Anaesthesia and intensive care management of face transplantation

A. Sedaghati-nia1*, A. Gilton1, C. Liger1, M. Binhas1, F. Cook1, B. Aït-Mammar1, E. Scherrer1, M. Hivelin2, L. Lantieri2, J. Marty1 and B. Plaud1

1 Université Paris-Est Créteil, Assistance Publique – Hôpitaux de Paris, GHU Henri Mondor – Albert Chenevier, Service d’Anesthésie, Réanimation Chirurgicale, Créteil F-94010, France
2 Université Paris-Est Créteil, Assistance Publique – Hôpitaux de Paris, GHU Henri Mondor – Albert Chenevier, Service de Chirurgie Plastique et reconstructive, Créteil F-94010, France
* Corresponding author: Groupe hospitalier Albert Chenevier-Henri Mondor, Assistance Publique – Hôpitaux de Paris, Service d’anesthésie, réanimation chirurgicale, 51, avenue du maréchal de Lattre de Tassigny, Créteil F-94010, France. E-mail: amir.sedaghati@hmn.aphp.fr

The face-grafting techniques are innovative and highly complex, requiring well-defined organization of all the teams involved. Subsequent to the first report in France in 2005, there have been 17 facial allograft transplantsations performed worldwide. We describe anaesthesia and postoperative management, and the problems encountered, during the course of seven facial composite tissue grafts performed between 2007 and 2011 in our hospital. The reasons for transplantation were ballistic trauma in four patients, extensive neurofibromatosis in two patients, and severe burns in one patient. Anaesthesia for this long procedure involves advanced planning for airway management, vascular access, technique of anaesthesia, and fluid management. Preparation and grafting phases were highly haemorrhagic (> one blood volume), requiring massive transfusion. Median (range) volumes given for packed red cell (PRC) and fresh-frozen plasma (FFP) were 64.2 ml kg\(^{-1}\) (35.5–227.5) and 46.2 ml kg\(^{-1}\) (6.3–173.5), respectively. Blood loss quantification was difficult because of diffuse bleeding to the drapes. The management of patients with neurofibromatosis or burns involving the whole face was more difficult and haemorrhagic than the patients with lower face transplantation. Average surgical duration was 19.1 h (15–28 h). Postoperative severe graft oedema was present in most patients. Most patients encountered complications in ICU, such as renal insufficiency, acute respiratory distress syndrome, and jugular thrombosis. Opportunistic bacterial infections were a feature during the postoperative period in these highly immunosuppressed patients.

Keywords: allograft; anaesthesia; intensive care; face; transplantation

Accepted for publication: 26 March 2013

Since the First World War, a number of surgical aesthetic reconstructive techniques for patients who have suffered facial trauma have been developed. However, the limits of those reconstructive procedures quickly became apparent in the most severe patients. These issues, in those extreme cases, led to the exploration of allotransplantation of composite tissues.1 Subsequent to the first report in France in 2005, there have been 17 facial allograft transplantsations performed worldwide. These face-grafting techniques are innovative and highly complex, requiring well-defined organization of all the teams involved. Here, we describe anaesthesia and postoperative management during the course of seven composite tissue grafts performed between 2007 and 2011 in our institution.

Case reports

Patient 1 was a 27-yr-old male with a massive plexiform neurofibroma, Type 1. Patient 2 was a 25-yr-old male suffering ballistic trauma with avulsion of the mandible and maxilla and nasal septum. Patient 3 was a 37-yr-old male who suffered severe burns from an explosion; the facial and scalp aesthetic sequelae were severe and he lost all fingers on both hands. Patient 4 was a 33-yr-old male who suffered ballistic trauma with mandibular, superior maxillary, and nasal substance loss. Patient 5 was a 35-yr-old male with a voluminous plexiform neurofibroma, Type 1. Patients 6 and 7 were 49- and 48-yr-old males, respectively with severe lower face defect from ballistic trauma.

