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Anaesthetic Management for Face Transplantations: The Experience of Akdeniz University

Necmiye Hadımoğlu[1], Melike Cengiz[1], Atilla Ramazanoğlu[1], Özlenen Özkan[2], Mustafa Gökhan Ertosun[2], Nilgun Bilal[3], Ömer Özkan[2]

[1]Department of Anaesthesiology and Reanimation, Akdeniz University School of Medicine, Antalya, Turkey
[2]Department of Plastic and Reconstructive Surgery, Akdeniz University School of Medicine, Antalya, Turkey
[3]Akdeniz University Hospital, Transplantation Center, Antalya, Turkey

ORCID IDs of the authors: N.H. 0000-0001-7469-7646; M.C. 0000-0001-6417-6214; A.R. 0000-0002-7215-6237; Ö.Ö. 0000-0001-6744-9193; M.G.E. 0000-0002-2557-7346; N.B. 0000-0002-7154-4908; Ö.Ö. 0000-0002-9031-5596

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Abstract

Objective: Solid organ transplantation is a rescue therapy, whereas face transplantation, as well as other composite tissue allotransplantations, offers treatment options to enhance the quality of life. Difficult airway, severe haemorrhage and prolonged operative length are among the frequently encountered complications of anaesthetic management in patients with a history of multiple reconstructive surgeries.

Methods: Five face allotransplants that were performed in our institute, arising from four full and one partial face transplantations, were reviewed. The pitfalls encountered before, during and following surgery were then summarised.

Results: Two of our patients (patients 3 and 4) underwent permanent tracheostomy preoperatively. Transplantation was initiated after surgical tracheostomy under local anaesthesia and under sedation in cases 2 and 5. Patient 1 was orally intubated without difficulty under general anaesthesia and was operated following tracheal cannulation via surgical tracheostomy. Thirteen units of red blood cells were transfused each for patients 2 and 4. Two other patients (patients 1 and 4) each received 5 units of red blood cells. Patient 5, who underwent mid-face transplantation lasting for 7.5 h, was not transfused. No major life-threatening complications were observed intraoperatively or following surgery.

Conclusion: Face transplantation is a surgical procedure in which anaesthetic management may be problematic. The anaesthetist may encounter difficulties, such as difficult airway, severe bleeding, a prolonged operative time and postoperative complications. Side effects and complications may be reduced by strict follow-up and haemodynamic monitoring of patients.

Keywords: Anaesthesia, complications, face transplantation

Introduction

Organ transplantation involves the transfer of an organ, part of an organ or tissue from a living or brain-dead donor to a patient with organ or tissue insufficiency, as well as associated arrangements, procurement, protection, preservation and practice (1). Organ transplantations are performed to save lives, extend survival, improve the quality of life and for therapeutic purposes. As a result of advances in science and medicine since the 1980s and the introduction of immunosuppressive agents used following transplantation, the number of organ transplantations has increased rapidly, and kidney, heart, liver, lung and pancreas transplantations have been successfully performed worldwide and also in Turkey. Composite tissue transplantation was a new development in the field of transplantation in the early 2000s. Composite tissues consist of the dermis, fat tissue, muscle, tendon, nerve, lymph node, bone, bone marrow, blood vessels and combinations of each, originating from the ectoderm or mesoderm. In other words, composite tissue transplantation represents the transfer of multiple tissue and organ fragments, such as the intestine, anterior abdominal wall, uterus, face, scalp, hand, foot, larynx, vessel, nerve, cartilage and bone, according to Agich et al. (2). Cadaver-derived composite tissue transplantation may be

Corresponding Author: Necmiye Hadımoğlu E-mail: necmiye@akdeniz.edu.tr

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performed in conditions leading to extensive defect and additional morbidity, such as trauma, burn, congenital deformities or tumour resection. Owing to recent advances in microvascular surgery and transplantation immunology, composite tissue transplantation has become an important therapeutic option and potential solution to reconstruction problems for extremity amputations and large tissue defects.

