Anaesthetic implications of free-flap microvascular surgery for head and neck malignancies – A relook

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Abstr<u>act</u>

Head and neck free-flap microvascular surgery is a type of surgery where multiple anaesthetic factors play a very important role in the outcome of the surgery while the conduct of anaesthesia itself may be quite challenging for the anaesthesiologist. In microvascular reconstruction of head and neck malignancies, flaps are used to reconstruct a primary defect formed by wide local excision. A free flap is raised after removing the neurovascular pedicle from the donor site and transplanting it by microvascular anastomosis to the new location. This gives rise to a secondary defect which is then repaired by direct suture or skin graft. The anaesthesiologist's role includes optimizing the physiological conditions for the survival of the flap while decreasing morbidity at the same time. Failure of the free flap is attributed to numerous causes. This is an attempt to highlight them along with discussion of the anaesthesia-related issues that are faced during this type of surgery. The various pre-, intra- and postoperative factors affecting flap survival and overall postoperative outcome in the patient are discussed here.

Keywords: Anaesthetic factors, flap survival, free-flap, head and neck malignancies, microvascular

Introduction

Proper conduct of anaesthesia is required for good surgical outcome in any surgery. Multiple anaesthetic factors play very important role in the outcome of free-flap microvascular surgery for head and neck malignancies while the conduct of anaesthesia itself may be challenging for the anaesthesiologist due to difficult airway, massive resection and long duration surgery. The anaesthesiologist's role includes optimizing the physiological conditions for the survival of the flap while decreasing morbidity.^[11] These patients have a mortality rate of 2.1%, median length of stay 11 days and a flap survival rate of 95%.^[2] Failure rate of free flaps is approximately 4% with a rate of re-exploration about 10%.^[11] This is an attempt to highlight the numerous causes of free-flap failure along with discussion of the anaesthesia-related issues faced during this

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Access this article online		
Quick Response Code:	Website: www.joacp.org	
ostation Statemen		
	DOI: 10.4103/joacp.JOACP_22_20	

type of surgery. Search was carried out using a combination of keywords such as microvascular surgery, free-flap surgery, head and neck reconstruction, anaesthetic factors, hypothermia, steroids, vasopressors, duration of surgery, preanesthetic checkup, free flap thrombosis, free flap necrosis and difficult airway, from various databases such as Pubmed, Cochrane and Google Scholar.

Surgical Procedure

A free flap is raised after removing the neurovascular pedicle from the donor site and transplanted by microvascular anastomosis to a new location. Whereas the flaps are used to reconstruct a primary defect formed by wide local excision around the head and neck malignancy, it gives rise to a secondary defect which is then repaired.^[11] Various donor sites include radial/ulnar forearm, latissimus dorsi, rectus

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 How to cite this article: Goswami U, Jain A. Anaesthetic implications of

 free-flap microvascular surgery for head and neck malignancies – A relook.

 J Anaesthesiol Clin Pharmacol 2021;37:499-504.

 Submitted: 18-Jan-2020
 Revised: 06-Apr-2020

 Accepted: 19-Jun-2020
 Published: 06-Jan-2022

abdominis muscle and groin flap.^[3] The preference for donor sites changed significantly over the last decade. For example, the fibula came to be preferred over the iliac crest for mandibular reconstructions as it can be harvested easily under tourniquet and its cutaneous unit used for lining the aerodigestive tract and/or for skin coverage.^[2]

Causes of Free-Flap Failure

Numerous causes of free flap failure that have been cited include arteriovenous thrombosis, vasospasm; mechanical compression due to dressings or positioning; inadequate surgical anastomosis, insufficient venous drainage, flap edema due to excessive use of crystalloids/haemodilution, histamine release; excessive flap manipulation; generalized vasoconstriction due to hypovolemia, hypothermia, pain, respiratory alkalosis; myocardial depressor drugs (anaesthetics, Ca2+ channel blockers). Various anaesthesia-related factors may affect both central haemodynamic stability and regional blood flow.^[1,3,4] Poor blood flow to the flap is cited to be the primary cause of flap failure as per evidence.^[5] Way back in 1985, Aps *et al.*^[6] reported that local vasospasm could be prevented by the use of direct arteriolar vasodilators (Sodium Nitroprusside).

The various factors affecting flap survival and overall post-operative outcome in the patient are discussed below [Table 1].