The preoperative screening included coagulation studies and cardiac evaluation with transthoracic echocardiography. Particular attention to the face injury and previous reconstructive surgery that may influence airway access was needed. Otolaryngology consultation was organized in this clinical research protocol to evaluate potential risks which can influence airway management. Vascular access evaluation in light of the haemorrhagic risk was crucial. Clinical research protocol was...
Anaesthesia for face transplantation

Anaesthesia was induced with both propofol (2.5 mg kg$^{-1}$), sufentanil (0.15–0.2 μg kg$^{-1}$), and rocuronium (0.5 mg kg$^{-1}$). In all patients, a femoral central venous catheter was placed. The internal jugular and subclavian veins were excluded because of the risk of thrombosis and inaccessibility of upper body area, and to avoid haemo-pneumothorax risk in these long procedures. Invasive arterial pressure monitoring was used in anticipation of haemodynamic instability. Three patients with lower face defect had pre-existing tracheostomy Patients 2, 4, and 7). In Patient 6, the tracheostomy wound was reopened with local anaesthesia before induction. For the remaining three patients with tumours or burns involving the whole face Patients 1, 3, and 5), oro-tracheal intubation using a laryngoscope blade conventional Macintosh type English Profile, Blade 4 and oral tracheal tube with a 7.5 or 8.0 mm internal diameter (ID) was performed without any difficulties and converted to tracheostomy before surgery (Figs 1 and 2). In all patients, a Montandon tube (ID 7.0 or 8.0 mm), a straight and long J-shaped tracheal tube with a bend >90° to pass down a tracheostomy (to allow access for head and neck operations), was used. The tracheostomy tube was sutured but not tied with a circumferential tie because of the risk of venous outflow obstruction secondary to facial swelling. An oral gastric tube was inserted for patients who did not have existing gastrostomy and removed before surgery. At the end of surgery, the Montandon tube was replaced by a regular tracheostomy tube (ID 7.0 or 8.0 mm) in all patients.

The patients were placed in a slight head up position at 15° to enhance venous drainage, to reduce blood loss, and reduce the risk of pneumonia. This needed particular attention to the risk of air embolism, optimizing volume status should be adjusted to prevent wide gradients between the right atrium and the entraining vein and there are ample reasons to avoid the use of nitrous oxide. Installation of all the materials and monitoring were placed at the patient’s feet while leaving the surgeon free access to the head and neck.

Anaesthesia was maintained with sevoflurane (0.8–1.8 minimum alveolar concentration) and a continuous infusion of 0.1–0.25 μg kg$^{-1}$ h$^{-1}$ of sufentanil. Volatile anaesthetic agents were used for their protective effects on the free flap microcirculation. Peroperative intermittent positive pressure ventilation was used as it allows accurate control of arterial blood gases and depth of anaesthesia during a prolonged procedure, using a mixture of O$_2$ and air (with F$O_2$=0.5), a tidal volume of 8 ml kg$^{-1}$, and a ventilator frequency adjusted to maintain end-tidal CO$_2$ between 4.7and 5.3 kPa. Hyperoxia and hypocarbia were avoided as either may produce arteriolar vasoconstriction. Monitoring systems such as arterial pressure, heart rate, oxygen saturation, urine output, electrocardiography, delta pulse pressure and delta down were used to assess the adequacy of perfusion and oxygenation of vital organs. Routine laboratory-based coagulation, fibrinogen, complete blood count, blood gas analysis, and electrolytes measurements were repeated regularly (e.g. ≤2–4 h depending on the clinical evaluation). Bispectral index monitoring was restricted by the surgical field and was not applicable in these interventions.

The initial dissection of the recipient site leads to significant blood loss. Controlled hypotension (mean arterial pressure (MAP) up to ~50 mm Hg and systolic arterial pressure up to 85 mm Hg) using general anaesthesia (sevoflurane and sufentanil infusion) was used to reduce bleeding. Once anastomosis was achieved, the MAP up to ~65 mm Hg and systolic arterial pressure >95 mm Hg was respected, in order to enhance cardiac output and maintain an adequate graft perfusion.

