




Evaluation of the Effect of Regional Anaesthesia on Microvascular Free Flaps

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Objective: Multiple factors influence the success of microvascular free flap surgeries. Anaesthesia is an important factor to maximise the success rate of microvascular free flaps both by controlling haemodynamics and improving the perfusion of free vascularised tissue. The debate on the usefulness of regional and general anaesthesia for free tissue transfer is ongoing. This retrospective study was conducted to evaluate the effects of regional anaesthesia and other perioperative factors on outcomes of microvascular free flaps.

Methods: This retrospective observational study was conducted on 165 patients undergoing microvascular free flap surgeries between January 2014 and December 2015 after obtaining approval from the Institutional Ethics Committee (Nizams Institute Ethics Committee, Nizams Institute of Medical Sciences, India). Perioperative variables analysed included the type of surgery, indication, ASA physical status, type of anaesthesia, perioperative haemodynamics, fluids used, duration of surgery, re-explorations, blood transfusion and duration of hospital stay. The primary outcome measure was to assess the effect of regional anaesthesia on the success of free flap.

Results: Multivariate analysis identified the type of anaesthesia and preoperative haemodynamics as independent risk factors for predicting the failure of flap with an odds ratio of 0.208 and 7.469, respectively. A subgroup analysis of 55 acute trauma patients revealed preoperative haemodynamic instability as an individual independent risk factor for graft failure with an odds ratio of 11.90.

Conclusion: The results of this study emphasise the importance of the choice of anaesthesia and preoperative optimisation in improving the success of free flap surgeries.

Keywords: Anaesthesia, regional, general, microsurgical free flap

Introduction

Evolving technology in surgical management has permitted the microvascular reconstruction of face and limbs that were previously considered to be unsalvageable. Soft tissue coverage for huge defects is usually performed using microvascular free flaps. Free tissue transfer provides a reliable method to deal with difficult reconstructions and major defects. It is a complex surgical procedure, and despite improvements in surgical and technical skills, problems of hypoperfusion and necrosis of the free flaps continue to be intriguing (1).

The main limitations of microvascular reconstruction are prolonged surgery and its attendant complications. Several non-surgical factors determine the success of free flap, including age, comorbid conditions, haemodynamic status, rheology, temperature regulation, anticoagulants and other vasogenic drugs. Anaesthesia is an important determining factor in the success of the procedure through maintaining the haemodynamic stability and regional blood flow.

Factors determining the blood flow of the newly vascularized tissue can be understood from the Hagen-Poiseuille's equation. A patient's haemodynamic status during the perioperative period has a major influence on the viability of free flap. Vasoactive drug use, changes in the blood volume during the perioperative period and the maintenance of microcirculation form major determinants of the outcome of free vascularized tissues. Maintaining all parameters to improve the perfusion of the patient per se and the free flap is challenging. Acute trauma patients with pre-existing haemodynamic instability pose greater problems because microcirculation has to be re-established prior to soft tissue coverage in these patients.

The evidence regarding the influence of regional anaesthesia on the regional blood flow following microvascular free flap is inconclusive. Regional anaesthesia improves regional blood flow by vasodilation. However, the blood flow to the sympathetically denervated neo re-vascularized tissue can be adversely affected by the steal phenomenon (2, 3). Therefore, no clear recommendation exists for the use of regional anaesthesia for these procedures.

Although surgical factors influencing the viability of microvascular free flap are well established, there is paucity of studies in literature regarding the influence of anaesthetic factors on the outcome of free flaps. This retrospective study was conducted to analyse the effect of the anaesthesia technique and management on the outcome of microvascular free flaps.

Methods

The study was conducted by collecting retrospective data of all patients undergoing microvascular free flap surgery between January 2014 and December 2015. Patients of all age groups, both sex and any physical status undergoing both elective and emergency free flap surgeries for any indication were included. Data were collected from hospital records after obtaining approval from the Institutional Ethics Committee. Patients with incomplete data and/or records were excluded (Figure 1).

