Clinical Policy Bulletin: Hand Transplantation

Number: 0816

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Aetna considers hand transplantation experimental and investigational because of insufficient evidence of its effectiveness.

Aetna considers multi-digit allo-transplantation for reconstruction of the metacarpal hand experimental and investigational because of insufficient evidence of its effectiveness.

See also CPB 0399 - Myoelectric Upper Limb Prostheses

Background

Trauma (e.g., motor vehicle and industrial accidents), congenital birth defects (e.g., no limb or a very short limb), as well as systemic diseases (e.g., cardiovascular disease, diabetes mellitus, and osteosarcoma) may result in amputation of the hand and upper-extremity. Upper-extremity limb loss has a significant psycho-social impact on the individual, in terms of both esthetic and functional aspects. While amputees can be fitted with mechanical prosthesis and advances in upper-limb prostheses will offer more options for amputees, they cannot fully duplicate the intricate actions of a native hand. Hand transplantation aims to provide a hand that looks more natural than a prosthesis, and which restores some sensation and movement. Hand transplantation is a complex operation (can take up to 16 hours -- twice the time of the average heart transplantation); but is not as difficult as a hand replantation because the latter usually involves severely damaged tissues. When performing a hand transplant, surgeons first fix the bone, and then repair tendons, arteries, nerves and veins. Post-surgery complications can include poor circulation, infections and rejection.

Before the operation, psychological assessment is needed of a patient’s motivation and likely compliance with post-operative rehabilitation and immuno-suppressive medication. A cadaveric limb removed surgically from a donor, below the elbow, is used for the transplant. Its suitability for the recipient is evaluated by basic matching for sex, size, appearance, and sometimes genetic matching. Following the procedure the limb may be immobilized in a plaster splint for a number of weeks. The patient should undergo intensive rehabilitation, including physiotherapy, occupational therapy and possibly electro-stimulation for best restoration of function. Long-term immuno-suppression is needed to reduce the possibility of rejection.

The American Society for Surgery of the Hand (AASH) (Lee et al, 2003) stated that hand transplantation has been performed since 1998. Preliminary clinical experience based on 14 subjects
has underscored the importance of patient motivation and compliance, intensive hand therapy, and close post-transplantation surveillance. Acceptable functional and cosmetic outcomes, particularly for bilateral amputees, have been achieved and are similar to hand replantation at equivalent levels. However, major return of 2-point discrimination or intrinsic muscle function is not to be expected. At present, ongoing heavy immuno-suppression is needed for allograft survival with unknown long-term risks. Although there have been no life-threatening adverse events, complications include allograft rejection and loss, tissue necrosis, and osteomyelitis. Furthermore, the effects of chronic rejection on the allograft function and survival have not yet been determined. Because there are many significant contra-indications to both the surgical procedure and the immuno-suppressive protocol, careful pre-operative, medical and psychological screening is mandatory. In summary, hand transplantation is still an experimental procedure that may enhance the function and/or appearance of carefully selected patients. They stated that further research and progress in transplant immunology are needed before hand transplantation can be considered a safe and effective procedure.

Piza-Katzer et al (2009) noted that the first hand transplantation was carried out in 1964 but the hand had to be removed within 3 weeks due to rejection. Although he was the first one to be treated with more modern immuno-suppressants, the same fate overtook another patient who received a hand from a brain-dead donor in 1998 in Lyon. Since then only 32 persons worldwide have been provided with parts of the upper-extremity. The partly published histories of 3 patients who have had both hands transplanted were summarized and indication critically assessed once again. It is also stressed how difficult, multi-layered and complex the patient's education is. The patient has to be informed in many conversations beforehand not only about every stage of therapy but also about possible complications and even rejection. Can the psychological burden/stress while waiting for a donor, the difficult post-operative period, lifelong adherence to a rigorous drug-regimen, the complexity of the whole procedure be made comprehensible to a layman? To replace same with same is the goal of the best-possible reconstructive surgery. It is to hope that through future innovations in the immuno-suppressing therapy patients can be offered transplantation of one or both hands as a routine-operation. Until then indication has to be strict and the operation can possibly only be performed in a few centers. Long-time prospects, disadvantages and complications, as well as side effects have to be presented openly.

