Chapter 29

Basics of Facial Transplantation: Surgical Principles and Management of Risks

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Additional information is available at the end of the chapter

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Abstract

Facial transplantation offers an alternative approach towards restoring gross facial disfigurement. Since its advent in 2005, the surgical principles have become continually refined depending on the nature of the injury and anatomical requirements posed by the recipients. Owing to the complex nature of the procedure, it bears a number of different risks. These have included graft rejection from alloimmune responses, complications from the effects of immunosuppression and risk of mortality; in addition, there is an inherent predisposition for the development of psychological complications. This chapter outlines the stepwise process of conducting a facial transplantation with emphasis on key surgical principles. It also provides details with case examples of how to minimize complications associated with the procedure.

Keywords: risks, facial transplant, surgical principles, complications, composite tissue allograft

1. Introduction

Facial transplantation has revolutionized complex forms of reconstruction where conventional procedures have produced suboptimum results [1–3]. Originally conducted in 2005 [4], it has redefined the technical boundaries of plastic surgery with many more having been conducted globally. However, performing a facial composite tissue allotransplantation (CTA) poses a significant number of challenges, which were anticipated early on [5]. Psychological complications can be profound [1] and therefore pre-operative mental assessment is vital [6, 7] to ensure engagement with the long-term multidisciplinary team therapy. Failure to do so has resulted

in mortality in one case due to lack of compliance with the immunosuppressive regime [1]. Acute rejection episodes have affected all allograft recipients [1, 8, 9] with one patient having had sustained a chronic rejection of the CTA [10]. The adverse effects of immunosuppression have been depicted within the literature, most notably an increased predisposition towards acquiring infections, which have affected a significant proportion of recipients [1]. Functional outcomes have so far exceeded expectations with all patients having demonstrated good motor and sensory development [4, 8, 11]. Motor recovery has, however, been slightly lagging in comparison to neurosensory restoration [1, 3, 12]. There have been three post-operative mortalities associated with facial CTAs so far [1]. Miscellaneous complications including renal insufficiency, blood loss and neoplasia development have been encountered too [1]. This chapter aims to draw focus towards the management of risks in facial transplantation and offers an insight into revising existing protocols. In addition, an overview concerning the principles of surgical approach in performing the procedure is addressed.

1.1. Ethical aspects

Ethical debates raised in the case of facial transplantation emphasize on the significance of the risks associated with the procedure taking into account that is not considered life saving but life changing [13]. In addition, the face unlike other forms of organ transplantation is unique to each person and represents one's individuality; the ethical dilemma, therefore, of a transfer of identity is an issue debated by many. So far, however, many of these concerns have been answered with the promising results of transplanted CTAs. No psychological complications of an identity crisis have yet been reported in the literature. All individuals have shown great functional improvement thus justifying the importance of the procedure [1]. Despite this, the associated risks have still meant that clinical and public opinion remains divided regarding the ethics of the surgery.

1.2. Malformations

Severe facial malformations not amenable to routine reconstructive methods serve as ideal indications for facial transplantation. So far, reports have included injuries sustained from shot-gun injuries, animal attacks, carcinomas and burns [1]. Such is often the severity of these defects that it would require countless surgeries over many years and still this would only be expected to produce suboptimum results. The unique ability of facial composite tissue allografts to correct gross disfigurement successfully in a single procedure has made it an ideal option.

1.3. Donor and recipient matching

It is important to identify the correct donor and recipient match for the surgery to be successful. Age, race, skin colour and blood type are some of the important considerations to take into account. This will lead to a more aesthetic outcome in keeping with the rest of the recipient's physical makeup. Also, a closer anatomical match will allow for an easier apposition of the procured CTA on to the donor.

1.4. The surgical experience

1.4.1. Pre-operative workup

1.4.1.1. Imaging

Prior to transplanting a facial CTA, thorough pre-operative imaging is necessary in order to outline the anatomical characteristics of the recipient [14]. This will help to guide the surgery in accordance with an individualized protocol. Computerized tomography (CT) scanning of the head and neck will delineate the bony structure of the recipient and can produce accurate specifications of the disfigurement. Three-dimensional (3D) reconstruction of the CT images can then help guide osteosynthesis of the recipient's bony framework to allow for finer anatomical apposition with the donor CTA.

Detailed venous and arterial assessment of the recipient has so far been best achieved by CT angiography. This has allowed for identifying inflow and outflow vessels aided by spatial resolution. It has shown to be more superior than magnetic resonance imaging (MRI) angiography as it has a greater potential to detect smaller vessels and with less artefacts. CT angiograms have therefore been identified as the first-line modality for delineating the recipient's vascular makeup [15] (**Figure 1**).

