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Composite Tissue Allotransplantation of the Face and Hand

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Coverage

Composite tissue allotransplantation of the face **is considered experimental, investigational and/or unproven.**

Composite tissue allotransplantation of the hand **is considered experimental, investigational and/or unproven.**

Policy Guidelines

Currently, there are no specific CPT codes for this procedure; however, should these procedures receive codes, it is likely that a combination of existing codes or the unlisted code for the anatomic area would be used (e.g., 26989).

Description

Composite tissue allotransplantation (also referred to as vascularized composite allotransplantation) is defined as transplantation of histologically different tissues. This type of transplantation is being proposed for facial transplants in individuals with severely disfigured faces, and for hand transplants in individuals dissatisfied with prosthetic hands. The treatment has potential benefits in terms of improving 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

Composite tissue allotransplantation refers to the transplantation of histologically different tissue that 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.

Hand and face transplants have been shown to be technically feasible. 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 United States, the first facial transplant was done in 2008; it 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 United States took place in 1999.

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. Bone fixation occurs first, and this is generally followed by the 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 transplantations (e.g., kidney and heart transplants), composite tissue allotransplantation is not life-saving, and its primary aim rests mainly in a patient's cosmetic satisfaction and quality of life. In the case of facial transplantations, there is immense potential for the psychosocial benefits when a surgery is successful. Moreover, the goal of composite tissue allotransplantation is to improve function (e.g., grasping and lifting after hand transplants, blinking and mouth closure after face transplants) without alternative interventions such as prosthetics. Additionally, 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 only involves a few operations.

Adverse Events

Composite tissue allotransplantation is associated with potential risks and benefits, and 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. A review of 115 facial or upper extremity transplants found an overall acute rejection rate of 89% with 11% of recipients with chronic rejection. (1) Other challenges include the need to participate actively in intensive physical therapy to restore functionality and the potential for frustration and disappointment if functional improvement 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. Furthermore, in the case of hand transplants, there is a risk that functional ability (e.g., 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.

Regulatory Status

Hand and face allotransplantations are surgical procedures and, as such, are not subject to regulation by the U.S. Food and Drug Administration (FDA).

Rationale

The policy was created in January 2016 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through July 1, 2024.

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be

adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Face Allotransplantation

Clinical Context and Therapy Purpose

The purpose of composite tissue allotransplantation in individuals who have a severely disfigured face due to burns or trauma is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals who have a severely disfigured face due to burns or trauma.

Interventions

The therapy being considered is composite tissue allotransplantation.

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 scalp. (2) 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.

Comparators

The following therapy is currently being used to treat a face after burns or trauma: standard care without facial allotransplantation.

Outcomes

The general outcomes of interest are functional improvement, graft failure, QOL (e.g., psychosocial well-being), and treatment-related adverse events (e.g., surgical complications, immunosuppression, infections).

Due to the complex nature of this lengthy surgical procedure, immediate postsurgical follow-up is needed, and lifelong follow-up will be necessary due to the immunosuppressive drugs required to prevent graft failure.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

As of 2021, 46 patients have received 48 face allotransplantations. (3) A systematic review of these patients by Hadjiandreou et al. (2024) found a total of 36 (75%) patients with acute rejection, while only 7 (14.6%) had chronic rejection. In the short-term (<36 months), patient and graft survival were 93.5% and 88.6%, respectively. Long-term (>36 months) patient survival was 84.8% and graft survival was reduced to 64.3%. A malignancy incidence rate of 10.9% was reported over the full reporting period. Short-term metabolic and infection complications were high (29.2% and 58.3%, respectively), and long-term rates were 13.5% and 16.2%, respectively.

A systematic analysis of outcomes was published by Smeets et al. (2014). (4) Reviewers included English-language articles, published through September 2013, that provided data on at least 1 face transplant in humans. Thirty-six articles reported on 27 worldwide face transplantations. Of the 27 cases, 10 were full face transplants (the first successful full face transplant was in 2010) and the remainder were partial face transplants. The literature does not report any case of graft loss, hyperacute (within the first 48 hours) or chronic rejection, or graft-versus-host disease (GVHD). However, all transplant recipients who were at least 1-year postsurgical follow-up reported experiencing at least 1 episode of acute rejection after the procedure. Other common complications were 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 a multidrug-resistant infection and graft necrosis (an early transplant). The third patient died of recurrent cancer. In terms of function, tactile sensitivity recovered at a mean of 4.1 months postsurgery when nerve repair was performed or at a mean of 7.3 months otherwise. Temperature sensitivity recovered at a mean of 4.3 months with nerve repair and at 12.5 months without nerve repair. Motor recovery began at a mean of 7.8 months after surgery. Trialists indicated that recovery of motor function started with contractions of single muscles, and complex movements 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.

