

Impact of COVID-19 on Corneal Transplantation: First *EuCornea Education Webinar*

Impacto da COVID-19 na Cirurgia de Transplantação Corneana: Primeiro *EuCornea Educational Webinar*

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The ophthalmic scientific community has been put to test throughout the COVID-19 disease pandemic, and the several, successful virtual scientific meetings and webinars have demonstrated the great impact of social media in scientific communication.¹ In 11th March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. One year later, the ophthalmologist community “e-gathered” to attend the first *EuCornea Educational Webinar* in 11th March 2021, which addressed the subject of corneal grafting and COVID-19.

During the pandemic, four main issues regarding risk management have been recognized: 1) the risk to sufficiency and sustainability of donor corneas, 2) the risk regarding viral status of the donor tissue, 3) the risk to eye bank and ophthalmology department staff, and 4) the risk to corneal graft recipients. Rethinking eye surgery and ocular tissue processing and preservation strategies was essential from the outset, as the ocular surface harbours proteins which allow SARS-CoV-2 virus entry into ocular surface cells, and as the virus RNA has been detected in conjunctival swabs of patients with COVID-19. In addition, a spectrum of ocular manifestations has been described in patients with COVID-19, although the incidence of conjunctivitis and other ocular complications appears to be low.²

In response to the COVID-19 pandemic, Ophthalmology departments and Eye Banks worldwide were placed in lockdown or reorganized into “COVID-19 units” in the early phase of the pandemic, and since then have resumed their activity at variable rates. Early in the pandemic, eye banks adapted quickly, and reduced procurement led to an excess of available tissue, with the problem of limited tissue shelf time. In Europe, the number of procurements decreased by 38%-68% between March-May 2020, compared with the mean of the two previous years.³ Later, with the progressive adaptation of both eye banks and cornea departments, increased pressure has been imposed on eye banks due to increased deferrals. Importantly, during the webinar it was highlighted that these changes were felt more strongly in smaller eye banks compared with higher-volume eye banks. Several strategies have been proposed to address these issues, including storage of dehydrated corneas (which may last up to 6 months in storage) particularly for anterior lamellar keratoplasty^{4,5}; the use of hemi- and quarter-DMEK grafts⁵; and the use of one donor cornea for multiple recipients.⁶

Additional complexities in transplantation during the pandemic include questions regarding donor and recipient screening. It is still not definitive whether donor corneal tissues harbour the SARS-CoV-2 RNA, with conflicting findin-

gs in the literature,⁷⁻⁹ including findings of both RNA and the envelope and spike proteins in one study,⁹ and positive findings in asymptomatic donors in another study.¹⁰ From 588 donors from the Veneto Eye Bank Foundation without medical evidence nor epidemiological links to COVID-19 cases, only three cases (0.5%) tested positive for SARS-CoV-2 in nasopharyngeal rt-PCR samples, of which two corneal specimens yielded SARS-CoV-2 RNA.¹⁰ During the webinar, speakers pointed out that positive genomic tests may not relate to viral replicability, as cases with detectable SARS-CoV-2 RNA in corneal tissue have low small genomic RNA expression, which suggests low or no viral replicability; and Dr Thuret mentioned that no bilateral positive cases were found, although unilateral infection may be possible. Besides, Dr Thuret found high inter-individual variability of ACE-2 and TMPRSS2 expression, meaning donors with positive nasopharyngeal PCR may not have corneal positivity. Despite these controversies, it is generally considered that the overall risk of transmission of SARS-CoV-2 through keratoplasty may be low, but that further research is warranted to assess the rate of SARS-CoV-2 transmission. Dr Dickmann pointed out that this is supported by the fact that there is no known transmission of other respiratory viruses in corneal grafts. Even so, until further data is available, most international guidelines avoid donor tissues from patients with COVID-19 disease. Current EEBA guidelines state that patients with active COVID-19 disease at time of death must be excluded from corneal donation, but that people with a positive PCR >14 days before death may be eligible 2 weeks after complete recovery and symptom-free at the time of death.¹¹ Post-mortem nasopharyngeal PCR testing is therefore critically important,^{9,12} particularly in individuals with unknown status prior to death.¹¹ According to the webinar speakers, further testing (including Western blot testing) likely has no added value to the validation of PCR results.

Regarding donor ocular tissue preparation, although concerns have arisen for potential ocular infectivity and infection of collection team staff,¹³ with adequate protective measures this risk may be very low.⁸ Since it appears that SARS-CoV-2 viral replication and its lytic activity restricts to epithelia, removal of all conjunctival tissue and corneal epithelial removal with povidone-iodine (PVI) is a crucial step in donor preparation.⁹ Although further evidence is required to demonstrate its efficacy on SARS-CoV-2 in corneal tissues, coronaviruses in inanimate surfaces appear to be rapidly inactivated following PVI exposure; the European Center for Disease Control considers PVI exposure to be validated for enveloped virus, and the current EBAA Medical Standard requires double exposure to PVI at the ocular surface before tissue recovery. However, eye banks and ophthalmologists must remain aware that PVI does not accomplish complete sterilization, nor does it eliminate the possibility of viral retention within ocular structures.¹⁴

It is recommended that patients undergo RT-PCR before keratoplasty and that PCR-positive patients are postponed, unless the emergent cases, in which all surgical staff should wear full protective equipment.¹³ Dr Ponzin suggested that endothelial keratoplasty may be a safer procedure compared with penetrating keratoplasty, since the corneal endothelial

layer lacks ACE-2 and TMPRSS2. The postoperative follow-up must take into account the possibility of the patient being infected with SARS-CoV-2, which may increase susceptibility for immune rejection episodes, possibly to viral induction of a proinflammatory state.¹⁵ Finally, Dr Dickmann stated that COVID-19 vaccination is safe in corneal transplant patients. However, it may be advisable to increase immunosuppressive treatment in patients with corneal allografts undergoing COVID-19 vaccination, particularly in patients at increased risk of rejection such as patients with corneal re-grafts; webinar speakers mentioned two cases of rejection episodes shortly following vaccination. Dr Dickmann suggested increasing topical steroids to 4 times daily 2 days before vaccination and for a period of 2 weeks, and highlighted the importance of keratoplasty patients to watch out for potential signs of graft rejection under the “RSVP” acronym for redness, sensitivity to light, vision blurring, and pain.

In conclusion, the first *EuCornea Educational Webinar* weaved sound considerations into corneal transplantation and eye banking during the COVID-19 pandemic. Key messages are that transplant activity during a pandemic should be fluid and tailored, with careful donor and recipient selection. International existing networks including EuCornea and the EEBA facilitate communication and foster cooperation to minimize the influence of the pandemic on donation and corneal transplantation activity. Prompt adaptation by eye banks and cornea departments allowed normalization of corneal grafting activity throughout Europe; that is, the “corneal transplantation chain” is rapidly adaptive, albeit at variable rates throughout Europe. With the appropriate measures for donor collection and preparation, and with careful perioperative protective measures, healthcare professionals and keratoplasty recipients likely have a low infectivity risk. Future challenges ahead will include the management of corneal patients undergoing COVID-19 vaccination, as well as further identification of potential donors among those with previous history of COVID-19 disease.

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