Anaesthesia for microvascular free tissue transfer

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Free vascularised tissue

Microvascular surgical techniques allow the transfer of free vascularised tissue (free flaps) which may include skin, muscle, bone and bowel. Despite improvements in surgical technique, hypoperfusion and flap failure are still major concerns. Anaesthesia can be an important factor in determining success of this type of surgery through alterations in central haemodynamics and regional blood flow. In addition, regional anaesthesia, changes in blood volume and the use of vasoactive drugs may influence blood flow in the free flap.

Tissue defects can be repaired using skin grafts, local flaps or free flaps. Local flaps are raised and rotated around their neurovascular bundle but the blood supply is never interrupted. In free flaps, the neurovascular bundle is removed from a donor site and transplanted to a new site and microvascularly re-anastomosed.

A flap is transferred to reconstruct a primary defect (see below) and then insert into this defect. This often leaves a secondary defect, which is usually closed by direct suture or by a skin graft. Common flap donor sites include radial and ulnar forearm, latissimus dorsi, rectus abdominis muscle and the groin. Conditions requiring free flap surgery vary widely and include:

- Reconstructive hand surgery using complex autografts (*e.g.* toe-to-hand transfers) or replantation after traumatic amputation
- Trauma (*e.g.* fractures with overlying tissue loss)
- Burns
- Malignancy (*e.g.* head and neck cancers, malignant melanoma)
- Breast reconstructive surgery (*e.g.* transverse rectus abdominis muscle [TRAM] flap following mastectomy)

Physiological considerations

A sound understanding of the physiology of the circulation and of denervated tissue is essential when providing anaesthesia for free tissue transfer. Laminar flow through a rigid tube is described by the Poiseuille-Hagen equation:

$$\text{Blood flow} = \frac{\Delta P\, \pi\, r^4}{8\, \eta\, l}$$

where ΔP = pressure difference between two ends of a tube, r = radius of the tube, η = viscosity and l = length of the tube. Although not strictly applicable to the circulation, it is apparent that changes in perfusion pressure, viscosity and cross-sectional area will all influence blood flow. The systemic arterial pressure is the main determinant of the pressure gradient across the transplanted tissue. As flow is related to the fourth power of the radius, a small decrease in vessel cross-sectional area will result in a large fall in flow. In addition, Laplace's law states that intraluminal pressure will itself influence blood vessel diameter. Transmural pressure is decreased by either an increase in extravascular pressure (*e.g.* oedema, haematoma, dressings) or a decrease in intravascular pressure.

There is a non-linear relationship between blood viscosity and haematocrit; viscosity rises steeply when the haematocrit exceeds 40%. Haemodilution increases blood flow but also decreases the oxygen carrying capacity of the blood. A haematocrit of approximately 30% is thought to give the best balance between blood viscosity and oxygen content for oxygen transport to the tissues.

The properties of free vascularised tissue are summarised in Table 1. Once dissected out, the tissue is effectively denervated. However, the feeding artery and draining vein

Key points

Maintain adequate mean arterial pressure and cardiac output.

Induce hypervolaemic haemodilution with colloid solutions.

Maintain normothermia and keep core-peripheral temperature gradient < 1°C.

Ensure good analgesia but use epidurals with caution.

Measures initiated in the theatre must be continued in the postoperative period.

Old age is not a contraindication to microvascular free tissue transfer.

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Table 1 Properties of free vascularised tissue

- Subject to warm ischaemia during transfer
- Denervated
- Still responds to physical and chemical stimuli
- Blood flow frequently decreases to half its original (*in situ*) flow
- No intact lymphatic drainage leading to increased risk of interstitial oedema

at the recipient site still respond to physical, humeral and chemical stimuli such as cold, catecholamines and pharmacological agents. Blood flow to the flap often decreases to less than half during the immediate postoperative period and may take days or weeks to return to normal. In addition, free flaps have no intact lymphatic drainage making them very sensitive to extravasation of fluids and pressure effects.

