Family refusal to donate a cornea for transplantation: associated factors and trends

Recusa familiar para doação de córneas para transplante: fatores associados e tendência

Negativa familiar para donación de córneas para trasplante: factores asociados y tendencia

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Abstract

Objective: To analyze family refusals to donate a cornea for transplantation in an Organ Procurement Organization.

Methods: This was a quantitative cross-sectional study on corneal donation refusals from potential brain-dead donors. The data source was based on the Terms of Authorization for Donation of Organs and Tissues signed from January 2001 to December 2020 in an Organ Procurement Organization. Data were collected, tabulated, and analyzed in a descriptive and inferential manner. The present study was approved by the Research Ethics Committee.

Results: Of the 2,447 Terms of Authorization for Donation of Organs and Tissues signed in the above period, 620 (25.34%) of them refused to donate a cornea. Regarding the time trend of corneal donation refusals, the period 2001-2009 was the only one that showed significance, when the 0-11 and 12-19 age groups showed a decreasing trend and that of 60 years or older showed an increasing trend. In the period 2001-2020, the age groups of 20-40, 41-59, and 60 years or older had lower rates of refusal to donate a cornea (48%, 59%, and 73%, respectively).

Conclusion: The age group is associated with refusal because older individuals had the highest refusal rates.

Keywords
Tissue and organ procurement; Tissue donors; Corneal transplantation; Refusal to participate; Family

Descritores
Obtenção de tecidos e órgãos; Doadores de tecidos; Transplante de córnea; Negativa de participação; Família

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Introduction

The cornea is a transparent tissue in the anterior portion of the eyeball, allowing the entry of light and still exerting a focus-related function. In many cases, corneal diseases can lead to a decrease in visual acuity, causing reversible blindness in 4-5% of cases.

Corneal transplantation is an important alternative that should assist in the partial or total recovery of vision in cases of more severe pathology; some of the major corneal pathologies, such as Fuchs’ dystrophy, keratoconus, primary corneal edema, and sequelae of infectious keratitis, require transplantation as a form of treatment.

Tissues, including the cornea, can be donated after the diagnosis of both brain death and death due to cardiopulmonary arrest. Brain death consists of the complete and irreversible stoppage of all structures of the human brain; in Brazil, the diagnosis is made based on two clinical exams and a complementary exam, which must be performed by two different doctors and with an interval of hours, according to the patient’s age. Death by cardiopulmonary arrest is the cessation of the heart’s work of pumping oxygenated blood into the brain and other structures of the human body.

Corneal donation can be performed in both cases, but obtaining it is often associated with cardiac arrest; in this case, only the tissues for donation (including the cornea) can be removed up to 6 h after death. However, donation after brain death is feasible; the lower rate of refusal to donate corneas observed in these cases contributes to meeting the demands of the population.
of donation is discussed and the organs and tissues that can be removed are decided.\(^{13}\)

Given the importance of family authorization for the process to continue, establishing public policies is necessary to make the population aware of the importance of donations and the safety of the process, so that all doubts of family members of potential donors are resolved, thus reducing the refusals and serving the population who is waiting for a transplant.

It is believed that the lack of information to potential donor families about the process and the importance of the donation are some obstacles to corneal donation for transplantation, in addition to legal, logistical, or religious issues.\(^2\) The education and kinship degree of the family members interviewed, as well as the shift in which the interview is carried out, also influence the consolidation of donations.\(^{1}\)

Therefore, analyzing family refusals to donate a cornea for transplantation in an Organ Procurement Organization was the aim of this study.

**Methods**

This was a quantitative cross-sectional analytical study of an exploratory and retrospective character on the refusals of family members of potential corneal donors in a situation of brain death.

The scenario for this research was the territory where an Organ Procurement Organization (OPO) encompasses 96 hospitals in the State of São Paulo.

The analysis material consisted of all Terms of Authorization for Donation of Organs and Tissues signed by donor family members from January 2001 to December 2020.

The data of interest were collected and tabulated in a Microsoft Excel spread sheet. The study variables related to refusal of corneal donation were as follows: year (2001-2020), donor age (0-11, 12-19, 20-40, 41-59, and 60 years or older), gender (female and male), cause of death (cerebrovascular accident, traumatic brain injury, anoxic encephalopathy after cardiac arrest, external causes, etc.), type of hospital (public and private), and refusal to donate cornea.

The final version of the database was transferred from Microsoft Excel to the Stata (v. 15.0) software, in which the analyses were performed. Chi-square tests were sequentially applied to test hypotheses of association between acceptance or refusal of donation and sociodemographic, clinical, and administration-type variables.