In contrast to solid organ transplantations, composite tissue transplantations are performed to improve the quality of life rather than to save life. Major factors limiting these kinds of transplantations are chronic rejection and systemic toxicity caused by lifelong immunosuppression.

Reconstruction of facial deformities resulting from severe burns, trauma and cancer-related surgeries is one of the most compelling issues for plastic and reconstructive surgeries. The aim of face transplantation, classified under composite tissue transplantations, is to gain functionality while providing aesthetic improvement that has not been achieved by classic reconstruction surgeries. Face transplantation was first introduced in 2005. Some 40 partial or full face transplants have been performed in various countries to date (3-6). Complications related to the use of immunosuppressive agents may be encountered following these surgical procedures. Complications, such as opportunistic infections, metabolic complications and malignancies, may have catastrophic effects since face transplantation is not regarded as a life-saving procedure.

Five (four total and one partial) face transplantations have been performed in our hospital since 2012 (7). This is the largest number of face transplantation cases from a single centre to date. The purpose of the present study was to report the management of anaesthesia and details of surgery, postoperative results and difficulties encountered in each case.

Methods

The study was approved by the Institutional Review Board (IRB). Written informed consent was obtained from all subjects. Ethical permits for transplantation surgery were obtained from the Review Board of the General Directorate of Curative Services of the National Ministry of Health. A vascularised composite tissue transplantation directive (No. 13984) including face, extremity, larynx and upper aerodigestive tract and intestinal transplantations was issued in 2011. Based on that directive, our institute has been certified as the first authorised vascularised composite tissue transplantation centre in Turkey. The internal scientific and ethical committee of our institution investigated and verified patients' suitability for possible transplantation and selected patients recorded on the national transplantation list after evaluation by the national scientific committee on vascular-

Table 1. Characteristics of face-transplanted patients

Characteristic		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	Donor	37	19	42	31	34
	Recipient	19	35	26	54	22
Blood type	Donor	A, Rh-positive	O, Rh-positive	B, Rh-positive	A, Rh-positive	A, Rh-negative
	Recipient	A, Rh-positive	A, Rh-positive	B, Rh-positive	A, Rh-positive	A, Rh-positive
Date of transplantation		21.01.2012	15.05.2012	18.07.2013	23.08.2013	28.12.2013
Type of injury and when		Burn-35 days	Burn-3 years ago	Gunshot injury-6 years ago	Gunshot injury-4 years ago	Gunshot injury
Type of face transplantation		Full face	Full face	Full face	Full face	Middle face
Total allograft ischaemia (h)		4	4	5	5	4 h and 20 min
Duration of anaesthesia (h)		10	10	12	16	12
Duration of operation (h)		9	9	11	15	11
Units of packed red cells transfused (no.)		5	5	13	13	–
Stay in intensive care unit		2 days	3 days	7 days	4 days	2 days
Duration of intubation (via tracheostomy)		2 days	1 day	5 days	2 days	1 day
Duration of tracheostomy		1 day	2 days	25 days	20 days	1 day