Preparation and grafting phases were highly haemorrhagic (>one blood volume), mandating massive transfusion. Taking into account the negative aspects of the low values, a minimum haematocrit of 27% was respected. Transfusions during the procedure most often were started at 4 h and maximum rate was between 8 and 12 h after the start of surgery. Packed red blood cells (PRC) were administered to maintain haemoglobin (Hb) concentration >9 g dl$^{-1}$, platelet concentrates (PC) (refer to one unit of platelets as either plasmapheresed from one donor or collected from 4 to 6 whole-blood donations and containing ~2–8×10$^{11}$ platelets) were used to obtain platelets count >50×10$^9$ litre$^{-1}$, fresh frozen plasma (FFP) to maintain activated partial thromboplastin time (APTT) and prothrombin time (PT) at <1.5 times control, and pasteurized human fibrinogen concentrate (Clottagen, LFB SA, Les Ulis, France) to maintain fibrinogen concentration >1 g litre$^{-1}$, Median volumes given for PRC were 64.2 ml kg$^{-1}$ (range 35.5–227.5), median volumes for FFP were 46.2 ml kg$^{-1}$ (range 6.3–173.7), median volumes for PC were 9.2 ml kg$^{-1}$ (range 0–36.2). A combination of crystalloid and colloid fluids was used to maintain an optimal blood flow. The median volume of crystalloid was 9.5 ml kg$^{-1}$ (range 11.4–8.4).

Patient 1 experienced severe arterial hypotension and sinus tachycardia concomitant with the administration of i.v. antithymocyte globulins (ATG) and required norepinephrine (0.2–1.5 mg h$^{-1}$) infusion >3 h. Patient 3 underwent dual hand grafts before face grafting. Subsequent facial grafting was highly haemorrhagic (>three blood volume), associated with major haemodynamic and haemostatic disorders requiring transfusion of: 60 PRC; 60 FFP; 9 PC units; two preparations of clotting factors (2,7,9, and 10); and six vials of fibrinogen.$^2$

The immunosuppressive regimen, designed for high immunological risk recipients, consisted of ATG, mycophenolate...
<table>
<thead>
<tr>
<th>Preoperation</th>
<th>Transplantation</th>
<th>Postoperative evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient number</td>
<td>Sex</td>
<td>Age</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>27</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>37</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>35</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>49</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>48</td>
</tr>
</tbody>
</table>
mofetil, oral tacrolimus, and prednisolone. Hypothermia was prevented by forced-air warming technique and fluid and blood warming devices. Rectal probe was used for a continuous reading. The average core temperature at the end of the procedure was 37.4°C (range 36–38). Long surgical duration required thrombosis prevention with anti-embolism stockings and Flowtron® inflatable anti-deep venous thrombosis leggings.

Patients 4, 6, and 7 had pre-existing gastrostomy, and for the remaining patients, surgical gastrostomy or jejunostomy was performed at the end of intervention. Average (range) surgical duration was 19.1 h (15–28). Two anaesthetists and one nurse anaesthetist were present in the operating room for each patient.

ICU management

All patients were transferred to ICU. Patients were ventilated with a volume-controlled mode (Servo 900, Siemens, Elema AB, Solna Sweden) with 5 cm H₂O of positive end-expiratory pressure. FIO₂ (0.3–0.6) was adjusted to keep Pao₂ levels between 13.3 kPa (100 mm Hg) and 20 kPa (150 mm Hg). The combination of sufentanil (0.25 μg kg⁻¹ h⁻¹) and midazolam (0.25 mg kg⁻¹ h⁻¹) were used for postoperative sedation. Vasocostriction caused by hypothermia, hypovolemia, and pain are the natural causes to compromise the free flaps.

Normothermia, a MAP up to 65 mm Hg, a haematocrit of >27%, urine output up to 1–1.5 ml kg⁻¹ h⁻¹, appropriate analgesia and anxiety treatment were the goals of postoperative care.

Most of the patients were weaned from mechanical ventilation after a median of 1 day, except Patient 2, who experienced acute respiratory distress syndrome (ARDS) on Day 2 with Pseudomonas aeruginosa pneumonia. Most patients were haemodynamically stable except Patient 1, who required nor-epinephrine infusion (0.2–1 mg h⁻¹) for >2 h to achieve MAP 60–65 mm Hg. Graft perfusion monitoring was performed by Doppler velocities control of the external carotid artery and no graft hypoperfusion was observed in this patient but he experienced reversible moderate renal failure with serum creatinine >1.4 mg dl⁻¹. Patient 4 was returned to surgery on Day 5 for thrombosis of the right external jugular vein because of surgical lesion.

Postoperative severe graft oedema was present in most patients. A head up at 45° position was used for enhanced venous drainage, and prophylaxis of pneumonia. Preventive anti-coagulation was continued with low-molecular-weight heparin.

