FREE FLAP MANAGEMENT

SUMMARY

Successful free flap management focuses on three areas: close monitoring of the patient and fresh flap, anticoagulation, and fluid resuscitation. Close ICU monitoring is paramount to early intervention in the event of complications. Anticoagulation appears beneficial only in preventing venous thromboembolic events in high risk patients. Fluid resuscitation is associated with complications at the extremes of delivery with both limited and excessive fluid delivery resulting in flap failure and end-organ dysfunction. Vasopressors, after fluid resuscitation is adequate, can be useful in optimizing cardiac function and blood flow to the flap. Near-infrared spectroscopy (NIRS) has been proven to identify microvascular complications in free flaps prior to clinical signs, and therefore, is beneficial to utilize for flap salvage.

RECOMMENDATIONS

- **Level 1**
  - ➢ **None**
- **Level 2**
  - ➢ **Free flap patients should be monitored in an ICU for the first 24-48 hours post-operatively**
  - ➢ **Pharmacologic venous thromboembolism prophylaxis should be initiated immediately post-operatively when a patient's Caprini risk score is ≥ 8 but should be held until 24-48 hours post-operatively if the score is < 8.**
  - ➢ **Crystalloid fluid resuscitation should be used to ensure adequate flap and renal perfusion with a goal urine output of 0.5-1.0 mL/kg/hr.**
  - ➢ **Crystalloid volumes should not exceed 130 mL/kg per 24-hour period.**
  - ➢ **Colloids should be used with caution in free flap patients.**
  - ➢ **Patients should not be "left dry" for the sake of improved flap survival.**
  - ➢ **Once a patient's fluid status is adequate, norepinephrine is the vasopressor of choice if the patient remains hypotensive.**
  - ➢ **Continuous NIRS monitoring can recognize early stages of arterial and venous thrombosis and is a dependable method for noninvasive postoperative flap surveillance.**
  - ➢ **StO2 ≤30% and the drop rate indicator ΔStO2/Δ t ≥ 20% per hour sustained more than 30 minutes predicted vascular complications**
- **Level 3**
  - ➢ **None**

INTRODUCTION

Free flaps are heterotopic tissue transfers with harvested and re-implanted blood supply. They may be used for breast augmentation or restoration after mastectomy, coverage of open wounds following trauma or

EVIDENCE DEFINITIONS

- **Class I:** Prospective randomized controlled trial.
- **Class II:** Prospective clinical study or retrospective analysis of reliable data. Includes observational, cohort, prevalence, or case control studies.
- **Class III:** Retrospective study. Includes database or registry reviews, large series of case reports, expert opinion.
- **Technology assessment:** A technology study which does not lend itself to classification in the above-mentioned format. Devices are evaluated in terms of their accuracy, reliability, therapeutic potential, or cost effectiveness.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Convincingly justifiable based on available scientific information alone. Usually based on Class I data or strong Class II evidence if randomized testing is inappropriate. Conversely, low quality or contradictory Class I data may be insufficient to support a Level I recommendation.
- **Level 2:** Reasonably justifiable based on available scientific evidence and strongly supported by expert opinion. Usually supported by Class II data or a preponderance of Class III evidence.
- **Level 3:** Supported by available data, but scientific evidence is lacking. Generally supported by Class III data. Useful for educational purposes and in guiding future clinical research.

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burns, and reconstruction after tumor excision to restore function and cosmesis. While there are no standardized management guidelines, a 95+% flap survival in expected. Failures occur due to a multitude of factors, including pre-operative patient characteristics as well as peri- and post-operative management decisions. Pre-operative factors, such as type of tumor, past medical history, comorbid conditions, and radiation therapy are important determinants of outcome. Patient selection is paramount to good outcomes.

Four major factors contribute to free flap failure: venous thrombosis, arterial thrombosis, condition of the tissue, and mechanical compression. Venous thromboses have been found to be largely made of fibrin, while arterial thromboses are platelet predominant. These facts have suggested the concept of using anti-platelet agents or heparin to prevent arterial and venous thrombosis respectively (1). Surgical technique is a contributor to the condition of the tissues used for free flaps. Beyond the innate quality of the flap (e.g., atherosclerotic disease), rough handling of the tissues results in worsening edema and inflammatory responses with associated hypercoagulability in the area of injury. Some older animal studies that looked at vasopressor usage in free flaps have noted that, once dissociated from the innate nervous structure of the original location, flaps can become more sensitive to vasopressors (2). Fluid resuscitation can contribute to both dehydration and tissue edema. Mechanical compression can come from patient positioning, surgical tailoring, or uncontrolled and recurrent bleeding resulting in hematoma formation.

