REVIEW ARTICLE

Ethical, clinical and technical analysis of face transplantation

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Abstract:

Introduction: Face transplants constitute a new reality in reconstructive surgery, allowing a new perspective on the restoration of complex facial defects and the possible complications resulting from this procedure.¹ Methods: The purpose of this work is to perform a bibliographic review on the techniques used to perform face transplantation, their difficulties of execution, possible post-operative clinical repercussions and the bioethics of face transplantation. Results: Since 2005 more than 30 face transplants have been performed in the world, the patients submitted to this procedure showed a good sensory recovery, successful motor and functional recovery slower and variable. Regarding the aesthetic and psychological issues, all patients have reported improvements. However, acute rejection is common to solid organ transplants and allograft, while chronic rejection has not been reported in even one face transplant case.¹ Discussion: One of the controversial aspects of face transplantation is that it is a high-risk procedure for a non-life threatening condition; lifelong use of immunosuppressants; and complications affecting the individual after transplantation. Conclusion: Therefore, face transplantation presents itself as a therapeutic option, which applies to a very limited number of patients, in which conventional reconstructive techniques have not been successful, which have brought functional, psychological and social comorbidities to the transplanted patient.¹ Keywords: Face transplantation; Bioethics; "Surgical Procedures, Operative"; "Elective Surgical Procedures"; "Contraindications, Procedure."

INTRODUCTION

According to Pedro Augusto Amoroso de Passos Canão (2014), face transplants emerged as a new treatment perspective for complex three-dimensional facial deformities fourteen years ago.² The first partial face transplant was performed in 2005 by Devauchelle and Dubernard's team in France, who restored a patient's nose, lips, cheek and chin after an accidental attack by their pet dog.

Currently, about fifty-two face transplants have been performed in the world, including a quarter performed in France. According to the literature, face transplantation is titled in composite tissue allotransplantation, which consists of a set of nonvital tissues with structural, functional and aesthetic units, which may consist of tissues of epidermal or mesodermic origin, namely dermis, nails, hair, nerves, vessels, muscles, tendons, ligaments, bone, cartilage, connective tissue and/or fat.^{3,4-5} Nowadays, face, hand, abdominal wall, flexor tendons, knee, nerves, larynx, penis and tongue transplants have been performed.6 Thus, facial transplantation is a surgical procedure in which some structures of one person's face are transplanted to another, allowing the replacement of similar tissue in fewer stages than conventional techniques, with greater similarity in color and texture of the adjacent skin, eliminating morbidity, especially in reconstructions of large defects.7

According to Morris (2006), facial transplantation can be performed in a partial manner, which is the transplantation of the nose, lips, mandible, maxilla and variable amounts of adjacent tissue, including skin, mucosa, muscles, and sensory and motor nerve neurorrhaphies for the return of function, that is, neurorrhaphy consists of restoring the connection of a severed nerve. And finally, total transplantation, which is the transplantation of the nose, ears or eyelids, depending on the needs of the recipient.⁸

However, the surgical procedure of face transplantation in the recipient begins with the anastomosis of the main trunks of the external carotid artery and internal Jugular vein and the nerves (thickness 2 to 4 mm) infra and supra orbital, mentual and their branches, trigeminal, auricular and facial, and after the anastomosis is performed coaptation of nerves.

In short, facial transplantation is limited to severe lesions involving at least 25% of the facial surface area or the loss of one or more facial units, particularly those of the middle portion of the face, when conventional procedures are inadequate.^{7,9}

Therefore, this review aims to present the ethical, clinical and technical aspects of facial transplantation.

METHODS

The bibliographic research was carried out in relevant databases regarding the indexation of scientific publications: PubMed, Lilacs and Scoups, Web of Science.

In the PubMed database 189 publications were found with the keywords "Transplantation and Anatomy", "Facial Transplantation and Ethical Analysis" and "Surgical Procedures and Clinics", in the Lilacs database 58 publications were found with the keyword "Facial Transplantation and Principle"; 333 publications with the keyword "Facial Transplantation" were found in the Scopus database and 379 publications with the keyword "Facial Transplantation" were found in the Web of Science database with the topic "Transplantation Method Technical Surgical Procedures and "Facial Transplantation Clinics".