Mathes et al (2009) examined current attitudes regarding the emerging field of composite tissue allo-transplantation (CTA) from those who treat complex hand injuries. A web-based survey regarding CTA was sent to members of the AASH, which identified their demographical data and practice profiles. Respondents' support for CTA and their assessment of the level of risk associated with these procedures were addressed. Additional questions focused on the clinical application of CTA with current immuno-suppression, ethical issues surrounding CTA, and the indications for hand transplantation. Finally, 2 clinical situations that closely mirrored past hand transplantations were presented, and members evaluated their suitability for allo-transplantation. A total of 474 surgeons responded to the survey (22 % response rate), who were divided in their opinion of hand transplantation with 24 % in favor, 45 % against, and 31 % undecided. While 69 % of the responders consider this surgery to be a high-risk endeavor; 71 % still believe it to be an ethical procedure when performed on properly selected patients. The most accepted indications for hand transplantation were loss of bilateral hands (78 %) and amputation of a dominant hand (32 %). Only 16 % were in favor of performing transplants with the immuno-suppression available today. In response to the clinical situation, 66 % would offer transplantation to a bilateral hand amputee, whereas only 9 % would offer transplantation to a patient with diabetes who had lost the dominant hand. The authors concluded that this survey demonstrated support for hand allo-transplantation as a solution for dominant-hand and bilateral hand amputees. However, surgeons continue to be concerned about the adverse effects of immuno-suppression and the risks of acute and chronic rejection, and many want to wait for the development of better immunologic treatment options.

Jones and Schneeberger (2009) stated that based on the results of above-elbow replantation, it is possible that above-elbow arm transplantation will be successful and result in a superior functional outcome. Above-elbow arm transplantation is probably technically simpler than distal forearm or wrist
transplantation, especially since the macro-anastomoses do not require micro-surgical expertise. However, hand function depends on re-innervation of forearm muscles and the distance for nerves to regenerate for re-innervation of intrinsic muscles of the hand is significant. The vascularized bone marrow transplanted with the arm holds potential to induce chimerism and promote tolerance but could also make the recipient more susceptible to graft-versus-host disease. The authors stated that prospective clinical studies comparing the functional results after above-elbow arm transplantation with the functional results achieved by the best neuronal-controlled above-elbow prosthesis are needed to determine the gold standard of upper-extremity reconstruction.

Amirlak and associates (2010) noted that between 1998 and 2008, a total of 44 hand transplantations were performed. The clinical success of hand transplantation has fueled the desire to start hand transplantation programs in many medical centers. Although the public demand for reconstructive transplantation is increasing, hand transplantation is far more complex and difficult than other solid organ transplantation. Furthermore, the medical ethics of hand transplantation have been debated. Solid organ transplantation for life-threatening disease is now a widely accepted procedure; however, reconstructive transplantation is less widely accepted.

Schunid (2010) stated that composite tissue allograft (CTA) is defined as heterologous transplantation of a complex comprising skin and subcutaneous, neurovascular and mesenchymal tissue. Such techniques allow complex reconstruction using matched tissue, without donor site morbidity. The potential indications in orthopedics-traumatology could in the future be more frequent than the present indications of heart, liver, lung, kidney and pancreas transplantation. International clinical experience clearly demonstrates the feasibility of CTA, both surgically and immunologically. However, immuno-suppression remains indispensable, exposing the patient to risks that are not acceptable for purely functional surgery, except in very particular indications. The main hope for the future lies in induction of graft-specific tolerance.