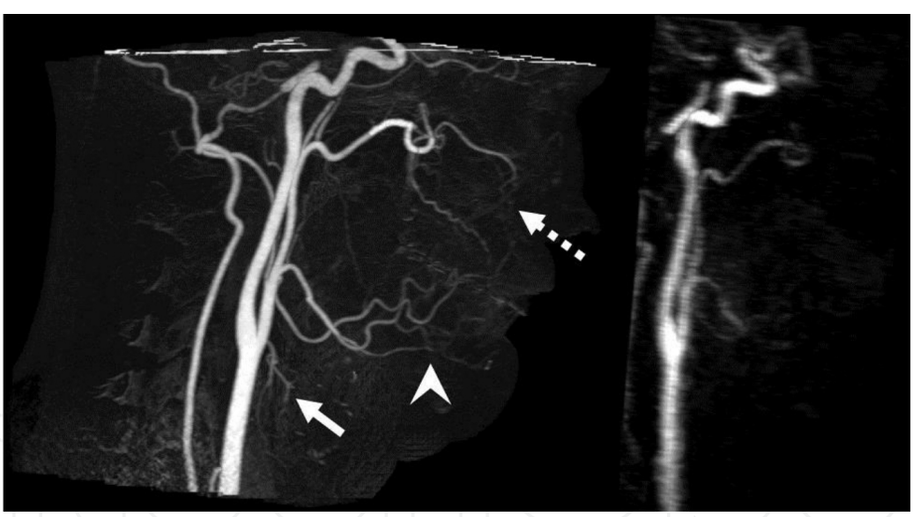

Figure 1. CT angiogram (left) demonstrating fine anatomical outline of internal maxillary, lingual and superior thyroid arteries in contrast to MR angiography which offers less resolution (right). Image reproduced from Shigeyoshi et al. [15].

1.4.1.2. Nerve function

Sensory-motor status of the recipient is assessed through electromyographic (EMG) studies. This helps evaluate the current neurological status and guides microscopic anastomosis of the nerves. This form of mapping is essential towards the success of the surgery. In addition, post-operative EMG results can be later compared to assess recovery and guide rehabilitation.

1.4.1.3. Oropharyngeal assessment

This is important so as to identify any underlying dental abscesses or periodontal disease which may require treatment prior to surgery. Such conditions can reduce the rate of post-operative recovery as it leads to immunomodulation, which could manifest in acute graft rejection.

1.4.1.4. Screening for carcinomas

The detection of underlying carcinomas in recipients is important as it can result in significant complications. In addition, it may also lead to reconsideration as to whether the recipient is at all a suitable candidate for the procedure. Immunocompromised states such as carcinomas would predispose individuals to a greater risk of opportunistic infections; also, immunomodulation due to reducing the immunosuppression regime can result in acute graft rejection. Recipients need to undergo screening for any oropharyngeal carcinomas, women over the age of 40 should be up to date with mammography and all patients above the age of 40 should undergo upper as well as lower endoscopy to detect underlying undiagnosed carcinomas [14]. The literature has depicted the severity of carcinomatous conditions on recipients of facial transplantation. A recurrent squamous cell carcinoma in one individual resulted in a mortality [3], which ultimately undermined the indication for performing the procedure in the first instance.

1.4.1.5. Anaesthetic assessment

The anaesthetic workup for performing facial CTAs just like other forms of solid organ transplantation begins with the routine evaluation of cardiovascular and respiratory status. This is aided by transthoracic echo and lung function tests, respectively. These tests although routinely conducted in those aged greater than 50 years should also be considered for younger patients if they possess risk factors for cardiopulmonary disease. Routine bloods to identify pre-existing coagulopathies or biochemical deficiencies are an important step in any pre-surgical workup [14].

An essential aspect of the anaesthetic assessment is delineating the airway anatomy in recipients of facial CTAs and this can be a complex process due to the severe nature of the injuries sustained. Often, there is gross disfigurement of the normal anatomy not only from the physical injury itself but also from numerous failed reconstructive attempts, which poses greater challenges in airway management. Pre-planning can be aided by reviewing the relevant imaging including both CT and MRI scans to obtain greater detail. Intraoperative management often involves the use of a tracheostomy; this not only avoids the difficulties in obtaining a definite airway as is a problem in recipients of facial CTAs but also keeps the facial-operating field clear for the surgeon.

Owing to the complexity of facial transplantation surgery as well as the haemorrhagic risk, obtaining adequate vascular access is an important element that requires careful consideration. Femoral lines not only provide a good mode of intraoperative monitoring but also abide in keeping the surgical field clear [16]. This is an important anatomical consideration.

