Current Global Bioethical Dilemmas in Corneal Transplantation

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Purpose: To analyze some of the bioethical dilemmas that may arise during the process required for corneal transplantation.

Methods: We conducted a narrative review based on the available literature and the experience of cornea specialists from 3 different countries.

Results: Bioethical dilemmas related to informed consent for organ and tissue donation, allocation of corneal tissues, transplant tourism, corneal tissue exportation and importation, and for-profit eye banking were analyzed and discussed.

Conclusions: Around the world, the number of required corneal transplants exceeds the number of donated corneas that are available and suitable for transplantation. This shortage of corneal tissue has led to the emergence of practices that may put the 4 basic principles of bioethics at risk: autonomy, beneficence, nonmaleficence, and justice. Therefore, it has been necessary to create ethical guidelines such as the Barcelona Principles and the World Health Organization Principles of Transplantation that attempt to regulate these practices.

Key Words: corneal transplant, bioethics, transplants bioethics, eye bank, informed consent

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Corneal tissue is the most frequently and highly successfully transplanted tissue worldwide, allowing many people to recover their eyesight.[1] Nevertheless, there are more people requiring corneal transplant than the availability of tissue. A recent study demonstrated that for each of the 70 required corneas in the world, only 1 cornea is available.[2] This tissue shortage has led to an increase in unethical practices[3] that put at risk the 4 basic principles of bioethics described by Beauchamp and Childress:[4] 1) *Autonomy:* the right for an individual to make his or her own choice, 2) *Beneficence:* the principle of acting with the best interest of the other in mind, 3) *Nonmaleficence:* the principle of "above all, do no harm," as stated in the Hippocratic oath, and 4) *Justice:* a concept that emphasizes fairness and equality among individuals.

As a measure to avoid unethical practices, bioethical guidelines on the subject have been published by different groups of experts, of which the most important are the World Health Organization (WHO) Principles of Transplantation[5] (Table 1) and the Global Alliance of Eye Bank Associations Barcelona Principles[6] (Table 2).

This article discusses some of the significant ethical dilemmas currently faced around the world in the field of corneal transplantation and the way in which the basic principles of bioethics could be compromised.

INFORMED CONSENT FOR ORGAN AND TISSUE DONATION

Informed consent is an important legality in medical practice because it ensures that the patient's *autonomy* is being protected.[7] For organ and tissue donation, informed consent means that an individual gives their authorization by free will, without pressure or reward of any kind, for the procurement of his/her organs and tissues—in this case, corneas. For corneal transplantation, an important issue to consider is that the donor is usually cadaveric and, therefore, cannot provide consent at the time of the procedure. Thus, in this situation, emphasis is on the consent given either before death or by the participation of the donor's family in respecting that decision.

There are 2 types of informed consents for donation: expressed and presumed. The first refers to the consent that must be written and signed, and the agreement to be a donor is explicitly stated. Expressed consent has to be either signed by the donor during his/her lifetime or by the donor's family after death. On the other hand, when presumed consent is used, it is assumed that any individual who did not formally oppose being a donor during his/her lifetime is, therefore, considered a donor by default.[5,7]

Each country defines, by law, the type of consent required for corneal donation. Although, for both types of consents, it might be argued that the *autonomy* principle is respected, the

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TABLE 1. The WHO Principles of Transplantation[5]

1. Cells, tissues, and organs may be removed from the bodies of deceased persons for the purpose of transplantation if, 1) any consent required by law is obtained and 2) there is no reason to believe that the deceased person objected to such removal.
2. Physicians determining that a potential donor has died should not be directly involved in cell, tissue, or organ removal from the donor or subsequent transplantation procedures, nor should they be responsible for the care of any intended recipient of such cells, tissues, and organs.
3. Donation from deceased persons should be developed to its maximum therapeutic potential, but adult living persons may donate organs as permitted by domestic regulations. In general living donors should be genetically, legally, or emotionally related to their recipients.
4. No cells, tissues, or organs should be removed from the body of a living minor for the purpose of transplantation other than narrow exceptions allowed under the national law. Specific measures should be in place to protect the minor and, wherever possible, the minor's assent should be obtained before donation. What is applicable to minors also applies to any legally incompetent person.
5. Cells, tissues, and organs should only be donated freely without any monetary payment or other reward of monetary value. Purchasing, or offering to purchase, cells, tissues, or organs for transplantation, or their sale by living persons or by the next-of-kin for deceased persons should be banned.
6. Promotion of altruistic donation of human cells, tissues, or organs by means of advertisement or public appeal may be undertaken in accordance with domestic regulation.
7. Physicians and other health professionals should not engage in transplantation procedures, and health insurers and other payers should not cover such procedures, if the cells, tissues, or organs concerned have been obtained through exploitation or coercion of, or payment to, the donor or the next-of-kin of a deceased donor.
8. All healthcare facilities and professionals involved in cell, tissue, or organ procurement and transplantation procedures should be prohibited from receiving any payment that exceeds the justifiable fee for the services rendered.
9. The allocation of organs, cells, and tissues should be guided by clinical criteria and ethical norms and not financial or other considerations. Allocation rules, defined by appropriately constituted committees, should be equitable, externally justified, and transparent.
10. High-quality, safe, and efficacious procedures are essential for donors and recipients alike. The long-term outcomes of cell, tissue, and organ donation and transplantation should be assessed for the living donor as well as the recipient in order to document benefit and harm.
11. The organization and execution of donation and transplantation activities, as well as their clinical results, must be transparent and open to scrutiny, while ensuring that the personal anonymity and privacy of donors and recipients are always protected.