Shores (2010) noted that recent advances in transplant immunology are shifting the focus from immuno-suppression to immuno-regulation, making CTA with novel and less potent immuno-suppressive regimens a possibility. Hand transplantation has been the most frequently performed human CTA, with more than 50 upper-extremity based transplants done worldwide. The author stated that further research is needed regarding immuno-modulating protocols, and careful oversight and individualized screening procedures will be needed as patients seeking improved quality of life through human CTA come to accept a certain level of risk in these experimental procedures.

Hand transplantation is available at the Atlanta Veterans Affairs (VA) Medical Center and its affiliate, Emory University, as well as at a few medical centers nationwide. The United States Department of VA (2010) noted that the surgery team with VA and Emory University will track outcomes of 9 patients who have received a hand transplant in the United States. This tracking program/study is funded by VA, the Department of Defense and other sources. Eligible participants are upper-limb amputees (below the elbow; regardless of when the amputation was performed) who are between the age of 18 and 55 years. Siemionow and co-workers (2010) stated that since 1998, nearly 50 hand transplantations in 40 patients have been performed around the world at various levels ranging from wrist level to shoulder level. However, the risk-to-benefit ratio remains controversial in bilateral versus unilateral transplantation and has yet to be determined. From recent experience, the 2 most important determinants of the success of each patient's upper-extremity transplant are patient compliance and intense rehabilitation.

While hand transplantation has received international attention in recent years, the economic impact of this innovative treatment is uncertain. Chung et al (2010) estimated the costs of hand transplantation and the use of hand prostheses for forearm amputations. Quality-adjusted life years (QALYs) were calculated for each outcome to create decision trees. Cost data for medical care were estimated based on Medicare fee schedules using the Current Procedural Terminology code for forearm replantation. The cost of immuno-suppressive therapy was estimated based on the wholesale price of
drugs. The incremental cost-utility ratio was calculated from the differences in costs and utilities between transplantation and prosthesis. Sensitivity analyses were performed to assess the robustness of the results. For unilateral hand amputation, prosthetic use was favored over hand transplantation (30.00 QALYs versus 28.81 QALYs; p = 0.03). Double hand transplantation was favored over the use of prostheses (26.73 QALYs versus 25.20 QALYs; p = 0.01). The incremental cost-utility ratio of double transplantation when compared with prostheses was $381,961/QALY, exceeding the traditionally accepted cost-effectiveness threshold of $50,000/QALY. The authors concluded that prosthetic adaption is the dominant strategy for unilateral hand amputation. For bilateral hand amputation, double hand transplantation exceeds the societally acceptable threshold for general adoption. Improvements in immuno-suppressive strategies may change the incremental cost-utility ratio for hand transplantation. The authors admitted that cost is not the only factor that needs to be taken into account. In kidney transplants, for example, society has determined that the cost of the procedure is offset by the major increase in QAL. Other, even more expensive, procedures such as heart and liver transplants have found wide acceptance due to a lack of alternative treatments for life-threatening conditions. However, they argued that cost is a viable consideration in hand amputation, given its non life-threatening nature.

The National Institute for Health and Clinical Excellence's guideline on hand transplantation (2011) states that current evidence on the safety and effectiveness of hand allo-transplantation is inadequate in quantity. In addition, there are risks from the prolonged immune suppression required after the procedure. Therefore this procedure should only be used with special arrangements for clinical governance, consent and research. Further research into hand allo-transplantation should include data on long-term functional outcomes, and any occurrence of malignancy associated with long-term immuno-suppression should be published. Furthermore, the Specialist Advisers listed adverse events reported in the literature as acute and chronic rejection (when immuno-suppression was stopped), poor neurological function of the hand and immuno-suppression-induced diabetes. They considered theoretical adverse events to include malignant changes or tumor development and graft–versus–host disease.