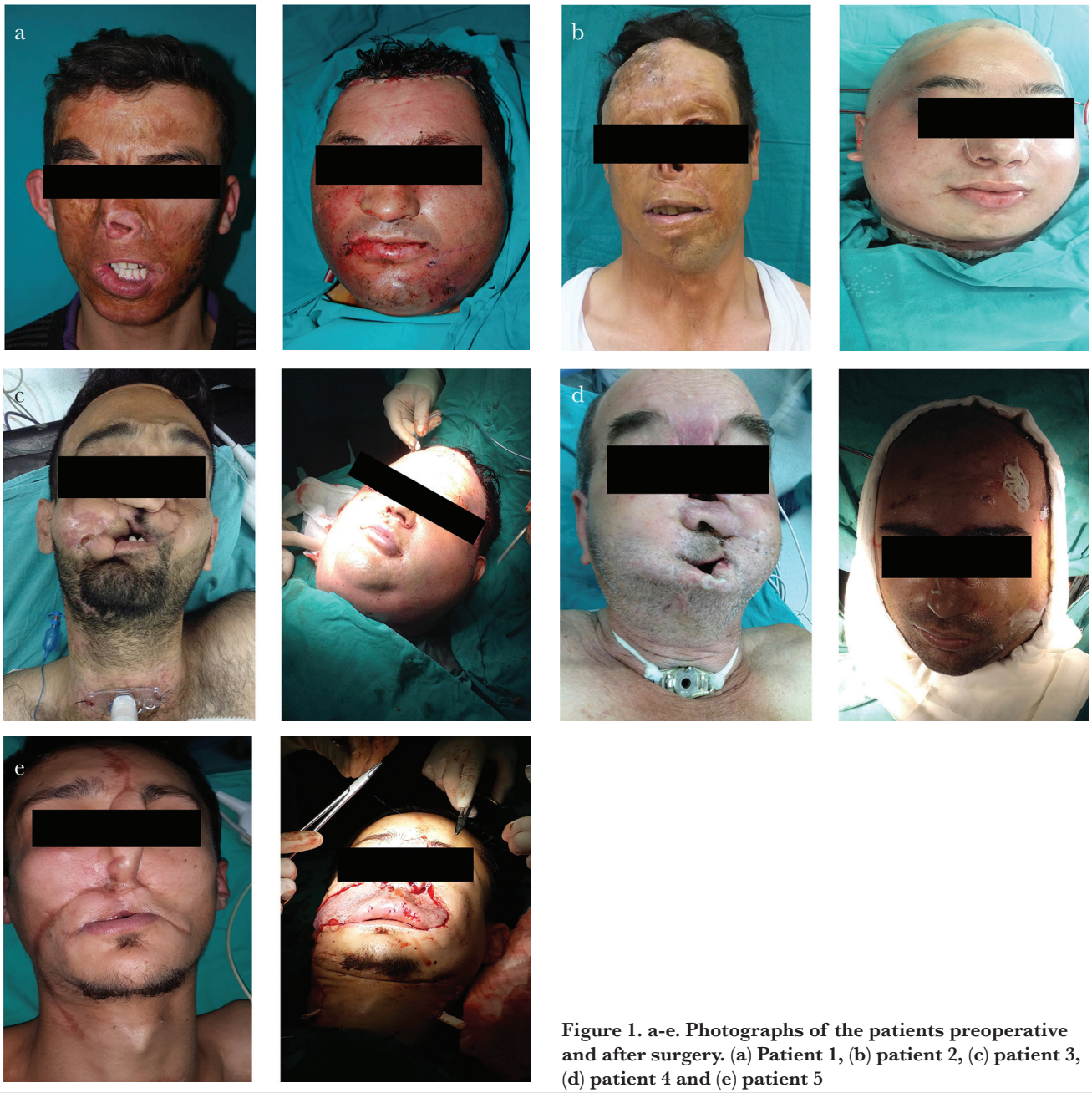

Figure 1. a-e. Photographs of the patients preoperative and after surgery. (a) Patient 1, (b) patient 2, (c) patient 3, (d) patient 4 and (e) patient 5

ised composite tissue transplantation (date 20.01.2012, No: 001). The patients were registered with a regional organ procurement organisation. We also made a detailed informed consent form and a legal contract. This contract referred to all potential complications associated with this potentially life-threatening and non-life-saving procedure, especially well-known or foreseeable drug-related complications, such as severe infections, diabetes, kidney failure, lymphoma and bone necrosis. The male patients in this series underwent face allotransplantation between January 2012 and December 2014. Table 1 lists the relevant demographic data. Causes of large deformity were burn scars in two patients and gunshot injuries in three patients. All patients had already undergone multiple conventional reconstruction surgeries (Figure 1). Facial grafts were obtained from brain-dead donors allocated by the National Organ and Tissue Coordination Centre. The surgical teams were divided into two groups as the donor and the recipient.