A discussion of the pre-operative, anatomical, and oncological factors affecting free flap survival is beyond the scope of this review. The focus here will be on the peri-operative management using a literature review to develop recommendations for four specific aspects: 1) how long should patients be monitored in an ICU setting?, 2) what is the timing and appropriateness of anti-coagulative medications?, 3) what is the proper management of hypotension with regards to peri-operative fluids and vasopressors?, and 4) is near-infrared spectroscopy (NIRS) monitoring of free flaps effective?

LITERATURE REVIEW

Monitoring, flap failure, and salvage

In 1996, Kroll et al. published a study of 990 patients who received free flaps for reconstruction of the breast, extremities, or head and neck between 1988 and 1994 (3). In general, the patients were monitored hourly for 3 days, every 2 hours for the next 1-2 days, and then every 4 hours until discharge or until post-op day 7. The group noted a 5.1% flap thrombosis rate with a subsequent 3.2% flap loss rate after attempted salvage. Several characteristics of the flap thromboses were noted. First, 80% of the flaps that developed problems did so in the first two days. Only 5% of flaps developed thromboses after day 3, and no salvage was obtained for those with late failures. 54% of the thrombosed flaps were primarily venous failures, 20% arterial, and 12% mixed. 90% of the arterial thromboses occurred on the first day, suggesting either technical problems or severe innate flap pathology.

In 2002, Chen et al. published a retrospective review of patients receiving free flaps between January 2002 and June 2003 with a focus on the failed flaps and salvage rates (4). 1142 free flaps were performed and 113 failed. 63% of the flaps were completely salvaged, 20% partially salvaged, and 16% failed completely. Confirming Kroll's 1996 observation, 82% of the flaps failed within 24 hours and 96% within 72 hours. 85% were able to be salvaged. Flaps that failed one week out had a meager 33% salvage rate.

If salvage is not an option, perhaps a second free flap is. Ross et al. published a retrospective review of their experience in the 1990's and 2000's with second free flaps for head and neck reconstruction after neoplastic excision (5). The first group consisted of patients with late problems, such as tumor recurrence, second primary tumor, or reconstructive complications (fractured plate, osteoradionecrosis, or an orocutaneous fistula). The second group had a second free flap following primary free flap failure. Not unexpectedly, the first group had similar patterns of failure to primary free flaps, with 96% success of the second flap. The second group, with the innate patient comorbidities and tissue problems that led to primary failure, had only 73% successful flap survival.

Since most flaps fail in the first 1-2 days, and the highest salvage rate is in the first 3 days, the current literature appears to support monitoring in an ICU setting for 1-2 days, followed by an in-patient stay for another 2-3 days to assure flap success and aid in quick action for flap salvage.

Near-infrared spectroscopy (NIRS) is a noninvasive modality to continuously measure free flap tissue oxygenation and perfusion. It is a well-accepted technique to assess flap viability at the bedside (6). In order to prevent flap failure, the time between onset of a microvascular incident and intervention is paramount. By the time clinical changes of the flap are observed, it is usually too late to successfully salvage the flap. (7). NIRS can provide the surgeon with prompt, objective information directing attention to impending flap failure, allowing timely surgical intervention.

Tissue oximetry is a technology that estimates % oxygen saturation (StO2%) in a volume of tissue beneath the sensor. Two light sources spread the light to the tissue, which is then collected by 4 photo detectors located in each sensor. Tissue oximetry uses 2 wavelengths of 690 and 830 nm near-infrared light each specific to HbO2 and Hb for the noninvasive measuring of StO2% (8). Keller et al. studied 208 breast free flaps, of which 5 patients demonstrated tissue oximeter waveforms representative of microvascular complications prior to clinical signs (7). They reported StO2 ≤30% and the drop rate indicator ΔStO2/Δtime ≥ 20% per hour sustained more than 30 minutes predicted vascular complications (7). NIRS detected all cases of flap compromise prior to clinical changes with no false positives or negatives.

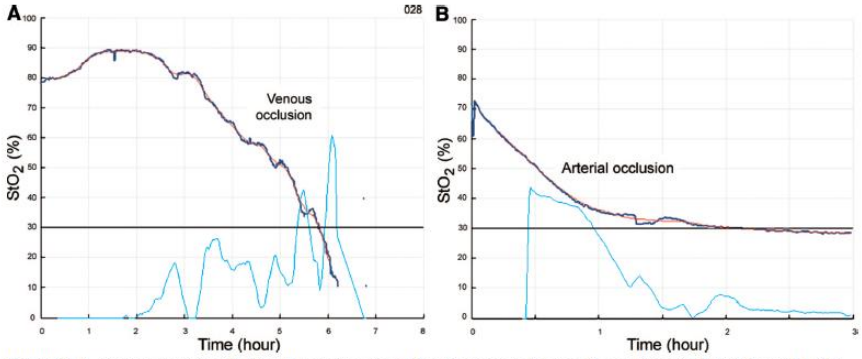

FIGURE 9. A, Venous occlusion. B, Arterial occlusion. The dark blue curve on the top of each figure is directly from the StO_2 data, the red curve for the StO_2 average and the blue curve in the bottom for the StO_2 drop rate.