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1.4.1.6. Donor prosthesis

Procurement of the facial CTA is known to create significant disfigurement at the donor site. In abiding to transplantation principles, which have previously stated that a sufficient aesthetic appearance should be obtained post organ retrieval [17], it is therefore important to take this factor into account. The process of producing a suitable prosthesis can be initiated pre-operatively whilst the donor is in ITU, an alginate material can be employed to obtain an impression of the donor's face, which is converted to a plaster of Paris (POP) cast in the laboratory. After this stage, a silicone putty material can be poured over this cast and a facial plaster of Paris structure can be obtained. Adhesive dental carding wax can be applied to reproduce the dimensions of skin and subcutaneous tissues over the POP prosthesis. A silicone elastomer can be finally mixed with it in the last stage. Artificial hair and eyebrows can be fabricated on to the prosthesis [18]. This can then be used post-operatively to cover the donor's facial defect.

1.4.2. Intraoperative period

The intraoperative period involves two surgical teams working simultaneously with one group involved in the procurement of the donor CTA and the other concerned with the preparation of the recipient to undergo implantation of the donor allograft.

1.4.2.1. Retrieval of the donor allograft

A major aim of transplant teams in the procurement of facial CTAs is to limit the ischaemia time. Heart-beating donors offer a greater period in which to arrange for the retrieval of the allograft and transfer it to the recipient [19]. The process of procurement begins after the anaesthetic teams perform a tracheostomy of the donor.

The next stage involves marking the boundaries of the CTA to be dissected as displayed in **Figure 2**:

Figure 2. Marking the boundaries for dissection on the donor. Note the extension of margins into the neck to provide additional tissue as part of the allograft. The extra section allows for adjustments to be conducted during transplantation on to the recipient as well as providing tissue for obtaining grafts to aid reconstructing residual defects.

A silastic sheet can be employed as a template to delineate the margins that need to be incised. This template is produced based on the specifications of the defect of the recipient and is then placed on to the donor to guide the surgeons of the retrieval margins. Models produced by 3D printers specifying the exact dimensions of the recipient's defect can help guide the depth of dissection on the donor. Depending on the structural and functional needs of the recipient, discretion is advocated as to what facial component and nerve structure is required for preservation.

After the initial incisions, the facial flap is elevated and the major vessels are identified including the facial arteries and external jugular veins. Vascular loops can be employed in labelling them. The facial artery is often preserved and dissection involves separating it from its point of attachment with the external carotid artery. A bi-coronal incision is often employed in removing the donor CTA; this is extended along the subperiosteum up towards the level of the orbits. It is then extended laterally and may include the ears if they are needed; however, if not, then a rhytidectomy incision can be employed. A deep plane is usually required for the incision so that when undermining of the facial CTA is being performed, skin, soft tissues and muscles can all be obtained. Nerves that require transection can be tested by stimulators to assess their functional status before deciding whether to transfer them with the facial CTA [14, 19, 20] (**Figure 3**).

Figure 3. Elevation of flap after creating a bi-coronal incision. Arrow heads depicting incision trajectory.

In procurement of the craniofacial skeleton, superior osteotomies can be employed just above the lateral canthi bilaterally [20, 21]. These can be advanced forward to include variable sections

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of the maxilla, zygoma and orbits depending on the anatomical requirements of the recipient. These structures can be elevated by pressure underneath after having been transected at the appropriate points. Haemostatic control is important when the facial CTA is being removed from the donor. The facial arteries and veins are clamped bilaterally and transected. The defect produced within the donor can be covered up with a silicone prosthesis as aforementioned.

