Composite Tissue Allotransplantation of the Hand and Face

I. Description

Composite tissue allotransplantation is defined as transplantation of histologically different tissues. This type of transplantation is being proposed for facial transplants in patients with severely disfigured faces, and for hand transplants in patients unsatisfied with prosthetic hands. The treatment has potential benefits in terms of functional status and psychosocial well-being. It also has potential risks, most notably those associated with a lifelong regimen of immunosuppressive drugs.

Background

Composite tissue allotransplantation refers to the transplantation of histologically different tissue which may include skin, connective tissue, blood vessels, muscle, bone, and nerve tissue. The procedure is also known as reconstructive transplantation. To date, primary applications of this type of transplantation have been of the hand and face (partial and full), although there are also reported cases of several other composite tissue allotransplantations, including that of the larynx, knee, and abdominal wall.

The first successful partial face transplant was performed in France in 2005 and the first complete facial transplant was performed in Spain in 2010. In the U.S., the first facial transplant was done in 2008 at the Cleveland Clinic; this was a near-total face transplant and included the midface, nose and bone. The first hand transplant with short-term success occurred in 1998 in France. However, the patient failed to follow the immunosuppressive regimen, which led to graft failure and removal of the hand 29 months after transplantation. The first hand transplantation in the U.S. took place in Louisville, KY in 1999.

Hand and face transplants have been found to be technically feasible. The most commonly performed face transplant procedure has been to restore the lower two thirds of facial structure, especially the perioral area (i.e., lips, cheeks, chin) and in some cases the forehead, eyelids and
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scalp. Facial transplantation has been performed on patients whose faces have been disfigured by trauma, burns, disease or birth defects and who are unable to benefit from traditional surgical reconstruction. Hand transplants have been done in patients who lost a hand due to trauma or life-saving interventions causing permanent injury to the hand. To date, hand transplants have not been performed for congenital anomalies or loss of a limb due to cancer.

Composite tissue allotransplantation procedures are complex and involve a series of operations using a rotating team of specialists. For face transplantation, the surgery may last 8 to 15 hours. Hand transplant surgery typically lasts between 8 and 12 hours. In all hand transplants, bone fixation occurred first and this was generally followed by artery and venous repair and then by suture of nerves and/or tendons. In all surgeries performed to date, the median and ulnar nerves were repaired. The radial nerve was reconstructed in about half of the procedures.

Unlike most solid organ transplants such as kidney and heart transplants, composite tissue allotransplantation is not life-saving, and its primary aim is to increase a patient’s quality of life, eg, by having a more normal appearance and a sense of wholeness. In the case of facial transplantations in particular, there is a large potential psychosocial benefit of successful surgery. Moreover, it is hoped that function may be better following composite tissue transplantation than with alternative interventions eg, grasping and lifting after hand transplants and basic functions such as blinking and mouth closure after facial transplants. In addition, in the case of face transplantation, the procedure may be less traumatic than “traditional” facial reconstructive surgery using the patient’s own tissue. For example, traditional procedures often involve dozens of operations, whereas facial transplantation involves only a few operations.

Composite tissue allotransplantation is associated with potential challenges and risks as well as potential benefits. Patients who undergo face or hand transplantation must adhere to a lifelong regimen of immunosuppressive drugs. Risks of immunosuppression include acute and chronic rejection, opportunistic infection that may be life-threatening and metabolic disorders such as diabetes, kidney damage, and lymphoma. There are also potential adverse impacts on quality of life including the need to commit to a lifetime immunosuppression regimen. Other challenges include the need to actively participate in intensive physical therapy in order to obtain functionality and the potential for frustration and disappointment if functionality does not meet expectations. Moreover, there is the potential for allograft loss, which would lead to additional procedures in hand transplant patients, and there are limited reconstructive options for facial transplantation patients. Furthermore, in the case of hand transplants, there is a risk that functional ability eg, grasping and lifting objects, may be lower than with a prosthetic hand, especially compared with newer electronic prosthetic devices. Due to the importance of selecting candidates who can withstand these physical and mental challenges, potential hand and face transplant recipients undergo extensive screening for both medical and psychosocial suitability.

II. Policy

Composite tissue allotransplantation of the hand and/or face is not covered as it is not known to be effective in improving health outcomes.
III. Policy Guidelines

There are no specific CPT codes for this procedure. It would be reported using combinations of existing codes or the unlisted code for the anatomic area (e.g., 26989 unlisted procedure, hands or fingers).

IV. Scientific Background

This policy was created with a search of the MEDLINE database through January 14, 2013. Following is a summary of the key literature to date. The policy was updated regularly; most recently, the literature was reviewed through January 7, 2015.