Enteral feeding was started in all patients as soon as bowel sounds reappeared, usually on the first postoperative day. High-protein formulas were used to help ensure adequate healing (25–30 kcal kg⁻¹ day⁻¹ and 1.5–2.0 g of protein kg⁻¹ day⁻¹), and water needs were estimated at 25–30 ml kg⁻¹ day⁻¹.

Immunosuppression was continued after operation. Two patients (2 and 4) experienced acute cellular rejection in ICU. Deep and superficial bacterial mapping and analysis of the drains and preservation solution were performed during the ICU stage. Most patients experienced opportunistic infections, with bacterial infections predominant (Table 1). Patient 3 suffered multi-resistant P. aeruginosa affecting the face and left hand allograft, despite extensive antibiotherapy and surgical excisions. He developed infected and necrotic facial allograft tissues and septic rupture on a radial bypass. This patient required removal of the left hand and upper part of the facial transplant, and suffered cardiac arrest on Day 33 with irreversible anoxic cerebral lesion revealed by magnetic resonance imaging, leading to death on Day 65.

Three patients experienced viral infection and fungal infection by Candida albicans was found in Patients 2 and 4 (Table 1). Infections related to over immunosuppression were remarkable.

Average duration of ICU admission was 17.4 days (range 4–65).

Discussion

These seven patients illustrate the problems consistently encountered and the strategies that were deployed. The
mechanism of injury was ballistic trauma in four patients, extensive neurofibromatosis in two patients, and severe burns in one patient. Most of the patients had undergone extensive previous reconstructive surgery.

During the preoperative phase, it is mandatory to evaluate: (i) tracheal intubation difficulties, (ii) possible problems with venous access in light of the haemorrhagic risk, and (iii) patient’s infectious and immunological status.

In the operating room, airway management required advanced planning. A Montandon tube was used for the extended tube design which locates breathing system away from the operative field allowing easier access and connection to the breathing system.

A central venous line was required in the inferior vena cava region. The femoral catheter was removed in ICU 24–48 h after surgery. In Cases 1, 2, and 3 which needed a longer period of catheterization, it was replaced by subclavian access at Day 2 to reduce infectious risk in these immunosuppressed patients. Several studies found that catheter related local infection incidence was higher for femoral than for internal jugular or subclavian access routes.

Anaesthesia was maintained with volatile agents. Sevoflurane when compared with i.v. anaesthetics such as propofol could have beneficial effects on the microcirculation by decreasing extravasation of plasma into the interstitial space, and thus limiting tissue oedema. Sevoflurane could also have a protective effect on endothelial cells against ischaemia-reperfusion injury. In experimental models of free flaps, propofol can cause significant endothelial oedema by increasing the number of leucocytes and lymphocytes adhering to the endothelial and migrating outside the post-capillary venule.

Facial preparation and grafting phase proved to be highly haemorrhagic (> one blood volume). For some of the patients, blood loss quantification was initially difficult because of diffuse bleeding to the drapes and also the non-visualized or posterior aspect of the graft. For this significant blood loss, several explanations were retained: new and haemorrhagic
surgical techniques (incision of scalp, first arterial and then venous vascular anastomoses, non-systematic use of aspiration by surgeons, synchronizing difficulties for the teams responsible for facial preparation and grafting), diffuse bleeding of microvascular beds that were difficult to control surgically, and vascular fragility caused by neurofibromatosis associated with arterial and neurofibromatous venous invasion.

Rheological factors make a relatively low Hb level desirable (9 g dl⁻¹) when microvascular free flaps are performed. The cell saver was difficult to use in this type of surgery because of the diffuse bleeding result from not tying several vessels to prevent any omission at graft.

All patients received PRC and FFP units; average PRC was 22.7, ranging from 9 to 60, while average FFP was 19.8, ranging from 2 to 60. Five patients received platelet, averaging 13.7 in a range from 0 to 54. Average ratios for FFP/PRC were 0.87; average ratios for platelet/PRC were 0.60. In massively injured patients, the treatment of coagulopathy with plasma administered in a 1:1 ratio with PRC has a certain degree of face validity and growing support in observational studies. The increased use of plasma, however, is not without risk. Immunomodulation and nosocomial infection are all higher in transfused trauma patients and should be considered in these highly immunosuppressed patients. Higher risk of ARDS has been reported.