Preoperative factors

Age per se has no direct effect on free flap outcome but age over 55 years may increase medical complications following surgery.^[2]

Higher American Society of Anaesthesiologists (ASA) class, cigarette smoking and weight loss more than 10% before surgery have been shown to be associated with flap failure.^[2,7,8] Preoperative comorbidity did not have any

statistically significant effect but it did seem to increase the absolute risk more than four-fold. $\ensuremath{^{[2]}}$

Other factors such as sex, chemotherapy, radiotherapy, stage IV cancer, tobacco use, and preoperative use of blood products have been shown not to correlate with postoperative complications.^[9]

Even though some studies have shown a negative effect of irradiation due to its adverse effect on blood vessels and delayed healing,^[2] others reported no association with either flap outcome or medical complications.^[10] Preoperative radiation may affect the airway however.^[11]

A study involving 2,846 patients with head and neck cancer found diabetes mellitus, peripheral vascular disease, renal failure, preoperative radiotherapy to be significant predictors.^[12]

Intraoperative factors

Type of anaesthesia/anaesthetic drugs

Balanced anaesthesia with benzodiazepines and opioids along with inhalational or intravenous agents are used across centres. Air/oxygen combination may be used with a volatile agent or Total Intravenous Anaesthesia (TIVA).^[3] Induction with sevoflurane is preferred in cases where a difficult intubation is anticipated as spontaneous ventilation can be preserved for managing the airway. In 2016, a randomised controlled trial [RCT] comparing balanced anaesthesia with sevoflurane and TIVA (propofol/remifentanil) monitored regional tissue oximetry to conclude that sevoflurane reduces ischemia-reperfusion injury.^[13] However, a recent study by Chang et al.^[14] comparing TIVA with inhalation anaesthesia (sevoflurane/desflurane) observed that the TIVA group required less perioperative fluids and developed fewer pulmonary complications. Infusion of remifentanil, a short-acting opioid, provides excellent intra-operative analgesia, rapid control of blood pressure, marked vasodilatation and also obviates the need for a muscle relaxant.^[3]

Table 1: Perioperative parameters affecting flap outcome		
Preoperative factors	Intraoperative factors	Postoperative factors
Age	Type of Anaesthesia/anaesthetic drugs	Hypothermia
Sex	Hypothermia	Hypoxia (SaO ₂ >94%)
ASA status	Crystalloids/colloids	Haematocrit
Smoking/tobacco abuse	Blood loss	Hypotension
Preoperative use of blood products	Goal-directed fluid therapy	Postoperative bleeding/edema in flap
Preoperative haemoglobin	Vasoactive drugs	Urine output
Preoperative haematocrit	Antithrombotic therapy	Airway complications
Preoperative comorbidity e.g., Diabetes Mellitus, peripheral vascular disease, renal failure	Duration of surgery	Pulmonary complications, e.g., pulmonary edema, pneumonia, atelectasis
Preoperative Chemotherapy	Number of surgeons	
Preoperative Radiotherapy		
Weight loss $>10\%$		

Intravenous dexmedetomidine may be continued as an infusion for up to 12 hours in the ICU postoperatively. The reservation against the use of this $\alpha 2$ agonist in free flap surgeries is that it could cause vasoconstriction leading to flap failure. It has however been found that dexmedetomidine maintains postoperative hemodynamics without any increase in flap compromise. It also decreases postoperative agitation.^[15,16]

After induction of anaesthesia the trachea has to be intubated with a cuffed endotracheal tube (ETT) followed by careful packing around the tube to prevent aspiration of blood. Controlled ventilation is then maintained while avoiding both hyperoxia and hypocarbia as they can trigger arteriolar vasoconstriction.^[6]

Analgesia in free flap harvesting site may be achieved with regional anaesthesia techniques like epidural or local perineurial catheter. The evidence regarding the influence of regional anaesthesia on microvascular free flap surgery is inconclusive. Sympathetic blockade with regional anaesthesia has been thought to cause vasodilatation leading to better flap survival but was not helpful in preventing vasospasm due to surgical manipulation whereas sodium nitroprusside infusion was. Also the sympathetically denervated neo- revascularized tissue may be adversely affected by a steal phenomenon.^[6,17] Mini-catheters have been used safely to inject local anaesthetic into the fibular^[18] and abdominal donor site with resultant decrease in opioid and antiemetic use as well as shorter hospital stay.^[19]

Continuous paravertebral block at levels T1 and T2 has been shown to improve tissue perfusion in cases of maxillofacial free flap surgery.^[20] Heparin (unfractionated) administered during flap harvesting warrants careful monitoring before and after removal of epidural catheter.^[21]

Local anaesthesia with monitored anaesthesia care is used for procedures like flap thinning after free flap reconstruction in head and neck malignancies.