Case Series

Fischer et al. (2015) identified 29 face transplants performed through December 2013 and reported functional outcomes in 5 patients treated at their center. (5) The investigators compared each patient's pre- and postsurgical functioning on various dimensions. Before surgery, all 5 patients had compromised respiration, breathing, sensation, and facial expression. After surgery, patients had substantial recovery in all these areas. In terms of breathing, all were able to breathe through their noses postsurgery, and 2 with tracheostomy tubes had them removed. Speech became understandable to an unfamiliar listener 3 to 9 months after

surgery and at that time most 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 with their functioning before the facial trauma. All 5 patients developed opportunistic infections (viral or bacterial) after facial transplantation.

Section Summary: Face Allotransplantation

The available case series studies on composite tissue allotransplantation of the face have suggested that the surgery is technically feasible. To date, however, given the limited number of patients worldwide who have undergone the procedure, the evidence is not sufficiently robust to determine whether the potential benefits to patients outweigh the potential risks (e.g., surgical complications, immunosuppression, opportunistic infections).

Hand and Upper-Extremity Allotransplantation

Clinical Context and Therapy Purpose

The purpose of composite tissue allotransplantation in individuals who have had hand or upper-extremity amputation is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals who have had a hand or upper-extremity amputation.

Interventions

The therapy being considered is composite tissue allotransplantation.

Hand transplantations have been done in patients who lost a hand due to trauma or life-saving interventions that caused permanent injury to the hand. To date, hand transplants have not been performed for congenital anomalies or loss of a limb due to cancer.

Comparators

The following therapy is currently being used to treat a hand or arm after amputation: standard care without hand and upper-extremity allotransplantation.

Outcomes

The general outcomes of interest are functional improvement, graft failure, QOL (e.g., psychosocial well-being), and treatment-related adverse events (e.g., surgical complications, immunosuppression, infections).

Due to the complex nature of this lengthy surgical procedure, immediate postsurgical follow-up is needed, and lifelong follow-up will be necessary due to the immunosuppressive drugs required to prevent graft failure.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Case Series

The most comprehensive reporting of the worldwide experience with hand and upper-limb transplants was published by Shores et al. (2015). (6) They identified 72 patients who received a total of 107 transplanted hand/upper extremities (35 received bilateral transplants, 37 unilateral). There are 4 known mortalities: 1 occurred after a bilateral hand transplant; the others followed multitype composite tissue allotransplantation (i.e., combined upper- and lower-limb or combined upper-limb and face transplants). Twenty-four graft losses have been reported; 8 of them were also associated with multiple composite tissue allotransplantation procedures and another 7 occurred in China during early efforts 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 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 was published by Pertuzzo and Dubernard (2011). (7) At the time data were extracted, hand transplants had been reported to the registry for 39 patients. The authors stated that 85% of transplant recipients experienced at least 1 episode of acute rejection in the first year after transplant. Acute rejection episodes were reversible in all patients compliant with treatment. The most commonly reported complications were metabolic complications (35/39 [90%]) and opportunistic infections (30/39 [77%]). Transient hyperglycemia occurred in 17 (44%) patients and cytomegalovirus reactivation in 10 (26%) patients. Ten patients required surgery for complications (2 arterial thromboses, 1 venous thrombosis, 6 small area of skin necrosis, 1 venous fistula). Five cases of graft loss were reported between day 5 and day 275 after transplant. The early (day 5) graft loss occurred in a patient who underwent a 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. Specific hand function data (e.g., mean function scores) were not reported.