Anaesthetic management

Routine anaesthetic evaluation was performed for each patient preoperatively. Those patients who were considered non-problematic were admitted to surgery after preparation of 10 units of packed red blood cells (PRBCs) and fresh frozen plasma (FFP) each. Two of the patients (patients 3 and 4) had undergone permanent tracheostomy. The tracheostomy cannula was inserted under sedation, and local anaesthesia was adminis-

tered prior to surgery in patients 2 and 5. Patient 1 underwent tracheostomy following tracheal intubation accompanied by general anaesthesia. Standard monitoring consisting of electrocardiography, pulse oximetry and end-tidal carbon dioxide, among others, was performed in all cases. Sodium thiopental, fentanyl and rocuronium bromide were used for anaesthesia induction. Invasive blood pressure monitoring was performed via the radial artery in patients 1, 2 and 3 or the arteria dorsalis pedis in patients 2 and 3. A large-bore peripheral venous cannula and central venous catheter were inserted via the femoral vein following induction of general anaesthesia, and central venous pressure was monitored in all cases. Urine excretion was monitored hourly using a Foley catheter. A peripheral temperature probe was used to monitor body temperature.

Surgical procedure

The facial graft was perfused with preservation solution and transferred in slush ice following excision. Donor and recipient surgical procedures were performed by two groups of transplant surgeons in a synchronised manner. The surgical team performing recipient procedures removed the deformed skin and connective tissues, while the other surgical team simultaneously excised the facial graft from the donor body.

Critical care management

Duration of critical care follow-up varied between 2 days (patients 1 and 5) and 7 days (patient 3). All patients were ventilated with assisted pressure-controlled mode using a fractional inspired oxygen concentration (FiO_2) of 40% and a positive end-expiratory pressure of 5 cm H_2O via tracheostomy cannula. Ventilation parameters were titrated to achieve the goals of peripheral O_2 saturation above 90% and partial arterial oxygen saturation (PaO_2) exceeding 80 mmHg. The mean duration of mechanical ventilation was 3.6 days, and patients were discharged from the intensive care unit (ICU) with tracheostomy cannulas shortly after a successful weaning period.

Immunosuppression protocol

Anti-thymocyte globulin and prednisolone were initially administered at the beginning of the transplantation procedure. Tacrolimus was added to the immunosuppressant regimen on postoperative day 4. Mycophenolate mofetil was medicated subsequently. Prophylactic antibiotherapy was used for 10 days after the transplantation in all cases. Immunological follow-up was performed using dermal biopsies twice a week for the first 3 months, once a month for the next 3 months and once every 3 months after 6 months following transplantation. Topical tacrolimus cream application and augmentation of systemic tacrolimus dosages were used to solve the problems of rejection attacks.

No anaesthetic or surgical complication occurred in the early postoperative period in our patient group.

Patients

Patient 1: A 40-year-old man who had lost his face as a result of flame burn at the age of 40 days and who had since undergone multiple surgical procedures for reconstruction. Routine pre-transplantation evaluation was performed since his medical history was unremarkable except for controlled epileptic activity. Difficult airway was not indicated preoperatively, and orotracheal intubation was achieved after routine anaesthesia induction. Tracheostomy was subsequently performed, and surgery then began. In addition to standard monitoring methods, arterial and central venous pressures were monitored via catheters inserted in the radial artery and femoral vein, respectively. Peripheral cannulas were also inserted into the brachial vessels. Five units of PRBCs and 8000 mL of balanced crystalloid solution were administered during the course of transplantation, which lasted for 9 h. No inotropic or vasopressor drugs were required, and 2100 mL of urine was excreted throughout the operation. Blood gases on admission to the ICU revealed 180 mmHg PaO_2, 35 mmHg PCO_2, pH 7.42, 7.9 g dL^{-1} haemoglobin (Hb), 24% haematocrit (Hct) and 1.6 mmol L^{-1} lactate. The patient was discharged to the ward with tracheostomy cannula on day 3 of ICU stay. Oral nutrition was started on day 5, and physiotherapy on day 8 postoperatively. The patient underwent full face transplantation protecting his own lower and upper eyelids and nasal bone and was medicated for seizure prophylaxis because of his history of epilepsy.