The intraoperative crystalloid infusion rate was 9.5 ml kg⁻¹ h⁻¹ and the risk associated with dilusional coagulopathy was considerable. Conventional coagulation analyses were used to identify those patients in need of plasma or platelet substitution. These analyses describe only isolated parts of the haemostatic process, and a platelet count does not reflect whether the platelets are functionally intact. Viscoelastic whole-blood assays, such as thrombelastography and rotational thrombelastometry provide a rapid evaluation of clot formation, strength, and lysis and may lead to improved outcomes while optimizing blood utilization.

In most cases, moderate hypotension was begun before posing of graft between 4 and 8 h after the start of surgery. In Patient 1, who required norepinephrine infusion, no graft hypoperfusion was observed after operation. Catecholamines are traditionally avoided, despite there being little evidence of them adversely affecting flap blood flow. Free flap surgery results in the disruption of the autonomic nerve fibres. In the short term, sympathectomy may reduce vascular tone and improve microcirculation. Animal studies have shown that at least in the short term there is a reduced response to circulating vasoconstrictors post-sympathectomy.

Management of patients with extensive neurofibromatosis or burns involving the whole face was more difficult and haemorrhagic than the patients with lower face transplantation (Fig 3). No respiratory failure, favoured by massive transfusion like transfusion-related acute lung injury was observed intraoperatively or immediately after operation. No signs of disseminated intravascular coagulation or fibrinolysis were observed. The technical progress made with diminished blood loss for the last cases was remarkable. Because of length of these surgeries, it required the successive availability of anaesthesia and surgical teams as several teams were required to accomplish the procedures.

Most patients encountered complications in ICU (Table 1). Patient 1 experienced moderate renal failure because of extra-cellular dehydration and possible overdose of Mycophenolate mofetil. Venous thrombosis occurred in Patient 4 on Day 5. Head and neck free flaps are different from other recipient sites and although most extremity microvascular complications occurred within the first 48 h, the same was not true for head and neck reconstructions and they should be monitored for at least 5 days because of the potential for pedicle kinking with neck movement.

Postoperative severe graft oedema was present in most patients. Flap tissues are susceptible to interstitial oedema having had their lymphatic drainage disrupted. Oedema reduces flow to the flap and may be a result of extreme haemodilution, trauma from handling or a prolonged ischaemia time. Postoperative head up position and negative fluid balance were used to reduce face oedema.

Patient 2 experienced ARDS with P. aeruginosa pneumonia. A prospective cohort study of ICU patients identified that pulmonary aetiology of injury (pneumonia, aspiration) and transfusion of > 8 units of packed RBC were associated with a higher risk of ARDS.

The risk of infection was severe. Most patients experienced opportunistic infections. This high risk of infection has been reported previously in hand transplant recipients. Early infections were mostly bacterial. Patient 3 suffered from extensive infected and necrotic face and hand allograft tissues and died on Day 65. The risk of infection mandates early removal of all invasive lines and subsequent frequent screening. Opportunistic infections and length of ICU admission were decreased in the last cases (Table 1).

Two patients experienced acute cellular rejection in ICU. This high incidence is consistent with another report, and may be because of the importance of antigenicity in skin and easy detection of this rejection in clinical evaluation. Rejections were controlled by complementary treatments.

In conclusion, these seven patients illustrate constant and consistent difficulties encountered in face grafts and the strategies used to circumvent them. Anaesthesia for this long procedure involves advancing planning for airway management, vascular access, technique of anaesthesia, and fluid management; and plays an important role in influencing outcome. All of the face transplant recipients were considered at the risk of massive blood loss and consequent transfusion. ICU management involves a number of special issues for maintenance of adequate graft perfusion. Postoperative opportunistic infections in these highly immunosuppressed patients were remarkable. Intraoperative transfusion quantities and postoperative complications have been reduced over the past 5 years.

Declaration of interest

None of the authors has any conflict of interest to disclose in relation to the study material. We confirm that we have read the...
Journal’s position on issues involved in ethical publication and declare that this report is consistent with those guidelines.

Funding
This work was supported only by institutional funding.

References

Handling editor: R. P. Mahajan