Hand transplantation

The most comprehensive reporting of the worldwide experience with hand/upper limb transplant was published by Shores et al in 2014. The authors identified 72 patients: 37 received bilateral transplants and 35 unilateral, for a total of 107 transplanted hand/upper extremities. There are 4 known mortalities: 1 occurred after a bilateral hand transplant, and the other 3 followed multitype CTAs (ie, combined upper- and lower-limb or combined upper-limb and face transplants). Twenty-four graft losses have been reported; 8 of these were also associated with multiple CTA procedures and another 7 occurred in China during their early experience with hand transplantation. In the United States, 21 known patients have undergone isolated upper limb transplantation; 13 were unilateral and 8 were bilateral (limb or digit) procedures. There was 1 immediate graft loss of the bilateral transplanted limb/digit. An additional 3 patients experienced hand loss at approximately 9 months, 2 years, and 4 years posttransplant, respectively. Few data on functional outcomes after hand transplantation have been reported. The authors noted that there is a lack of agreement on appropriate outcome measures and the level of transplantation varies greatly among patients, making it difficult to compare functional improvement.

An article describing data from the International Registry on Hand and Composite Tissue Allotransplantation (IRHCTT) published an article describing registry data in 2011. At the time data were prepared for the article, hand transplants had been reported to the registry in a total of 39 patients. The article stated that 85% of transplant recipients experienced at least one episode of acute rejection in the first year after transplant. Acute rejection episodes were reversible in all patients who were compliant with treatment. The most commonly reported complications were metabolic complications (35 of 39, 90%) and opportunistic infections (30 of 39, 77%). Transient hyperglycemia occurred in 17 patients (44%) and cytomegalovirus reactivation in 10 patients (26%). Ten patients required surgery for complications (n=2 arterial thrombosis, n=1 venous thrombosis, n=6 small area of skin necrosis, and n=1 venous fistula). Five cases of graft loss were reported between day 5 and 275 after transplant. The early (day 5) graft loss occurred in a patient who underwent face and bilateral hand transplant, and this patient died at day 65 from cerebral anoxia. This was the only reported death in this series of patients. Hand function was reported in figures included in the article, but specific numbers eg, mean function scores, were not included in the text of the article.
No studies comparing health outcomes in patients undergoing hand transplantation versus receiving hand/lower limb prostheses were identified.

Face transplantation

In 2014, Smeets et al systematically reviewed published reports of face transplants.4 The authors included English language articles published through September 15, 2013, that provided data on at least 1 face transplant in humans. A total of 36 articles reported on 27 worldwide face transplantations. University Hospital Henri Mondor in Creteil, France, and Brigham and Women’s Hospital in Boston, Massachusetts, were the centers with the most experience. Ten of the 27 cases were full face transplants (the first successful full face transplant was in 2010) and the remainder were partial face transplants. The literature did not report any case of graft loss, hyperacute (within the first 48 hours) or chronic rejection, or graft-versus-host disease. However, all of the face transplant recipients with at least 1 year post-surgical follow-up were reported to experience at least 1 episode of acute rejection days or months after the procedure. Other common complications related to drug toxicity from immunosuppressive therapy, leading to opportunistic infections, metabolic disorders, and increased incidence of malignancy. There have been 3 reported cases of malignancy to date. Three deaths occurred in transplant recipients. One patient died 27 months after surgery due to lack of compliance with immunosuppressive therapy. A second death occurred in a French recipient who had multidrug-resistant infection and graft necrosis (this was an early transplant in France). The third patient died of recurrent cancer.

In terms of function, tactile sensitivity recovered a mean of 4.1 months after surgery when nerve repair was performed, and a mean of 7.3 months otherwise. Temperature sensitivity recovered a mean of 4.3 months with nerve repair and 12.5 months without nerve repair. Motor recovery began a mean of 7.8 months after surgery. Recovery of motor function has started with contractions of single muscles, and complex movements have appeared within the first year in a number of patients. Long-term results are still pending in most cases. After 5 years of follow-up, the first face transplant recipient was able to fully open her mouth, smile, speak, chew, and swallow.

Also in 2014, Fischer et al identified a total of 29 face transplants performed through December 2013 and reported functional outcomes in 5 patients treated at their center. The investigators compared each patient’s pre- and post-surgical functioning on various dimensions. Before surgery, all 5 patients had compromised respiration, breathing, sensation, and facial expression. After surgery, they had substantial recovery in all of these areas. In terms of breathing, the 5 patients were able to breathe through their noses post-surgery, and the 2 patients who previously had tracheostomy tubes had them removed. Speech became understandable to an unfamiliar listener 3 to 9 months after surgery. Three to 9 months post-surgery, the majority of allografts were responsive to light touch, and patients could distinguish between heat and cold. Facial expression, including the ability to smile, recovered after transplantation in all patients. Three of 5 patients were unable to chew solid food before surgery, and 2 patients had liquid leakage. All patients were capable of oral food intake 3 to 29 days after surgery, and 3 to 12 months after surgery, all had unrestricted or nearly unrestricted eating and drinking. The 2 patients with compromised ability to
smell both reported a substantial improvement in smelling, comparable to their functioning before facial trauma. All 5 patients developed opportunistic infections (viral or bacterial) after facial transplantation.