Patient 2: A 35-year-old man with a severe facial deformity due to accidental burn at the age of 4 years. He had undergone six previous reconstructive surgeries. His medical history was unremarkable, and routine pre-transplantation evaluation was therefore performed. Surgical tracheostomy under local anaesthesia and sedation was performed to provide a safe airway considering the scar tissue enclosing his face and mouth and the deformity in the nose. In addition to standard monitoring methods, arterial and central venous pressures were monitored via catheters inserted in the radial artery and brachial vein (Cavafix; Braun™), respectively. Five units of RBC, 4 units of FFP, 9000 ml of balanced crystalloid solution and 1000 ml of colloid solutions were administered during the course of transplantation, which lasted for 9 h. No inotropic or vasopressor drugs were required. Blood gases on admission to the ICU revealed 170 mmHg PaO_2, 37 mmHg PCO_2, pH 7.36, 11 g dL^{-1} Hb, 34.4% Hct and 1.9 mmol L^{-1} lactate. He was discharged to the ward after removal of the tracheostomy cannula on day 4 of ICU stay. Oral nutrition and physiotherapy were initiated on postoperative day 7. Full face transplantation including the scalp, upper and lower eyelids and right auricle was achieved. Two additional reconstructive operations were performed to achieve upper eyelid functionality (levator muscle) and to avoid ectropion at the end of 2 months and 1 year, respectively.

Patient 3: A 26-year-old man who lost his face at the age of 20 years due to gunshot trauma. The patient had already been tracheostomised preoperatively. Arterial and central venous pressures were monitored via catheters inserted in the left dorsalis pedis artery and femoral vein, respectively. Duration of anaesthesia was 12 h, and the transplantation procedure lasted for 11 h. Cold ischaemia time was 6.5 h. Thirteen units of RBC, 2 units of FFP, 11,000 ml of crystalloid and 1000 ml of colloid solutions were administered. Noradrenaline infusion was initiated to maintain haemodynamic stability, and total urine excretion was 2000 ml at the end of the operation. Full face transplantation involving the mandible and maxilla was performed. Blood gases on admission to the ICU revealed 190 mmHg PaO_2, 41 mmHg PCO_2, pH 7.36, 10.3 g dL^{-1} Hb, 26.2% Hct and 3.7 mmol L^{-1} lactate. Noradrenaline infusion could not be discontinued postoperatively. Enteral nutrition was started on day 5. The patient subsequently underwent another reconstructive procedure to achieve better chin occlusion. The patient was intubated awake with the help of a fiberoptic bronchoscope due to his limited chin mobility.

Patient 4: A 54-year-old man who had lost his face and had already been tracheostomised as a result of gunshot injury. The patient was anaesthetised with a standard protocol since his history and physical examination were unremarkable. Arterial and central venous pressures were monitored via catheters inserted in the left dorsalis pedis artery and femoral vein, respectively. Duration of anaesthesia was 16 h, and the transplantation procedure lasted for 15 h. Cold ischaemia time was 9.10 h. Thirteen units of RBC, 3 units of FFP, 13,000 mL of crystalloid and 1000 mL of colloid solutions were administered. Noradrenaline infusion was initiated to maintain haemodynamic stability. Total urine excretion was 1900 mL at the end of the operation. Blood gases on admission to the ICU revealed 150 mmHg PaO_2, 39 mmHg PCO_2, pH 7.33, 10.6 g dL^{-1} Hb, 29.4% Hct and 13.6 mmol L^{-1} lactate. Noradrenaline infusion could not be discontinued postoperatively. Enteral nutrition was started on day 4. Although no early complication occurred, squamous cell carcinoma developed in the upper and lower extremities on month 5, and post-transplant lymphoproliferative disorder was diagnosed on month 6 after transplantation. The malignity was treated both medically and surgically. No airway difficulty was observed during post-transplant surgeries, and orotracheal intubation was performed. Opportunistic pulmonary and cerebellar aspergillosis occurred subsequently. The face graft was removed to reduce the metabolic and immunological load hampering the clinical status and replaced with a free flap. The patient died on month 11 after transplantation due to multiorgan deficiency resulting from progressive infectious and metabolic complications.