Demographic data including age, sex, ASA physical status, co-morbidities and preoperative data, such as indication for surgery, preoperative investigations, haemodynamics and optimisation if any (fluid resuscitation, transfusions and vasopressor use required for maintaining mean arterial pressure at >60 mmHg), were collected.

In the operating room, ASA standard monitoring was applied to all patients. They received regional anaesthesia, general anaesthesia or a combination of both. In surgeries involving only lower limb, spinal or combined spinal epidural was used depending on the expected duration. The techniques were invariably blind because our institution had no ultrasound during that period. If there was a failure of any of these techniques as evidenced by a patient complaining of pain or any other haemodynamic issues, then general anaesthesia was administered. General anaesthesia was induced by fentanyl 1.5-2 $\mu\text{g kg}^{-1}$, thiopentone (3-5 mg kg^{-1}) or propofol (1-1.5 mg kg^{-1}) and muscle relaxant atracurium 0.5 mg kg^{-1} , followed by inhalational agents. Intraoperative haemodynamics was considered stable if the mean arterial pressure was ≥ 60 mmHg, and if this decreased, then it was managed by 200 mL crystalloid bolus over 10 min. Patients not responding to fluids were treated with phenylephrine 50 μg increments. If more than five such increments were needed, then patients were started on dopamine. Haematocrit was maintained between 25% and 30% as per the institutional protocol. If there was a reduction in this level, then

blood was transfused. Fluid and vasopressor requirements and the number of transfusions during the perioperative period were noted. Temperature was maintained with the core to surface gradient at no more than 2°C in all cases, as per the institutional protocol. Care was taken to prevent hypothermia by monitoring temperature and using forced air warming devices and warm fluids. The type of flap, anaesthesia technique, haemodynamics, use of dextran, transfusions, duration of surgery and postoperative elective ventilation (most head and neck surgeries were electively ventilated for immobilisation as per the institutional protocol) were documented from the anaesthesia records.

During the postoperative period, haemodynamics, re-explorations, surgical site infection, fever, antibiotics, duration of intensive care unit stay if any, duration of hospital stay and anticoagulants and dextran use were recorded.

The main outcome measure studied was the effect of regional anaesthesia on the success of free flap. Secondary outcome measures were the role of perioperative haemodynamics, blood transfusions, re-explorations and haematocrit values on the success of free flap. Flap was considered to be failed when there was a need to completely remove the flap or if any other measures had to be applied. The project was undertaken in accordance with the protocol accepted by the Institutional Ethics Committee (NIEC) of the Nizam's Institute of Medical Sciences.

Statistical analysis

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (IBM SPSS Corp.; Armonk, NY, USA) version 20. All categorical parameters were presented as number (n) and percentage (%). Perioperative data were univariately analysed as predictors for the successful outcome of free flap, and logistic regression model was developed based on the identified univariate predictors. Forward selection within the regression model was stepwise, where variables were retained if their p value was <0.05.

Results

Data of 165 patients were complete as shown in Figure 1.

Demographic data

A total of 165 patients were included in the study, with male predominance contributing to 78.8%. Among the patients, 72.7% belonged to the age group of 18–50 years, with the mean age being 28.04 years. Seventy-three (44.2%) patients had undergone lower limb surgeries compared with upper limb (49 patients), head and neck region surgeries (39 patients) (Table 1). Only 12 patients of 165 had comorbidities such as diabetes mellitus or hypertension and belonged to the ASA physical status grade II. Majority of patients were operated for trauma or posttraumatic sequelae [76 (46%)]. Overall, there were 13 flap failures without any mortality.

