REVIEW ARTICLE
Surgery

JKMS

http://dx.doi.org/10.3346/jkms.2015.30.6.669 • J Korean Med Sci 2015; 30: 669-672

Facial Transplantation Surgery Introduction

Seok-Chan Eun

Department of Plastic and Reconstructive Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea

Received: 15 January 2014
Accepted: 24 June 2014

Address for Correspondence:
Seok-Chan Eun, MD
Department of Plastic and Reconstructive Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 463-707, Korea
Tel: +82.31-787-7223, Fax: +82.31-787-4055
E-mail: sceun@snubh.org

Funding: This work was supported by the National Research Foundation 2012R1A1A2021731, of Ministry of Science, ICT and Future Planning, Korean Government.

Severely disfiguring facial injuries can have a devastating impact on the patient's quality of life. During the past decade, vascularized facial allotransplantation has progressed from an experimental possibility to a clinical reality in the fields of disease, trauma, and congenital malformations. This technique may now be considered a viable option for repairing complex craniofacial defects for which the results of autologous reconstruction remain suboptimal. Vascularized facial allotransplantation permits optimal anatomical reconstruction and provides desired functional, esthetic, and psychosocial benefits that are far superior to those achieved with conventional methods. Along with dramatic improvements in their functional statuses, patients regain the ability to make facial expressions such as smiling and to perform various functions such as smelling, eating, drinking, and speaking. The ideas in the 1997 movie "Face/Off" have now been realized in the clinical field. The objective of this article is to introduce this new surgical field, provide a basis for examining the status of the field of face transplantation, and stimulate and enhance facial transplantation studies in Korea.

Keywords: Facial Transplantation; Facial Reconstruction; Surgery; Surgical Flaps

INTRODUCTION

The history of facial reconstructive surgery has progressed slowly and naturally and is punctuated by highlights from sudden profound changes. Facial transplantation has only recently become possible through the discovery of innovative drugs and the courage of innovative surgeons. Facial allotransplantation is a new surgical technique that could be considered a new paradigm in facial reconstruction. Facial transplantation is among the most prominent areas of composite tissue allotransplantation (CTA) or vascular composite allograft (VCA), along with hand transplantation. Since the first facial allograft transplantation was reported in France in 2005, 25 cases have been performed worldwide with encouraging results (1). As with any novel and previously developed procedure, many questions have been posed and many concerns have emerged. For example, what is an acceptable risk-benefit ratio, and what are the indications for transplantation? Today, the number of facial transplantations remains small; however, the total number of allograft recipients, including those receiving hands, faces, bones, joints, and abdominal walls, has surpassed 150, and more than 10 yr of follow-up data are available for some of these patients (2).

INDICATIONS FOR FACIAL TRANSPLANTATION

The indications for facial transplantation require considerable discussion. Although many superb techniques and solutions exist, all reconstructive surgeons agree that specific unmet needs and limitations also exist. Bullet injuries and severe burn trauma seem to be definite and primary indications for transplantation, as these injuries include severe skin damage, tissue loss, and disfigurement (3). However, reconstructive options, multiple conventional surgical reconstructive procedures, and even very sophisticated supermicrosurgical techniques cannot facilitate recovery and thus reveal the limits of autologous tissue. Facial composite tissue allotransplantation is the best currently available option for such cases. Full or partial facial transplantation can be selected as the surgical strategy according to the anatomic deficiencies.

Inequitable patient characteristics such as immunosensitization or mental illness can present hurdles to such surgeries (4). The transplantation team should thoroughly examine the previous medical histories of blood transfusions or cadaveric skin grafts. Human leukocyte antigen screening is mandatory for the detection of presensitized patients. Psychological issues such as major depressive, psychotic, cognitive, and behavioral disorders represent another contraindication because of problems with a postoperative loss of control and cooperation. A comprehensive psychological evaluation should be conducted prior to transplantation surgery. Postoperative immune therapy is associated with many harmful complications such as renal toxicity, malignancy, diabetes, and metabolic disorders. Ultimately, patients should decide whether the benefits of facial transplantation outweigh the risks of surgery and immunosuppression. Each practicing physician has the duty and responsibility to provide his/her patients with the best treatment options available,

pISSN 1011-8934
eISSN 1598-6357

and patients should be allowed to decide for themselves whether to accept these risks and proceed with CTA. In most Asian countries, patients and their families may experience feelings of guilt regarding the procedure of facial harvesting from the donor patient. This guilt acts as another major hurdle that is not as prominent in the USA and European countries. After donor facial harvesting is completed, a prefabricated facial mask should be applied to the facial deficit area (5). The recipient might experience problems with identity because of the expected transformation resulting from the transplantation surgery. A follow-up psychological consultation should be conducted.

