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Review

Efficacy of the postoperative management after microsurgical free tissue transfer

N. Sigaux [a,*], P. Philouze [b], F. Boucher [c], M. Jacquemart [a], P. Frobert [d], P. Breton [a]

[a] Department of Maxillofacial Surgery, Stomatology and Facial Plastic Surgery, Hospices Civils de Lyon – Claude-Bernard-Lyon 1 University, 165 Chemin du Grand Revoyet, 69495 Pierre-Bénite, France
[b] Department of Otorhinolaryngology, Head and Neck Surgery, Hospices Civils de Lyon – Claude-Bernard-Lyon 1 University, 103 Grande Rue de la Croix-Rousse, 69004 Lyon, France
[c] Department of Plastic, Reconstructive and Esthetic Surgery – Croix Rousse Hospital, Hospices Civils de Lyon – Claude-Bernard-Lyon 1 University, 103 Grande Rue de la Croix-Rousse, 69004 Lyon, France
[d] Department of Plastic, Reconstructive and Esthetic Surgery, Centre Léon-Bérard – Cancer Treatment Center, 28 rue Laënnec, 69008 Lyon, France

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ABSTRACT

Introduction: The physical and medical postoperative measures after free flap reconstruction vary substantially between surgical units. The objective of this review was to identify the postoperative measures which proved a significant positive effect on free flap survival.
Method: A review was conducted in the MEDLINE database on the English and French literature.
Results and discussion: Twenty-eight articles were retained. A meta-analysis of 4984 patients who were given antithrombotics (viz. antiplatelets and anticoagulants) postoperatively found that these treatments were of no significant benefit to free flap survival and increased the risk of postoperative hematoma. Postoperative transfusions did not favor free flap survival and were associated with a higher incidence of medical complications. Preoperative anemia was a risk factor for free flap failure. Blood pressure control, vasodilators, antioxidants, corticotherapy, oxygen therapy, and prolonged immobilization were of no proven benefit.
Conclusion: No postoperative therapy, whether drug-based or not, has been shown to have a significant positive effect on free flap survival.

1. Introduction

Free tissue transfer has become an indispensable tool in Reconstructive Surgery. The success rates reported in the literature for this procedure range between 90% and 99% [1,2], but failure has severe functional, esthetic, psychological and economic consequences. Although the surgeon's technical skills can guarantee a successful operation, this does not by itself prevent the failure of the procedure. The postoperative phase is indeed fundamental for the prevention of complications. The importance of the associated physical and drug treatments therefore require a close medical and surgical follow-up. However, postoperative protocols differ widely between surgical units. This is the reason why the objective of this review was to identify the postoperative measures that proved a significant positive effect on free flap survival.

2. Major causes of free flap failure

2.1. Thrombosis

Pedicle thrombosis is the most common complication following free flap reconstruction. According to a large majority of authors, thrombosis of the vein is roughly three times as frequent as arterial thrombosis. Most thrombi (80%) form within 48 h of surgery [3].

The risk factors are multiple, corresponding to Virchow's triad of blood flow stasis, endothelial damage and hypercoagulability. The causes can furthermore be classified as either intra- or extravascular. The former include hypercoagulability due to chronic or acute hematological disorders (e.g. hemoconcentration, polycythemia, thrombophilia), hemodynamic disorders (blood pressure variations), and microsurgical errors (e.g. endothelial clamping damage, transfixing or stenotic sutures). The main extravascular cause of thrombosis is pedicle constriction. Compression (from hematoma, edema or bandaging for instance) and torsion of the vascular are suspected to be the main risk factors for failure.

* Corresponding author.
E-mail address: n.sigaux@gmail.com (N. Sigaux).

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Several metabolic factors (viz. undernutrition, heat) favoring thrombosis have also been reported.

Thrombosis prevention is therefore crucial, both before surgery and after, as discussed in more detail below. Many methods have been described in the literature, employing both drug-based (using antithrombotic or blood pressure medication for example) and physical measures (e.g. immobilization, bandaging). However, very few have been shown to have a significant effect.

2.2. Vasospasm

Vasospasm refers to a substantial reduction in vein diameter caused by the contraction of smooth muscle cells in the vascular wall. Vasospasm mainly affects arteries, whose walls are significantly richer in these cells than are those of veins. Vasospasm can be provoked by different stimuli, which are often associated. These can be mechanical (traction or excessive adventicectomy), chemical (vasoconstrictor medication), thermal (cold) or neurovegetative (through a sympathetic stimulus or bleeding). Vasospasm prevention must be initiated before surgery and continued postoperatively. This can be achieved using vasodilators or non-drug measures (e.g. warming, immobilization).

2.3. The no-reflow phenomenon

No-reflow occurs when prolonged ischemia (caused by cellular swelling, intravascular aggregation or leakage of intravascular fluid into the interstitial space) induces irreversible tissue lesions [4]. Intraoperative measures should therefore be taken to minimize the time during which the flap remains ischemic.

