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Research Article

Role of heparin in microvascular free flap surgery in head and neck reconstruction

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ABSTRACT

Background: Microsurgical reconstructions for free flap transfer have been highly successful applications in the past decades. Antithrombotic prophylactic agents, such as low molecular- weight heparin, aspirin and dextran have been routinely used for the prevention of microvascular thrombosis. Even though these agents are efficacious in microsurgery, some systemic morbidity is still reported.
Methods: The present prospective study was conducted in the Department of Surgical Oncology, Regional cancer center, Pt. JNMC, Raipur (C.G.), India from the January 2014 to June 2015. Each patient was informed and consent was taken to participate in the study. Detailed clinical history and examination of the patients was recorded. All Investigations relevant to the study were done before the surgical procedure. Outcome of the surgery were noted. Data was compiled in MS Excel and checked for its completeness and correctness. Then it was analyzed.
Results: During the study period, 20 microsurgery operations on 20 patients were performed. There were 17 male and 3 female patients. In all patients neck dissection was done and resective part was reconstructed with free flap. Out of 20 free flap 12 radial artery free flaps and 8 free fibula flap was harvested.
Conclusions: The free flap technique is safe but involves a significant learning period and requires careful postoperative monitoring of the patient. Early intervention is important for the salvage of free flaps and for lowering the failure rate.

Keywords: Heparin, Antithrombotic agent, Microsurgical free flap, Head and Neck Reconstruction

INTRODUCTION

Due to the complex anatomy and function of the head and neck region, the reconstruction of ablative defects in this area is challenging. In addition, an increasing interest in improving the quality of life of patients and achieving good functional results has highlighted the importance of free flaps. Over the past decade, techniques in free tissue transfer with microvascular anastomosis have advanced and this procedure is now widely used for the reconstruction of defects following cancer ablation in the head and neck. With improvements in technique and surgical devices, the reported overall rates of success of free flaps in the literature are as high as 95% to 97% in the case of experienced surgeons.[1,2] However, failures caused by vascular thrombosis are inevitable in some cases, and this frequently leads to devastating results[2,3]. Today, transfer of chosen composite tissue to a defect from a distant site by free micro-vascular technique is considered 'standard of care' in many reconstructive surgical situations. The operative technique requires involves vascular anastomosis and requires special instrumentation, Operative magnification, and training.[4,5]

Antithrombotic agents such as low molecular- weight dextran, aspirin and heparin have been thought to play a significant role in this success. Ninety-six percent of micro surgeons use antithrombotic agents such as dextran, heparin and aspirin alone or combination in free flap transfer and replantation.[3] Antithrombotic prophylaxis has been shown to be beneficial in these circumstances. Multiple antithrombotic agents such as low-molecular-weight heparin, aspirin, and dextran are routinely applied despite a lack of consensus about their use. Serious systemic complications from these agents have been reported. Reported complications from low molecular- weight dextran have included as prolonged bleeding time and abnormal bleeding from the site of surgery, acute pulmonary oedema, and adult respiratory distress syndrome, osmotic complications in free flap surgery and anaphylactic complication. An increasing number of reports of significant morbidity and mortality related to these agents have brought into question their routine use in microsurgery.[3,4]

Their adverse effects can cause morbidity and mortality in patients; with serious side effects from low-molecular-weight dextran have been reported. For example, Disa and colleagues reported that dextran did not improve benefit in free flap survival but increased the risk of systemic complications.[3]

The time interval between the onset of ischemia and its clinical recognition is of utmost importance in terms of free flap salvage in free flap surgery. Although microsurgical free-tissue transfer has become a reliable technique, between 5 to 25 percent of transferred flaps require surgical revision because of circulatory compromise either on the arterial or venous side. Regardless of the surgeon's experience or the reliability of the chosen free flap, immediate detection of perfusion failure and prompt revision is paramount for flap salvage as ischemic tolerance of the flap tissue is limited to a few hours and irreversible disseminated microvascular thrombi may form during malperfusion. After completion of the microsurgical anastomosis, the success of a free-tissue transfer is dependent on the continuous arterial inflow and venous outflow until the tissue is neovascularized by peripheral ingrowth of vessels. Consecutively, close monitoring of free flap perfusion is mandatory in the postoperative period for early diagnosis of perfusion failure.[3,6]

METHODS

The present prospective study was conducted in the Department of Surgical Oncology, Regional cancer center, Pt. JNMC, Raipur (C.G.), India from the January 2014 to June 2015. Each patient was informed and consent was taken to participate in the study.

Inclusion criteria

Patient eligible for the analysis were those with reconstruction of malignant tumors of the head and neck who underwent an immediate reconstruction with use of free flap surgery.

Exclusion criteria

Patient undergone primary closure, pedicle flap and other loco regional flap were excluded from the study.