SURGICAL PLAN

Anesthesia for the long facial transplantation procedure requires advanced planning for airway management, vascular access, anesthetic technique, and fluid management. The preparation and grafting phases are highly hemorrhagic (> 1 blood volume) and therefore massive transfusion is required (6). During facial allograft transplantation, the anesthesiologist must be prepared for a long period of anesthesia with rapid blood loss following graft reperfusion. Severe postoperative graft edema is present in most patients. In the intensive care unit (ICU), most patients encounter complications such as renal insufficiency, acute respiratory distress syndrome, and jugular thrombosis. Opportunistic bacterial infections are also an issue in these highly immunosuppressed patients during the postoperative period. The anesthesia team should be involved in the early planning phase and should have access to the donor's detailed medical history; alternative anticoagulation treatments for the donor and recipient have been suggested to avoid possible complications.

Craniofacial and orthognathic considerations should be emphasized with respect to functional effects when planning and executing facial transplants that include both bone and soft tissue elements. These steps are taken to restore the normal anatomy by fixing the face in a proper relationship with the skull base. Traditional orthognathic planning via cephalometric parameters yields the most anatomical restoration of occlusion, speech, and airway function (7). Typical candidates have extremely complex vascular anatomies due to severe injury and/or multiple prior reconstructive attempts; therefore, each procedure is uniquely determined according to the candidate's defects and vascular anatomy. CT angiography vascular mapping has demonstrated the clinical relevance of imaging, the angiosome concept, and noninvasive key vessel delineation as well as the current controversies related to the vascular anastomoses. The facial artery is the main arterial supply to the facial skin envelope and serves as the main pedicle for a number of facial flaps, including the facial transplant graft (8). Facial arterial dominance in the facial blood supply is common but unpredictable. A careful vascular workup prior to facial transplantation and a unipedicled flap procedure are therefore essential. Previously, surgical planning software was used to create specific facial defects (Mandibular, Midface, or Large) in recipient models, followed by restoration using allografts extracted from the donor models.

POSTOPERATIVE CARE AND LONG-TERM RESULTS

Most immunosuppression protocols are triple-therapy regimens, which comprise tacrolimus (FK-506), mycophenolate mofetil, and prednisolone. The initial functional and aesthetic outcomes have been very encouraging, and good motor and sensory recovery and improved important facial functions have been observed. Phonation recovery has been impressive and has allowed patients to talk, smile, chew, swallow, and blow normally (9). As predicted, episodes of acute rejection have been common but are easily controlled with increased systemic immunosuppression treatments. All candidates are fully informed with regard to the risks of cytomegalovirus/infection transmission and the institution of aggressive anti-viral, bacterial, and fungal prophylaxis. Despite some long-term complications, which are similar to the complications reported after solid organ transplantation, the patients have been generally satisfied with their new faces, and the results have led to the recovery of some social interactions. The psychological improvements have been remarkable and have resulted in the reintegration of patients into the outside world, social networks, and even the workplace (10). Cellular therapy in the context of transplantation can significantly benefit the allograft survival and reduce the healing time. The molecular characterizations of these cells and the mechanisms associated with their participation in allograft acceptance and rejection will contribute to the future of modern transplantology.

FACIAL TRANSPLANTATION RESEARCH IN KOREA

Anatomical research, immunosuppression, and immune tolerance are important topics in CTA research. Before initiating human facial transplantation in any country, the preclinical laboratory results should be determined and animal surgeries performed for 2 reasons: first, to develop an immune tolerance strategy and second, to provide surgical simulation opportunities. Because these fields do not target life-saving organs, there have been many debates regarding immunosuppression therapy. However, without this presurgical preparation, it is difficult to obtain appreciation and compassion from other scientists and the population. Review articles about transplantation immunology as well as a few research papers about topical immunosuppressive agents, immune tolerance strategies that incorporate cell culture, and pretreatments have been published (11-13). Additionally, a few preclinical animal allotransplantation

http://dx.doi.org/10.3346/jkms.2015.30.6.669

studies using rat, rabbit, dog, and cadaver models have been published (14-19). Surgical simulation opportunities in medium to large-sized animals are very important for transplantation surgeons. Although the facial transplantation technique has been described as similar to the currently used surgical methods, this is not true in reality. Experience with large animal transplantation research can lead to an understanding of the considerable existing differences.