Articles of clinical aspects were selected for analysis according to inclusion criteria, excluding articles from experimental works.

RESULTS

The results of this study were based on a documental review of the literature with the subjective selection of the author looking for articles and productions related to the ethical, clinical and technical aspects of face transplantation (Table 1).

ETHICAL CONSIDERATIONS:

Among the ethical questions of face transplantation we can cite: the identity of the donor, that is, the set of characteristics and traits proper to the individual;10 the awareness that the person has of himself/herself and that makes him/her different from the others;¹⁰ the loss of the characteristics of the donor, because of the prosthetic rehabilitation, with psychological commitment of the relatives and loss of the traits and characteristics of the donor;¹⁰ loss of personal identity on the part of the recipient, causing psychological and psychic problems in the transplanted patient, that is, in the ethical debate of facial transplants, 73 publications contrary to transplants have been observed, in favor or not, in the articles

| Team | Receiver- Gender / Age | Recommendation | Allograft | Current state |
|--|------------------------|--|---|----------------------------------|
| Devauchelle y Dubernard Amiens, France November 2005 | 38 / F | Trauma Bite of dog | Pectoral muscles, oral mucosa and nasal, nose, bilateral facial ves- sels, zygomatic, buccal and mandibular branches facial nerve, infra- orbital nerves and mentonian | alive |
| Guo Xian, China April 2006 | 30 / M | Trauma Bear Attack | Parotid, partial oral mucosa, partial masseter, zygomatic archparcial, floor and side wall of orbit, maxillary sinus, upper lip, nose, nasal bone | alive Dead after 27 months |
| Lantieri Crete, France January 2007 | 29 / M | Birth defect Neurofibromas plexiform bilateral | Parotid, nose, oral mucosa, nerves facial, infraorbital and mentonian, bilateral external carotid arteries, thyrolinguofacial veins | Live |
| Siemionow Cleveland, USA December 2008 | 45 / F | Trauma Gun Injury of fire | Nose, lower eyelids, lip upper, infraorbital floor, bilateral zygoma, anterior maxilla with alveoli, anterior hard palate, parotid arteries, bilateral facial arteries, external jugular vein, facial vein posterior left, facial nerves bilateral | Live |
| Lantieri Crete, France March 2009 | 27 / M | Trauma Gun Injury of fire | Parotid glands, masseter, mucosa oral, lips, ment, nose, jaw anterior, anterior sinus walls jaws, external carotid artery, external jugular vein, trunk thyrolinguofacial, facial, supra and infraorbital | Live |
| Lantieri Crete, France April 2009 | 37 / M | Burn | Scalp, ear pavilions, parotid glands, masseter, mucosa oral, upper and lower lips, artery external carotid artery, external jugular vein, thyrolinguofacial trunk, facial nerves, infraorbital and mentonian | Dead after 2 months |
| Pohamac Boston, USA April 2009 | 59 / M | Trauma Burn electrical | Mimetic muscles of the face, lip upper, nose, jaw, hard palate, oral mucosa, bilateral facial arteries, left facial vein, jugular vein right external, facial and infraorbital | Live |
| Lantieri Crete, France August 2009 | 33 / M | Trauma Gun Injury of fire | Lower 2/3 of the nose, muscles perioral, maxilla, oral mucosa | Live |
| Burrows Valence, Spain August 2009 | 42 / M | Radiotherapy | Mandible (from right angle to left condyle), tongue, floor of the mouth, hyoid bone, muscles suprahioideus, parotid glands, submaxillary and sublingual arteries facial, lingual, inner jaw left, common and internal carotids and external and internal jugular veins and tireolinguals | Live |
| Devauchelle y Dubernard Amiens, France November 2009 | 27 / M | Burn | Maxilla, mandible, lower lip, floor of the mouth and chin | Live |
| Gomez-Cia Seville, Spain January 2010 | 35 / M | Birth defect Neuro- fibromas plexiform bilateral | Lips, oral mucosa, muscles perioral, buccinators, glands parotid, facial nerves, mentonian and infraorbital, carotid arteries common, jugular veins, mandible previous | Live |
| Barret Barcelona, Spain April 2010 | 31 / M | Trauma Gun Injury of fire | Facial muscles, eyelids, ducts lacrimal, hard palate, floor of the mou- th, lips, oral mucosa, mandible, maxilla, 2/3 of the zygoma, nose, arteries external carotid arteries, jugular veins external, supraorbital nerves, infraorbital and mandibular and branches frontal, buccal and zygomatic nerve facial | Live |
| Barret Barcelona, Spain April 2010 Lantieri Crete, France July 2010 | 35 / M | Birth defect Neuro- fibromas plexiform bilateral | Facial muscles, eyelids, glands and tear ducts, nose, lips, ment, paro- tid glands, cartilage septal | Live |
| Pohamac Boston, USA March 2011 | 30 / M | Burn | Nose, lips, facial muscles, eyelids, parotid, septal cartilage | Live |
| Lantieri Crete, France April 2011 | 45 / M | Trauma Lesão por arma de fogo | Nariz, lábios, músculos faciais, mucosa oral, maxila e mandíbula com dentes | Live |

