The Prevalence of Fuchs' Endothelial Corneal Dystrophy in Cataract Patients within the Czech Population

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SUMMARY

Aims: To determine the incidence of Fuchs' endothelial corneal dystrophy (FECD) in patients undergoing cataract surgery in the Czech population.
Material and Methods: Consecutive group of 2804 eyes of 1499 patients undergoing cataract surgery at the Lexum Karlovy Vary clinic in the period from 4/2022 to 9/2024. The corneal endothelium was examined preoperatively using a slit lamp and an endothelial microscope. The corneas were divided into 6 grades (0–5) according to the Krachmer scale, or 4 clinical stages of the disease.
Results: The incidence of FECD in our group of patients undergoing cataract surgery was 29.6% (total 840 eyes). In 578 cases this concerned stage 1 of the disease, which had no effect on the outcome of the operation. In 81 cases it concerned a stage 3-5 disease, in which potential postoperative complications must be taken into account. In 13 cases (0.46%) we primarily performed a combined procedure of cataract surgery and DMEK (Descemet's membrane endothelial keratoplasty).
Conclusion: FECD in the population of cataract patients is probably often under-diagnosed. In our cohort of patients we registered some signs of the disease in more than a quarter of the patients.
Key words: Fuchs' endothelial corneal dystrophy, DMEK, cataract

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INTRODUCTION

Fuchs' endothelial corneal dystrophy (FECD) is a bilateral, slowly progressing, often asymmetrical disease of the cornea, characterized by damage to the corneal endothelium and the development of guttata – bumps and thickening of the Descemet's membrane (DM) [1–3]. In the next phase of the disease, these changes lead to corneal edema, deterioration of visual functions (glare, halo, reduced visual acuity) and in the advanced stages to loss of corneal transparency and painful attacks of recurring erosions of the corneal epithelium [4]. FECD is typically manifested in the fifth decade of life, more frequently in women. It is a heterogeneous genetic disorder, in which interaction between genetic and environmental influences leads to apoptosis of the corneal epithelial cells and extracellular matrix deposition [5].

The prevalence of the disease varies in different parts of the world, on average it is estimated at 7.3%, in which it is stated at 7.2% in persons aged under 50 years, in the age range of 50–69 years at 9.3% and over the age of 70 years in 10.9% of the population [6]. Nevertheless, these data are markedly influenced by the small number of published studies and the lack of data from different parts of the world.

FECD is also one of the most common indications for corneal transplantation, for example in the United States it is currently the most common indication [7]. In a worldwide overview study which processed data from 116 countries and incorporated indications for 184 576 corneal transplantations, this dystrophy was the most common indication, accounting for 39% of cases [8].

Like FECD, the incidence of cataract also has a significant correlation with age. The worldwide prevalence of cataract within the population is estimated at 17.2%, in which the prevalence in the age group of 20–39 years is stated at 3%, while in the age group over 60 years it rises to 54%. Nevertheless, these data also differ markedly depending on the region [9]. With reference to the fact that the incidence of both FECD and cataract demonstrably increases with age, the coincidence of both pathologies in older patients is relatively frequent. FECD is thus probably the most com-

mon corneal pathology which we may encounter in patients undergoing cataract surgery. At the same time, if this pathology is not detected preoperatively and subsequent postoperative corneal decompensation occurs, the result is disappointing for both the patient and the surgeon.

A finding of both clinical units within the framework of the preoperative examination is significant when planning cataract surgery, estimating the occurrence of potential postoperative complications and if applicable proposing an alternative surgical strategy (combined procedure – cataract surgery and transplantation of corneal epithelium, or two separate procedures).

Table 1. FECD classification according to Krachmer [2]

Grade	
G1	1–12 central, non-confluent guttae, usually asymptomatic
G2	More than 12 central guttae
G3	Confluent guttae in the central area, 1–2 mm horizontally
G4	Confluent guttae in the central area, 2–5 mm horizontally
G5	Confluent guttae in the central area, over 5 mm, with or without edema of the stromal or epithelial tissue

FECD – Fuchs' endothelial dystrophy

According to the Krachmer grading scale we divide FECD into 5 grades (Table 1) [2], or 4 clinical stages (Table 2 and Figure 1–4) of the disease [3,10]. The aim of our study was to determine the frequency of FECD in our own cohort of patients indicated for cataract surgery at our center, and to compare this data with the data published in the foreign literature.