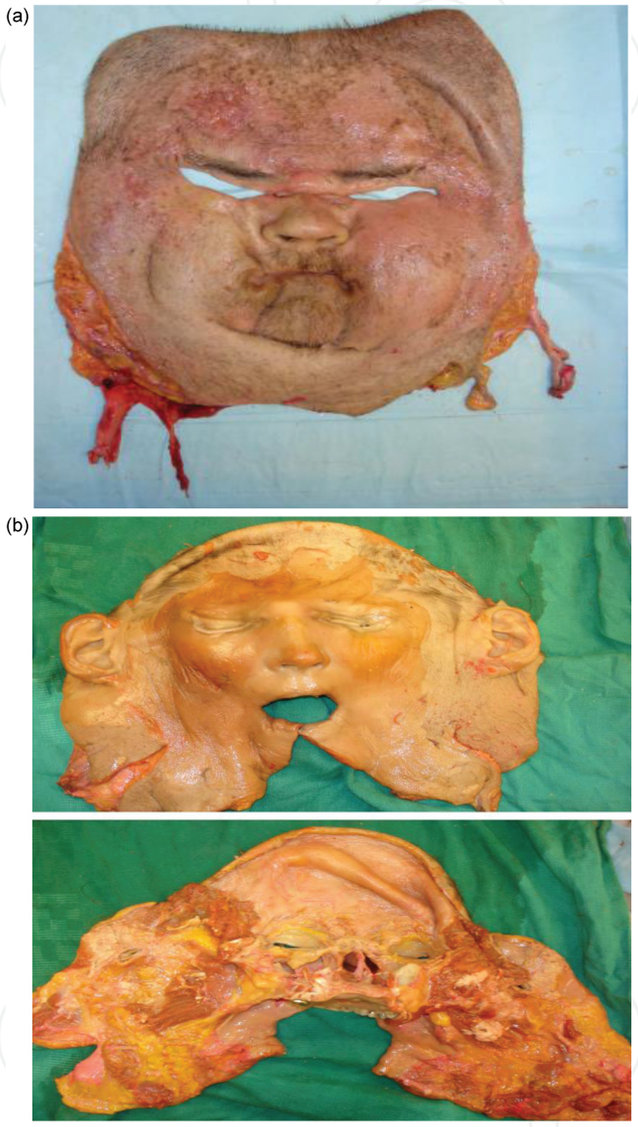

Figure 4. (a) Example of a sub-SMAS (subsuperficial muscular aponeurotic system) facial allograft in a cadaveric model after procurement containing skin and soft tissues. (b) Example of a subperiosteal Le Fort III graft. Image reproduced from Baccarani et al. [21].

The type of flap needed to be harvested and the structures required for preservation is dependent on the anatomical dimensions of the defect to be repaired. If only soft tissues are required, then a sub-SMAS (subsuperficial muscular aponeurotic system) graft can be obtained, which involves dissection from the vertex down towards the subplatysmal plane. If bony structures are necessary for procurement, then a subperiosteal Le Fort III harvest can be

conducted. This involves dissection down from the vertex towards the subperiosteal plane instead followed by a Le Fort III osteotomy to obtain sections of the facial skeleton in addition to soft tissues (**Figure 4**).

1.4.2.2. Preparation of the recipient

Often when bony reconstruction is required it commences with osteosynthesis of the donor's facial bones most notably the maxilla, zygomatic arch, orbital rim and mandible depending on the nature of the injury. The dimensions are surgically modified to match those of the donor allograft so as to allow for a more natural apposition. This in addition to offering a more aesthetic result bares an important physiological benefit because closer anatomical alignment of the sinuses reduces the risk of sinusitis from poor aeration. Conventional wires, plates and screws aid this phase of the reconstructive process. Initially, a temporary osteosynthetic method may be employed so as to proceed much earlier to microvascular anastomosis, which would reduce the duration of ischaemic insult to the facial CTA. When the risk of ischaemia has been alleviated, the completion of bony realignment can be carried through.

The next phase of the facial transplantation procedure will include coaptation of both motor and sensory nerves. This technique involves meticulous microsurgical reattachment of the nerves to enable functionalisation of the donor allograft. If recipient nerves have been damaged by previous deformities, then they can be reconstructed through the aid of donor cable grafts for which a number of host nerves can be employed. These include the facial, infraorbital, supraorbital, inferior alveolar nerves and mental nerves. A mastoidectomy can often be employed to obtain additional facial nerve length within the host. This enables for extrusion outside of the bony facial canal and allows for easier attachment during cable grafting. A similar method in the form of an orbital osteotomy can be conducted to provide the release of the infraorbital nerve. This technique will allow for a more tension-free attachment. Points of skin attachment of the facial CTA to that of the recipient should ideally be performed along natural lines of cleavage such as the nasolabial folds. This will allow for a more tension-free closure offering a better aesthetic outcome [22, 23]. The original surgical technique in full facial CTAs involved bilateral inclusion of superficial temporal and facial arteries often with the parotid gland, which gave poor aesthetic outcomes. This method became revised in 2012 when it was shown that the inclusion of the facial arteries alone was sufficient to produce desirable outcomes thus simplifying the surgery [23]. In addition, the exclusion of the parotids allowed for more distal nerve coaptation. Recently, there has been an increase in revision surgeries post transplantation [24]. Results have been favourable [1, 23, 24] without major complications, thus offering an additional option towards enhancing both aesthetic and functional outcomes of the CTA.

1.4.3. Revision surgeries

Secondary procedures post transplantation can be employed in order to revise residual functional and aesthetic defects. These have included bony realignment, soft-tissue resuspension, dermabrasion, skin grafting and fat injection [1].