One study identified had compared health outcomes in patients undergoing hand transplantation with those receiving hand/upper-limb prostheses. This study, by Salminger et al. (2016), compared outcomes for 5 patients who had below-elbow hand transplantation with 7 patients who had prosthetic hands. (8) There were 3 unilateral and 2 bilateral hand transplants, for a total of 7 transplanted hands. The prosthetic patients received myoelectric prostheses controlled by simple direct control. Functional assessments were undertaken a mean of 9 years (standard deviation, 3.9 years) after transplantation. The following standardized instruments were used to evaluate function: the Action Research Arm Test, the Southampton Hand Assessment Procedure, and the Disabilities of the Arm, Shoulder and Hand measures. In addition, QOL was assessed using the 36-Item Short-Form Health Survey (SF-36). There were no statistically significant differences between groups in functional scores on the standardized measures. For example, the mean Southampton Hand Assessment Procedure score was 75.0 in the transplanted group and 75.4 in the prosthetic group. For the QOL scores, transplant patients had significantly higher scores on the SF-36 role-emotional and mental health subscales and there were no significant differences on the SF-36 physical functioning, bodily pain, general health, or social functioning subscales. The authors did not report total SF-36 scores.

Section Summary: Hand and Upper-Extremity Allotransplantation

A total of 107 hand and upper-extremity transplants had been conducted worldwide as of 2015 and data are reported in a number of case series. The available studies on composite tissue allotransplantation of the hand have suggested that the surgery is technically feasible. A single study (N=12) has compared outcomes for patients who had hand transplants with those receiving prostheses. It found no statistically significant differences in functional outcomes between groups and no differences in 4 of 7, SF-36 subscales. Given the limited number of patients worldwide who have undergone the procedure and the limited amount of data comparing outcomes with the best available prosthetics, the evidence is not sufficiently robust to determine whether the potential benefits to patients outweigh the potential risks (e.g., surgical complications, immunosuppression, opportunistic infections).

Summary of Evidence

For individuals who have a severely disfigured face due to burns or trauma who receive composite tissue allotransplantation, the evidence includes a case series and several systematic reviews of case series. Relevant outcomes are functional outcomes, quality of life (QOL), resource utilization, and treatment-related mortality and morbidity. The available studies on composite tissue allotransplantation of the face have suggested that the surgery is technically feasible; however, to date, only a limited number of patients worldwide have undergone the procedure, and the data are not sufficiently robust to determine whether the potential benefits to patients outweigh the potential risks (e.g., of surgical complications, immunosuppression, opportunistic infections). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have hand and upper-extremity amputation(s) who receive composite tissue allotransplantation, the evidence includes a case series, several systematic reviews of case series, and a nonrandomized comparative study. Relevant outcomes are functional outcomes, QOL, resource utilization, and treatment-related mortality and morbidity. The available studies on composite tissue allotransplantation of the hand have suggested that the surgery is technically feasible. The only study comparing outcomes in patients who had hand transplants with those who received prostheses included 12 patients. It found no differences between groups in functional outcomes and little difference in the QOL. Given the limited number of patients worldwide who have undergone the procedure and the limited amount of data comparing outcomes with the best available prosthetics, the evidence is not sufficiently robust to determine whether the potential benefits to patients outweigh the potential risks (e.g., surgical complications, immunosuppression, opportunistic infections). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

National Institute for Health and Care Excellence (NICE)

In 2011, NICE published guidance on hand allotransplantation. (9) The guidance stated that the quantity of current evidence on the efficacy and safety of hand allotransplantation was inadequate.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this medical policy are listed in Table 1.

Table 1: Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01459107	Human Upper Extremity Allotransplantation	30	Jun 2036
NCT05699187	Face Transplantation	4	Dec 2030

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	26989
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
11/15/2024	Document updated with literature review. Coverage unchanged. Added references 1 and 3; others removed.
01/01/2024	Reviewed. No changes.
10/15/2022	Document updated with literature review. Coverage unchanged. No new references added.
10/01/2021	Reviewed. No changes.
12/15/2020	Document updated with literature review. Coverage unchanged. No new references added.
10/15/2019	Reviewed. No changes.
12/15/2018	Document updated with literature review. Coverage unchanged. References 2 and 7 were added, none removed. The title changed from “Composite Tissue Allotransplantation of the Hand and Face”.
10/15/2017	Reviewed. No changes.
06/01/2016	New medical document. Composite tissue allotransplantation of the hand is considered experimental, investigational and/or unproven. Composite tissue allotransplantation of the face is considered experimental, investigational and/or unproven.