Table 1. Demographic variables and perioperative data for success and failure of free flap by univariate analysis

Variable	Total	Success	Failure	Probability
Age	152/13	31.54±14.075	28.05±13.849	0.654
Sex- M/F	130/35	119/33	11/2	0.738
Region				
Upper limb	49	40 (81.6%)	9 (18.4%)	
Lower limb	73	70 (95.9%)	3 (4.1%)	0.013
Head and neck	39	38 (97.4%)	1 (2.6%)	
Trunk	4	4 (100%)	0	
Cause				
Trauma and post-traumatic	76	65 (85.5%)	11 (14.5%)	
Neoplasia	59	57 (3.4%)	2 (96.6%)	0.005
Burns and others	30	30 (100%)		
ASA physical status				
I/II	153/12	141 (92.2%)/11 (91.7%)	12 (7.8%)/1 (8.3%)	0.064
Type of surgery				
Elective	113	109 (96.5%)	4 (3.5%)	0.004
Emergency	52	43 (82.7%)	9 (17.3%)	
Preoperative variables				
Stable haemodynamics	159	149 (93.7%)	10 (6.3%)	0.007
Unstable	6	3 (50%)	3 (50%)	
PCV		37.26±6.911	35.92±6.198	0.317
Haemoglobin		12.49±2.356	11.92±2.06	0.540
Platelets		2.43±0.811	2.54±0.877	0.640
Total leucocyte count		10749±4040	11670±3498	0.573
Anaesthesia technique				
General	115	111 (96.5%)	4 (3.5%)	
Regional/ Combined	50	41 (82%)	9 (18%)	0.006
Duration of surgery		6.819±1.55 h	7.123±1.64	0.379
Perioperative transfusion	53	44 (83%)	9 (17%)	0.005
Re-exploration	21	13 (68.9%)	8 (31.1%)	0.000
Elective ventilation	33	33	0	0.048
Duration of hospital stay		11.89±4.07 days	15.77±6.94 days	0.398

PCV: packed cell volume; ASA: American society of Anesthesiologists

Table 2. Multivariate predictors of success of free flap by logistic regression analysis

Parameter	Odds ratio	95% confidence interval		Coefficient	p
		Lower	Upper		
Anaesthesia technique	0.208	0.39	1.091	-1.572	0.33
Preoperative haemodynamics	7.469	1.331	5.117	2.011	0.28

Of the total surgeries, 113 flap procedures (68.5%) were performed as elective surgery and the remaining 52 (31.5%) were emergency surgeries. Failure rate in emergency trauma cases (16.7%) was significantly higher than that in elective surgeries ($p=0.004$). The proportion of failures in upper limb surgeries was significant ($p=0.013$) than other areas. Patients who had haemodynamic instability during the preoperative period had an incidence of flap failure as high as 50%, which

was significantly greater than that in those without ($p=0.007$). Preoperative variables such as haemoglobin, packed cell volume, platelet count or total leucocyte count did not have an influence on the flap outcome.

Fifty patients received regional anaesthesia in the form of neuraxial blockade (spinal, combined spinal epidural or epidural and general anaesthesia), and one of the patient re-

ceived supraclavicular block along with general anaesthesia. All of these patients were grouped together for statistical analysis of patients who received regional anaesthesia. The use of regional anaesthesia had a significant impact on the outcome. The graft failure was measured as 18% in patients who underwent regional anaesthesia, whereas it was only 3.5% in those who received general anaesthesia alone (p=0.006). Other intraoperative variables such as fluids used, dextran and anticoagulant use and duration of surgery had no influence on the outcome of free flap surgery.

Perioperative transfusion had a statistically significant negative impact on the outcome (p=0.005). The flaps that had failed

among patients who received transfusion in the perioperative period were 17%. Re-explorations for any reason ranging from those detected at the end of surgery to those at 4 days postoperatively had poor outcomes with statistical significance (p=0.0001). Re-exploration had to be performed in 21 patients, and 8 (31.1%) of them had flap failure because of circulatory problems longer than 24 h. One patient had to be explored twice for venous thrombosis, but that flap survived.

All other postoperative parameters such as haemodynamics, dextran and anticoagulant use, antibiotics and elective ventilation had no role on the flap outcome.

Of the above-mentioned variables, anaesthesia technique and preoperative haemodynamics were independent risk factors for the failure of free flap. The p value, odds ratio and confidence interval of these parameters are presented in Table 2.

Subgroup analysis

A subgroup analysis was conducted in 55 acute trauma patients because of the high failure rate in this group. They had higher risk factors as emergency surgery, preoperative haemodynamic instability and trauma (Table 3). Preoperative haemodynamic instability warranting fluid or blood infusions carried a significant risk for failure along with the use of regional anaesthesia technique. Haemodynamic instability in trauma patients was an independent predictor for flap failure as shown in Table 4.