Anaesthesia

Pre-operative assessment

All patients presenting for free flap surgery must be thoroughly assessed and investigated prior to anaesthesia. Elderly patients with head and neck cancer are often heavy smokers and drinkers and may have significant cardiac and respiratory co-morbidity as well as poor nutritional state. Airway anatomy may be distorted, especially in patients who have had previous chemotherapy or radiotherapy, and a difficult intubation must be anticipated. Paediatric patients may have associated abnormalities of anaesthetic importance (*e.g.* congenital cardiac disease). Baseline investigations should include full blood count, urea and electrolytes, clotting screen and blood sugar. Chest X-ray, ECG, respiratory function tests, arterial blood gases and echocardiogram should be considered in patients with cardiac and respiratory risk factors. All patients require a 'group and save' and blood should be cross-matched for all surgery requiring extensive dissection and reconstruction.

A careful explanation to the patient about the anaesthetic is required, including the use of epidurals, PCA machines, invasive monitoring, urinary catheter and postoperative care. A sedative premedication is often prescribed (*e.g.* lorazepam 1–2 mg orally 1 h before surgery). Chronological old age in itself is not a contraindication to free flap surgery and is not a risk factor for postoperative morbidity or flap failure.

Conduct of anaesthesia

The basic requirements for free tissue transfer are the provision of a full hyperdynamic circulation and maintenance of a normal body temperature. All patients usually require large bore intravenous access, an arterial cannula and central venous catheter. Appropriate sites for these should be discussed with the surgeon beforehand. In head and neck cases, direct access to central veins may be impossible. Lines placed from peripheral veins (*e.g.* in the antecubital fossa) have a high failure rate for correct placement and their position should be verified by X-ray prior to their use.

Positioning of the patient requires meticulous attention to detail in order to avoid well recognised problems (*e.g.* peripheral nerve damage, pressure sores). Pneumatic calf compression should be utilised routinely; some recommend regular passive limb movements during prolonged surgery. The patient's position may need to be adjusted several times during surgery. Hypothermia must be avoided by minimising patient exposure and maintaining an adequate ambient temperature. Forced air convection heating is recommended.

In general, a balanced anaesthetic technique is used with adequate analgesic supplementation to reduce the stress response and catecholamine release. As the duration of surgery is often > 5 h, nitrous oxide is best avoided. Most anaesthetists favour air and oxygen in combination with a volatile agent or a propofol infusion. The addition of a remifentanil infusion has also become very popular. This short-acting opioid provides excellent intra-operative analgesia, rapid control of blood pressure and marked vasodilatation. It usually obviates the need for a muscle relaxant.

Emergence and extubation can be very challenging, even for the most experienced anaesthetist. Whilst it is desirable to have an awake co-operative patient, it is also important to avoid excessive surges in blood pressure associated with coughing and retching. This is especially true in head and neck surgery and it is vital to ensure optimal analgesia before discontinuing the anaesthetic. Techniques used to reduce the risk of blood pressure surges at the time of extubation include:

- Allowing the patient to wake gradually, breathing spontaneously with the endotracheal cuff deflated
- Exchanging the endotracheal tube for a laryngeal mask airway prior to reversing muscle relaxation
- Intravenous lidocaine 0.5 mg kg^{-1} may reduce coughing during waking and extubation
- Carefully titrated boluses of a short-acting β-blocker (*e.g.* esmolol)

None of these methods are foolproof. If surgery has been particularly prolonged and there is concern about the anastomosis, a period of ventilation on the intensive care unit may be considered.

Fluid therapy

A hyperdynamic circulation with a high cardiac output, peripheral vasodilatation and a large pulse pressure is required to maintain adequate microcirculatory perfusion of the transplanted tissue. An adequate arterial pressure with vasodilatation provides good tissue perfusion by providing high regional blood flow, improving the patency of the microvasculature and maintaining the fluidity of the blood in the microcirculation.