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Dermabrasion is a method of surgical planning that can be conducted under local anaesthetic. The epidermis is abraded to a variable extent; however, this certainly carries the risk of bleeding as well as acquiring infections. Refined techniques including CO_2 laser resurfacing as well as electrobrasion have become more renowned and carry less risks [25]. These can help eliminate scars post transplantation as well as remove abnormal pigmentation of the CTA giving enhanced skin texture and appearance.

Both skin grafts and fat injections can be employed to correct residual anatomical defects within the hybrid facial structure. Skin grafts, however, expose the patient to the added risk of anaesthesia as well as post-surgical infections which may provide a challenge to eliminate especially in the presence of immunosuppressant medications.

Bony realignment post-transplantation is one of the more invasive revision procedures and carries a greater risk of complications since it involves the resection of the facial CTA to obtain access to the craniofacial skeleton. For this reason, effective pre-operative surgical planning is vital to avoid this clinical scenario.

1.4.4. Pre- and post-operative outcomes

In the subsequent text, we provide example cases of pre- and post-operative outcomes (**Figure 5**).

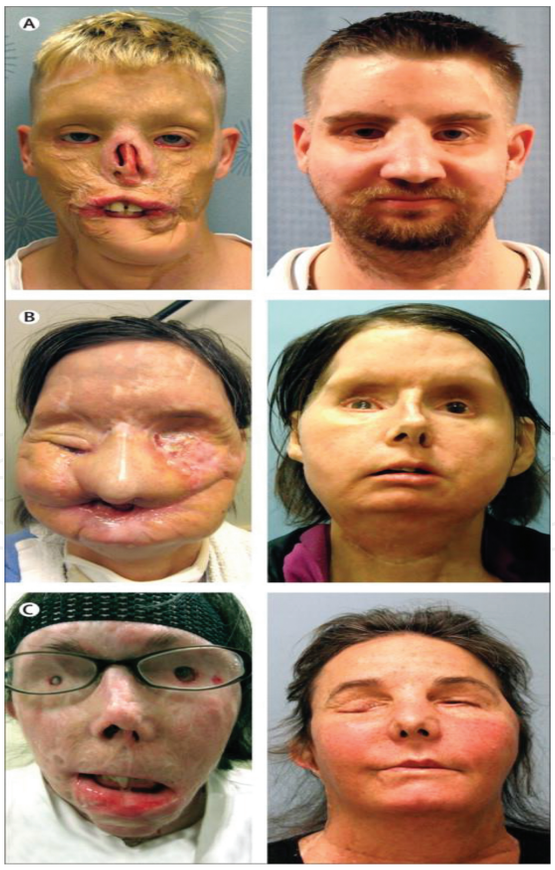

Figure 5. Pre- and post-operative outcomes for facial transplantation, adapted from Khalifian et al. [1].

1.4.5. Post-operative management

1.4.5.1. Rehabilitation

The post-operative period is an essential time when effective multidisciplinary team rehabilitation can help maximize function of the allograft. This process includes a host of different teams constituted by speech and language therapists, occupational as well as physical therapists. In addition, engagement with psychological teams and dietary teams is crucial too.

The patient needs to cognitively recognize the new facial structures he/she has been transplanted with. Research has shown that early and extensive rehabilitation of facial musculature is important in aiding cerebral recognition [26]. The recipient needs to learn how to make the newly acquired musculature functional. Exercises with physical therapists can help achieve this process by practising different facial expressions. Speech therapy is essential in order for the patient to not only be able to regain full vocal ability but also be able to safely swallow.

It is important to assess nerve innervation post transplantation to not only establish the technical success of the microsurgical reattachment but also ensure that rehabilitation will be a success. Nerve function is best assessed with EMG studies.

Occupational therapists can help ensure that patients are able to cope with activities of daily living at home prior to discharge and clinical psychologists are able to address any concerns regarding the development of identity issues. Ultimately, the post-operative period involves a strong multidisciplinary approach to allow for the functional success of the transplanted CTA.

1.5. Management of risks

Minimizing risk in the case of facial transplantation requires effective pre-operative planning as well as robust measures to tackle any post-operative complications. Over the years as the transposition of facial CTAs has increased, important lessons have been learnt about avoiding adversities. This has helped to continually refine protocols to minimize risks.