MATERIAL AND METHOD

Consecutive cohort of patients undergoing cataract surgery at the Somich (now Lexum) center in Karlovy Vary in the period from 4/2022 to 9/2024. The cohort consisted of a total of 2804 eyes of 1498 patients, of whom 623 were men and 875 women. The mean age of the patients at the time of operation and examination was 71.1±8.8 years (min. 39, max. 95). Besides the regular preoperative examination, all patients underwent a corneal examination on a slit lamp, in which the clinical condition of the cornea was assessed. According to the finding, the corneas were divided according to the Krachmer grading scale into 6 grades (G0–G5) of FECD (G0 is designated as a cornea without signs of disease), or 5 clinical stages (stage 0–4). All the examinations were conducted by a single doctor – surgeon (PS). We also conducted an examination of the corneal epithelium on all the patients before surgery with the aid of the automatic endothelial microscope EM 3000 (Tomey GmbH,

Table 2. Stages of FECD disease [3,10]

Stage	Symptoms	Slit-lamp findings	Endothelial microscopic findings
1	Asymptomatic	Central guttae, non-confluent, thickening of the DM	
2	Blurred vision, glare, especially upon awakening	Confluent guttae	Polymegatism, pleomorphism, cell loss
3	In case of rupture of the bullae pain	Epithelial bullae/corneal stromal edema	
4	Haze, reduced visual acuity	Graying, scarring, vascularization	

FECD – Fuchs' endothelial dystrophy, DM – Descemet's membrane

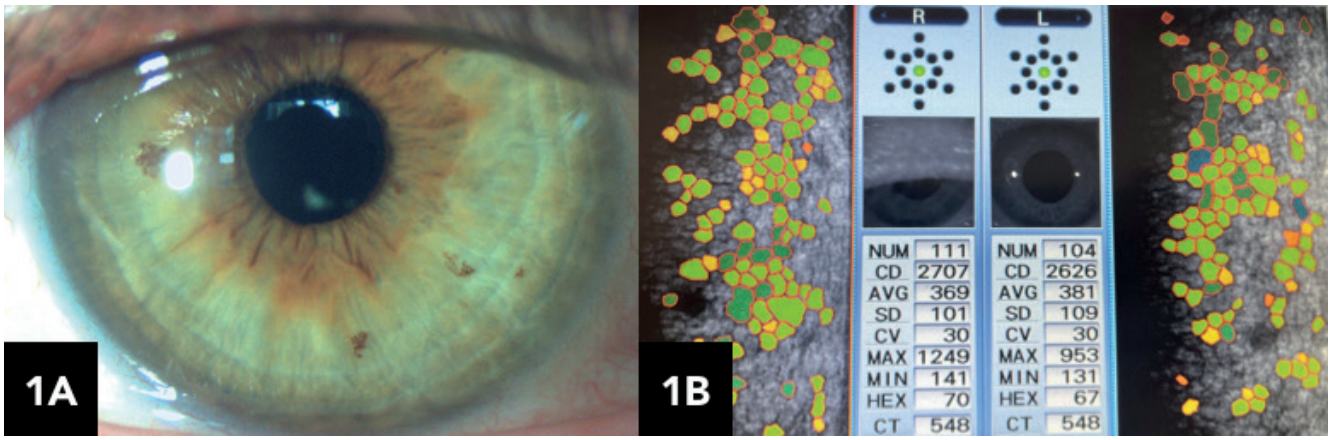

Figure 1. Stage 1 FECD (**A**) slit lamp (**B**) endothelial microscope
FECD – Fuchs' endothelial dystrophy