2.4. Ischemia-reperfusion syndrome

Reperfusion injuries occur in all tissues that are vascularized again after a period of ischemia [5,6] and are therefore inevitable in free flap reconstruction with microanastomosis.

Ischemia induces anaerobic mechanisms in the tissues, which thus produces less ATP than normal. This in turn inhibits the sodium-potassium pump, leading to the accumulation of sodium and calcium in the cell. Glycolysis and the concentration of lactic acid increase while the pH decreases. After some time, ischemia inevitably leads to cellular necrosis. Because the mitochondrial metabolism is disturbed, reperfusion also induces lesions, but these differ from those caused by ischemia. The production of reactive oxygen species (ROS) increases, as does the release of cytochrome C by the mitochondria, triggering apoptosis. The resulting edema and release of free radicals imparts oxidative stress, leading to endothelial dysfunction and thereby to arterial vasoconstriction.

The production of ROS is thought to be the key step in reperfusion injuries. Several studies have therefore investigated the potential benefit of ROS-targeting treatments (e.g. antioxidants, corticosteroids), both pre- and postoperatively. Some of their conclusions are noted below.

Nitric oxide is another molecule that has been implicated in ischemia-reperfusion syndrome. However, its precise effect is controversial with conflicting evidence as to its role as a risk or protective factor. Note finally that while the value of ischemic preconditioning is currently a matter of debate, this measure, being intraoperative, is beyond the scope of this review.

3. Method

A literature review was conducted in the MEDLINE database on papers in English or French published between 1975 and 2015. The following keyword combinations were used: "free flap" AND/OR "microsurgical anastomosis" AND "postoperative management"; then "free flap" AND/OR "microsurgical anastomosis" AND ["antithrombotics" OR "anticoagulants" OR "antiplatelet" OR "blood transfusion" OR "hemodynamic" OR "vasodilators" OR "corticotherapy" OR "antioxidants" OR "mobilization" OR "coffee"]. The location of tissue loss, etiology, and type of free flap used were not considered specifically. Single case reports were excluded. In total, 28 scientifically valid articles were retained.

4. Results and discussion

4.1. Drug-based postoperative measures

4.1.1. Antithrombotics

The prevention of pedicle thrombosis, first cause of free flap failure, is essential. Antithrombotic treatments (anticoagulants, platelet antiaggregants, dextrans) are widely administered postoperatively. However, while their efficacy has been demonstrated in animal studies, there is no scientific proof of their benefit in humans. Lee and Mun [7] conducted an extensive literature survey to exploit data from 12 large-scale studies totaling 4984 cases. This recently published meta-analysis investigated the association between common antithrombotics (aspirin, clopidogrel, unfractionated heparin, low molecular weight heparin (LMWH), dextrans) pedicle thrombosis, hematoma and flap failure rates. None of the antithrombotics significantly improved flap survival. Although heparin did reduce the failure rate by 35% on average, this result was not significant (relative risk, 0.65; 95% confidence interval: 0.25–1.69). Furthermore, heparin dosage had no effect on the outcome. In contrast, all these treatments significantly increased the risk of postoperative hematoma (relative risk: 1.78, 95% confidence interval: 1.20–2.63).

On the basis of this powerful meta-analysis, the authors recommended restraint in the administration of antithrombotics after free flap surgery, with an indication (preferably LMWH) only for patients at risk of lower-limb deep vein thrombosis and no expected benefit in terms of flap survival. Other authors suggested that in combination with aspirin, isocoagulant doses of LMWH increased the risk of bleeding [3], but we did not find any quantitative data to support or refute this claim.

Postoperative hematoma is indeed a severe complication requiring emergency surgery. Ahmad et al. [8] carried out a retrospective study of 1883 free flaps used for cervicofacial reconstruction, with no systematic administration of anticoagulants. Of the 88 patients who developed postoperative hematoma (4.7% of the study population), the flap was compromised in 20 cases, of which 12 involved pedicle thrombosis (most often venous). The sooner the hematoma was operated on, the greater the salvage rate of the flaps was (salvage rate if time to operation <5 h was 93.3%; 20% otherwise; $P = 0.0049$). The authors emphasized the fact that if anticoagulants had been administered systematically to these patients, the incidence of hematoma would have been much higher.

Some cases of heparin-induced thrombocytopenia (HIT) leading to thrombosis in microanastomoses were reported in the literature [9,10]. Heparin-induced thrombocytopenia is evidenced by a rapid decrease in platelet counts that can occur up to 14 days after the initiation of thromboprophylaxis. Its incidence was higher (0.5–3% vs 0.2%) when unfractionated heparin is used rather than LMWH (e.g. enoxaparin). These results highlighted the importance of twice-weekly platelet monitoring during heparin treatment.

4.1.2. Blood transfusion

Maintaining normal plasma hemoglobin levels by red blood cell transfusion seems justified in order to avoid ischemic compromise