1.5.1. Graft rejection

1.5.1.1. Acute rejection

Graft rejection is a universal drawback to all forms of transplantation [27, 28] and was considered a definite risk to recipients of facial allografts in 2006 [5]. Despite advancements in immunosuppressant therapy, acute graft rejection has been evidenced in the literature [29, 30]. All current documented cases of facial transplants have sustained episodes of acute rejection [8, 9]. However, they have been well controlled with changes in immunosuppressive therapy preventing graft loss. An incidence of 50% [31] (in reference to hand transplants) was predicted initially [5]; however, until present 100% of reported cases in the literature have succumbed to modes of acute rejection [1, 8, 9].

Facial transplant	Acute rejection – Time Period	Treatment	Outcome
November, 2005 Amiens, France, performed by Devauchelle and Dubernard[32]	Acute rejection episode sustained on post op day 24	Prednisolone was used at a higher dose from 25 to 60 mg/kg daily. Tacrolimus and clobetazol ointments were employed. The dose of mycophenolate mofetil was increased	Normal outcome
April, 2006 Xi'an, China Guo[33]	Episodes of acute graft rejections occurred in months 3, 5, and 17 after transplantation	Tacrolimus dose adjustment and methylprednisone therapy for 5 days. The steroid regime was tapered subsequently by a gradual reduction of the dose	Normal outcome
January, 2007 Paris, France Lantieri[1]	Two episodes of rejection occurred on days 28 and 64.	Prednisolone was increased to 60mg for 3 days along with 3 daily 500mg IV boluses which were administered	Resolution of the rejection episode clinically however biopsies still demonstrated evidence of graft rejection
December, 2008 Cleveland, OH, USA Siemionow[1]	On day 47, biopsy revealed Banff III/IV). rejection of the graft	A single dose of IV corticosteroids	Normal outcome shown by negative biopsy
March, 2009 Paris, France Lantieri[1], [34]	Biopsies showed a grade 1 acute T cell mediated acute rejection	Intravenous methyrlprednisolone for 3 consecutive days with ATG therapy	Normal resolution
April, 2009 Boston, MA, USA Pomahac[35]	On post-op day 17, the patient developed facial redness. Flap biopsies showed a grade 1 rejection	A methylprednisolone bolus was given. And MMF was switched to mycophenolic acid At day 74 and 107, topical treatment included clobetazol cream. This was given between days 27-35 and 37-45 as well. Tacrolimus cream was used on day 107-113. Metronidazole cream was given on day 115 for rosacea infection	Normal outcome (An undiagnosed case of rosacea infection went undetected in the donor allograft tissue which delayed treatment)
August, 2009 Paris, France Lantieri[2]	One episode at day 5 of acute rejection	Intravenous methylprednisolone doses on 3 consecutive days as well as administration of ATG	Normal outcome
August, 2009 Valencia, Spain[36]	Two acute rejection episodes occurred on postoperative days 14 and 350 (Banff l, grade III)	Methylprednisolone 500 mg/24 hrs for 5 days.	Normal outcome
November, 2009 Amiens, France Devauchelle [9]	5 episodes of acute rejection on day 41, day 103, month 6, 16 and 18th	Antithymocyte globulin, tacrolimus and prednisolone were all employed	Normal outcome

Table 1. Example cases of acute rejection episodes with treatments and outcomes.

Analysing all current documented cases of facial transplants, they have all sustained episodes of acute rejection [1], which contrasts to the initial predicted incidence of 50% based on hand transplants [5]. However, all episodes have been well controlled with changes in immunosuppressive therapy therefore preventing graft loss in the acute stage. **Table 1** demonstrates some cases where the timelines of acute rejection episodes have been reported along with the treatment method and outcome. Currently, no graft loss from acute rejection has been reported [1, 8, 9]; however, detailed explanation of the nature of all acute rejections in the literature is still pending.

Although the majority of acute rejection episodes have been well controlled, greater clinical research is needed to reduce the incidence when performing facial transplantation as it hinders post-operative recovery. For now, strict early recognition protocols should be adapted to allow for timely detection and treatment.

1.5.1.2. Chronic rejection

Chronic graft rejection can result in progressive fibrosis of skin with ultimate graft failure [37]. So far, there has been one case reported within the literature. This occurred subsequent to the minimization of immunosuppressive therapy due to an Epstein-Barr virus (EBV)-positive B-cell lymphoma [10]. The chronic rejection ultimately compromised graft function with evidence of reduced mouth opening [10]. Such a rejection event can be avoided if better donor and recipient matching for EBV is conducted. Also, strict management protocols of acute rejection episodes should be adapted for the prevention of any potential progression towards a chronic mode of rejection.