Technique

Detailed clinical history and examination of the patients were recorded. All Investigations relevant to the study were done before the surgical procedure. All procedures were performed by the same group of surgeons and were performed as per standard protocol. Firstly, tried to limit the operative time by two teams performing free flap transfer simultaneously, one team harvesting the donor flap and the other team preparing the recipient site. The tissue was performed under a magnifying glass. Just before transecting vessels 5000 IU bolus heparin given Secondly, to preserve the tissue, the donor flap and amputated part were cooled with cooled lactated Ringer's solution. After good preparation of both the recipient and the donor vessels, they were irrigated with heparinized solution (5000IU mixed with 100ml saline) to remove blood from the vessel end. The vessel was anastomosed under an operating microscope and irrigated with heparinized solution to ensure a clear view during suturing without touching the vascular wall. All microvascular anastomosis were performed by one surgeon. Postoperatively 5000 IU heparin mixed with 500 ml saline was given over 24 hrs for the next 5 days. No other agent was used in this study. Outcome of the surgery were noted. Data was compiled in MS Excel and checked for its completeness and correctness. Then it was analyzed.

RESULTS

Table 1: Different type of variable associated with the study.

Variable	No.	Percentage
Sex		
Male	17	85%
Female	3	15%
Free flap		
Radial Artery	12	60%
Fibular flap	8	40%
Outcome		
No complication	18	90%
Bleeding	1	5%
Arterial thrombus	1	5%

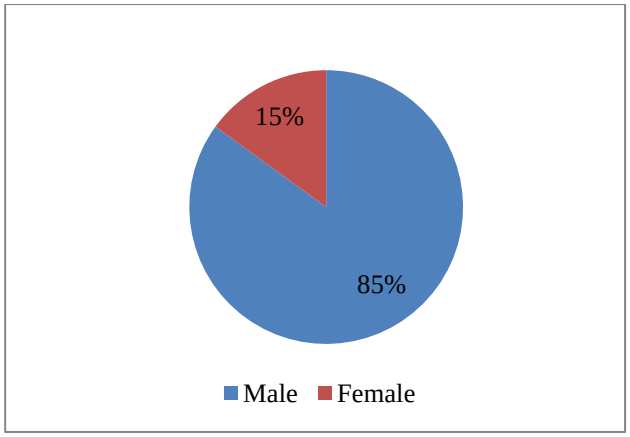

Figure 1: Sex wise distribution of study subjects.

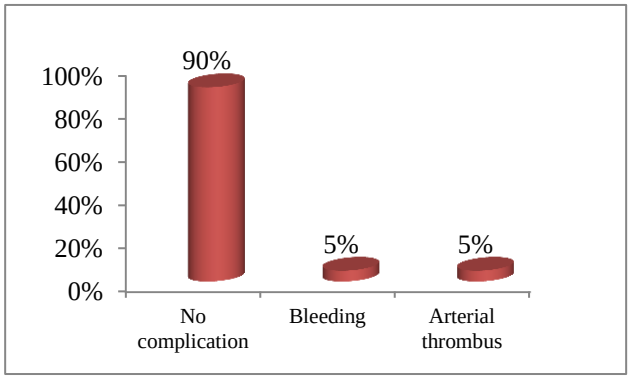

Figure 2: Outcome of the study.

During the study period, 20 microsurgery operations on 20 patients were performed. There were 17 male and 3 female patients ranging in age from 35 to 70 years. In all patients neck dissection was done and resective part was reconstructed with free flap. Out of 20 free flap 12 radial artery free flaps and 8 free fibula flap was harvested. All patients receive heparin postoperatively. In only one case bleeding was encountered which was managed by blood transfusion and in one case arterial thrombus encountered postoperatively day one which was managed by a reanastomosis. In current study, we have not encountered any flap loss (Table 1 & Figure 1, 2).

DISCUSSION

Based on a recent literature review Brinkman et al recommended the use of LMWH monotherapy as this seems to be as effective as acetylsalicylic acid, and has the additional advantage to prevent systemic thromboembolic events and unlike acetylsalicylic acid does not increase the risk of gastrointestinal bleeding[7].

Stephan et al concluded that the combined use of acetylsalicylic acid with another anticoagulant would increase the risk of bleeding.[7]

Ashjian et al compared a thromboprophylactic regimen consisting of 325 mg acetylsalicylic acid once daily with 5,000 units of LMWH once daily in a population of patients undergoing free flap surgery for reconstruction of the head and neck, upper and lower extremity, trunk and breast and concluded that LMWH and acetylsalicylic acid 325 mg daily are equally effective as postoperative anticoagulation agents in oncological free flap reconstruction. Chien et al concluded that 325 mg acetylsalicylic acid once daily and subcutaneous heparin twice a day at 5,000 IU in head and neck free flap reconstruction was equally effective in preventing microvascular complications and flap failure compared with other existing regimens[7]. Florian G Draenert at all apply standard anti-thrombosis prophylaxis with low molecular weight heparin, for instance, Fragmin P, but do not preoperatively use any further anti-coagulatives, such as ASS or high dose heparin.[8]