Monitoring

Apart from the routine monitoring (electrocardiography-ECG, Non-invasive Blood pressure-NIBP, Pulse Oximetry-SPO2, End tidal carbon dioxide-ETCO2, temperature and neuromuscular monitoring), other monitors like Central venous pressure (CVP) and Invasive arterial blood pressure (IBP) may be required in these cases where huge amount of blood loss may occur. Clinical monitoring of the patient is important with intraoperative urine output, blood loss, glucose and Arterial Blood Gas (ABG) assessment. Postoperatively too the patient has to be carefully monitored for sedation level and pain apart from vitals monitoring. Various studies where goal directed fluid therapy has been followed used arterial pulse contour device for Cardiac output (CO), Cardiac Index (CI) and Stroke Volume (SV) monitoring.^[22,23]

Airway management

Being prepared for difficult airway is of utmost necessity. Many a patient may present for surgery post-radiation which further complicates matters due to involvement of various tissues.^[11]

Awake fibreoptic intubation of the trachea is usually the preferred method. Fibreoptic intubation after induction of anaesthesia is another option when there is no risk of loss of the airway after induction. In extremely difficult cases of massive resection followed by reconstruction, elective tracheostomy is desirable. Different types of cuffed ETT that may used are:

- Polyvinyl chloride (PVC) ETT
- Reinforced ETT
- Ring Adair Elwyn (RAE) tubes
- Tracheostomy tubes.

Routes of insertion of ETT may be per oral, nasal, submental or retromolar in some cases.

Tissue edema may compromise airway patency postoperatively and mechanical ventilation for a few hours allows edema to subside before extubation. The difficult airway trolley has to be available for extubation. Prophylactic administration of intravenous steroids (dexamethasone, methylprednisolone) reduces the incidence of laryngeal oedema and reintubation rate after extubation in adults.^[24-26] Due to the area of surgery, peritubal leak may not be easy to assess. Use of the airway exchange catheter (AEC) may aid tracheal reintubation in these patients.^[27]

Intravenous access and fluid management

Wide bore intravenous access is a must for these patients. The limb from where free flap is to be harvested should be marked preoperatively to avoid securing venous access in this arm.

Central venous catheter (mostly subclavian vein) should be inserted in these patients for guidance in fluid resuscitation. Goal-directed fluid therapy using minimally invasive cardiac output monitoring could improve haemodynamics which in turn would lead to less fluid administration during the perioperative period. Cardiac output measurement, Cardiac Index (CI), Stroke volume index (SVI) may be monitored intraoperatively with the arterial pulse contour device.^[22] No significant difference in patient outcome was seen when goal-directed fluid management (GDFM) was followed in another RCT with Stroke Volume (SV) monitoring. GDFM however led to a decrease in the overall volume of crystalloids infused while increasing the volume of colloids.^[23]

Exaggerated tissue edema due to low colloid oncotic pressure after crystalloid use of more than 7 L may worsen edema due to tissue handling.^[2,6] Huge blood loss may warrant blood transfusion in many cases with its inherent complications. A postoperative transfusion trigger of haematocrit less than 25 percent has been shown to decrease the rate of blood transfusion while decreasing flap failure rates.^[28]

Vasoactive drugs

Vasopressors used during anaesthesia have been traditionally thought to be one of the causes of poor blood flow to the flap.^[29] Other studies however have shown that the type (dopamine, noradrenaline and metaraminol) or method of usage of vasoconstrictors could not be associated to flap failure directly and in fact vasoconstrictors such as noradrenaline have been shown to be beneficial by maintaining blood flow to the flap.^[5,30,31] Sodium nitroprusside improves blood flow in the free flap on direct administration onto the vessels being anastomosed.^[6] It has the advantage over alpha blocker (labetolol), of fast and profound vasodilation in the sympathetically denervated free flap without undue effect on the sympathetic nervous system.^[32]