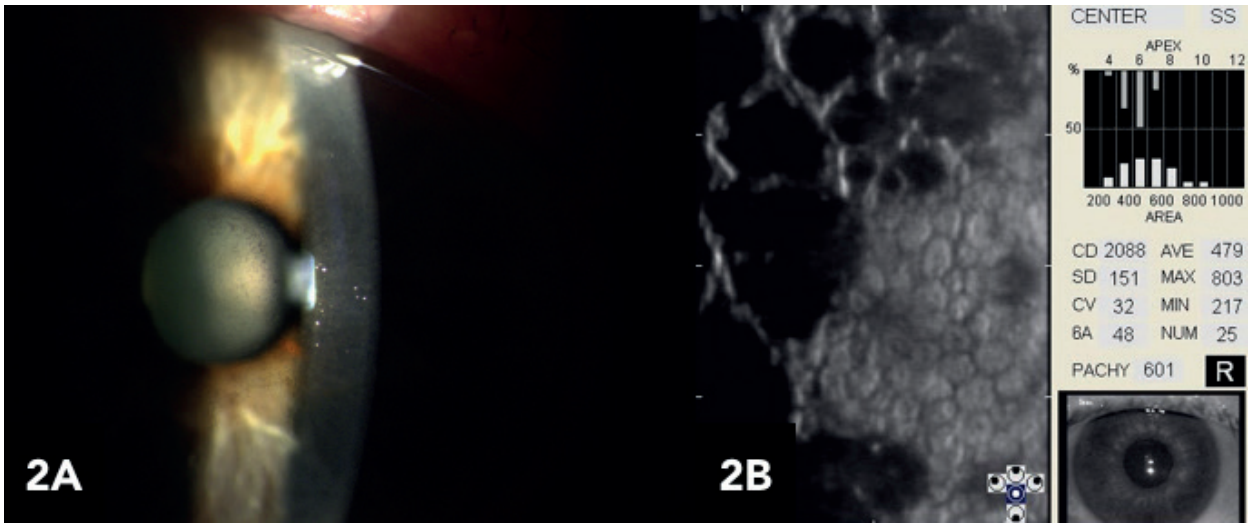

Figure 2. Stage 2 FECD (**A**) slit lamp (**B**) endothelial microscope
FECD – Fuchs' endothelial dystrophy

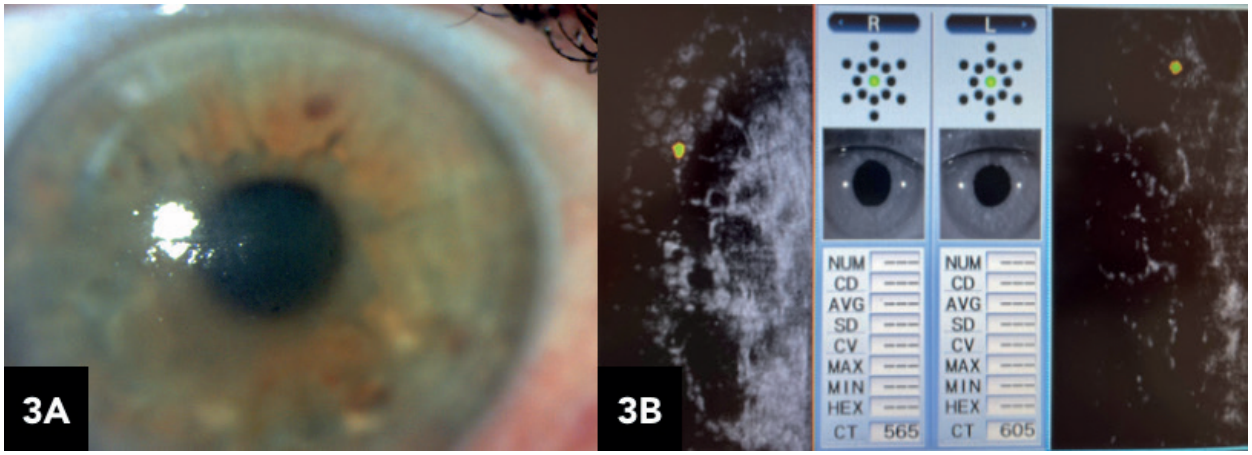

Figure 3. Stage 3 FECD (**A**) slit lamp (**B**) endothelial microscope
FECD – Fuchs' endothelial dystrophy