Table 1. Summary of the characteristics of facial transplants performed until July 2013 (adapted from Shanmugarajah K, et al. Clinical outcomes of facial transplantation: A review. International Journal of Surgery 2011 Oct; 9: 600-7.

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| Lantieri Crete, France April 2011 | 41 / M | Trauma Gun Injury of fire | Nose, lips, facial muscles, mucosa oral, maxilla and mandible with teeth | Live |
|---|--------|-----------------------------|---|-------------------|
| Pomahac Boston, USA April 2011 | 30 / M | Burn | Facial muscles, nose, eyelids, lips, oral mucosa, septal cartilage | Live |
| Pomahac Boston, USA May 2011 | 55 / F | Trauma Attack by chimpanzee | Facial muscles, eyelids, nose, lips, oral mucosa, maxilla with teeth, hard palate | Live |
| Ozkan Antalya, Turkey January 2012 | 19 / M | Burn | Total osteomyocutaneous | Live |
| Rodriguez Baltimore, USA March 2012 | 37 / M | Burn | No information | No information |

published on the subject. The frequency of opposites to facial transplants increased to 100% in 2008, due to a change in identity and psychological effects, followed by immunosuppression by 69.1%, risks and benefits by 64.8%; immunosuppression and identity appeared both before and after the first transplant. Facial transplantation hurts personal identity and the principle that each individual is unique, because according to the literature, after the serial facial transplant it is possible to identify the donor in 2.6% of the cases and the recipient in 66% of the cases. Other ethical problems are: advertising, i.e., invasion of privacy through media vehicles, which expose information about the identity of the donor and recipient, and the latter can react with great psychological stress; obtaining the face for donation, according to Masquelet $(2007)^{11}$ there are three main characteristics of a face: uniqueness, if you identify the individual singularly through his or her face; expressiveness, the face transmits emotions and internal attitudes, and recent research has shown that the expression of the face can have an influence on emotions; foundation of intersubjectivity, this is, the relationship between individual and individual.

In this way, autonomy can be harmed, because the choice is not entirely free, that is, the risks are still unknown and thus it is not possible to explain to the patient the real risks for this procedure, so a high risk procedure is offered for a condition in which the patient is not in danger of life.

Therefore, the issue of face transplantation has fragile boundaries between ethics in research, clinical bioethics and minority ethics, especially when aspects related to the protection of research participants or surgeries, such as who would be responsible for the costs of the research or procedure or how immunosuppressants would be guaranteed throughout life, how the waiting list for transplants would be constructed and what the criteria and who would make this call, since face transplantation encompasses particularities regarding ethnicity, blood type, gender, race, facial morphological aspects.¹²

Clinical Considerations:

The following drugs have been used in facial transplants in the scheme Immunosuppressive; Induction: Polyclonal Antibodies, Tacrolimus, Mofetil Mycophenolate, Prednisolone, Methylprednisolone, Interleukin 2 monoclonal and Basiliximab Antibodies;^{7,13} and for Maintenance: Prednisolone, Mofetil Mycophenolate and Tacrolimus.^{7,13,14}

Thus, the continuous use of immunosuppressants causes an increase in the index of pathologies such as: diabetes, hypertension, infections, renal toxicity, disorders of blood lipid levels, cushing syndrome, guillain barre syndrome and malignant neoplasms.

