using a cluster random sampling method, a total of 24810 flight trainees who participated in the annual physical examination at the Flight Personnel Physical Examination and Appraisal Center of China Civil Aviation Flight Academy Hospital from March 2019 to March 2024 were selected for investigation. All flight trainees underwent comprehensive ophthalmic examinations. A total of 55 flight trainees (80 eyes) were detected to have corneal endothelial lesions, all of whom were male. The oldest at the time of onset was 29 years old, the youngest was 17 years old, and the average age was (20.71 ± 0.36) years old. All flight trainees have signed informed consent forms, which comply with ethical requirements.

2.2 Method

All flight trainees participating in the annual physical examination were assessed according to the Detailed Rules for the Implementation of Medical Standards for Civil Aviation Medical Examination and Certification [5]. Each flight trainee underwent examinations including uncorrected distance visual acuity, near visual acuity, color vision, extraocular muscles, slit-lamp microscopy, and direct ophthalmoscopy. For trainees whose uncorrected distance visual acuity did not meet the standard of 0.7 on the "C" chart, vision correction was performed, and the refractive error was recorded in detail. For trainees diagnosed with corneal endothelial disorders, further consultations at higher-level hospitals or internal departmental discussions were conducted to clarify the nature of the condition. Each trainee with corneal endothelial disorders underwent confocal microscopy and corneal endothelial cell count examinations. Among them, those with corneal endothelial opacities accompanied by vesicular changes were diagnosed with posterior polymorphous corneal dystrophy (PPCD), while those with only corneal endothelial opacities were recommended for further observation and follow-up. All ophthalmological examinations were performed by two qualified ophthalmologists appointed by the Civil Aviation Administration.

2.3 Slit-lamp examination method [6]

The detection of corneal endothelial disorders primarily relies on slit-lamp microscopy. During the examination, the subject sits opposite the examiner, with their head stabilized on the adjustable chin rest and forehead strap of the slit lamp. The slit beam is projected onto the cornea to create an optical section. Under high magnification of the slit-lamp microscope, the inner surface of the cornea is carefully observed. Small punctate opacities of the corneal endothelium should be differentiated from corneal precipitates. If there are widespread clusters of small vesicles on the corneal endothelium, the width of the slit beam should be adjusted to carefully observe the extent and morphology of the lesions. The findings are then recorded in detail in the medical examination report.

2.4 Diagnosis of posterior polymorphic corneal malnutrition [7]

Relying on medical history and typical clinical manifestations, corneal endothelial microscopy or clinical confocal microscopy examination has important diagnostic value. Under the corneal endothelial microscope, typical vesicles, inner bands, or abnormal corneal endothelial cells can be found on the inner surface of the cornea.

2.5 Equipment and Instruments

Uncorrected distance visual acuity was measured using the Landolt "C" ring chart. For automated refraction, the Topcon RM-800 autorefractor from Japan was used. Slit-lamp examination was performed using a Topcon slit-lamp microscope. Fundus examination was conducted using the Suzhou Liuliu YZ6F ophthalmoscope. Visual field testing was carried out using the Haag-Streit Octopus 900 automated perimeter from Switzerland.

2.6 Statistical analysis

SPSS 23.0 statistical software was used for statistical processing. The measurement data is

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represented by $\bar{x} \pm s$, and the data are normally distributed. The count data is represented by rate, and the comparison between groups is performed using the chi square test or continuous correction chi square test, P<0.05 indicates a statistically significant difference.

3. Results

3.1 General Information Analysis

From March 2019 to March 2024, a total of 24,810 flight students underwent annual physical examinations at the Aeromedical Assessment Center of the Hospital of Civil Aviation Flight University of China. Among them, 55 students (80 eyes) were diagnosed with corneal endothelial disorders, resulting in an overall detection rate of 0.22%. Specifically, 30 students (37 eyes) exhibited corneal endothelial opacities with cystic changes, with a detection rate of 0.12%. All these students were diagnosed with posterior polymorphous corneal dystrophy. Additionally, 25 students (43 eyes) had simple corneal endothelial opacities, with a detection rate of 0.10%. These students were recommended for follow-up and observation. Among the affected students, 32 had unilateral involvement, while 23 had bilateral involvement. All detected cases of corneal endothelial disorders were male, with the oldest being 29 years old and the youngest 17 years old, and an average age of (20.71 ± 0.36) years. (See Table 1 for details)