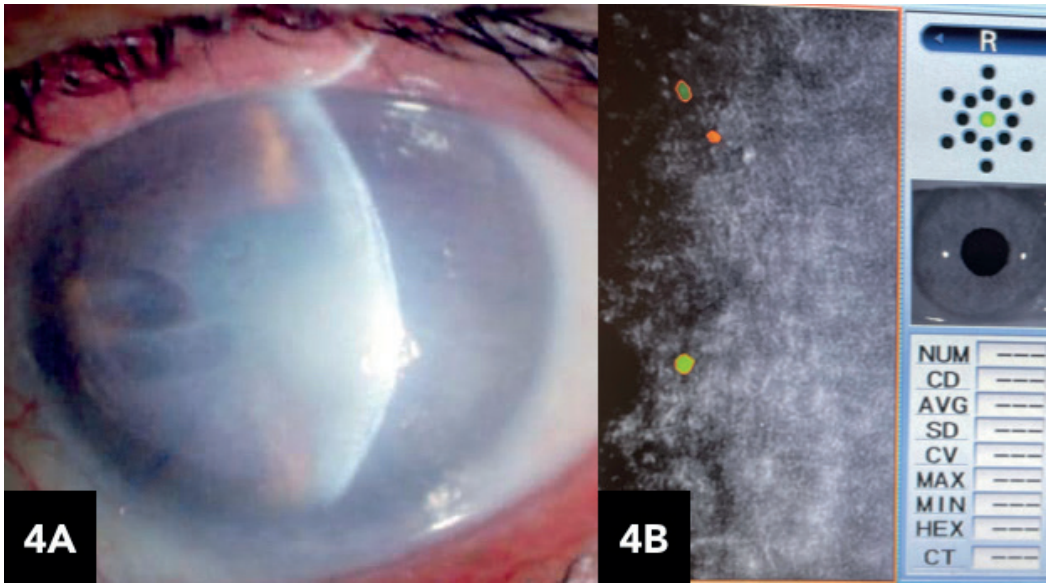

Figure 4. Stage 4 FECD (**A**) slit lamp (**B**) endothelial microscope
FECD – Fuchs' endothelial dystrophy

Erlangen, Germany). The measured value of endothelial cell density (ECD) was recorded, expressed in the number of cells per square millimeter of the surface (bb/mm^2). In cases of significant depletion of the endothelium, when it was not possible to effectively identify endothelial cells and measure their density using the instrument, a referential ECD of 500 bb/mm^2 was recorded in the protocol.

The data analysis was performed with the aid of the program Microsoft Excel for Mac, version 16.16.3. The descriptive statistics were processed for the median values, standard deviations, minimum and maximum values. We assessed statistical significance with the aid of a t-test, and we considered values of $p < 0.05$ to represent the level of statistical significance.

RESULTS

Mean endothelial cell density in the cohort was 2452 ±411 bb/mm^2 (min. 500, max. 3420). Endothelial cell density in the individual clinical stages and grades of FECD is presented in Tables 3 and 4. Values of ECD progressively decreased between the individual clinical stages and grades, and in all cases these differences were statistically significant. Overall there was no presence of any sign of FECD in 70% of the patients in our cohort, while in 30% we recorded presence of certain manifestations of FECD. In 47 patients we preoperatively recorded presence of clinical symptoms of edema of the stroma or corneal epithelium, i.e. clinical stage 3 or 4. In a total of 13 cases (0.5% of all eyes in the cohort) we indicated and performed combined surgery for cataract and DMEK (Descemet's membrane endothelial keratoplasty), in one case we performed the operations separately at an interval, with cataract surgery first followed by DMEK.

DISCUSSION

FECD is probably the most common corneal comorbidity in patients with cataract. The stated frequency of the disease within the population fluctuates markedly. These differences may be due in part to the method of examination and evaluation, and in part to regional differences.

In 2022 Aiello et al. published an extensive meta-analysis drawing upon 4 relevant published studies (Eghrari [11], Higa [12], Zoega [13], Kitagawa [14]) and incorporating a total of 4746 persons aged over 30 years, of whom 2233 were men and 2322 were women. Presence of FECD was recorded in 269 of these subjects (81 men, 188 women). In the conclusion, the authors of the study presented a summary estimate of worldwide prevalence at 7.33% [6]. The main risk of the aforementioned meta-analysis is that it drew upon data obtained in relatively small, usually island populations (Singapore, small regions of Japan – Ishikawa prefecture and Kume Island, Iceland and Tangier Island in the USA). In our study we determined a higher prevalence of FECD. In 30% of patients we found at least minimal signs of FECD, in 9.4% FECD in grade G2 or higher, and in 2.9% of patients we found signs of the disease in grade G3 or higher (according to the Krachmer scale). This difference is undoubtedly influenced to a certain extent by the age composition of the cohort of patients under investigation. In the aforementioned meta-analysis the average age of the examined subjects was 61.9 years, in our case the average age of the patients undergoing cataract surgery was 71.1 ±8.8 years.