Increasing cardiac filling pressures leads to an increase in cardiac output with skin and muscle vasodilatation. Both normovolaemic and hypovolaemic haemodilution have been shown clinically and experimentally to improve the chance of survival of tissues with compromised circulation. Most patients can tolerate a drop in haematocrit to 18–20%, although oxygen delivery to the tissues is probably optimal at around 30%. Also, a very low haematocrit is associated with increased bleeding time. Target CVP values of 10–15 cmH_2O or 3–5 cmH_2O above baseline are often quoted despite the fact that CVP does not provide accurate information on the state of the peripheral circulation. CVP trends are more useful and should be considered with other relevant information such as urine output and Δt (difference between core and peripheral temperatures). In the absence of major blood loss, hypotension is likely to be due to the vasodilatory effects of the volatile agent or propofol and remifentanil infusions. This can be treated by a reduction in the agent, relief of postural stress and by judicious use of fluids.

Patients with documented ischaemic heart disease or left ventricular dysfunction may not tolerate volume loading well and are probably better managed with normovolaemic haemodilution. Fluids should be administered cautiously whilst monitoring for signs of ischaemia and hypoperfusion (*e.g.* ST segment depression, fall in urine output, rising blood lactate concentration and increasing Δt). Measurement of pulmonary capillary wedge pressure, stroke volume index and cardiac output may provide useful additional information. It may be that some patients with significant cardiac disease are better served with a less ambitious, although less cosmetically satisfying, procedure. Left ventricular failure guarantees free flap failure.

A combination of crystalloid and colloid infusions is used. Electrolyte solutions alone are less effective in producing volume expansion and haemodilution; resultant interstitial oedema may put the flap at risk. In the UK, gelatin and albumin solutions are usually used for volume expansion, although there is no evidence that one is better than the other. Synthetic colloids have the advantage that they are readily available, stable, relatively inexpensive and without the risk of transmitting infectious diseases. However, gelatins have a relatively short half-life and may predispose to postoperative hypovolaemia. In continental Europe, dextran solutions, starch solutions and hypertonic saline are very popular as plasma substitutes in microvascular surgery. Dextran has been shown to be a more efficient plasma substitute than both large volumes of crystalloids and gelatin and appears to have beneficial effects on the microcirculation. It has antithrombotic effects through a reduction in platelet adhesiveness and depression of Factor VIII activity. This is an advantage in terms of thromboprophylaxis but limits the amount that can be given during major blood loss. Both hydroxyethyl starch and pentastarch have characteristics that may be beneficial in microvascular surgery. They are efficient plasma volume expanders, have a low incidence of anaphylactic reactions and may reduce reperfusion injury and capillary hyperpermeability after temporary ischaemia. Their disadvantages include prolonged bleeding time if used in excessive amounts and a high incidence of postoperative pruritus.

Hypertonic saline solutions have been the subject of recent interest. They appear to be effective plasma volume expanders and to have beneficial cardiovascular effects (*i.e.* increased myocardial contractility, decreased afterload and increased preload). They produce a high transcapillary osmotic gradient, which draws fluid out of the microvascular endothelial cells and red blood cells, leading to arteriolar vasodilatation, re-opening of occluded capillaries and a reduction in reperfusion injury. The duration of action of hypertonic saline solutions is only 15–20 min but can be prolonged to 30–60 min by the addition of a colloid. Other potential disadvantages include hypernatraemia, hypokalaemia and intracellular hypovolaemia, although these do not appear to be a problem clinically.

Our policy in adults is to infuse 10–20 ml kg^{-1} of 0.9% NaCl followed by 1000–1500 ml of 4.5% human albumin solution over the next 1–2 h. Thereafter, fluid therapy is guided by urine output, CVP and haematocrit measurement. Blood loss may be extensive during a prolonged procedure and may be covert (*e.g.* latissimus dorsi donor site). Red cells should only be transfused if the Hb falls below 8 g dl^{-1}. Clotting factors and platelets may be required if blood loss is significant.