Patient 5: A 22-year-old man with a history of traffic accident that severely damaged his face at the age of 13 years. No comorbidity was present. He underwent approximately 30 reconstructive surgical procedures after the accident. Transplantation was started following tracheostomy performed with local anaesthesia and general anaesthetic agents. Desflurane, remifentanil and vecuronium were used for the. Wide-spectrum antibiotic prophylaxis was administered in line with the recommendations of infectious disease consultants. The transplantation procedure lasted for 11 h. Cold ischaemia time was 7.5 h, and 5000 mL of crystalloid and 1000 mL of colloid solutions were administered. No blood or blood products were used. Total urine excretion was 1900 mL by the end of the operation. Blood gases on admission to the ICU revealed 185 mmHg PaO_2, 34 mmHg PCO_2, pH 7.36, 12 g dL^{-1} Hb and 1 mmol L^{-1} lactate. Partial face transplantation was performed, including the nose and upper lip. The patient was reoperated for minimal excisional scarring 1 year subsequently, and orotracheal intubation was easily achieved with laryngoscopy.

Discussion

Face transplantation is classified as a composite tissue transplantation procedure, those which improve the quality of life, in contrast to solid organ transplantations intended to save life. The numbers of face transplants are increasing rapidly worldwide at various centres. However, the surgical procedure is still more problematic and complex than other transplantation surgeries (8-10). Anaesthetic pitfalls may also arise during these procedures. The aim of the present study was to evaluate the anaesthetic management of five face transplantations performed over 2 years at our institution.

Extensive facial deformities necessitating face transplantation were caused by burns in patients 1 and 2, gunshot injuries in patients 3 and 4 and traffic accident in patient 5. All patients had undergone several reconstructive procedures before face transplantation.

Another important issue for anaesthesia management is the possibility of difficult airway due to facial deformations (11-13). Tracheostomy may be performed following fiberoptic orotracheal intubation in patients with potential airway difficulty. Another option is to initiate the transplantation procedure after tracheostomy following placement of a tracheostomy cannula applying local anaesthesia and sedation. However, if difficult airway is not indicated, standard anaesthesia induction and intubation followed by tracheostomy may be preferred. Circular fastening of the tracheostomy cannula to the neck may hamper venous return flow in the facial graft. Fixation of the tracheostomy cannula by means of sutures may therefore be recommended.

Two of our patients (patients 3 and 4) received permanent tracheostomy before face transplantation. Surgery began following tracheostomy by the use of local anaesthesia and sedation in patients 2 and 5. The first patient was intubated with direct laryngoscopy with no difficulties in terms of airway patency, and transplantation began after tracheostomy. Another important issue, in addition to airway patency, is the preparation of large-bore venous access considering the duration of surgery and the risk of major bleeding during excision of the recipient tissues for preparation for transplantation.

Femoral vein and arterial cannulation are often used for vascular access and haemodynamic monitoring. Use of the internal jugular or subclavian veins is not recommended due to the risks of thrombosis and disruption of facial graft venous flow (11-13). However, only limited data are currently available regarding the risks associated with femoral catheter infections in an immunosuppressive patient. We used the femoral vein for central vein access in four patients and the subclavian vein via the brachial vein in one patient. Invasive blood pressure monitoring was performed in all cases, and the radial artery was preferred for cannula insertion. Anaesthesia induction was achieved by fentanyl, rocuronium and sodium thiopental for each patient, and desflurane was used as an inhalation anaesthetic during anaesthesia maintenance. Remifentanil infusion and repetitive rocuronium boluses were administered to provide analgesia and muscle relaxation for the rest of the anaesthetic procedure.