Ongoing Clinical Trials

**Human upper extremity (hand and forearm) allotransplantation (NCT00722280)**: This study aims to evaluate the risk of rejection after allograft transplantation and minimize the need for long-term high dose immunosuppression. It will test the “Pittsburgh Protocol”, an immunomodulatory strategy using donor bone marrow stem cells. Recipients will be selected from a population of adults 18-60 years-old with upper limb loss. The primary outcome is graft survival, and there will be up to 10 years of follow-up. This study aims to evaluate the risk of rejection after allograft transplantation and minimize the need for long-term high dose immunosuppression. It will test the “Pittsburgh Protocol”, an immunomodulatory strategy using donor bone marrow stem cells. Recipients will be selected from a population of adults 18-60 years-old with upper limb loss. The primary outcome is graft survival, and there will be up to 10 years of follow-up. The study is sponsored by the University of Pittsburgh. Estimated enrollment is 300 patients, and the estimated date of study completion is January 2018.

Several case series are under way in the United States evaluating the outcomes of hand transplants in small numbers of patients. These include a study sponsored by the Christine M. Kleinert Institute for Hand and Microsurgery in Kentucky (NCT00711373) and a study sponsored by Brigham and Women's Hospital (NCT01293214). Each of these studies is recruiting 10 patients. Small (recruiting 2-5 patients) trials of facial transplants in patients with severe facial deformities are also under way. Trial sponsors consist of the Brigham and Women’s Hospital (NCT01281267), the University of Maryland (NCT01140087), and Cleveland Clinic (NCT01269164).

Summary

Preliminary experience with composite tissue allotransplantation of the hand and face suggest that the surgery is technically feasible. To date, however, only a limited number of patients worldwide have undergone such allotransplantation of the hand and/or face. There are insufficient data on whether the procedure improves the net health outcome, ie, whether the potential benefits to patients’ quality of life outweigh the potential risks, eg, of surgical complications, immunosuppression and opportunistic infections. In addition, for hand transplantation, no published data are available comparing functional and quality-of-life outcomes compared with use of lower limb prostheses. Thus, composite tissue allotransplantation of the hand and/or face is not known to be effective in improving health outcomes.

Practice Guidelines and Position Statements

In November 2013, the American Society for Surgery of the Hand published a position statement on hand transplantation. The organization recognized that hand transplantation is an alternative to prostheses and rehabilitation in appropriately selected patients yet continued to consider it an “innovative intervention”. The statement emphasized the need for further advances in the areas of patient selection, surgical technique and immunosuppression and recommended that, at this time,
the procedure be carried out only in centers with extensive experience in both hand surgery and solid organ transplantation.

In March 2011, the National Institute for Health and Clinical Excellence in the United Kingdom published guidance on hand allotransplantation. The guidance stated that current evidence on the efficacy and safety of hand allotransplantation is inadequate in quantity. They recommended that the procedure only be available under special arrangements, eg, in a research setting.

In 2006, The American Society for Reconstructive Microsurgery and the American Society of Plastic Surgeons published guiding principles on facial transplantation for plastic surgeons. Selected principles are listed below:

1. “Facial transplantation should only be utilized for patients with severe facial deformities who cannot be helped through traditional reconstructive surgical measures.
2. Facial transplantation should only be undertaken in institutions with appropriate Institutional Review Boards familiar with the many intricacies for approval and application of new clinical procedures and protocols.
3. Facial transplantation should be conducted in the context of a transplant team having appropriate institutional resources and commitment to the project...
4. Appropriate patient selection criteria should be established and a complete risk/benefit ratio must be considered for each patient on a case-by-case basis.
5. To facilitate informed consent:
   a. The physician must provide the patient with the latest and complete information on the risks associated with facial transplant.
   b. The preoperative evaluation of potential donors may involve additional considerations as more experience is gained. At this time the results of facial transplantation are unknown. If early results are less than optimal, potential patients should be informed of any newly identified limitation of the procedure.
   c. Patients must demonstrate a thorough understanding of all the known risks and benefits.
   d. The physician should regard the facial transplantation procedure as experimental and it should be subjected to the evaluation of an independent research ethics committee.
   e. The informed consent should include an alternative and acceptable solution for management of the recipients’ face in the event of transplant failure... “

Medicare National Coverage

There is no national coverage determination.

V. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.
Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

VI. References

14. American Society for Reconstructive Microsurgery (ASRM) and the American Society of Plastic
http://www.microsurg.org/assets/1/13/ftGuidelines.pdf