importance and weight given to the donor's family varies, and thus, the implementation and acceptance of presumed consent in societies with strong family ties is problematic.[8,9] Many countries with presumed consent laws, such as Spain and Argentina, have a "soft approach" in this matter and always consult the relatives for consent before proceeding.

The recently published Barcelona Principles[6] established in the first principle that the *autonomy* of both donor and next-of-kin must be respected during the consent process. However, as previously mentioned, depending on the required type of consent (expressed or presumed), the *autonomy* of the donor's next-of-kin might be particularly affected because it would have more or less weight.

The success of organ and tissue donation programs does not depend only on the consent type by law. Society's perception of this activity, transparency of the process, the quality of service in the health care given, and respect given to the family at a very delicate time are equally important to guarantee acceptable results. That is why, each country should individually evaluate the cultural variables of its population and establish the most appropriate consent type. This avoids jeopardizing the cultural principles of its population while simultaneously favoring and promoting tissue donation.

TABLE 2. The Barcelona Principles[6]

1. Respect the autonomy of the donor and their next-of-kin in the consent process.
2. Protect the integrity of the altruistic and voluntary donation and its utility as a public resource for the shared benefit of all.
3. Support sight restoration and ocular health for recipients.
4. Promote fair, equitable, and transparent allocation mechanisms.
5. Uphold the integrity of the custodian' s profession in all jurisdictions.
6. Develop high-quality services that promote ethical CTO management, traceability, and utility.
7. Develop local/national self-sufficient services.
8. Recognize and address the potential ethical, legal, and clinical implications of cross-border activities.
9. Ensure ethical practice and governance of research (nontherapeutic) requiring CTO.

CTO, cells, tissues, and organs.

CORNEAL TISSUE ALLOCATION

Taking into account the worldwide shortage of corneal tissues, the manner in which the available tissues are assigned is controversial because it is sometimes challenging to determine which conditions should be prioritized. For organ and tissue transplantation, each country regulates its own distribution; in some countries, this distribution is at the national level and in others at the regional or local level. Furthermore, each country must seek for covering its need for corneal tissue to achieve self-sufficiency.[10]

Both WHO in its ninth principle and the Global Alliance of Eye Bank Association in its fourth Barcelona principle state that organ and tissue distribution must be fair, equitable, transparent, and externally justified and in addition independent of gender, ethnicity, religion, and social or economic position.[5,6]

Based on these statements, the bioethics' principle that is at stake is *justice*. Therefore, prioritizing a patient can only be justified under circumstances in which there is a real and proven urgency or in a condition that is more acutely severed than the conditions presented by those patients who have been on the waiting list for longer. In the case of corneal tissue, this usually refers to acute corneal perforation or threatened

potential loss of the eye. Excluding that, allocation normally aligns with geographical criteria and time on the waiting list.

Another dilemma regarding tissue allocation arises when patients who do not reside in their country of origin require a corneal transplant. The Declaration of Istanbul[11] establishes that corneal transplantation for foreigners should be considered only when the needs of the country in question were already met, but requirements for a foreigner to be able to get a cornea vary greatly from country to country. Many countries require the patient to be a legal resident with a history of medical care in the country or a detailed referral from his/her country of origin that brings transparency to the process; other countries forbid them altogether.

In general terms, residents have priority over foreigners. However, although this may cause some controversy because it does not seem proper to deny tissue transplantation to a foreign patient, this action is not based on selfishness or exclusion of foreigners but rather is thought to stimulate countries to achieve self-sufficiency. This may help avoid unethical practices such transplant tourism and organ and tissue trafficking that may affect vulnerable populations.