The temporal trend analysis was performed using the Prais-Winster-type generalized linear regression, in which the beta 1 coefficients (\(\beta_1\)) (with first-order temporal autocorrelation correction) and the respective 95% confidence intervals were estimated. Refusals to donate corneas in the general population and subgroups (male gender, public administration, and the age groups of 0-11, 12-19, 20-40, 41-59, and 60 years or older) were considered as dependent variables. The estimated coefficients were used to calculate the percentage trend or change evidenced by the Annual Percent Change (APC) parameter and the respective 95% confidence intervals. The APC values were calculated based on the formula demonstrated by Antunes and Cardoso.\(^{14}\)

In addition, the relative variation coefficients in the periods of interest were calculated. For this, the difference between the percentages of refusal in the final and initial years of the analyzed period was divided by the percentage in the initial year. To interpret the results, the increasing (mean annual percent change, APC, significantly positive; \(p<0.05\)), decreasing (significantly negative change rate; \(p<0.05\)), and stationary (accepting the null hypothesis that there is no significant difference between the variation and zero; \(p>0.05\)) tendencies were considered.\(^{14}\)

A multiple logistic regression-type multivariate analysis was performed to estimate the chances of refusing to donate organs and/or tissues. Initially, the crude odds ratios (OR) and the respective 95% confidence intervals were estimated for the following subgroups: male gender, public administration, and the age ranges of 12-19, 20-40, 41-59, and 60 years or older. The 5% significance level was adopted in all analyses.

This study is part of a larger research project (Analysis of donations of organs and tissues for trans-
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In the period studied, 2,447 Terms of Authorization for Donation of Organs and Tissues were signed; 1,827 (74.66%) of them were for donation and 620 (25.34%) for refusal of corneal donation. Regarding the characteristics of individuals who refused to donate corneas, the age range was significant \( (p < 0.001) \), and the highest number of refusals was observed in the 41-59 age group (Table 1).

### Results

In the period 2001-2009, the temporal trend of corneal donation refusals for the age groups of 0-11 \( (APC: -0.99; CI: -1.09; -0.27; p = 0.040) \) and 12-19 years \( (APC: -0.99; CI: -1.08; -0.82; p = 0.008) \) decreased. In the age group of 60 years or older, the temporal trend of refusals showed to be increasing \( (APC: 140.25; CI: 3.78; 424.67; p = 0.011) \) (Table 2). In the second period (2010-2020), no variable showed a significant trend. The other variables (male gender; public administration; 20-40 and 41-59 years old; general population) showed a stationary temporal trend in the analyzed periods (Table 2).

In the period 2001-2009, the age groups of 41-59 \( (p = 0.002) \) and 60 years or older \( (p < 0.001) \) had lower chances of refusing cornea donation (66.0 and 81.0%, respectively) compared to the age group of 0-11 years (Table 3). In the period 2010-2020, the age groups of 20-40 \( (p = 0.040) \), 41-59 \( (p = 0.008) \), and 60 years or older \( (p < 0.001) \) showed lower chances of refusal (47.0, 55.0, and 69.0%, respectively), when compared to the age group of 0-11 years (Table 3). In the period 2001-2020, the age groups of 20-40 \( (p = 0.025) \) and traumatic brain injury \( (p = 0.028) \) showed lower chances of refusal (39.0 and 23.0%, respectively), compared to other diagnoses (Table 3).

### Discussion

With basis on the above results, the specific family refusal to donate cornea was analyzed in an Organ Procurement Organization in the State of São Paulo. After analysis, the age group was associated with refusal, whereas older individuals had higher refusal indices.

A study carried out in Australia (2006) also indicated an association between the potential donor’s age and specific refusal to donate a cornea, and increasing age was positively related to the chances of donating a cornea. (15) However, the positive relationship of this study is opposed by our results. A Brazilian study, which was carried out in the period 2007-2008 at a University Hospital in the State of Paraná, did not observe a significant association between donor age and effective donation. (16) Thus, the variation observed in the results on this theme...
suggests an additional study to better understand this aspect.

As the donor’s age does not affect the procedure’s success, this result is also relevant if the endothelial cell count was adequate. Then, even the donation of the cornea from older individuals (the age group that most refused donation) would significantly contribute to supplying the eye bank, favoring future transplants.16,17

Analyzing the temporal trend in the period 2001-2009, a decreasing trend was identified in the age groups of 0-11 and 12-19 years (and an increasing trend in the age group of 60 years or older) indicating an increase in refusals simultaneously with
the increase in age. In the period 2010-2020, no variable showed a significant trend. In a study carried out at an Organ Procurement Organization in the city of São Paulo in the period 2001-2016, it was observed that corneal donation remained stationary for more than a decade, whereas donation of other tissues presented lower rates.\(^{(18)}\)