The example in Figure 9A was a deep inferior epigastric perforator flap that was not elevated or needed and had the vein clamped. Figure 9B is a deep inferior epigastric perforator flap that was not elevated or needed that had the artery clamped. These graphs illustrate the effect of pure vessel occlusion with known start times on ΔStO2. (7).

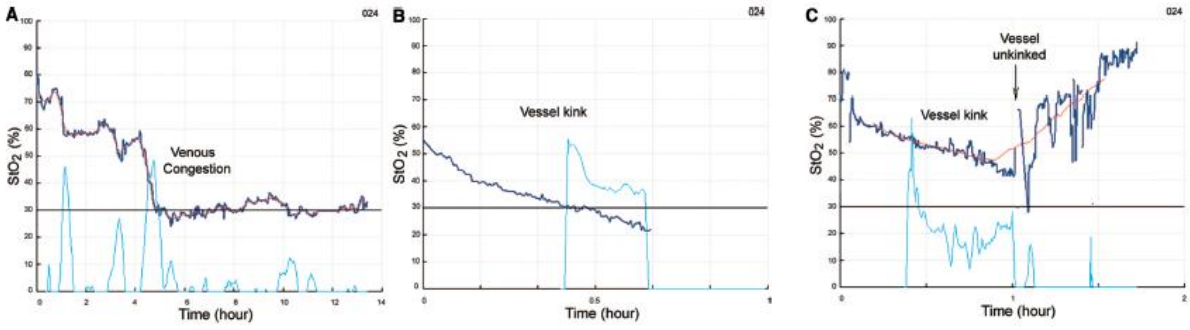

FIGURE 4. Flaps with complication: A, venous congestion; B, an initial vessel kink; and C, a subsequent vessel kink.

Figure 4 represents a patient in the Keller et al. study that experienced 3 flap complications in series: venous congestion during the initial surgery (Fig. 4A), thrombosis of the superficial vein after a second anastomosis was performed to resolve this venous congestion (Fig. 4B), and a second kink of the superficial vein (7).

Several studies advocate the use of noninvasive optical spectroscopy for monitoring flap viability (9-12). Although the spectroscopy machines and their study designs were different, all studies concluded with evidence supporting the use of NIRS for monitoring flap viability.

Measurements can be influenced depending upon changes in probe position (13,14). Due to this variability, it is difficult to standardize exact NIRS threshold values that would indicate a threat to a free flap. Therefore, it is vital to observe trends of NIRS changes instead of exact values (6).

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An experimental study on a pedicled flap conducted by Payette et al. indicated that optical spectroscopy was more dependable than laser doppler examination in identifying problems with arterial inflow (15). NIRS has many advantages over laser Doppler and other monitoring modalities. Primarily, NIRS has the light capability to penetrate a greater depth of tissue and provide data of events occurring in a relatively large volume of tissue. In contrast, laser Doppler flowmetry can only observe superficial microcirculatory changes in tissue. Another benefit of NIRS, unlike laser Doppler, is that its' measurements are not influenced by patient movement (6,9,11,13-16).

Venous Thromboembolism (VTE) Prophylaxis

In 2012, Shuman et al. studied a diverse group of 2016 otolaryngologic surgical patients between 2003 and 2010 who had no chemoprophylaxis (17). The Caprini risk score (Figure 1) was used to stratify patients. Overall venous thromboembolism (VTE) rate was 1.3%. A Caprini risk score up to 6 resulted in a VTE rate of 0.5%. A score of 7 or 8 yielded a VTE rate of 2.4%. Patients scoring >8 had a VTE rate of 18.3%.

Due to the concern for platelet predominant arterial thromboses and fibrin predominant venous thromboses, many studies have been performed to evaluate the risks and benefits of using some type of anticoagulant during free flaps. In 2015, Swartz et al. published a retrospective multi-center analysis of free radial forearm flaps as well as a systematic review of the literature (18). Across their own and 5 other reviewed studies with a total of 759 patients, the flap failure rate was 5.3%. Several different anticoagulation regimens were used (aspirin, low molecular weight dextran, unfractionated heparin, prostaglandin-E1, and no treatment). Unfractionated heparin was associated with a higher rate of flap failure though this finding was confounded by the elevated number of patients requiring revision surgery of the free flap's anastomosis. Notably, anticoagulants were not associated with improved flap survival or decreased flap related complications.

Together, these two papers suggest that a Caprini risk score >8 should initiate consideration for early pharmacologic VTE prophylaxis. Theoretical benefit still exists for anti-coagulative strategies to enhance free flap survival, but this is not reflected in the current literature.