Discussion

The overall success rate of free flaps was 91.6%, which was similar to the reported rate in most previously published

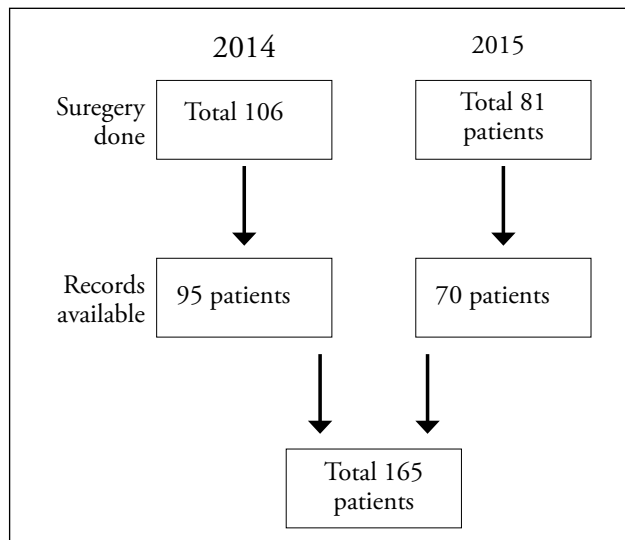


Figure 1. Flow diagram of the study

Table 3. Subgroup analysis in acute trauma patients

Variable	Total	Success	Failure	Probability
Time of surgery	53	44	9	0.218
<4 days	43	37 (84.1%)	6 (15.9%)	
>4days	10	7 (66.7%)	3 (33.3%)	
Haemodynamics				
Stable	44	10 (22.7%)	34 (77.3%)	0.003
Unstable	9	7 (77.8%)	2 (22.2%)	
Transfusion				
Given	15	10 (22.7%)	5 (55.6%)	0.061
Not given	38	34 (77.3%)	4 (44.4%)	
Anaesthesia				
General	21	20 (45.5%)	1 (11.1%)	0.056
Regional/ combined	32	24 (54.5%)	8 (88.9%)	

Table 4. Multivariate predictors of success of free flap in acute trauma by logistic regression

Parameter	Odds ratio	95% confidence interval		Coefficient	p
		Lower	Upper		
Preoperative haemodynamics	11.90	2.126	16.615	2.477	0.005

studies. Free tissue transfer is a reliable method for the reconstruction of defects in various sites. A patient's physiological status has a greater influence on flap viability; however, anaesthetic management and postoperative care also have a direct effect on the outcome. Regional anaesthesia and preoperative haemodynamic instability were the two independent risk factors for flap failure observed in this study. Among trauma patients, the failure rate was higher in those who underwent emergency surgeries, and the incidence of haemodynamic instability was also higher in this subgroup.

The effects of different anaesthetics on free flap blood flow remain unclear (3). Furthermore, little is known regarding the effect of anaesthetics on microvascular parameters related to fluid distribution (4). Sevoflurane, compared with intravenous anaesthetics such as propofol, has been suggested to have beneficial effects on microcirculation, reducing plasma leakage into interstitial space and therefore, decreasing oedema (5). Moreover, there has been evidence suggesting beneficial effects of inhalational agents on different mechanisms of ischaemia-reperfusion injury (6, 7). In the present study, as per the institutional protocol, inhalational anaesthesia was used for patients who had received general anaesthesia either alone or in combination with regional anaesthesia.

Perceived advantages of regional anaesthesia are excellent analgesia, reduction in stress hormones, decrease in blood loss, reduced incidence of deep vein thrombosis and improved perfusion (2, 8-10). Habib et al. (11) have demonstrated an improvement in the signs of tissue perfusion using continuous infusion of local anaesthetics in the paravertebral block for maxillofacial free flap.