Hidalgo et al identified venous problems (35%) as the most common etiology of flap failure followed by arterial problems (28%), hematoma (26%) and recipient vessel problems (11%). Late flap failures (i.e. > 48 hours) were most often due to infection or mechanical stress around the anastomosis. In 756 cases Miyasaka et al performed 22 explorations for vascular pedicle compromise, 17 (77%) of which were due to venous compromise and five due to an arterial problem. Most cases of venous compromise were identified within the first 25 hours following surgery. Brown et al reviewed 427 free tissue transfers with 16% requiring return to the operating theatre within seven days for compromised flap or hematoma. Venous compromise (83%) was once again much higher than arterial compromise.[9]

Low molecular weight heparins (LMWHs) were used in treatment of ischemic heart disease, myocardial infarction and prophylaxis of thromboembolism in different fields of surgery. Low-molecular weight- heparin (LMWH) is a new class of synthetic anticoagulant that selectively binds and potentiates antithrombin III, thereby specifically inhibiting factor Xa in the coagulation cascade. This is opposed to other anticoagulants (i.e., heparin), which binds to multiple factors in the coagulation cascade. Heparin has been used with variable success rate in the literature for the salvage of ischemic pedicle flaps.[10]

Successful outcome after microvascular reconstruction of the head and neck has been reported to range from 93% to 99%. This success rate is dependent on 3 basic components that include the preoperative evaluation of the patient, technical aspect of the operation, and postoperative management.[11]

Free flap failure occurs in 1 to 9% of the cases and is generally caused by microvascular thrombosis in the area of the vascular anastomosis or the distal flap microcirculation, while early diagnosis and revision of a thrombosed anastomosis have been shown to salvage free flaps, prevention of microvascular thrombosis remains of primary importance. Several studies made different recommendations based on a review of existing literature.

Conrad et al proposed an anticoagulation algorithm for free flap thromboprophylaxis, consisting of low dose acetylsalicylic acid at a dose of 1.4 mg/ kg/d starting 2 weeks preoperatively which has to be continued for 2 weeks postoperatively, and heparin which is given intraoperatively as a bolus and local topical agent. Lecoq et al recommended the intraoperative use of heparin in microsurgery and the use of acetylsalicylic acid for inhibition of platelet aggregation.[7]

Free flaps suffer from ischemia between tissue harvesting and anastomosis of the adherent blood Vessels. This poses a major threat to the tissue due to the ischemia reperfusion injury which can ultimately result in partial or total flap loss.[5] Prevention of thrombosis at the microvascular anastomosis of the free flap has been a concern for the microvascular surgeon since the earliest days of free tissue transfer[12]. Microvascular thrombosis has an alterable etiology for failure, addressing Virchow's triad of stasis, hypercoagulability, and vessel injury. More than 21 pharmacological agents have been used; however, aspirin, heparin, and dextran remain the mainstays of treatment.[13]

Khouri et al. reported that only postoperative subcutaneous heparin treatment had a statistically significant effect on preventing thrombosis. Although they recognize experimental evidence which shows that heparinized irrigation has a beneficial result in preventing thrombosis.[13]

The selection of recipient vessels that are suitable for microvascular anastomosis within the head and neck is an important component affecting patency. The vascular anatomy of the head and neck is complex with numerous arteries and veins from which to choose. The decision is usually based on the location of the defect and the proximity of a recipient artery and vein. Recipient vessels that are in close proximity to the defect are usually anastomosed to the donor vessels in an end-to-end or end-to-side fashion. However, in circumstances in which the local vascular access is not available or when the quality of the local vasculature is inadequate, remote vascular access could be required.[11] Ichinose et al recommended the use of dual venous drainage (external and internal jugular systems) for the radial forearm free flap. They reported no venous failure in 405 consecutive cases. Significant medical co-morbidities, such as diabetes, hyper-coagulable disorders and alcohol withdrawal may result in an increased risk of flap failure.[9]

No studies have demonstrated that anticoagulant will improve the patency rate of technically well performed microvascular anastomosis nevertheless failure of microvascular flap is always associated with microvascular thrombosis there may be subset of patients who may be benefited from the anticoagulant therapy[12]. Vascular occlusion (thrombosis) remains the primary reason for flap loss, with venous thrombosis being more common than arterial occlusion. The majority of flap failures occur within the first 48 hours.[9]

CONCLUSION

The free flap technique is safe but involves a significant learning period and requires careful postoperative monitoring of the patient. Early intervention is important for the salvage of free flaps and for lowering the failure rate. Irrespective of the type and use of anticoagulant or nor result depends upon the quality of anastomosis and tissue handling. However, this series is small and would require further study for validation. In conclusion, the free flap technique is safe but involves a learning period for the surgeon and careful postoperative monitoring of the patients.

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