The cited meta-analysis also demonstrated statistically significant differences in the prevalence of FECD in connection with sex, specifically a higher incidence in women – OR (odds ratio): 2.22 [6]. This fact is confirmed also by other studies [15]. In our cohort also we recorded a higher incidence of women (OR in our cohort was 1.63, in the case of more advanced forms of G3 or higher 1.88); nevertheless, these values were lower than in the aforementioned meta-analysis (OR = 2.22).

Some published studies present a markedly lower frequency of FECD. For example, Xie (China) states the incidence of FECD at 0.8% of cases in 2026 consecutive patients for cataract surgery. The authors determined

Table 3. Endothelial density and number of eyes in individual clinical stages of FECD

	Total	Without FECD	Stage 1	Stage 2	Stage 3	Stage 4
Number	2804	1962	689	106	45	2
%	100	70	24.6	3.8	1.6	0.1
ECD (cc/mm^2)	2452	2520	2413	2132	950	500
SD	±411	±326	±367	±497	±570	N/A

FECD – Fuchs' endothelial dystrophy, ECD – endothelial cell density, SD – standard deviation

Table 4. Endothelial density and number of eyes in individual stages of FECD

	Total	G0	Gx	G1	G2	G3	G4	G5
Number	2804	1962	842	579	182	62	16	3
%	100	70	30	20.6	6.5	2.2	0.6	0.1
ECD (bb/mm^2)	2452	2520	2295	2435	2263	1589	639	500
SMODCH	±411	±326	±527	±361	±428	±669	±639	N/A

FECD – Fuchs' endothelial dystrophy, ECD – endothelial cell density, SD – standard deviation, G0 – group of eyes without signs of FECD, Gx – group of eyes with some stage of FECD, G1–5: groups of eyes in individual stages of FECD

Table 5. Gender representation in individual FECD groups

	Total	G0	Gx	G1	G2	G3	G4	G5
Number	2804	1962	842	579	182	62	16	3
Men	1144	867	277	213	42	12	8	2
Women	1660	1095	565	366	140	50	8	1
Representation of women in the given group of patients (%)	59.2	55.8	67.1	63.1	76.9	80.6	50.0	66.7

FECD – Fuchs' endothelial dystrophy, G0 group of eyes without signs of FECD, Gx group of eyes with some degree of FECD, G1–5 groups of eyes in individual degrees of FECD

the diagnosis on the basis of an examination by specular microscope; nevertheless the division into individual stages was not clear, and neither were the criteria set by the authors for the definition of this diagnosis [16].

Based on cases reported in the Medicare system (the system of health insurance in the USA), Sing stated an estimated prevalence of the disease in 1.2% of the population aged over 65 years [17]. However, this raises a question concerning the extent to which the disease is detected in the preclinical significant stages, and subsequently reported in the Medicare system.

It was determined that the risk of developing FECD is associated with the incidence of a mutation in gene TCF 4 (transcription factor 4), in which an expansion of CTG trinucleotide repeat occurs [18,19]. Zhang determined the incidence of this mutation in gene TCF4 in a variety of ethnic groups. The incidence in the USA was 3.1% in Afro-Americans, 8.1% in Americans of European origin, and 3.3% in Latinos. Globally the incidence of the mutation was determined in 2.7% of Africans, 9.5% of Europeans, 5.2% of East Asians, and 7.2% of South Asians [20]. These conclusions confirm the fact that the incidence of FECD is highest in the European population.

In general, therefore, the determined incidence of FECD in our study exceeds the previously published data. The question naturally arises as to whether it is necessary to consider the appearance of individual guttata on the corneal epithelium in a number of 1–12 without further clinical manifestations of the pathology (classification G1 according to the Krachmer scale) to constitute dystrophy. In addition, endothelial cell density in the G1 group in our cohort is not statistically significantly lower in comparison with corneas without the appearance of any guttata, i.e. in the G0 group (2435 compared with 2520 bb/mm^2). For these patients we are not adjusting the procedure for cataract surgery in any way, and the risk of transition to further stages of the disease is probably relatively low, also taking into account the average age of the patients undergoing cataract surgery.

