EDITORIAL

Facial transplantation: what does the future hold?

> "We cannot solve our problems with the same thinking we used when we created them."
>
> *Albert Einstein*

Oral and Maxillofacial Surgery has been involved in facial reconstructive surgery since its birth as a specialty. Whether it has been to correct a facial deformity secondary to a facial skeletal deficiency, trauma, infection, cancer related defect, temporomandibular joint (TMJ) disease or a congenital cleft lip/palate defect, the objective of the reconstructive surgeon has been to restore both the function and the aesthetic form of the face. To achieve this goal, all aspects of facial reconstruction, including normal speech and swallowing, correct perioral/periocular function, adequate nasal airflow, and dental rehabilitation, need to be addressed, all while recreating natural-appearing aesthetically appealing hard and soft tissue facial subunits.

Through the development of modern reconstructive techniques (i.e., microvascular surgery, computer-assisted virtual surgical planning, computed tomography−guided navigation, and robotic surgery) and with the advancement in biomaterial sciences (i.e., titanium and resorbable hardware fixation, dental implants, TMJ prostheses, custom 3-dimensional printed facial implants, and tissue expanders), our ability to restore pre-existing facial appearance and function in our patients has increased significantly. Despite the medical advancements, there are clearly situations in which our reconstructive techniques fall short and patient quality of life is reduced dramatically. Examples that are all too familiar to most reconstructive surgeons include those cases involving the destruction of multiple subunits secondary to significant trauma (i.e., ballistic injuries) or massive tumor-extirpative defects. To further complicate matters, these malnourished and medically compromised patients often have undergone previous surgeries or radiation therapy, contributing to suboptimal results.

Since the first reported face transplantation performed by Devauchelle et al. in 2005,[1] there has been a large interest in the facial reconstructive surgery community to utilize this technique for correcting numerous facial defects and deformities. Despite its proven success, albeit in a very limited case series worldwide, few other facial reconstructive techniques could be more controversial, leading to heated discussions regarding its utility and applications. At its fundamental level, facial transplantation involves standard microvascular techniques utilized daily for head/neck reconstruction, coupled with other modern techniques used in orthognathic surgery, TMJ surgery, maxillofacial trauma fixation, cosmetic facial surgery, and facial nerve dissection (parotid/skull base surgery). At the heart of its complexity is the requirement for lifelong immunosuppression, resulting in significant risk of mortality, chronic organ rejection, alternative contingency surgery, and financial costs. Patients need to be carefully selected on the basis of compliance and expectations regarding both aesthetic and functional outcomes. Opponents of facial transplantation cite the underreporting of complications, immunosuppression-associated malignancies, and failure of a truly dynamic functional facial unit. Of the 37 cases of facial transplantation reported worldwide from 2005 to 2015, 6 patients (16%) died as a result of organ rejection, multisystem organ failure, infection, malignancy, or suicide.[2]

Immunosuppression is required to suppress the antigenic activity that will result in transplant rejection. As with all organ transplantations, rejection is classified into hyperacute rejection (immediate), acute rejection (within 3 months), and chronic rejection. Although most cases of acute rejection can be managed with adjustments in immunosuppressive medication, it is chronic rejection that will result in a catastrophic outcome. Unlike chronic rejection of the transplanted kidney or the liver, in which organ donation is more common and numerous, allowing for a viable second organ transplantation or alternative life-sustaining therapy (i.e., dialysis), there is no real viable option for a second attempt at facial transplantation that results in any functional or aesthetic normalcy. Salvage plans include large bulky soft tissue flap coverage, which results in dismal quality of life postoperatively.

Advancements in cancer research have clearly demonstrated the role of the immune system in cancer prevention and therapy. This causal relationship helps explain why patients on immunosuppressive medications, such as those required for organ transplantation, are at high risk of cancer development. The high level of antigenic activity associated with facial transplantation may require higher immunosuppressive levels, thereby increasing the lifelong risk of development of a cancer.

To date, facial transplantation has been considered the costliest treatment with respect to finances

compared with other solid organ transplantation programs. Ruegg et al.[3] reported on the estimated cost of facial transplantation around as €125,000 compared with heart transplantation (€80,000) or kidney transplantation (€20,000). Currently, most transplantation programs are funded by research grants through military defense, national health systems, and industry. Costs will likely decrease as techniques and team experience improve; however, the extensive resources required
in terms of health care personnel and cost, throughout the life of the facial transplant recipient, will always make facial transplantation one of the more financially expensive procedures compared with all other transplantations.

Who then is the ideal facial transplant recipient? Unfortunately, many of the patients considered for facial transplantation are young, most being victims of some form of trauma. As discussed previously, these patients are likely to experience organ rejection during their lifetime or develop a secondary cancer as a result of immunosuppression. The patient with head and neck cancer who undergoes a large ablative procedure to treat his or her disease is clearly a poor candidate for facial transplantation because this patient will most certainly be at high risk of recurrence of a primary cancer. Currently, the ideal patient is one who is already receiving immunosuppressive therapy for some other disease or is a previous organ transplant recipient. The defect must be critically assessed, and an expert reconstructive team must have evaluated the patient and have considered other surgical options with conventional techniques. Patients considered for facial transplantation need to undergo extensive psychological testing with regard to true understanding of the psychological aspects of receiving another individual's face ("the notion of self"), compliance with antirejection medication regimens, realistic expectations of what the surgery can offer, and risk of mortality or organ failure. Patients with an extensive psychiatric history or who have suffered a self-inflicted injury add another layer of complexity and are the subject of a serious ethical debate. We, as health care providers, treat these patients on a daily basis without pause; however, the stakes are lower with conventional techniques, both in terms of health risks (morbidity) and health care financial costs. Few studies have looked at the psychological aspects of facial transplantation, but findings suggest that many patients have no problem with accepting the new face and that their fear of transplant rejection, although present, does not differ from that in other organ transplant recipients. Patients with the highest risk of compliance issues or suicide are those with preexisting mental disease or untreated depression.[4]

There is definite value in the pursuit of facial transplantation as a treatment option, from both clinical and research standpoints. Clearly, there are select patients suffering from massive facial defects who can benefit from their improved "self," which would facilitate their reintegration into society and a better quality of life. One must be cautious about extending this technique to all situations such as smaller subunit defects that can be managed with more conventional modern techniques, as well as about accurate reporting of complications, facial nerve regeneration, speech/swallowing outcomes, and patients' true reintegration into society. We must also ask ourselves how many face transplantation centers are truly required as the case numbers (both current and in the future) are extremely small with very significant morbidities and financial costs.

Future research needs to be directed at true tissue engineering, the creation of functional autogenous innervated musculo−mucosal−cutaneous junctions (oral/eyelid sphincters), nerve regeneration, 3-dimensional printed bioresorbable scaffolds, and elimination of antigenic transplanted tissue.

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