Antithrombotic therapy

Some agents that are used with varied protocols to decrease platelet functioning, improve blood flow or decrease blood viscosity are Aspirin, Dextran 40 and Unfractionated Heparin. Statins have vasoprotective and anti-inflammatory actions but their role in preventing anastomotic thrombosis is not known.^[33]

Dextran infusion has traditionally been used to improve perfusion in the free flap vessels.^[33,34] However, the routine use of dextran has been questioned due to adverse effects such as anaphylactoid reactions, adult respiratory distress syndrome, cardiac overload, haemorrhage, and renal damage. The patency rates of free flap reconstructions and thrombotic complications were not statistically different from patients not receiving dextran infusion.^[35,36]

Once a thrombus is formed, options that are available are mechanical re-exploration, thrombolysis with agents like tPA.^[37]

Temperature control

Long duration of surgery under GA, multiple exposure sites to cool OR temperatures and cool intravenous fluids often lead to hypothermia. Hypothermia has been implicated in causing various postoperative complications like partial or complete flap loss, delayed wound healing, local vasoconstriction, increased viscosity/haematocrit, coagulopathy leading to haematoma formation and infectious complications. Postoperative shivering may lead to increased oxygen consumption, hypoxia, arrhythmias and myocardial events.^[1,9,38-40]

Surgical factors

Operative time has been shown to be positively associated with postoperative complications, morbidity, and prolonged length of stay in various type of surgeries.^[41,42] A study on 2,008 patients^[7] observed a correlation between operative time and the incidence of early flap failure and postoperative complications following microvascular tissue transfer surgery using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Other studies have however observed that duration of surgery did not per se influence the medical or surgical outcomes.^[2]

The number of surgeons may affect the outcome which has been shown to improve when preoperative selection and postoperative management is handled by one person.^[2] Another study has however reported same outcome even with multiple surgeons.^[43]

Postoperative factors

Postoperative care should include maintaining normothermia, normal blood pressure, haematocrit around 30%, urine output >1 ml kg–1 h-1, SaO₂ >94% (oxygen for the first 24 h), regular inspection of the flap and continuous monitoring of blood flow in the flap by temperature and laser Doppler.^[3] Edema and bleeding in the flap site may lead to airway obstruction. Common modalities of postoperative pain management are intravenous non-steroidal anti-inflammatory drug (NSAID), paracetamol, and opioids. Mini-catheters have been used safely to inject local anaesthetic into the fibular donor site after flap harvesting for reconstruction of the head-and-neck area with successful outcome.^[18] Pulmonary complications such as pulmonary edema, pneumonia or atelectasis may occur in these patients.^[14]

Grafts should be monitored for 24 hours for arterial spasm, graft oedema and venous occlusion. Re-exploration of the graft may be required if signs of ischaemia occur. Graft oedema can be reduced by elevation of the recipient site, IV drugs like single dose of dexamethasone (40 mg) and mannitol 10% (0.5 g/kg).^[6] Routine use of IV heparin and dextran infusion are not followed by many centres due to concern over rebleed.^[6,36]