Jensen et al (2012) noted that as reconstructive transplantation emerges as an increasingly viable option for upper limb amputees, a better understanding of quality of life (QOL) outcomes is needed to evaluate the benefits and risks of the procedure from the patient perspective. To address this need, these investigators searched PubMed (1998 to 2011) to characterize QOL outcomes among upper limb transplant recipients. They identified 27 articles reporting on QOL outcomes in hand transplantation. Common instruments to assess domains of QOL in hand transplantation include the Disabilities of the Arm, Shoulder, and Hand questionnaire, the Medical Outcomes Study Short Form- 36, and the International Registry on Hand and Composite Tissue Transplantation's Hand Transplantation Score System. Preliminary reports using standardized measures indicated that most hand transplant recipients described improved QOL. Several studies also qualitatively reported that recipients expressed satisfaction with cosmetic, sensory, functional, and social outcomes after transplantation. However, this review suggested that the measurement of QOL in hand transplantation is limited, although it is largely driven by QOL considerations. The authors concluded that this review high-lighted the need for improved measurement of QOL in hand transplantation. The preliminary QOL findings across published hand transplantation articles will aid in improving the future assessment of QOL in hand transplantation.

Murphy and colleagues (2013) noted that in vascularized composite allotransplantation (VCA), multiple types of tissue are transferred from donor to recipient as a single functional unit. This technique has been performed for upper extremity, face, and abdominal wall transplants, among many others. These investigators reviewed the existing cases of face and upper extremity VCA performed to-date and described the functional outcomes and challenges associated with this new procedure. They also reviewed the immune suppression protocols required for these procedures. A literature review was performed using PubMed and online registries where available to identify patients who have undergone upper extremity and face transplant procedures. These were compiled and cross-
referenced to abstracts, conference presentations, and press releases in the media to create a list of procedures performed to-date. More than 70 patients have undergone upper extremity transplantation with very good functional outcomes routinely achieved; 25 face transplants were identified that have been completed to date and details regarding patient outcome were included. One cases of human face allotransplantation with pre- and post-operative images was included as an example of what can be achieved with this technique. The authors concluded that VCA is an emerging field that provides an exciting new avenue for reconstructive procedures and achieves functional and cosmetic outcomes not previously possible with existing techniques. However, these investigators stated that VCA is not without its challenges and considerable work is still needed before widespread adoption of these new reconstructive techniques.

Hand transplantation is a treatment option for complex injuries that leave patients with structural, functional, and aesthetic deficits that cannot be addressed by other means. It is a form of VCA, which is the highest rung the reconstructive ladder due to its complex technical and immunologic challenges. Despite completion of the first successful hand transplant in 1999, the understanding of hand transplantation is still evolving. Ongoing research is needed to improve functional outcomes and decrease the morbidity associated with long-term immunosuppression (No authors listed, 2014).

Pomahac et al (2014) stated that VCA is a novel therapeutic option for treatment of patients suffering from limb loss or severe facial disfigurement. To-date, a total of 72 hand and 19 facial transplantsations have been performed worldwide. Vascularized composite allotransplantation in hand and facial transplantation is a complex procedure requiring a multi-disciplinary team approach and extensive surgical planning. Despite good functional outcome, courses after hand and facial transplantation have been complicated by skin rejection. The authors concluded that long-term immunosuppression remains a necessity in VCA for allograft survival. To widen the scope of these quality-of-life-improving procedures, minimization of immunosuppression to limit risks and side effects is needed.

Petruzzo et al (2015) evaluated the outcomes and the risk/benefit balance in bilateral hand allo-transplantation. The study included 5 cases of bilateral hand allo-transplantation performed in a single center, with a follow-up ranging from 3 to 13 years. The recipients (4 men, 1 woman) were young. The level of amputation was distal in all cases except for 2 patients amputated at the mid-forearm level. All the recipients initially received the same immunosuppressive treatment that included tacrolimus, mycophenolate mofetil, prednisone, and, for induction, anti-thymocyte globulins. Patient and graft survival was 100 %. All recipients showed adequate sensorimotor recovery (protective and tactile sensitivity and partial recovery of intrinsic muscles), they were able to perform the majority of activities of daily living, and had a normal social life. Most complications occurred in the first post-transplant year and were successfully managed. All recipients experienced at least 1 episode of acute rejection, which was easily reversed by increasing oral steroid dose or by intravenous steroids, except for patient 3, who presented 6 episodes of acute rejection, the latest 2 treated with Campath-1H. The authors concluded that although bilateral hand transplantation may be a satisfactory treatment option for amputees, a careful selection of candidates and a rigorous evaluation of recipients after transplantation are imperative.