Table 1 General Situation of Corneal Endothelial Disease Detection in Flight Trainees

Lesion type	Number of detected persons (person)	Number of eyes (eyes)	Age of onset
Vesicular changes+turbid spots	30	37	21.11±2.38
Simple turbid spot	25	43	20.37±2.79
Total	55	80	20.71±0.36

3.2 Comparison of corneal endothelial cell counts among 55 flight trainees with corneal endothelial lesions in the past three years

As the years increased, the corneal endothelial cell count of flight trainees detected with corneal endothelial lesions gradually decreased, but the difference was not statistically significant (P<0.05). (See Table 2 for details)

Table 2 Comparison of corneal endothelial cell counts of 55 flying cadets with corneal endothelial lesions in recent three years

Lesion type	Number of eyes (eyes)	2022	2023	2024
Vesicular changes+turbid spots	37	2798.53±349.55	2747.40±348.63	2742.04±338.86
Simple turbid spot	43	2592.94±251.46	2859.11±239.19	2835.94±244.51
Normal eye	30	2995.79±292.08	2994.30±336.02	2887.42±329.57
Total	110			

4. Discussions

Posterior Polymorphous Corneal Dystrophy (PPCD) is relatively rare in clinical practice. While there have been sporadic case reports in European and American countries, detailed epidemiological data are lacking. Reports of this disease in Asian countries are even fewer, and clinical reports of PPCD cases in China are extremely scarce. PPCD is an autosomal dominant genetic disorder, with approximately 30% of patients having a clear family history. It is currently believed that the occurrence of PPCD may result from mutations in certain genes leading to abnormal protein expression, which subsequently triggers a series of pathological processes. Known genetic loci include 20p11.2-q11.2, 1p34.3-p32.3, and 10p11.22 [8].

The onset of PPCD is often insidious. It can be non-progressive or progress very slowly, and patients frequently exhibit no subjective symptoms. The condition is often detected during routine health examinations, making it difficult to determine the exact age of onset, which contributes to its underdiagnosis in clinical practice. Clinically, PPCD is classified into three types: vesicular, band-like,and diffuse, with lesions located at the level of the corneal endothelium and Descemet's membrane. The vesicular type of PPCD is the most frequently reported subtype in multiple studies [9-10].Due to the location of the lesions on the posterior corneal surface and the diverse range and morphological distribution of the lesions, the diagnosis of PPCD is particularly challenging.

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The diagnosis of PPCD primarily relies on slit-lamp examination, anterior segment OCT, corneal endothelial microscopy, corneal confocal microscopy, and corneal topography. Using the retroillumination method under a slit lamp, various forms of corneal lesions can be observed in the deep cornea, such as vesicular, band-like, or diffuse opacities [11]. Vesicular lesions are often clustered together, presenting a cystic appearance with varying sizes. In typical cases, calcified crystalline plaques in the deep corneal stroma can be seen under the slit lamp, and cystic lesions may be observed in the endothelial layer. Edema may occur in the deep stromal layer, and in severe cases, both the epithelium and the entire stromal layer may become edematous [12]. The pathological features of PPCD include endothelial cell changes and collagen deposition [13]. In Krachmer's literature review in 1985 [14],the most significant pathological change in PPCD was the presence of epithelial-like endothelial cells in the cornea. The clinical manifestations, surgical prognosis, visual acuity improvement, and intraocular pressure reduction are directly related to these endothelial pathological changes.

During the physical examination of flight students at the Civil Aviation Flight University of China, slit-lamp examination of the cornea using the retroillumination method revealed small patchy opacities in the corneal endothelium. Some of these opacities contained isolated or clustered small vesicles, while band-like and diffuse types were rarely observed. Typical PPCD generally presents bilaterally, with both corneas exhibiting asymmetric appearances, though unilateral cases have also been occasionally reported. Some studies have found unilateral vesicular presentations, which may be related to smaller or concealed vesicles hidden within the Descemet's membrane without protruding into the endothelial layer, making them difficult to detect. Sheng Xunlun et al. [15] reported four cases of band-like posterior polymorphous corneal dystrophy, all of which were unilateral. In this investigation, the number of flight students with unilateral disease was slightly higher than those with bilateral disease, which may be attributed to differences in the selected population[16].