Two surgical teams, one for excising the facial graft and the other for preparing the recipient face for transplantation, are required during the transplantation procedure. Preparation of vascular patterns and nerves may be problematic, especially in recipients with histories of frequent multiple surgical procedures for reconstruction. Vascular and nerve anastomoses of the graft are achieved after the preparatory step, and the graft is perfused subsequently. At this stage, major blood loss at the surgical site may be underestimated. It is therefore essential that Hb concentrations be monitored, and that transfusion be performed if required. Some surgical teams prefer to administer replacements using a cell saver. However, this method involves the risks of immunisation and infection. Some authors also recommend limiting transfusion of procoagulant products, such as FFP and platelet suspensions in terms of the risk of facial graft thrombosis. Corticosteroids are used prior to perfusion of the graft in intermittent bolus doses (total of 10-15 mg kg^{-1} methylprednisolone) intraoperatively.

Severe haemorrhage has been reported in previous studies, especially during the face preparation stage. Major bleeding also occurred in the patients transplanted at our clinic, particularly while the recipient's face was being excised for grafting, and transfusions were performed during this stage. Two of our patients (patients 2 and 4) each received 13 units of RBC, and two others each received 5 units of RBC. Patient 5, who underwent partial midline face transplantation lasting for 7.5 h, required no transfusion. Transfusion requirements were notably higher in patients 2 and 4, whose operations lasted for >14 h. Although cell saver use is encouraged in patients with suspected high risks of bleeding, we elected not to use this method. Another major subject of debate in prolonged operations is warming the patient. Maintenance of body temperature can be achieved by using heated infusion solutions and blankets. Warming blankets placed on operating tables and heated blood products and solutions were used in all our cases. However, despite these measures intended to prevent hypothermia, all our patients were hypothermic during admission to the ICU. They were therefore re-warmed during the first hours of ICU care. Balanced crystalloid solution was administered at an infusion rate of 8-10 mL kg^{-1} h^{-1} in addition to RBC and FFP transfusions for fluid replacement. Blood gas analysis and blood coagulation tests were performed every 1 and 3 h, respectively. Intraoperative RBC, FFP and electrolyte replacements were titrated according to the results of these analyses. No transfusion-related complication was observed intraoperatively or in the early postoperative period.

Haemodynamic instability, pancytopenia and delirium were determined in patient 3, and progressive haemodynamic instability and anaemia were observed in patient 4 during ICU stay in the early postoperative period. No serious complications were observed in the other cases at this time. The mean time to discharge from the ICU was 3.6 days, and patient care and physiotherapy were continued on the ward.

Progression of infectious complications in immunosuppressive patients may have severe consequences. Fungal infections known as opportunistic infections are the leading factors involved in severe morbidity. One of our five patients first lost his face and subsequently his life. Respiratory insufficiency worsened by month 9 after transplantation during follow-up. Mortality in this case was related to sepsis, multiorgan insufficiency, pulmonary aspergillosis and acute respiratory distress syndrome. No severe complication has to date been encountered in our other face-transplanted patients. Routine dermal biopsies are performed, and topical corticosteroids are used when rejection is suspected.

Conclusion

Face transplantation is a crucial surgical procedure in anaesthesiology practice. The anaesthetist has to overcome problems, such as management of difficult airway, prolonged operative time and postoperative ICU care. Side effects associated with medications and complications due to transplantation surgery may be minimised by strict haemodynamic monitoring and detailed follow-up.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Akdeniz University School of Medicine (Date: 20.01.2012, No: 001).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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