FACIAL TRANSPLANTATION PROGRAM ESTABLISHMENT IN KOREA

In any country, it is very difficult and challenging to establish a facial transplantation program. The development of such a program in Korea would involve a successful collaboration between a strong project leader with a vested clinical research interest, a multidisciplinary team of investigators, an Institutional Review Board (IRB), the Korean Network For Organ Sharing (KONOS), and a special fundraiser (20) as this program far exceeds the presently occurring tasks in plastic surgery departments. There had been intense debate regarding the risks and benefits of this type of experimental surgery prior to the start of the facial transplant program. A sound research protocol, solid infrastructure, expert personnel, and adequate funding will be required before launching human applications. To date, only a few active facial transplantation programs have been implemented worldwide in areas with growing interests. The members of the facial transplantation team responsible for carrying out the protocol will include a team leader, a program manager/coordinator, clinical and rehabilitation specialists, social workers, bioethicists, nurses, and administrative staff. The demonstrated experience of this team indicates that patients will receive optimal care both before and after facial transplantation via the collaborations, creativity, and unique multidisciplinary approaches of the members. The establishment of this process can be slow and lengthy; therefore, the project leader must strive to maintain the enthusiasm and continue to drive the project forward (21).

Many Korean surgeons expected that this program would begin at an earlier time point; however, there remain a few hurdles to overcome. First, facial transplantation should be categorized as a new medical technology and protected under the organ transplantation law with respect to facial harvesting from a brain-dead patient. Second, during the donor harvest, close and intimate coordination is necessary between the teams harvesting the face and those harvesting other organs such as the heart, liver, kidney, and cornea. The related situations and circumstances differ between countries; therefore, each program must find its own way. The risk/benefit balance must be weighed carefully by each program and individually for each patient. Our duty as doctors and scientists is to collect and report the informative data and knowledge needed to develop a social consensus regarding these important issues. This will only be possible through candid discussions and presentations of the strategic protocols among many interested stakeholders.

FACIAL TRANSPLANTATION COSTS

The costs associated with facial transplantation are higher than those associated with heart or any other solid organ transplantation and are 2-fold higher than the costs associated with liver transplantation (22). This cost might decrease as the surgical teams gain experience, which might also reduce the requirement for postoperative intensive care and the overall hospital stay durations. The 2 largest areas of cost utilization are surgery and nursing, followed by anesthesia and pharmacy. The cost of facial transplantation is similar to that of multiple conventional reconstructions (23). Although the cost of facial transplantation is considerable, the alleviation of psychological and physiological suffering, exceptional functional recovery, and fulfillment of long-lasting hopes for social reintegration may be priceless. The overall early outcomes of the facial transplant program have been generally more positive than many had predicted. Dissemination of the outcomes and ongoing refinement of the process might eventually allow facial transplantation to become a first-line reconstructive option for patients with extensive facial disfigurements.

CONCLUSION

Facial transplantation has the unique potential to restore the facial form and function in patients with severe facial defects. This procedure represents the most comprehensive type of transplantation performed to date. To effectively address this challenging surgery, a comprehensive multidisciplinary approach should be devised. The establishment of a facial transplantation program is complicated by multiple problems concerning the various involved medical fields, administration, society, ethics, and laws; however, if we cooperate, this paradigm change in facial reconstruction can deliver new hope to the few patients with no other alternatives. The establishment strategy involves the foundation of a basic science laboratory, the cultivation of a supportive institutional clinical environment, and the innovative application of technologies. Patients should be extensively educated about the risks and benefits of facial transplantation and then allowed to act as the primary decision-makers. Improving patients' quality of life is a major goal of plastic surgery, and facial transplantation can help us to accomplish this goal.

DISCLOSURE

The author has no conflicts of interest to disclose.