Both confocal microscopy and corneal endothelial microscopy can be used as instruments to assess the status of the corneal endothelium. Corneal endothelial cells are terminal cells with limited regenerative capacity and cannot regenerate after injury [17]. Additionally, approximately 0.3%-0.5% of these cells are lost annually due to apoptosis. The density and morphology of endothelial cells are important indicators for evaluating corneal endothelial function, and changes in the morphological structure of endothelial cells are highly sensitive to early subtle alterations in corneal endothelial function.

Confocal microscopy, as a new type of high-magnification optical microscope with an 800x magnification, enables real-time, non-invasive observation of each layer of living corneal tissue at the cellular level. It has been widely used in the diagnosis and research of PPCD [18]. Although confocal microscopy offers high magnification, allowing for detailed observation of the location of vesicles and changes in affected cells, it has limitations, such as a small scanning area per session, which may lead to missed observations.

Corneal endothelial microscopy, on the other hand, can be used to observe the size, morphology, and number of corneal endothelial cells in the absence of corneal edema. It is a simple and convenient diagnostic tool that allows both qualitative and quantitative assessment of corneal endothelial cells. The density of endothelial cells may be related to the size, number, and distribution patterns of vesicles, such as whether they are clustered or arranged in chains.

The aviation medical concern regarding corneal endothelial dystrophy primarily lies in the fact that the function of corneal endothelial cells directly affects corneal transparency. Endothelial cell dystrophy leads to degeneration of corneal endothelial cells and disruption of normal corneal tissue structure. In flight environments characterized by high altitude, hypoxia, low pressure, and excessive load, this condition poses potential risks. Currently, there are no reports in China's civil aviation regarding the impact of early-stage corneal dystrophy on pilots. In the past, when recruiting flight students, cases of corneal dystrophy were identified, and considering the potential risks associated with the condition, these candidates were deemed unfit. For active pilots, if corneal dystrophy or corneal endothelial opacities are detected later, they undergo comprehensive evaluations, including confocal microscopy, corneal endothelial microscopy, central visual field testing, and contrast sensitivity testing, before a medical assessment conclusion is issued.

In July 2024, the Civil Aviation Administration of China revised and issued the Detailed Rules for the Implementation of Medical Standards for Civil Aviation Medical Assessment. Regarding the assessment of corneal endothelial disorders or corneal dystrophy, applicants for a first-class medical certificate with corneal endothelial disorders or corneal dystrophy may be deemed qualified if their central visual field meets the standards, contrast sensitivity is normal, and corneal physiological

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functions show no abnormalities. The implementation of this new standard indicates a relaxation of the medical assessment criteria for recruiting flight students compared to previous standards. However, it also introduces unknown risks, and further in-depth research is needed to understand the visual function of flight personnel with corneal dystrophy in the long term.

5. Conclusion

This study systematically analyzed the detection of corneal endothelial lesions among flight students at the Civil Aviation Flight Academy of China, revealing the characteristics of corneal endothelial lesions in the flight student population and their impact on visual function. The research results show that the overall detection rate of corneal endothelial lesions among flight trainees is low, and the lesions are mostly in the early stages of the disease. These students generally have good visual functional status and meet the standards of aviation medical identification.

Further analysis revealed that although the corneal endothelial cell count of patients with corneal endothelial lesions has shown a gradually decreasing trend in the past three years, this change did not reach statistical significance ($P<0.05$), indicating relatively slow progression of the disease. However, considering the special nature of flight activities and the high demand for visual function in high-altitude environments, even if corneal endothelial lesions are in the early stages, sufficient attention should be given.

Therefore, it is recommended to track and observe flight trainees who have been detected with corneal endothelial lesions, and regularly review visual and corneal physiological function indicators. In addition, further in-depth research is needed in the future on the long-term effects of corneal endothelial lesions in the pilot population, as well as the specific mechanisms by which high-altitude environments affect the function of corneal endothelial cells, in order to provide theoretical basis for the development of more scientific and reasonable aviation medical identification standards.

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