Analgesia

The main choices are an opioid technique, regional block or a combination of the two. Conventional NSAIDs (COX1 and COX2 inhibitors) are usually avoided in the acute peri-operative

period because of the risk of bleeding and flap haematoma formation. Regional anaesthesia usually consists of a lumbar epidural for lower limb flaps or a brachial plexus block for upper limb work. In both cases, a catheter technique allows continuation of the block into the postoperative period. An opioid may be required to provide analgesia for the donor site (*e.g.* latissimus dorsi flap). Most commonly, morphine PCA is utilised. Prophylactic anti-emetics should be given to prevent retching and vomiting.

Perceived advantages of regional analgesia include excellent analgesia and vasodilatation with improved flap blood flow during and after the operation. Other possible advantages include a reduction in the stress response to surgery and anaesthesia, reduced incidence of deep vein thrombosis, decreased blood loss and a hastened postoperative recovery. It is also felt by some that regional anaesthesia can prevent vasospasm after replantations. However, there are some major concerns regarding the use of regional anaesthesia, especially epidurals, in microvascular free tissue transfer. Because the flap is denervated, a chemical sympathectomy produced by an epidural may decrease microcirculatory blood flow in free flaps by decreasing MAP (and hence perfusion pressure) and by diverting flow away from the flap to normal intact tissues (steal phenomenon). There is particular concern in patients who are hypovolaemic; animal models have demonstrated that epidural anaesthesia in the presence of only 10% hypovolaemia may reduce flap microcirculatory blood flow by 40%.

Our policy is to start using the epidural towards the end of the case when the blood pressure is satisfactory and the cardiovascular system is adequately filled. We use small increments of 0.125% or 0.25% bupivacaine followed by an infusion of 0.15% bupivacaine with or without fentanyl 2 μg ml^{-1}.

Temperature regulation

Patients must not be allowed to become hypothermic. Maintenance of normothermia can be difficult with large tissue areas often exposed for prolonged periods of time and large blood and fluid losses. In addition, anaesthetic agents may interfere with the normal thermoregulatory mechanisms. Cold induces vasoconstriction, an increase in haematocrit, increased aggregation of red cells, and increased whole blood and plasma viscosity. Patients must be actively warmed by means of underheating mattresses, forced air warming blankets (*e.g.* Bair Hugger), warmed intravenous fluids, humidification of anaesthetic gases and by maintaining operating room temperature around 24°C. Both core and peripheral temperatures should be monitored and the difference between them (Δt) should ideally be < 1°C. The volume status of the patient can be reflected by Δt. Core temperature is usefully measured by means of a specially adapted urinary catheter which allows continuous measurements, easily continued in the postoperative period. At the end of surgery, patients should be immediately transferred to a dedicated warmed area for continued monitoring.

Postoperative shivering should be treated as it can more than double oxygen consumption, increase circulating catecholamine concentrations and cause peripheral vasoconstriction. It has also been shown to cause a profound drop in free flap blood flow. It can usually be stopped with external warming together with doses of intravenous meperidine (10–20 mg), chlorpromazine (2.5–5 mg) or clonidine (100–150 μg). However, flap blood flow may not return to normal for over an hour.

Control of blood pressure

During the dissection stages of surgery, especially for major tumour resection, controlled hypotension may be requested to improve the surgical field and reduce blood loss. Other measures which may assist include positioning to improve venous drainage or local anaesthetic infiltration. Blood pressure can be controlled with a variety of anaesthetic techniques. Combinations that are flexible and rapidly reversible include: (i) vapour and remifentanil infusion ± glyceryl trinitrate infusion; and (ii) propofol and remifentanil total intravenous anaesthesia.

β-Blockers are best avoided as they can cause a relative vasoconstriction in peripheral tissues. During harvesting and anastomosis of the flap, mean arterial blood pressure should be maintained at a normal or slightly elevated level to ensure an adequate perfusion pressure through the graft tissue bed.

