

SPECIAL CONSIDERATIONS IN FACIAL TRANSPLANTATION: A SYSTEMATIC REVIEW

Melanie Shpigel, B.S., B.A., Sammy Othman, B.S., Jason Cohn, D.O., Christopher Hill, M.D., Paige Bunderick, M.D., Gabriel F. Santiago, M.D., Chad Gordon, D.O.



ABSTRACT

Background
Vascularized composite allotransplantation (VCA) of the face is an exceedingly complex procedure, requiring extensive planning and surgical precision in order to successfully manage patients with facial disfigurements. This review aims to present an overview of the salient anatomic considerations in facial transplantation, as well as give attention to unique patient populations and special considerations.

Methods
A literature review was performed in search of articles pertaining to considerations in facial transplantation using the databases PubMed, Web of Science, and Cochrane. Articles selected for further review included full-text articles with an emphasis on specific anatomic defects and how they were addressed in the transplant process, as well as management of special patient populations undergoing facial transplantation.

Results
This systematic review of the literature pertaining to considerations in facial transplantation revealed common themes, as well as the importance of a multidisciplinary approach to the procedure. The ultimate outcome is dependent upon the synchronization of subunits of the allograft and the desired functional outcomes, including osseous, ocular, oral, and otologic considerations. Management of specific pathology and subgroups of patients are critical aspects. Although pediatric face transplantation has not yet been performed, it is a likely a future step in the evolution of this procedure.

Conclusion
When performing a face transplantation, many components must be considered pre-, intra-, and post-operatively. This systematic review presents specific anatomic considerations, as well as information about special patient populations within this cross-section of multidisciplinary microsurgery, psychiatry, and transplant immunology.

Anatomic Considerations

Considerations in Special Patient Populations

Anatomic Region	Examples of Salient Characteristics in the Literature and How They Were Addressed
Nasomaxillary	<ul style="list-style-type: none"> Lack of nasal/septal structures and passageway due in part to excessive scarring, as well as absence of maxilla, zygoma, both orbital rims Include "redundant glandular tissue" (submandibular and also parotid so that recipient gets facial nerve) in the allograft Include muscles of midface, upper lip, buccal mucosa in allograft Harvest entire hard palate with the goal of facial arterial system providing complete supply Implants were used to reconstruct orbital floor
Otologic	<ul style="list-style-type: none"> Extensive thermal injury (3rd degree burns on face/scalp) Patent canals but post-operative bilateral stenotic external auditory meatus Ear-containing allograft with follow-up meatoplasties Post-operative ofloxacin regimen for Pseudomonas prophylaxis
Salivary Glands and Facial Nerve	<ul style="list-style-type: none"> Various reasons to include submandibular and parotid glands in allograft (facial artery, facial/lingual/hypoglossal nerves) or to not include (increased risk of infection) Of studies reviewed with gland complications, parotid was most common cause—mainly due to bulk and fluid collection (bulk is sometimes advantageous for patients lacking contour) Sialadenitis, parotitis, wound dehiscence treated with antibiotics Intraparotid botox injections for sialoceles Coaptation of facial nerve as close as possible to main trunk to reduce scarring at distal portions
Ocular	<ul style="list-style-type: none"> Most common ocular post-operative complication involves eyelids, usually lower lid ectropion Tailor donor periorbital components to prevent long term consequences of vision impairment, corneal disease, scarring of conjunctiva, etc. Re-draped eyelid tissue Post-operative use of topical corneal lubricants, "therapeutic bandage contact lens", prosthetic "scleral lens device" Tracked eyelid movements to assess blinking and overall function Monitored aperture and synchronicity of eyes
Dental and Maxillofacial	<ul style="list-style-type: none"> Pre-existing dental disease increases infection risk when immunocompromised in the context of transplant; avoid dental work for 3-6 months post-operative for same reason Risk for malocclusion or airway obstruction if bony elements of transplant are not properly aligned Dentures/prostheses for edentulous recipients complicated by "reduced bone density, increased epithelial fragility, and increased infection risk" Endosseous dental implants are standard of care for edentulous patients and also for ongoing dental caries Can lengthen incisors for adequate esthetic visibility and for speech/functional purposes
Osteocutaneous	<ul style="list-style-type: none"> First step of transfer was fixation of skeletal subunits Avoided cutaneous incisions across face because of probably scar formation (also helps with psychosocial aspect long term) Performed 3-Dimensional craniofacial computerized tomography scan and angiogram pre-operatively to help guide the procedure Used surgical modeling software to superimpose the allograft and plan Intraoperatively, used alternate current nerve stimulation and perfusion angiography to ensure perfusion and function Performed nasofrontal osteotomy to correct skeletal defect
Intraoral	<ul style="list-style-type: none"> Assess intra- and extraoral sensation with sharp versus dull testing, thermal stimuli, light touch Angle classification system to evaluate occlusion Blood supply of dental pulp was evaluated with modified pulse oximetry Sensation of dental pulp evaluated with EPT (electric pulp test) and thermal testing Quantification of salivary flow was determined as a means to evaluate orofacial muscle function/control May have limited mouth opening ability due to temporomandibular joint dysfunction or palatal fistulas (can predispose to dental caries, poor hygiene, infection) Teeth can be included in allograft; must include adequate vascular structures Follow-up surgery to correct the fistula and allow for adequate mouth opening