Fluid and blood pressure management

Clark et al. described predictors of major complications following free flap reconstruction for head and neck cancer in 2007 (19). After retrospectively reviewing 185 patients, their comorbidities, and peri-operative care, his team developed three major conclusions. First, major complications of all types were predicted by increasing age, ASA class, and smoking history. Second, medical complications (myocardial infarction, congestive heart failure, multi-organ failure, etc…) were predicted by ASA class, smoking, and >130 mL/kg/day of crystalloid replacement. Surgical complications (flap failure, wound breakdown, etc...) were predicted by the placement of a tracheostomy, a pre-operative hemoglobin <11 gms, and pre-operative radiotherapy. Surgical complications (such as flap failure) were not affected by large volume fluid resuscitation.

Zhong et al. reviewed 260 patients with 354 flaps (often bilateral reconstructions) and noted a 0.8% failure rate (20). Upon reviewing the intravenous fluid infusion rate, they noted that infusion rates at the extremes predicted complications and that colloids trended toward more complications. Based on their data, they recommend a daily dose of 3.5-6 mL/kg/hr of crystalloid (245-420 mL/hr for a 70 kg patient). They note that the important principle of optimizing cardiac performance to enhance free flap perfusion is the goal of fluid management.

Nelson et al. studied 682 patients receiving autologous breast reconstruction, stratifying them into three groups based on urine output (21). Normal urine output was defined as 0.5-1.0 mL/kg. No differences were noted intra-operatively, but post-operatively there were large differences between delayed thrombotic complications and flap loss. The low urine output group had a 10.3% delayed thrombotic complication rate and 8.8% flap loss rate. This finding sharply contrasts with rates of 3.3 and 3.1% thrombotic complications and 2.2 and 0.6% flap loss, suggesting that adequate fluid resuscitation to maintain adequate urine output provides the best chance for flap survival. They also noted that a hitherto unrecognized use of intra-operative vasopressor by the anesthesia team had no effect on flap complications or survival.

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In contrast to these studies, Ettinger et al. in 2017 noted that in 154 head and neck reconstruction patients, there were no flap losses and a partial failure rate of only 3% (22). They found that the total peri-operative fluid predicting complications was 5.5 L, and that 7 L of fluid predicted major complications. Comparing this to Nelson's figures, these amounts translate into a rate of 3.2-4.1 mL/kg/hr, 224-287 mL/hr, or 80-100 mL/kg/day in a 70kg patient. This suggests that in the head and neck population, fluid requirements may be lower than in breast reconstruction.

Chen et al. studied vasopressor usage in 187 patients with 258 free flaps (23). Overall complication rate in a group that had intra-operative vasopressors was 24% with complete flap loss in 0.7% of patients. Despite expectations to the contrary, the cohort that received no vasopressors had a similar overall complication rate of 24%, but a much higher complete flap loss rate of 4.2%. The study supports maintaining adequate hemodynamics as the best way to improve flap survival.

Monroe et al. in 2011 described a similar study to the Chen breast flap study in which 169 head and neck patients received intra-operative vasopressors vs. no vasopressors (24). There were no statistical differences between the two groups in either complications or early flap failure.

Eley et al. used power spectral analysis of the effects of epinephrine, norepinephrine, dobutamine, and dopexamine on microcirculation (25). They infused each vasopressor into patients at random intervals post-operatively and used a laser-doppler at the deltoid region as a control. They demonstrated the expected denervation of the flap and noted that norepinephrine was most effective in maintaining average blood pressure and flap blood flow.

Figure 1: Caprini Risk Score

One point	Age 41-60 years Swollen legs Varicose veins Obesity (BMI >25) Minor surgery planned Sepsis <1 month prior Serious lung disease (pneumonia) < 1 month prior Oral contraceptives or hormone replacement therapy Pregnancy or post-partum <1 month prior History of unexplained stillborn infant, recurrent spontaneous abortion (>2), premature birth with toxemia or growth restricted infant Acute myocardial infarction Congestive heart failure <1 month prior Medical patient currently at bed rest History of prior major surgery < 1 month prior Abnormal pulmonary function (e.g. COPD)
Two points	Age 61-74 years Arthroscopic surgery Malignancy (present or previous) Laparoscopic surgery (>45 minutes) Patient confined to bed >72 hours Immobilizing plaster cast (< 1 month) Central venous access Major surgery >45 minutes
Three points	Age 75 years or older History of DVT/PE Positive factor V Leiden Elevated serum homocysteine Heparin-induced thrombocytopenia Elevated anticardiolipin antibodies Family history of thrombosis (most frequently missed risk factor) Positive prothrombin 20210A Positive lupus anticoagulant
Five points	Stroke <1 month prior Elective major lower extremity arthroplasty Hip, pelvis, or leg fracture Multiple trauma <1 month prior

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