TRANSPLANT TOURISM, TRAVEL FOR TRANSPLANTATION, AND TISSUE TRAFFICKING

When referring to transplant tourism, some terms need to be defined and differentiated to avoid confusion because the term "transplant tourism" is commonly—but incorrectly—used to refer to both legal and illegal transplants performed in a foreign country. In the recent 2018 edition of the Declaration of Istanbul,[11] different terms are recommended for naming these activities based on their legality. Hence, when a patient travels to another country and both surgery and tissue procurement are performed legally, the correct term to use is "travel for transplantation." The term "transplant tourism" should be reserved only for those cases in which the obtained tissue and/or the performed surgery are illegal and undermine the country's capacity to achieve self-sufficiency.

For indisputable reasons, transplant tourism violates the 4 basic principles of bioethics. It is illegal almost everywhere in the world and puts both the recipient and potential donors at risk from vulnerable populations of the country where it is performed. When a transplant is performed illegally, it is not usually performed under proper sanitary conditions nor with the appropriate technology, instruments, or infrastructure to guarantee safe and optimal outcomes, thus violating the bioethical principles of *beneficence* and *nonmaleficence*.

When the tissue is illegally obtained and without consent, it is called "tissue trafficking," which in addition to being a crime infringes the principle of *autonomy*. Moreover, it does not guarantee tissue quality, recipient safety, and above all, equality and fairness. Therefore, it also violates the principle of *justice*.[11]

With "travel for transplantation," the above conditions are usually not an issue because these surgeries are legally performed and are generally offered by recognized ophthalmic institutions. This modality is commonly used by people with the financial means to travel, who have difficulty in accessing a corneal transplant in their country of origin either because of the cost of the procedure or because tissues are unavailable. Thus, travel for transplantation is usually performed by countries where the available tissues surpass the number of performed corneal transplants or by countries where importation of foreign corneas is possible. It is important to consider whether travel for transplantation puts local vulnerable populations at risk and whether this practice may ultimately hinder the need for countries with a shortage of tissue or a lack of corneal specialists to create initiatives to achieve self-sufficiency.[10]

Under any of the mentioned transplantation circumstances, the patient does not live in the place where his/her transplant was performed, which puts the patient's follow-up and safety at risk during the postoperative period,[12] requiring the patient to assume the responsibility for finding a trained ophthalmologist at his place of residence who is willing to follow him postoperatively. This situation is far from ideal or adequate for both patient and medical practitioner. It violates both *beneficence* and *nonmaleficence* principles of bioethics because corneal transplantation is a delicate surgery that requires close monitoring and proper management of possible complications that may have devastating consequences. In addition, for the eye banks supplying these corneas, follow-up data of the transplanted tissue—which are fundamental for eye bank self-assessment and continuous quality improvement—are challenging and the follow-up is seldom carried out in detriment of transplant safety, transparency, and traceability.

CORNEAL TISSUE EXPORTATION AND IMPORTATION

Currently, there are 116 countries actively performing corneal transplants. Only 82 of these countries procure corneas, which has led to exportation and importation of corneal tissues. Gain et al[2] recently published the results of a Global Survey of Corneal Transplantation and Eye Banking and reported that 11% of corneal transplants in the world are performed using imported corneas and 8% of the procured corneas are exported, primarily from the United States, Sri Lanka, and Italy.

The international mobilization of corneal tissues from one country to another has both positive and negative implications. On the positive side, it allows countries with an excess of procured corneas to export these tissues, satisfying the needs of countries where tissue procurement is lacking or where there is shortage of corneas. However, the countries may also have negative implications: First, it is important to understand that for exportation/importation of tissues to occur, the legislation of the two countries must be compatible, since countries may have different economic, technological, and cultural variables that must be respected according to beneficence and non-maleficence principles. Moreover, there is always a cost that comes with the import and export of corneal tissues that is usually covered by the patient. This generates financial inequality in the access to transplantation.

In addition, as described in the Declaration of Istanbul[11] and in the previously mentioned WHO Principles of Transplantation[5] and Barcelona Principles,[6] it should always be kept in mind that each country must work constantly to achieve self-sufficiency; importing tissue may inhibit the

development of eye banks and procurement systems that increase the availability of local corneas. The term "self-sufficiency" refers to the relationship between the number of required corneas and national/regional procured available corneas, a ratio that can often be difficult to determine because there may be a large number of people without access to the healthcare system and in need of corneal transplantation. However, because these patients have no access to medical attention, corneas cannot be ordered for them, and, therefore, statistical data may indicate the existence of a "surplus" donor tissues inaccurately. In such cases, tissue exportation may be beneficial for the exporting eye banks, but it does not promote an increase in local population coverage.