According to Rodrigues (2019),15 acute rejection occurred in 10% of the cases reported in the literature, already chronic rejection occurred in 30 to 50% of the cases in a period of 2 to 5 years after face transplantation, so it was possible to conclude based on this survey that graft recipients are susceptible to viral infections (cytomegalovirus) and fungal infections.

Other clinical consequences of face transplantation are: 50% of transplant patients develop squamous cell cancer; 2% of transplanted face recipients have post transplant lymphoproliferative disease that varies in severity from a type of glandular fever to highly malignant lymphoma syndrome.¹⁶

However, according to Özel (2015), dental disease represents a potential risk for infection in face transplanted patients.

Therefore, all transplanted patients have experienced metabolic, hematological complications

resulting from immunosuppression. These include the establishment of Diabetes Mellitus, Transient Acute Steroid-induced Confusion Syndrome, Early Transient Leukopenia, Anemia Microangiopathic Hemolytics with Thrombocytopenia, Hypertension and Acute Kidney Failure.^{7,13,14}

Technical and Anatomical Considerations:

Among the technical questions of face transplantation we can mention: the difficult task of identifying vascular pedicles and nerves in the face due to anatomy distortion; fibrosis and tissue retraction.

According to Masquelet (2007),¹¹ dissection of the recipient's face is difficult, because the tissue underlying the scar is very vascularized and overflows copiously, during the excision of the scar; moreover the interrupted anatomy makes it difficult to identify vital structures, such as nerves, veins and muscles, which are severely damaged by atrophy or hypertrophy, either by burns, trauma, among other incidents.¹¹

DISCUSSION

Nowadays, facial transplantation is a therapeutic reality, applicable to a very restricted number of patients, whose functional, psychological and social morbidity of the disfigurement has not been diminished through the current reconstructive techniques and overlaps with the risks of a lifetime immunosuppression.^{7,18,19}

Thus, the main obstacle to the acceptance of facial transplantation as a therapeutic action is the exposure of patients to immunosuppression for the rest of their lives¹, which is considered a high risk procedure for a non-life threatening condition.

However, facial transplantation is generally accepted by patients, since they wish to have a less disfigured face, but, according to the author, there are difficulties in reconstituting their new identity, since the face of another person has been transplanted over their bone frame, as well as the acceptance of this new face by their social network (family and friends), revealing a series of complexities generated from the procedure.

According to Katia Torres,¹⁰ the countries that performed the face transplant were able to understand that facial transplantation is a viable option for reconstruction of severe facial injuries, however, it is considered an experimental procedure with high risk of complications, high costs, involves multidisciplinary team and the need for lifetime use of immunosuppressants. So far, it is indicated for a small group of patients¹⁰. In short, according to Devauchelle, more than 30 patients have undergone facial transplantation worldwide, and some of these individuals are close to a decade after transplantation. A careful analysis of the causes of morbidity and mortality of these patients in the future will allow a better understanding of the natural evolution of this specific type of composite tissue transplantation. A better understanding of several factors, such as immune compatibility between the recipient and the donor, the relationship between the immunosuppressive drugs used in these patients and the development of malignant neoplasms and other chronic diseases, and the evaluation of the quality of life after facial transplantation will be central to establishing more precise criteria for indicating the procedure.

CONCLUSION:

Therefore, Facial Transplantation has been performed in cases with great facial deformity and, despite the positive results cited, there are reports in the literature of difficulties in performing emotional facial expression due to neuro musculoskeletal facial lesions, consequently affecting the recognition of facial expressions.

In short, facial transplantation is generally accepted by patients since they intend to provide the patient with a face with less deformity. However, there are difficulties on the part of individuals in reconstituting their new identity, since the face of another person has been transplanted into their bone structure, as well as the acceptance of this new face by their social network (family and friends), revealing a series of complexities generated, which involve ethical, bioethical and psychosocial issues.

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