If we narrow down the incidence of FECD to the further stages of the disease, which require caution in planning cataract surgery, namely stages G2 and higher, then the determined frequency of the pathology in our cohort of cataract patients is 9.4%. This data is therefore close to the values stated in studies conducted by other authors, especially taking into account the age and ethnicity of our cohort. In the case of patients in clinical stages 2–4, it is necessary to inform the patients of the potential occurrence of postoperative edema, the risk of prolonged healing and the potential necessity of a subsequent endothelial transplant.

At present, a range of authors recommend a combined procedure for distinctly risk patients, i.e. cataract surgery with implantation of an intraocular lens together with transplantation of a DMEK type endothelium within the framework of a single surgical procedure [21–24]. The advantage of this approach is above all faster convalescence, as well as the reduced risk of complications in comparison with two surgical procedures, and lower costs. A certain disadvantage is the greater difficulty of calculating the intraocular lens, as well as the unavailability of corneal tissue and a longer waiting period for the surgical procedure in certain regions.

Above all, timely detection of endothelial pathology is necessary for ensuring the correct procedure for patients with combined cataract and FECD. Patel recommends as standard examination with the aid of Scheimpflug tomography, primarily map of elevation of the posterior surface of the cornea and pachymetry map, which may detect early corneal edema [25].

Van Cleynenbreugel in his study states the result of pachymetry as the decisive factor in performing a triple procedure, in which he considers the borderline value to be a preoperative corneal thickness of 630 um, and the authors consider the most reliable factor to be light dispersion on the cornea determined with the aid of in vivo confocal microscopy, in which they consider ther borderline value to be 1894 units [26].

Arnalich-Montiel also states light dispersion on the anterior surface of the cornea within the region of 0–2 mm from the apex, as well as relative increase of central corneal thickness, as significant factors in estimating endothelial failure following cataract surgery. Examination was performed with the aid of a Scheimpflug camera [27]. Guindolet uses local changes of corneal thickness examined with the aid of OCT, or ratios of thickness between the individual regions measured in the 2, 5, 7 and 9 mm zone, as an effective examination in order to estimate subclinical postoperative edema following cataract surgery in patients with FECD [28].

Shah describes the significance of examining corneal densitometry in the central region with the aid of

a Scheimpflug camera, in which an increase of this value is significantly associated with worse visual acuity [29].

In our cohort of patients we performed combined surgery in a total of 13 cases (0.5% of all eyes in the cohort), in only one case we performed the operations separately at an interval following consultation with the patient, with cataract surgery first followed by DMEK.

In cases where combined surgery is not possible for whatever reason, cataract surgery alone may improve visual acuity of patients to a certain extent, and in some cases, upon a satisfactory finding on the cornea, transplantation may be temporarily deferred [30]. The stated criterion for considering deferring endothelial transplantation is lack of blurred vision in the morning in the patient's medical history and pachymetry of less than 630 µm. For example, Malandin in a cohort of 64 eyes stated that it was necessary to perform subsequent DMEK in only 14 cases (22%), in which the average observation period was 12 months [31]. If a procedure of cataract surgery alone is chosen for patients with FECD, some authors recommend an adjustment of the surgical procedure in the sense of greater safety and protection of the endothelium, such as the use of the soft-shell technique – namely a combination of dispersive and cohesive viscoelastic material or viscoadaptive material [32,33].

CONCLUSION

FECD is probably often under-diagnosed in the population of cataract patients. In our cohort of patients we registered certain signs of the disease in 30% of cases, and we recorded a grade of the pathology of G2 and higher in 9.4% of the eyes of patients undergoing cataract surgery. In 106 (5.5%) of a total number of 2804 eyes, the disease was already in a clinically significant stage (stage 2 or higher) – coalescent guttata, blurred vision in the morning etc. For these patients it is necessary to consider a possible combined procedure before proceeding to cataract surgery, and above all to inform the patient of the longer healing time and other potential risks.

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