1.5.2. Infections

Immunosuppression causes an increased predisposition to acquiring infections and Butler had collectively referred to all the adverse effects that could potentially surface from immunosuppressive agents [5]. Infective complications have affected 11 patients of transplanted allografts so far [1, 38]. Lack of pre-transplantation detection of cytomegalovirus has led to six recipients acquiring the infection [2, 38]. Bacterial infection has been reported in eight cases with five patients developing sepsis [3]. Leukopenia has also been experienced amongst two recipients who had their medication regime altered to lower doses [39, 40]. With respect to the high proportions of infections developing in the recipients of facial allografts, it is fair to say that we should employ better pre-op screening techniques to reduce the incidence of transmission. Certainly, viral screening of the allografts could have prevented cytomegalovirus transmission and reduced the incidence of infections encountered. Such a protocol should be considered for future transplantations. Also, early recognition is key as in one case an underlying Candida infection was misdiagnosed [3] as an acute rejection episode and this can lead to a delay in treatment. Maintenance immunosuppression certainly poses significant risks for facial CTAs and this like other forms of allotransplantation is dependent on the success of tolerance regimes to provide better functional outcomes. So far, clinical trials have included Tregs, which are regulatory T cells and are believed will be able to induce tolerance enabling graft survival. Recent evidence also points to focusing research on the role of effector cells such as T cells as

well as B cells as they are believed to possess key roles in regulating inflammatory responses [41, 42]. Tolerance would allow for better outcomes in facial CTAs as it would eliminate the need for long-term immunosuppression.

1.5.3. Mortality

There have so far been three reported mortalities in the case of facial transplantation [1]. The Chinese case failed in complying with long-term immunosuppressive therapy ultimately resulting in multi-organ failure [1]. A second case who received bilateral simultaneous below elbow upper limb transplants in conjunction with a facial transplant sustained a cardiac arrest in the post-operative period whilst in ITU after being treated for septic shock and pneumonia [2, 43]. Another patient who also underwent simultaneous hand and facial transplantation sustained upper limb ischaemia subsequent to septic shock and the hand transplants were removed with salvage of the facial allograft [2]. This indicates that perhaps concomitant limb and facial transplantation should not be conducted due to increased risk of post-operative complications. The third patient mortality stemmed from a squamous carcinoma development of the tongue in a human immunodeficiency virus (HIV)-positive patient [36, 43]. This indicates that patients with severe co-morbidities should not be considered as recipients particularly in those with immunocompromised states.

1.5.4. Functional outcome

Results concerning functional improvement have been positive with increased ability to perform basic facial functions [2, 4, 8]. Regression of normal motor function has been encouraging although slightly slower than sensory restoration [2, 12]. Despite this, the first case in France regaining the ability to eat and drink after 1 week [10] has displayed great promise. Equally, results have been paralleled globally with a case in Spain regaining full swallowing ability at 16 months [36, 44]. This demonstrates that motor function restoration can be just as swift as that of sensory. Gross return of lip motion has been reported too at 3 months [3]. Pomahac has reported restoration of olfaction as early as the third post-operative day and a return to facial sensation at 3–4 months time for the three cases he has addressed [3]. Chronic pain induced by skin contractures has also been obliterated and offered an additional mode of function improvement [1]. Fischer et al. have demonstrated significant improvement in numerous facial functions including speaking, breathing, eating, smelling, improved facial expression as well as sensation in the vicinity of a single study [45]. They report that between 20 days and 1 year, all patients were capable of oral food intake with removal of all feeding tubes, after 9 months all patients at their centre had regained intelligible speech, which correlated with other studies within the literature, olfactory sensation was recovered in 100% of cases where it was previously impaired, significant improvements in breathing were reported too, facial expression was, however, only reported to increase in 76% of reported cases. A unique finding that has been deduced from facial transplants is the efficiency of sensory nerve reinnervation even when they have not been directly opposed in terms of microvascular restoration. Restoration of sensory function has still been very good [2, 11]. This, however, has not been the case in terms of motor function where poor anastomotic recon-

struction has been reflected by lack of motor improvement [45]. Therefore, a standardized level of microvascular reconstruction should be aimed for so as to obtain both satisfactory motor and sensory reinnervation. Early rehabilitation of facial musculature is important in facilitating a normal outcome and therefore a multidisciplinary approach including speech and language therapy is important as it aids cerebral recognition of newly transplanted facial musculature [4].