Conclusion

Microvascular flap surgery for head and neck malignancies is a challenge to the anaesthesiologist and optimization of the physiological conditions for flap survival while keeping morbidity at check is the goal. Knowledge of the various aspects of this surgery along with close communication with the surgeon and regulation of the numerous factors that may affect flap survival are imperative to ensure a favourable outcome.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Pereira CM, Figueiredo ME, Carvalho R, Catre D, Assunção JP. Anesthesia and surgical microvascular flaps. Rev Bras Anestesiol 2012;62:563-79.
- Haughey BH, Wilson E, Kluwe L, Piccirillo J, Fredrickson J, Sessions D, *et al.* Free flap reconstruction of the head and neck: Analysis of 241 cases. Otolaryngol Head Neck Surg 2001;125:10-7.
- 3. Adams J, Charlton P. Anesthesia for microvascular free tissue transfer. Br J Anaesth 2003;3:33-7.
- Stepanovs J, Ozoliòa A, Rovîte V, Mamaja B, Vanags I. Factors affecting the risk of free flap failure in microvascular surgery. Proc Latvian Acad Sci 2016;70:356-64.
- Rose L, Prado N, Mulvey D, Laugharne D, Jones K, Stenhouse J. Vasoactive agents do not adversely influence the success of maxillo-facial microvascular free-flap surgery: A retrospective analysis. Int J Anesth Res 2016;4:327-30.
- Aps C, Cox RG, Mayou BJ, Sengupta P. The role of anaesthetic management in enhancing peripheral blood flow in patients undergoing free flap transfer. Ann R Coll Surg Engl 1985;67:177-9.
- Offodile AC II, Aherrera A, Wenger J, Rajab TK, Guo L. Impact of increasing operative time on the incidence of early failure and complications following free tissue transfer? A risk factor analysis of 2,008 patients from the ACS-NSQIP database. Microsurgery 2017;37:12-20.
- 8. Steidelman WK, Digenis AG, Tobin GR. Impediments to wound healing. Am J Surg 1998;176:395-475.
- Sumer BD, Myers LL, Leach J, Truelson JM. Correlation between intraoperative hypothermia and perioperative morbidity in patients with head and neck cancer. Arch Otolaryngol Head Neck Surg 2009;135:682-6.
- Kroll SS, Robb GL, Reece GP. Does prior irradiation increase the risk of total or partial free flap loss? J Reconstr Microsurg 1998;14:263-8.
- Balakrishnan M, Kuriakose R, Koshy RC. Radiation induced changes in the airway—anaesthetic implications, Southern African J Anaesth Analg 2004;10:19-21.
- Ishimaru M, Ono S, Suzuki S, Matsui H, Fushimi K, Yasunaga H. Risk factors for free flap failure in 2,846 patients with head and neck cancer: A national database study in Japan. J Oral Maxillofac Surg 2016;74:1265-70.
- Claroni C, Torregiani G, Covotta M, Sofra M, Scotto Di Uccio A, Marcelli ME, *et al.* Protective effect of sevoflurane preconditioning on ischemia-reperfusion injury in patients undergoing reconstructive plastic surgery with microsurgical flap, a randomized controlled trial. BMC Anesthesiol 2016;16:66.
- Chang YT, Wu CC, Tang TY, Lu CT, Lai CS, Shen CH. Differences between total intravenous anesthesia and inhalation anesthesia in free flap surgery of head and neck cancer. PLoS One 2016;11:e0147713.

- Rajan S, Moorthy S, Paul J, Kumar L. Effect of dexmedetomidine on postoperative hemodynamics and outcome of free flaps in head and neck reconstructive surgeries. Open Anesthesiol J 2016;10:12-8.
- Yang X, Li Z, Gao C, Liu R. Effect of dexmedetomidine on preventing agitation and delirium after microvascular free flap surgery: A randomized, double-blind, control study. J Oral Maxillofac Surg 2015;73:1065-72.
- 17. Jayaram K, Rao P, Gurajala I, Ramachandran G. Evaluation of the effect of regional anaesthesia on microvascular free flaps. Turk J Anaesthesiol Reanim 2018;46:441-6.
- Ferri A, Varazzani A, Valente A, Pedrazzi G, Bianchi B, Ferrari S, *et al.* Perioperative pain management after fibular free flap harvesting for head-and-neck reconstruction using mini-catheters to inject local anesthetic: A pilot study. Microsurgery 2018;38:295-9.
- Giordano S, Veräjänkorva E, Koskivuo I, Suominen E. Effectiveness of local anaesthetic pain catheters for abdominal donor site analgesia in patients undergoing free lower abdominal flap breast reconstruction: A meta-analysis of comparative studies. J Plastic Surg Hand Surg 2013;47:428-33.
- Habib AM, Zanaty OM, Anwer HF, Abo Alia D. The effect of paravertebral block on maxillofacial free flap survival. Int J Oral Maxillofac Surg 2017;46:706-11.
- 21. Horlocker TT, Wedel DJ, Rowlingson JC, Enneking FK, Kopp SL, Benzon HT, *et al.* Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American society of regional anesthesia and pain medicine evidence-based guidelines (Third Edition). Reg Anesth Pain Med 2010;35:64-101.
- 22. Funk D, Bohn J, Mutch WA, Hayakawa T, Buchel F. Goal-directed fluid therapy for microvascular free flap reconstruction following mastectomy: A pilot study. Plast Surg 2015;23:231-4.
- Cordero-Rochet MJ, McCluskey SA, Minkovich L, Gilbert R. Goal directed fluid management in free flap reconstructive surgery. Can J Anesth 2014;61:S75-6.
- 24. Fan T, Wang G, Mao B, Xiong Z, Zhang Y, Liu X, *et al.* Prophylactic administration of parenteral steroids for preventing airway complications after extubation in adults: Meta-analysis of randomised placebo controlled trials. BMJ 2008;337:a1841.
- 25. Markovitz BP, Randolph AG. Corticosteroids for the prevention of reintubation and postextubation stridor in pediatric patients: A meta-analysis. Pediatr Crit Care Med. 2002;3:223-6.
- 26. Francois B, Bellisant E, Gissot V, Desachy S, Boulain T, Preux P-M, et al. 12-h Pretreatment with methylprednisolone versus placebo for prevention of postextubation laryngeal oedema: A randomised double-blind trial. Lancet 2007;369:1083-9.
- Mort TC. Continuous airway access for the difficult extubation: The efficacy of the airway exchange catheter. Anesth Analg 2007;105:1357-62.
- Rossmiller SR, Cannady SB, Ghanem TA, Wax MK. Transfusion criteria in free flap surgery. Otolaryngol Head Neck Surg 2010;142:359-64.
- 29. Motakef S, Mountziaris PM, Ismail IK, Agag RL, Patel A. Perioperative management for microsurgical free tissue transfer: Survey of current practices with a comparison to the literature. J Reconstr Microsurg 2015;3:355-63.
- Monroe MM, Cannady SB, Ghanem TA, Swide CE, Wax MK. Safety of vasopressor use in head and neck microvascular reconstruction: A prospective observational study. Otolaryngol Head Neck Surg 2011;144:877-82.
- Chen C, Nguyen MD, Bar-Meir E, Hess PA, Lin S, Tobias AM, et al. Effects of vasopressor administration on the outcomes of microsurgical breast reconstruction. Ann Plast Surg 2010;65:28-31.
- 32. Inglis MS, Edwards JM, Robbie DS, Breach NM. The anaesthetic management of patients undergoing free flap reconstructive surgery following resection of head and neck neoplasms: A review