It is also important to recognize that when tissues do not come from local eye banks, the traceability for evaluating quality, safety, and efficacy—which are extremely important activities for proper functioning of the eye bank and for recipient safety—is considerably more difficult.[10]

Finally, one must also consider that when signed consent for donation is provided, it is commonly assumed that the tissue will be given to a person from the same country. For this reason, if there is a possibility that donated tissue might be exported, an explicit authorization for exportation should be included in the consent form. This is important to avoid violation of the bioethical principle of *autonomy*.

FOR-PROFIT EYE BANKING

Most eye banks are *nonprofit* entities because their activities are based on the altruistic act of tissue donation. However, some eye banks have recently reorganized as *for-profit* entities, a change that has generated widespread controversy and criticism as being contradictory to a free and selfless act, when the eye bank activity is predicated on the generation of resources and profit.

Defenders of the for-profit eye banking paradigm defend this model, arguing that the generation of resources especially through allied for-profit industry ensures the operation of the eye bank and facilitates ophthalmic research and the development and acquisition of new technology to fight blindness.[13] However, although the generation of resources for these purposes sounds reasonable and attractive, the implementation of for-profit models can easily lead to the management of eye banks just like other business, compromising the altruistic essence of the donation act.[14]

This relatively new eye bank model can lead to unethical practices, primarily compromising the bioethical principle of *justice*, because access to transplantation may be more dependent on the financial status of the patient. In addition, it is important that donors be made aware that the donated tissue is being used by a for-profit entity because it is almost always assumed by the deceased patient or his family that the donated cornea is a humanitarian gift, not an object of trade (a commodity).[15] If this were not mentioned to the donor or the donor's family, it would also affect the principle of *autonomy*, a betrayal of the common social contract norm.

Although this is a relatively recent development in the community of eye banks, multiple unanswered questions remain. For example, it has been suggested that despite the growth and excellent performance of some eye banks in the United States, in recent years, many other local eye banks have disappeared probably because of the increasing costs and the competition between eye banks. This competition is uneven when different eye bank models are taken into account (large eye banks, local eye banks, nonprofit eye banks, and for-profit eye banks). Therefore, the Eye Bank Association of America board has endorsed the Barcelona Principles and recently published a position statement in which it is stated that donation operation is largely based on cooperation and shared expertise of many participants: hospitals, eye banks, tissue banks and organ procurement organizations, and alliances between parties that affect the equitable distribution of corneal tissues and affect local eye banks should be avoided.[16]

The for-profit eye bank model may facilitate unethical practices and great caution needs to be taken in their

TABLE 3. Summary: Dilemmas and Recommendations to Avoid Unethical Practices

Dilemma	Recommendations to Avoid Unethical Practices
Informed consent for organ and tissue donation	Each country must individually evaluate the cultural variables of its population and establish the most appropriate consent type to avoid jeopardizing the cultural principles of its population while simultaneously favoring and promoting tissue donation.
Corneal tissue allocation	Each country must seek to cover its need for corneal tissue to achieve self-sufficiency and a fair, equitable, and transparent distribution independent of gender, ethnicity, religion, and social or economic position must be guaranteed.
Transplant tourism, travel for transplantation, and tissue trafficking	Each country must evaluate whether travel for transplantation puts local vulnerable populations at risk and develop strategies to avoid this damage. Transplant tourism and tissue trafficking are illegal and must be punished by law.
Corneal tissue exportation and importation	Each country must evaluate according to its level of self-sufficiency the pros and cons of allowing corneal tissue exportation and/or importation avoiding that these activities affect the local development to achieve self-sufficiency.
For-profit eye banking	The for-profit eye bank model may facilitate unethical practices, and great caution needs to be taken in its implementation. Countries with developing eye banking and corneal transplantation programs should aspire to become self-sufficient systems by strengthening their public programs and access to transplantation for all sectors of the population and by avoiding for-profit schemes.

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CONCLUSION

Although attempts have been made to create bioethical guidelines to avoid unethical practices in the field of corneal transplantation, there is a great lack of scientific evidence, so it is important and necessary to promote nonclinical research in this field.

The information presented in this article summarizes the available evidence about the aforementioned dilemmas, in addition to our analysis and interpretation of how existing ethical guidelines could be applied to current ethical issues (Table 3). It is important to mention that although the discussed points are valid globally, the authors' nationality could influence some of the presented interpretations.

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