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Perioperative considerations in free flap surgery: A review of pressors and anticoagulation

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ABSTRACT

Given the high stakes for microvascular reconstruction, the majority of reconstructive surgeons have developed paradigms for pre, intra, and postoperative management that have proven to result in individual high success rates. Much has been done to identify and avoid perioperative factors that could potentially increase flap failure rates. Two example of this practice has been the generalized use of anticoagulation in free tissue transfer and the prohibition against vasopressor use in patients that are undergoing free tissue transfer. This manuscript will discuss these issues.

Introduction

The head and neck plays a critical role in multiple homeostatic processes. Many of these are noticeable in everyday social interaction. From a physiologic perspective: eating, drinking, articulation, swallowing, and the ability to maintain weight are dependent on intact anatomy and function of the head and neck structures. Any procedure that interferes with the anatomy and thus the physiologic processes will have a debilitating effect on the patient. Whether it is psychological, a cosmetic deformity or a physiological dysfunction, these issues need to be addressed. Thus reconstruction following composite tissue loss is required to allow for adequate rehabilitation of the patient. This tissue loss may be the result of a composite tissue loss from an oncologic procedure, trauma, osteoradionecrosis, or less commonly infection. The best method of reconstructing composite tissue loss from any etiology is with a composite tissue replacement. Free tissue transfer allows the harvesting of multiple tissue components from one part of the body that is similar to the tissue that has been lost in the head and neck region. Over the last decade the use of free tissue transfer has become the optimal method for allowing maximal rehabilitation with restoration of functional outcomes.

The success rate of microvascular reconstruction in the head and neck is typically greater than 95% in experienced author's hands [1]. The use of vascularized non treated tissue allows for an improved functional result, superior aesthetic outcomes and improved quality of life [2–5]. Hospital stays can range from as little as a few days to a week or longer depending on medical comorbidities [6]. Unfortunately there is a small subset of patients in which free tissue transfer is unsuccessful. In these cases the entire composite tissue is lost resulting in a large composite defect. Multiple surgical procedures or multiple attempts at salvage, lead to prolonged morbidity with increased hospital cost and length of stay with poorer functional outcomes.

Given these high stakes for microvascular reconstruction, the majority of reconstructive surgeons have developed paradigms for pre, intra, and postoperative management that have proven to result in individual high success rates [2,6]. Much has been done to identify and avoid perioperative factors that could potentially increase flap failure rates. Two example of this practice has been the generalized use of anticoagulation in free tissue transfer and the prohibition against vasopressor use in patients that are undergoing free tissue transfer.

Anticoagulation in free tissue transfer

Patients requiring free tissue transfer, most often for cancer related defects, are at risk for clotting events postoperatively. A survey of reconstructive surgeons demonstrated that 97% of them used some form of anticoagulation when performing free tissue transfer [7]. In regards to the type of anticoagulation used in free flap management, practices and opinions differ [1]. This stems from both clotting and bleeding having the potential to compromise a free flap, by thrombosis or hematoma respectively. Common sense would also dictate that each patient must be approached individually, as with those cases where stopping anticoagulation could be life-threatening due to serious heart disease or another comorbidity. This has led to significant controversy and a wide variation in postoperative anticoagulation protocols from surgeon to surgeon [7,8]. The perfect balance remains unclear [6].

Many flap anticoagulation protocols exist with no consensus on which is best [7,8]. Part of the difficulty in determining this more

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definitively is that randomized-controlled trials in human patients could place some patients at higher risk for flap failure. Currently with very low reported flap failure rates at most major academic medical centers, the need to elucidate this definitively is arguably not an urgent necessity. When thrombosis does occur it is most often in the first three days post-operatively, presumably when vessel intimal damage is greatest [1,10,11]. The majority of these are venous thrombi and if not explored and corrected urgently can be devastating for the flap [9].

In a multicenter analysis of radial forearm flap survival, on multivariate logistic regression analysis, no anticoagulation regimen improved flap survival or decreased the rate of flap-related complications [8]. Despite this, the vast majority of surgeons report that they use some type of anticoagulation prophylaxis to prevent anastomotic thrombosis [1,7]. The most common medications include aspirin, heparin, and dextran. More recently statins have been discussed as another theoretical agent [12,13].

Aspirin works as an anticoagulant by inhibiting cyclooxygenase which decreases the amount of thromboxane A2 produced. Thromboxane A2 has prothrombotic properties. It stimulates activation of new platelets and increases aggregation. Aspirin use also has well-known potential complications associated with its use, including gastric bleeding [9]. When compared with other various anticoagulation regimens, aspirin has not shown to have a greater impact on reducing the incidence of flap loss or thrombotic complications [14].