The present study began in 2001 when the highest rate of family refusal of corneal donation was observed. On 09/06/2001, the Ministry of Health created the National Program for Implementation of Eye Banks (Ordinance 1559) within the scope of the National Transplant System. Through this Ordinance, the Program objectives were established. They must offer implantation conditions for the Eye Banks, in addition to other actions, enabling a wide collection of cornea for transplantation (with the necessary technical and safety conditions), thus increasing the number of transplants and reducing waiting lists.\(^{(19)}\)

It was possible to observe that the creation of the National Program for Implementation of Eye Banks enabled significant changes, as a drop was noted in the refusal rates in the following years. In addition, the Cornea-Fila Zero Campaign was launched in São Paulo in 2003 by Mayor Marta Suplicy to provide more information to the population about corneal donation for transplantation, thus contributing to the fall in refusal rates.\(^{(20, 21)}\)

The year 2009 was relevant because the lowest rate of refusal occurred in it within the entire study period. In that year, Ordinance 2600 (10/21/2009) approved the Technical Regulation of the National Transplantation System. However, the drop in refusals is probably not associated with this approval, as it occurred in the second half of the year and a significant change in the index for that year would not be possible.\(^{(22)}\) Thus, we presume that the drop is a reflection of the pattern observed in previous years.

The implementation of the Technical Regulation of the National Transplant System was not enough to generate positive results (relative to corneal donations in 2010); they completely diverged from the repetitive pattern observed in previous years, with the second highest rate of refusals in the period.

Also in 2010, the Transplant Center (that coordinates the State Transplant System of the São Paulo State Health Department) changed the Donation Authorization Term, which started to be used in family interviews. With the use of this new Term, a 17.2% increase was observed in authorizations for corneal donation. Thus, the evidence found in the literature was not sufficient to explain the reason for the increase in refusal rates in that year, indicating the need for further studies to explore the characteristics of this period.\(^{(23)}\)

Concerning 2020 (when the Covid-19 pandemic was declared), the non-increase in the refusal rate was an important observation; in fact, this index has also decreased throughout Brazil.\(^{(11)}\) One issue that may be related to this was the death of an important Brazilian artist due to brain death at the end of 2019: the donation of his organs and tissues was authorized by his family members, generating a lot of publicity on the subject on social media, thus bringing this subject for discussion in many families and social settings.\(^{(24)}\)

Regarding the association between corneal donation refusals and sociodemographic characteristics, the age groups showed a certain kind of percentage pattern in all analyzed periods. In all cases, older individuals had higher percentages of chance of refusing donation when compared to the 0-11 age group.

It is interesting to emphasize that the findings of the present study confirm those of previous studies that indicate specific refusal of corneal donation when donation of other organs and tissues was accepted.\(^{(15)}\) A study conducted in the East explains how donation-related terminology can influence effective donation.\(^{(25)}\) In the case of cornea donation, the use of terms such as “donation and/or eye bank” should be avoided, replacing them with “donation and/or ocular tissue bank” or specifically cornea donation. Not only the stigma associated with the removal of eyes for donation (and all its meanings in society) should be considered but also make the interpretation and expression of family members clearer in the choice of tissues to be donated.\(^{(25)}\)

Another study indicates that other aspects related to the population, in addition to those presented
here (such as marital status, place of residence, and legal or religious aspects), can also lead to the refusal of the donation of organs and tissues. However, it refers to a context in which no donation is made; differently, in the present study, donation of other organs and tissues occurred, but specific corneal donation was refused.\(^{(26)}\)

The character of this study can be considered original, as the data source was composed of the Terms of Donation of Organs and Tissues in which the family specifically refused to donate the cornea, but agreed to donate other organs and tissues. In addition, this is an analysis of donor refusals in cases of brain death, whereas most corneal removals for donation occurred in patients who died of cardiopulmonary arrest. The limitations of the present study consist in the fact that they could not explain the motivation for the refusals, although some variables showed a significant result. Therefore, carrying out new studies in the area is necessary to understand other variables related to both the donors and the family members interviewed, including age, sex, education, and the interviewees’ degree of kinship.

**Conclusion**

Age group is associated with refusal, as older donor individuals also had higher refusal rates. Conducting new studies is necessary to better understand the specific reasons for refusing to donate cornea. Actions and campaigns to raise public awareness about the importance of donating the cornea are also necessary, including older individuals, as the donor’s age does not affect the procedure’s success. This will contribute to supplying the corneal banks, helping to meet the demand and reduce the refusal rates.

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**Collaborations**

Silva ICN, Pimentel RRS, Moraes EL, and Santos MJ contributed to the study design, data analysis and interpretation, manuscript writing, relevant critical review of the intellectual content, and approval of the final version to be published.

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