Many pharmacological agents have been utilised in the past in an attempt to improve flap survival. Most commonly employed were drugs that influence vascular tone such as α-receptor blockers (*e.g.* chlorpromazine) and direct-acting vasodilators (*e.g.* sodium nitroprusside). These are used infrequently now (especially with the introduction of remifentanil) and there is little evidence to support their use. Systemic vasodilators may be harmful due to the risk of blood flow steal away from an already maximally vasodilated flap. Systemic sodium nitroprusside has been shown to cause a marked reduction in flap blood flow and may lead to reflex vasoconstriction in the postoperative period when the infusion is stopped.

Hypotension is usually secondary to blood loss or vasodilatation and should be treated with fluid replacement. Catecholamines are usually avoided, despite there being little evidence to show that systemically administered catecholamines adversely affect flap blood flow; indeed phenylephrine may actually improve it through an increase in MAP. Some units use agents such as

dopexamine or dobutamine that produce an increase in cardiac output with systemic vasodilatation, but these should only be considered in combination with intravenous fluid loading. It must also be remembered that the greater the skin vasodilatation produced, the greater the heat loss will be unless adequate measures are taken to prevent it.

Postoperative care

It is essential that all measures taken to ensure adequate tissue perfusion during surgery are continued in to the postoperative period, including maintenance of circulating volume with crystalloid infusions and colloid boluses, maintenance of normothermia and provision of effective analgesia. These measures are summarised in Table 2.

Monitoring the flap

Clinical observation of skin colour, capillary return and temperature are the traditional methods of monitoring free skin flaps. They are useful in experienced hands but cannot be used to monitor buried flaps such as muscle or bone. Other more invasive methods include use of radiolabelled microspheres and erythrocytes, dermofluorometry and ultrasound Doppler. However, perhaps the best of the currently available methods is laser Doppler flowmetry which allows monitoring of superficial and buried flaps and is reportedly reliable for skin, muscle, bowel and bone transfers. Light at a constant wavelength is emitted from a helium-neon laser source with a fraction being reflected back to cause a Doppler shift in receiving fibres. The shift depends on the number and velocity of the red blood cells and is expressed as arbitrary perfusion units indicating flux or flow.

Despite the development of increasingly sophisticated methods of monitoring flap blood flow, decisions regarding flap well-being are based on simple clinical observations with concerns leading to early surgical exploration.

Table 2 Postoperative care

- Maintain normothermia; $\Delta t < 1\,^{\circ}C$
- Hyperdynamic circulation – high cardiac output, low systemic vascular resistance
- Normal blood pressure
- Haematocrit 30% (checked every 6 h for the first 24 h)
- Urine output > 1 ml kg^{-1} h^{-1}
- SaO_2 > 94% (oxygen for the first 24 h)
- Regular inspection of the flap (if possible) and continuous monitoring of blood flow in the flap by temperature and laser Doppler if available.

Table 3 Factors decreasing blood flow in free flaps

Arterial	Arterial thrombosis
	Arterial spasm
Venous outflow	Venous thrombosis
	Venous spasm
	Mechanical compression (e.g. dressings)
Flap oedema	Excessive use of crystalloids
	Extreme haemodilution
	Prolonged ischaemia
	Histamine release (e.g. anaesthetics, antibiotics)
	Excessive tissue handling
Generalised vasoconstriction	Hypovolaemia
	Hypothermia
	Pain
	Respiratory alkalosis
Hypotension	Hypovolaemia
	Cardiac depressant drugs (e.g. anaesthetics, calcium channel blockers)
	Extensive sympathetic blockade (e.g. epidural)
	Profound vasodilatation
	Cardiac failure (e.g. ischaemia, fluid overload)
Prolonged flap ischaemia	

Reasons for flap failure are mainly surgical and are summarised in Table 3. Respiratory acidosis may actually reduce flap blood flow because of decreased compliance of red blood cells and an activation of the sympathetic nervous system. Respiratory alkalosis leads to peripheral vasoconstriction and decreased cardiac output.

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See multiple choice questions 23 and 24.