If spinal or epidural anaesthesia produces profound hypotension, then it can be disadvantageous for flap blood flow (12). Chemical sympathectomy produced by regional block can cause a diversion of blood flow due to the vasodilation of the intact tissue, resulting in steal phenomenon (9, 12). Regional anaesthesia usually comprises epidural for lower extremities and brachial plexus block for upper extremities. This study showed an increase in the incidence of flap failure in patients who received regional anaesthesia. Erni et al. (13) have demonstrated the reduction in blood flow to the free vascularized tissue using laser flow velocimetry after epidural anaesthesia. They reported a reduction in the mean arterial pressure following the administration of epidural equivalent to slightly hypovolemic status. If appropriate, regional block may be performed, preferably for harvesting the flap, taking advantage of the sympathetic block (14).

Preoperative haemodynamic instability, which is most often associated with acute trauma, is an independent risk factor for the survival of flap. Trauma results in alteration in tissue perfusion and impairment of microcirculation. Any cause of hypotension, such as hypovolemia, decreased myocardial contractility and low cardiac output, that are present in trauma can reduce the free flap blood flow (12). This un-

derlying deficit might play a role in the failure of flaps when acute trauma cases along with recently corrected haemodynamic instability are taken up for free flap procedures. The subgroup analysis conducted in this study on acute trauma patients showed that except for preoperative haemodynamic instability, no factors predict the outcome.

Extremity trauma is amalgamated with long bone fractures and soft tissue loss, which warrant the excess use of fluids in the form of crystalloids and colloids. The overzealous use of crystalloids results in oedema and extreme haemodilution, which may hamper flap blood flow and oxygenation (15). The importance of proper volume replacement has been widely accepted; however, the optimal strategy, including the type of fluid, is still open to debate (9). The preservation of physiological and patient-adapted systemic arterial pressure with wide pulse pressure is essential for flap survival.

Haematocrit is another major determinant of microvascular blood and blood viscosity. Higher haematocrit values result in higher viscosity and lower blood flow in the microcirculation and vice versa (16). Isovolemic haemodilution reduces viscosity, causes muscle reperfusion injury and increases the number of patent capillaries that reduces tissue necrosis. Haematocrit value of 30% provides the best balance between viscosity and oxygen carrying capacity (16). A classification of preoperative haematocrit to <25%, 25%–40% and >40% did not have a marked influence on the flap outcome in the present study probably because of the lesser number of cases in the extremes. Perioperative transfusion for the maintenance of haematocrit level, had no influence on the flap outcome. Both haematocrit and blood transfusion were not independent risk factors for flap failure.

Patients who had been re-explored earlier had higher success rate. The most common cause for exploration was pedicle thrombosis, and venous thrombosis was more salvageable than arterial thrombosis. Our results were consistent with findings of Duc Bui et al. (17) in terms of venous thrombosis, although our failure rate was higher. The early re-exploration of flaps probably resulted in such a significant success rate. However, re-exploration was not an independent risk factor predicting flap failure in our study.

Dextran as a plasma substitute is effective in decreasing platelet adhesiveness and aggregation by increasing the negative charge of platelets and erythrocytes. It is also a volume expander and decreases blood viscosity. Its benefit in terms of flap success has not been clinically demonstrated [9]. However, in contrast to the findings of Hanasano et al. (18), dextran use did not cause any complication in our study.

In contrast, hypertension also results in haematoma and bleeding. Patients with hypertension and coronary artery disease pose more challenge, particularly during emergency situations and extubation. None of our patients had coronary artery disease and seven had hypertension. Because of the small data, it is difficult to comment on the influence.

The main limitations of this study were its retrospective nature, heterogenous group and smaller sample size. Randomised controlled trials that are specific for the cause or the type of surgery should be conducted for better results.

Conclusion

Preoperative haemodynamic instability and regional anaesthesia are major factors that predict the flap outcome, particularly in acute trauma patients. The results of this study showed that regional anaesthesia and haemodynamic instability during the preoperative period are risk factors for the failure of microvascular free flaps.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Nizams Institutional Ethics Committee, Nizams Institute of Medical Sciences.

Informed Consent: Written informed consent was obtained from patients if they are major and from patients parents if the patients are less than 18 years of age.

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