1.5.5. Psychological risks

Psychiatric evaluation of patients for the receipt of donor facial CTAs is essential in order to minimize risk. Patients who are considered for selection must acknowledge the pros and cons of the procedure, be highly motivated as well as appreciate the importance of engagement with long-term multidisciplinary team therapy [32]. Some of the contraindications include active psychotic disorders, severe personality disorders as well as previous suicide attempts [32]. Viewing an altered facial structure can induce emotional stress as an individual fails to recognize his/her own identity [28]. However, until now there has been no documented psychological complications due to altered identity with recipients having had accepted their new appearance [5, 19, 25]. Recipients have also been shown to not possess donor resemblance [29, 30] as was initially predicted by Butler [16], thus nullifying these perceived risks. Results overall have shown positive outcomes with reports of reduced depression and a sense of greater social integration amongst patients treated with the facial CTAs [14].

Despite thorough psychological assessment for the selection of patients, there has been one case in China where lack of motivation in compliance with long-term immunosuppressive therapy has contributed to a mortality [14]. This emphasizes the importance of maintaining a robust pre-operative psychological workup as well as the need for post-operative psychological follow-up.

It is important to appreciate maintaining a quantitative method of assessing psychological changes. Coffman et al. have emphasized the use of various psychological scales in order to achieve this [46]. They followed outcomes for up to 3 years in a recipient of a facial CTA and quantified their findings. Scaling systems were used every 3 months for the first 2 years and then every 6 months. The Psychosocial Adjustment to Illness Scale (PAIS-SR) scoring system was employed in order to assess social reintegration and psychological distress. The patient's Perception of Teasing FACES scores decreased from 25 to 9 at the last follow-up. PASTAS-State (Physical Appearance State and Trait Anxiety Scale: State) was utilized in order to evaluate the patient's mental state in accordance to their body and facial image. Overall, it showed an improvement during the course of the 3 years. Other scales that were used included the Beck Depression Inventory, which decreased from 16 to 6 by 3 months, and the PAIN thermometer, which showed a reduction in the degree of pain post-surgery.

Quantifying the psychological outcomes will most certainly reduce risks as it will enable for timely recognition of mental problems that could develop post-operatively. Early detection and treatment will therefore allow for a quicker recovery, which will also maintain patient motivation in complying with the post-op multidisciplinary therapy.

1.5.6. Miscellaneous risks

1.5.6.1. Blood loss

Significant intraoperative blood loss was a complication that was initially overlooked in 2006 [16]; however, it was a concern amongst the initial transplants [2, 3] conducted and the associated indirect risks posed from subsequent transfusions. However, as surgical techniques have become more refined, the incidence of significant intraoperative blood loss has been reduced.

1.5.6.2. Chronic renal insufficiency

This has so far developed in two patients subsequent to immunosuppressive therapy [4, 39]. Such problems had been predicted [26] in relation to long-term immunosuppression; however, the incidence has so far been low [43]. Unless tolerance regimes become developed, the risk of this complication will persist.

1.5.6.3. Malignancy

Neoplasia has been evidenced in three cases so far with one patient sustaining mortality subsequent to a squamous cell carcinoma of the tongue [43]. This was due to the effects of immunomodulation from an underlying HIV infection in the recipient. Another patient developed a monoclonal B-cell lymphoma at 4 months [43] due to Epstein-Barr virus mismatch implicating that stricter viral screening measures of donors need to be adapted. Cervical dysplasia has also been reported in the first partial facial allograft in France for which the patient underwent hysterectomy [47].

1.6. Conclusion

In conclusion, we can see that acute rejections have shown to affect almost all patients. Although they have been well controlled with no graft loss, it should still draw focus towards more research in this field and how to limit its incidence as there has been a report of one case that has progressed towards chronic rejection impairing graft function. Infective complications have affected 11 patients. Almost half of these could have been avoided if stricter protocols were practised in terms of pre-operative viral screening of donor grafts. Six cases of cytomegalovirus and one case of EBV were acquired. These could have been prevented. Significant complications can arise as a result of infections as was evidenced in the case of Epstein-Barr virus acquisition from a donor graft causing monoclonal B-cell lymphoma. The risk of unpredictability in functional improvement has certainly been disproved. All reported cases so far excluding the three mortalities have demonstrated improved facial function to some degree apart from one case of reduced graft function due to chronic rejection. Psychological complications have been negligible apart from one case in China not complying to his immunosuppressive therapy. This can be avoided by better patient selection and a more thorough psychological assessment in terms of choosing transplant recipients. Also, it is important to quantify the psychological outcome as it will help to improve the post-op follow-

up and recognize mental problems that may develop. Concomitant limb and facial transplants should be avoided as it has shown to increase mortality and morbidity in the two cases where it has been attempted. Recipient co-morbidity status should therefore be considered pre-operatively as it can increase the complication incidence. This has been further highlighted by mortality in relation to one recipient with HIV succumbing to a malignant complication of the tongue again emphasizing the importance of considering co-morbid state.

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