Bernardon et al (2015) stated that between January 2000 and July 2009, 5 adults who had suffered bilateral traumatic below-elbow amputations, received bilateral hand-forearm allografts performed by the Lyon team. These investigators reported the functional benefits achieved over a mean follow-up period of 7.6 years (range of 4 to 13 years), up to December 31, 2013. Clinical measurement was hampered by the lack of specific validated assessment tools, obliging the authors to use non-specific standardized evaluation means. Their assessment showed that the restoration of motion, strength, and sensibility were fair. Functional results (Carroll upper extremity function test, 400-point test, Activities of daily living) were good, as well as quality of life evaluation (RAND-36). Subjective and overall results explored with questionnaires -- Disabilities of the Arm Shoulder and Hand (DASH), Hand Transplantation Score System (HTSS), were very good. Improvement was seen to continue during the first 3 years, and then tend to become stable. The authors concluded that continued efforts should be directed at designing comprehensive, condition-specific, reliable outcome measurement tools; and
continuous monitoring and evaluation of patients is needed to ascertain the long-term risk-benefit balance.

Breidenbach et al (2016) performed a rigorous statistical analysis of all hand and face transplantations to examine if hand and/or face transplantation is the standard-of-care. Data from September 1998 until March 2014 on all hand and face transplantations in the world were obtained through publications, news articles, personal communications, and presentations. Data on solid organ transplantation (SOT) were obtained from the Scientific Registry of Transplant Recipients for comparison with the results of hand transplantation. Re-sampling and permutation statistical analysis was used to compare structured cohorts of hand, face, and SOT. Routine immunosuppression can achieve intermediate- to long-term graft survival in hand transplantation that is empirically superior to SOT. Chronic rejection (CR) in hand transplantation is statistically significantly less than in SOT. Renal failure in hand and face transplantation is empirically less than in SOT. Bone marrow transplant with hand transplantation produces both statistically superior and statistically inferior results compared with hand transplantation without bone marrow. In hand transplantation, acute rejection did not appear to increase late allograft loss. The function of hand transplantation is statistically significantly superior to prosthesis yet inferior to hand replantation. Not all hand and face transplants have good results, yet those hand transplants completed within certain parameters obtained excellent results. The authors concluded that certain hand transplants arguably can be considered the standard-of-care; face transplantation requires more time and patient numbers and a clearer definition of inclusion and exclusion criteria before standard-of-care assessment can be made. However, the parameters that resulted in excellent results in hand transplantation are not clearly delineated.

In an update on “Chronic rejection in human vascularized composite allotransplantation (hand and face recipients)”, Kanitakis et al (2016) noted that VCA have become a viable option to restore severely damaged parts of the body that cannot be repaired with conventional surgical techniques. Acute rejection develops frequently in the early post-graft period both in human and experimental VCA, but the possibility of human VCA to undergo CR remained initially unknown. The experience gained over the years showed that, similar to SOT, human VCA can also develop CR. Chronic rejection is clinically mostly apparent on the skin and targets preferentially skin and deep vessels, leading, as in SOT, to graft vasculopathy and often to graft loss. Dermal sclerosis and adnexal atrophy are additional features of CR. The pathogenetic immune mechanisms involved (cell-mediated versus humoral) remain incompletely known. The changes of CR can be detected with skin and deep tissue biopsies. Modern in-vivo imaging tools can detect vascular narrowing and have the advantage of being non-invasive. However, the diagnosis and treatment of CR remain challenging, as several important questions remain to be answered: a more accurate definition of CR in VCA is needed to establish criteria allowing an accurate and early diagnosis. The authors concluded that the pathogenetic mechanisms of CR need to be better understood to allow more effective treatment; and favoring/triggering factors of CR need to be better understood so that they can be avoided. They stated that as in SOT, there is a need for efficient tolerance-inducing protocols that will favor graft acceptance and circumvent the necessity of lifelong immunosuppression.