ORCID

Seok-Chan Eun *http://orcid.org/0000-0003-4372-6955*

REFERENCES

1. Siemionow M, Ozturk C. *Face transplantation: outcomes, concerns, controversies, and future directions. J Craniofac Surg 2012; 23: 254-9.*
2. Murphy BD, Zuker RM, Borschel GH. *Vascularized composite allotransplantation: an update on medical and surgical progress and remaining challenges. J Plast Reconstr Aesthet Surg 2013; 66: 1449-55.*
3. Siemionow M. *Impact of reconstructive transplantation on the future of plastic and reconstructive surgery. Clin Plast Surg 2012; 39: 425-34.*
4. Pomahac B, Diaz-Siso JR, Bueno EM. *Evolution of indications for facial transplantation. J Plast Reconstr Aesthet Surg 2011; 64: 1410-6.*
5. Lantieri L. *Face transplant: a paradigm change in facial reconstruction. J Craniofac Surg 2012; 23: 250-3.*
6. Sedaghati-nia A, Gilton A, Liger C, Binhas M, Cook F, Ait-Mammar B, Scherrer E, Hivelin M, Lantieri L, Marty J, et al. *Anaesthesia and intensive care management of face transplantation. Br J Anaesth 2013; 111: 600-6.*
7. Gordon CR, Susarla SM, Peacock ZS, Kaban LB, Yaremchuk MJ. *Le Fort-based maxillofacial transplantation: current state of the art and a refined technique using orthognathic applications. J Craniofac Surg 2012; 23: 81-7.*
8. Lohn JW, Penn JW, Norton J, Butler PE. *The course and variation of the facial artery and vein: implications for facial transplantation and facial surgery. Ann Plast Surg 2011; 67: 184-8.*
9. Shanmugarajah K, Hettiaratchy S, Clarke A, Butler PE. *Clinical outcomes of facial transplantation: a review. Int J Surg 2011; 9: 600-7.*
10. Petruzzo P, Kanitakis J, Badet L, Pialat JB, Boutroy S, Charpulat R, Mouly J, Gazarian A, Lanzetta M, Brunet M, et al. *Long-term follow-up in composite tissue allotransplantation: in-depth study of five (hand and face) recipients. Am J Transplant 2011; 11: 808-16.*
11. Eun SC. *Composite tissue allotransplantation immunology. Arch Plast Surg 2013; 40: 141-53.*
12. Kim YE, Eun SC. *Effect of FK506 ointment (Protopic) on rat skin allograft model. Transplant Proc 2014; 46: 1222-5.*
13. Eun SC, Baek RM, Park CG. *Prolongation of the rat composite tissue allograft survival by the combination of tolerogenic immature dendritic cells and short-term treatment with FK506. Transplant Proc 2013; 45: 1792-6.*
14. Jeon YR, Hong JW, Kim YS, Roh TS, Lew DH, Rah DK. *Experimental hind limb & inguinal-femur osteocutaneous flap model in rats for composite tissue transplantation. J Korean Burn Soc 2011; 14: 85-92.*
15. Eun SC, Baek RM. *Rat hindlimb allotransplantation with short-term immune suppressants and dendritic cell pretreatment. J Korean Soc Microsurg 2012; 21: 34-40.*
16. Eun SC. *Skin allograft using donor antigen-pulsed dendritic cell therapy. J Korean Burn Soc 2012; 15: 127-30.*
17. Baek RM, Eun SC, Heo CY, Chang H. *Experimental facial transplantation surgery. J Craniofac Surg 2010; 21: 648-51.*
18. Lee KM, Eun SC. *Experimental canine facial transplantation. Transplant Proc 2014; 46: 1208-11.*
19. Kim CW, Do ER, Kim HT. *A new facial composite flap model(panorama facial flap) with sensory and motor nerve from cadaver study for facial transplantation. J Korean Cleft Palate-Craniofac Assoc 2011; 12: 86-92.*
20. Pomahac B. *Establishing a composite tissue allotransplantation program. J Reconstr Microsurg 2012; 28: 3-6.*
21. Singhal D, Pribaz JJ, Pomahac B. *The Brigham and Women's Hospital face transplant program: a look back. Plast Reconstr Surg 2012; 129: 81e-8e.*
22. Siemionow M, Gatherwright J, Djohan R, Papay F. *Cost analysis of conventional facial reconstruction procedures followed by face transplantation. Am J Transplant 2011; 11: 379-85.*
23. Rüegg EM, Hivelin M, Hemery F, Maciver C, Benjoar MD, Meningaud JP, Lantieri L. *Face transplantation program in France: a cost analysis of five patients. Transplantation 2012; 93: 1166-72.*

 http://dx.doi.org/10.3346/jkms.2015.30.6.669