of 64 patients. Ann Royal Coll Surg Eng 1988;70:235-38.

- Pršić A, Kiwanuka E, Caterson SA, Caterson EJ. Anticoagulants and statins as pharmacological agents in free flap surgery: Current rationale. Eplasty 2015;15:e51.
- Wolfort SF, Angel MF, Knight KR, Amiss LR, Morgan RF. The beneficial effect of dextran on anastomotic patency and flap survival in a strongly thrombogenic model. J Reconstr Microsurg 1992;8:375-8.
- Sun TB, Chien SH, Lee JT, Cheng LF, Hsu LP, Chen PR. Is dextran infusion as an antithrombotic agent necessary in microvascular reconstruction of the upper aerodigestive tract? J Reconstr Microsurg 2003;19:463-6.
- 36. Jayaprasad K, Mathew J, Thankappan K, Sharma M, Duraisamy S, Rajan S, et al. Safety and efficacy of low molecular weight dextran (dextran 40) in head and neck free flap reconstruction. J Reconstr Microsurg 2013;29:443-8.
- Hanasono MM, Butler CE. Prevention and treatment of thrombosis in microvascular surgery. J Reconstr Microsurg 2008;24:305-14.

- Steinbrook RA, Seigne PW. Total-body oxygen consumption after isoflurane anesthesia: Effects of mild hypothermia and combined epidural-general anesthesia. J Clin Anesth 1997;9:559-63.
- Pereira QJ. Anaesthesia for reconstrutive surgery. Anaesth Int Care 2006;7:31-5.
- Diaz M, Becker DE. Thermoregultion: Physiological and clinical considerations during sedation and general anesthesia. Anesth Prog 2010;57:25-33.
- 41. Jackson TD, Wannares JJ, Lancaster RT, Rattner DW, Hutter MM. Does speed matter? The impact of operative time on outcome in laparoscopic surgery. Surg Endosc 2011;25:2288-95.
- 42. Finical S, Doubek WD, Yugueros P, Johnson CH. The fate of free flaps used to reconstruct defects in recurrent head and neck cancer. Plast Reconstr Surg 2001;107:1363-6.
- 43. Jones NF, Johnson JT, Shestak KC, Myers EN, Swartz WM. Microsurgical reconstruction of the head and neck: Interdisciplinary collaboration between head and neck surgeons and plastic surgeons in 305 cases. Ann Plast Surg 1996;36:37-43.