Heparin binds antithrombin and inactivates multiple clotting factors. The primary risk of its administration is bleeding. It can be used topically, systemically, or by subcutaneous injection. Animal studies looking at topical use of heparin have shown a benefit in reducing microvascular thrombosis [15–17]. On the other hand, a prospective, clinical study did not show any difference in flap outcome with the use of topical heparin [18]. Other topical agents have also been studied and compared to heparin for intraoperative use. A blinded, randomized, parallel group study looked at recombinant human tissue factor pathway inhibitor as an antithrombotic additive to intraluminal irrigation solution. 622 patients undergoing free flaps were divided into three groups. Overall there was equivalent efficacy in the groups of low and high concentrations compared to standard heparinized irrigating solution [19]. In addition, intraoperative use of systemic heparin had no effect on thrombotic complication rate [16,20]. Postoperative subcutaneous heparin, however, has shown to decrease the incidence of microvascular thrombosis [18]. Other various retrospective studies have looked at combinations of anticoagulants compared to single agent regimens and found no significant differences in rate of complications, thrombosis, or flap failure [14,21–24]. The one exception is dextran.

Dextran, an artificial colloid, is an intravascular volume expander and works as an anticoagulant primarily by reducing platelet and erythrocyte aggregation. Some known complications include anaphylaxis, renal injury, and pulmonary edema [9]. Two studies have shown no benefit to dextran use, but rather have implied a potential harm. In a prospective, randomized trial, dextran did not have an effect on flap survival but increased the incidence of systemic complications compared to aspirin [25]. In a retrospective review of 1351 free flaps, dextran administration increased the rate of flap failure in high-risk patients while not effecting flap survival compared to no antithrombotic prophylaxis [26].

Statins have been widely used in the management of hyperlipidemia and for the prevention of coronary artery disease and stroke. They have a relatively low side-effect profile. The most common being myalgia and rhabdomyolysis. They work by inhibiting HMG-CoA reductase. This leads to reductions in inflammation, thrombogenicity, and improved vasodilation. They have also been shown to improve endothelial dysfunction. For these reasons they are theorized to have a potential benefit in microvascular free flap surgery, although no studies to date have looked at this specifically [13,27]. The majority of clinical data comes from cohort studies looking at patients with hyperlipidemia and other cardiovascular diseases [13,27]. Given the prevalence of cardiovascular disease in the Head and Neck cancer population it may be beneficial to start patients that have indications on statins. Whether this will be efficacious in reducing free flap morbidity is unknown.

Although data regarding the effect of the above mentioned agents is generally inconclusive, after a thorough review of the existing published evidence, Motakef et al. [28] made three definitive recommendations and provide the corresponding levels of evidence for each. First, with a level of evidence 2b, they recommend aspirin 325 mg or heparin 5000 units subcutaneously every day for antithrombotic prophylaxis. Second, and also with a level of evidence 2b, they state that there is no benefit to systemic heparin. Lastly, with a level of evidence 1b, they advise against the use of dextran due to a strong link with flap and systemic complications. Interestingly they acknowledge that the data regarding anticoagulation is inconclusive. A key factor for their conclusion is based on Chien et al.'s [29] review of their institutional data of flap survival with a regime that utilized aspirin and subcutaneous heparin in the post-operative setting. They demonstrated that their survival was similar to other protocols in the literature. Thus the basis for routine peri-operative anti coagulation is generally based on very low level data. A further limitation of Motakef's [28] study was that the populations studied were not exclusively head and neck reconstructions. Translating this information to the head and neck population must be done carefully as there are differences between flaps in this area and other body parts. Clearly more study is needed.

Two recent studies have focused on special situations. Rather than standard anticoagulation protocols for prevention of thrombosis post-operatively, Senchenkov et al. [30] addressed the use of anticoagulants to manage thrombosis after it has occurred. They constructed an algorithm to guide management in this situation using multiple anticoagulants. They performed a retrospective review of 395 free flaps and focused on the 15 thrombotic complications, of which two were ultimately lost due to arterial thrombosis. Upon return to the operating room for a postoperative thrombosis, a stat heparin bolus was given and optimized to therapeutic range. An intraflap injection of tPA was given followed by emergent exploration with thrombectomy, intra-arterial tPA injection, and vascular revision. Weight-based systemic heparin was then continued for at least 5 days. Dextran was added in cases where thrombus was considered extensive. All flaps with venous thromboses were salvaged with this protocol with no reconstructive site hematomas reported.

Nelson et al. [31] addressed specifically how patients with a preoperative history of hypercoagulability can be approached differently. They performed a retrospective study comparing a historical cohort of hypercoagulable patients with a newly designed and implemented protocol for thrombosis prevention. They identified hypercoagulable patients as those with a documented history of a blood clot or blood clot event or had been told that they are at a high risk for a clot. The anticoagulation protocol involved intraoperative administration of 5000 units subcutaneous heparin at induction, 2000 units IV heparin bolus prior to anastomosis, and initiation of a continuous 500 units/hour IV heparin infusion at the time of anastomosis. The heparin infusion was titrated to a therapeutic level post-operatively while an inpatient, and anticoagulation was transitioned to warfarin or enoxaparin and continued for one month. They looked at 32 flaps in 23 patients, 11 of which received the novel anticoagulation protocol. Three thrombotic events occurred in the control cohort and these flaps were lost. None of the patients in the novel protocol cohort had any thrombotic events or flap losses, but they were more likely to have had red blood cell transfusion (72.6% vs. 16.7%), hematoma (26.7% vs. 0%), and lower hemoglobin nadirs (6.9 vs. 8.9) post-operatively. Although this study was of low power, it illustrates the ongoing attempt by microvascular surgeons to balance prevention of thrombosis and bleeding complications.