Unique Population or Pathology	Examples of Salient Characteristics in the Literature and How They Were Addressed
Pediatric Patients	<ul style="list-style-type: none"> Has not yet occurred—youngest person to have face transplant was 21 Cosmetic (trauma, burns, disfigurement after tumor resection) and medical (vascular malformations, congenital diseases) indications Donors must be close in age to recipient in order to match the anatomical structures at the proper level of development Significant psychosocial element and impact; necessary involvement of pediatric psychologists, social workers, child care specialists in the multidisciplinary team Contraindications: HIV (+); current psychiatric instability; recent history of neoplasia Immunosuppression side effects pose an ethical dilemma, as well as lifelong immunosuppression
Bacterial Infections	<ul style="list-style-type: none"> Bacteria of concern in facial transplant include <i>Streptococcus</i> spp., anaerobes, <i>Capnocytophaga</i> spp. due to the flora of the transplanted structures Prophylaxis with ampicillin/sulbactam Prescription of multiple antibiotics puts patients at risk for <i>Clostridium difficile</i> diarrhea
Cytomegalovirus	<ul style="list-style-type: none"> Donor grafts containing mucosa and paranasal sinuses are unique because of their flora; also pose risk for mold infections due to external exposure In transplant setting, CMV infection could be due to reactivation of latent CMV or new infection (new infection is more serious because patient is immunosuppressed) Can present in three ways: asymptomatic viremia, CMV syndrome, tissue-invasive disease CMV induces immunomodulation and can affect efficacy and function of graft indirectly Other herpesviruses are also of concern Prophylaxis with antiviral therapy, most commonly with valganciclovir (3 month duration of prophylaxis)
Guillain–Barré syndrome (GB) following resistant cytomegalovirus (CMV)	<ul style="list-style-type: none"> More significant immunosuppression is required for face transplant than for transplant of solid organs because facial allografts have greater antigenic load Acute rejection is pro-inflammatory state which supports continued replication of virus Recipient became CMV positive at six months post-operative, even after consistent prophylaxis with valganciclovir, and developed polyneuropathy 5 months later, labeled an axonal form of GB Treated Guillain-Barré with intravenous immunoglobulin Performed repeat nerve conduction studies and electromyography; saw improvement and patient was discharged and instructed to continue physical therapy
Fungal Infections	<ul style="list-style-type: none"> Important to distinguish infection (e.g. candidal stomatitis) from mucosal graft rejection (both may present with erythema and edema) May receive antifungal prophylaxis if significant concern for mold colonization
Granulomatosis with polyangiitis (Wegener's granulomatosis)	<ul style="list-style-type: none"> Extensive craniofacial damage from GPA (granulomatosis with polyangiitis) with skin manifestation, presenting as malignant pyoderma Indication for face transplant was more urgent than for purely cosmetic or functional reasons (GPA is life-threatening) Recipient was close to losing both eyes and becoming completely blind due to granulomas, necrotizing inflammation, scar tissue Infection led to erosion of body skeleton → midface collapse, dural exposure; allograft, therefore, incorporated Le-Fort III skeletal subunits GPA was controlled with immunosuppression Allograft included soft tissue from entire face minus perioral area, as well as frontal scalp subunits Harvested bilateral superficial temporal arteries (STA) to supply scalp allograft Coapted facial nerve trunks and used grafts; also transplanted parotid lobes
Neurofibromatosis Type 1	<ul style="list-style-type: none"> Case of Neurofibromatosis type 1 (NF1) limited to face/head, affecting speech, vision, eating capabilities Infiltration of facial nerve → facial paralysis (complete on L side and partial on R) In removal of the neurofibroma, the recipient lost all native soft tissue of upper, middle, lower facial subunits; > 75% of donor soft tissues were harvested to accommodate the extensive defect Example of indication for facial transplantation that is not traumatic in origin Graft was supplied by bilateral external carotid arteries and included bilateral auricular, eyelids, and scalp Neurofibromas can be highly vascular—recipient required 27 units of packed RBCs intraoperatively

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