The U.S. Department of Health and Human Services (DHHS)’ Organ Procurement and Transplantation Network (OPTN) has formed a 18-member National Committee to develop nationwide standards and policies for hand and face transplantation (2014). While face and hand transplantation are currently the most widely known VCA procedures, other types of VCA transplantation may be developed in the future. In July 2013, the DHHS announced that VCAs will be added to the definition of transplantable organs covered by federal regulation and legislation effective July 3, 2014. Dr. Kenneth Andreoni, President of the OPTN/UNOS (United Network for Organ Sharing) noted that "The demand for VCA transplants and the potential for future forms of these transplants, is growing rapidly, and it is important to establish consistent, national standards at this point to ensure that all patients are considered fairly and that we maintain the best possible outcomes for recipients". The OPTN/UNOS Vascularized Composite Allograft Transplantation Committee will determine which organ combinations will be covered in policy and develop national standards and processes for VCA donor consent and recovery, as well as a system to prioritize VCA transplant candidates for available organs. Other tasks will
include developing a national set of clinical data to be collected on VCA transplants and establishing institutional standards for hospitals that perform VCA transplants. The committee will present its recommendations to the OPTN/UNOS Board of Directors for final action. https://optn.transplant.hrsa.gov/news/national-committee-formed-to-develop-network-policies-for-hand-face-transplantation/

Multi-Digit Allo-Transplantation for Reconstruction of the Metacarpal Hand:

Rampazzo et al (2015) stated that amputation of all fingers (metacarpal hand) can be functionally equivalent to hand amputation. These researchers noted that multi-digit allo-transplantation might benefit patients who require a full complement of fingers to return to their pre-injury activities. They investigated the feasibility of the transfer of 4 fingers and thumb as a single allograft. Four fingers and the thumb were harvested from 16 hands as an allograft based on the radial and ulnar arteries. Dorsal digital veins were dissected until confluent in the major veins. The common digital nerves were divided at the origin. The flexor and extensor tendons were transected, respectively, in zones V and VI. The fingers were disarticulated at the metacarpophalangeal (MCP) joint. After harvest, ulnar and radial arteries were injected with red and blue India ink, respectively, followed by injection of lead gel in the ulnar artery to study the perfusion of the fingers. Digital radiographs and computed tomographic scans were obtained. A bilateral mock transplantation was performed. The ulnar artery perfused the small, ring, long, and ulnar half of the index finger, whereas the radial artery vascularized the thumb. The index finger represented a watershed area. The presence of contrast in the 4 fingers, decreasing toward the radial fingers, was confirmed by computed tomography. The mock transplantation procedure was performed successfully. The authors concluded that multi-digit transplantation is an anatomically feasible procedure. Although the ulnar artery can supply the entire allograft, the variable anatomy of the palmar arches should be considered and the flap based on both ulnar and radial arteries. This was a feasibility study; further important aspects regarding this procedure have to be assessed in well-designed clinical studies.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

There are no specific CPT/HCPCS codes for hand transplant from a donor or for multi-digit allo-transplantation for reconstruction of the metacarpal hand:

ICD-10 codes not covered for indications listed in the CPB:

S48.011+ - S48.929+ Traumatic amputation of shoulder and upper arm
S58.011+ - S58.929+ Traumatic amputation of elbow and forearm
S68.011+ - S68.729+ Traumatic amputation of wrist, hand and fingers

The above policy is based on the following references:

AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0816 Hand Transplantation

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania
updated 11/18/2016