

Case Report

Heparin-induced bleeding treatment in microsurgery

Rodrigo A. Mendoza-Aceves¹, Rodrigo Banegas-Ruiz², Francisco Fabián Gómez-Mendoza³,
Rigoberto Román-Hernández⁴, Christian Porrás-Méndez⁵, Alan I. Valderrama-Treviño⁶,
Ismael Vejar Alba⁷, Baltazar Barrera-Mera^{8*}

¹Department of Anaesthesiology, Angeles del Pedregal Hospital, CDMX, Mexico

²Department of Traumatology, Rehabilitation Hospital, Luis Guillermo Ibarra Ibarra, CDMX, Mexico

³Department of Hand Surgery, ⁴Department of Peripheral Vascular Surgery, ⁷Department of Maxillofacial Surgery, Central Military Hospital, CDMX, Mexico

⁵Department of General Surgery, High Specialty Hospital, Veracruz, Mexico

⁶Laboratory of Experimental Immunotherapy and Tissue Engineering, ⁸Department of Physiology, Faculty of Medicine, UNAM, CDMX, Mexico

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*Correspondence:

Dr. Baltazar Barrera Mera,

E-mail: baltazar.barrera.mera@gmail.com

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ABSTRACT

Microsurgery is associated with prolonged surgical times with an increased risk of deep vein thrombosis, pulmonary embolism and myocardial infarction. The use of antithrombotic means is a commonly employed tactic to prevent vascular thrombosis after microvascular free flap surgery. Flap loss is a devastating complication of microsurgical procedures that leads to detrimental outcomes. A 32-year-old male patient has a ruptured calcaneal tendon. He underwent 5 surgical cleanings with multiple failed sequential attempts at wound closure. Traumatology department in its microsurgery division where it is proposed to perform neo-tendon with graft of palmaris longus of the right thoracic extremity and radial antebachial microvascular flap. The neo tendon was performed in addition to the micro surgical coverage with the radial antebachial flap. When having vascular control with micro-clamps, 6000 U of unfractionated heparin was initiated, approximately 20 minutes after the end of the microvascular anastomosis, there was incoercible bleeding, which is initially treated with spray fibrin. Continued bleeding after 3 hours, so it was decided to reverse the effect of heparin with transfusion of fresh frozen plasma, 10 mg of vitamin K and fibrinogen. The effect of heparin was reversed without having thrombotic complications of microvascular anastomoses. The flap was not reexplored since they showed no signs of vascular compromise. If anticoagulants have been used and an incoercible hemorrhage is found, the effect of heparin must be reversed. In the transfer of tissues with microsurgery, the recommended and safe anticoagulation are prophylactic doses and not therapeutic doses.

Keywords: Anticoagulation, Bleeding, Free flap, Heparin, Microsurgery, Thrombosis

INTRODUCTION

Skin defect at the distal end of the leg are difficult to treat, since the bone structures are percutaneously and there is poor coverage with less muscle layers, however reconstruction is possible through a variety of flaps and

microsurgery. Free flaps are distinguished by their dependence on a vascular anastomosis at the receptor site.¹ Prolonged surgical times from 5 to 20 hours may represent a risk factor for deep vein thrombosis, pulmonary embolism and myocardial infarction.^{2,3} It has been considered that a reliable anastomosis of vessels

with external lumen diameters of 0.5-2 mm with permeability rates of approximately 95% or more is possible, although technical refinement is precise, anastomotic thrombosis represents one of the main causes of surgery failure so the use of antithrombotic means is a tactic commonly used to prevent thrombosis after flap surgery.^{4,5} One of the most used antithrombotic agents is heparin which is a polyglycosaminoglycan that prevents arterial and venous thrombosis.^{6,7}

More than 50 years ago, unfractionated heparin (UFH) was introduced into clinical practice and continues to be used as an effective, low-cost and relatively safe anticoagulant. Although it has been partially replaced for several indications by low molecular weight heparin (LMWH), it still remains the parenteral anticoagulant of choice in selected groups of patients.⁸ It has two routes of administration: intravenous and subcutaneous. The first has greater bioavailability and lower latency, so it is used in patients who need a rapid anticoagulant effect. Subcutaneous UFH is reserved for thrombo-prophylaxis of hospitalized patients who require prolonged rest. Its excretion has two elimination pathways: a rapid and saturable one, which depends on the binding to endothelial receptors and macrophages; and another of renal elimination, which is slower and corresponds to the highest percentage of excretion.^{9,10}

Unfractionated Heparin (UFH) and low-molecular weight heparin (LMWH) UFH exerts its main anticoagulant effect after binding to the serine protease inhibitor antithrombin III in plasma. The resulting conformational change in the antithrombin III molecule increases its inhibitory effect on several coagulation enzymes (factor II and X). Smaller heparin fractions (LMWH) can still bind to antithrombin III and can inactivate factor Xa. UFH has a greater potential for causing bleeding than do its low-molecular weight derivatives, because of its simultaneous actions on factors II and X. By acting on antithrombin III, UFH have an important role in the ischemia-reperfusion phenomenon.¹¹ These effects have been studied in free flap transfer surgery, with better tolerance to ischemic injury in case of heparinized blood.¹² Until recently, UFH has been the drug of choice for the initial management of deep venous thrombosis and for thromboprophylaxis in a variety of settings. However, LMWH have been demonstrated to be similar regarding their efficacy, safer in terms of haemorrhagic risk, with considerably easier administration.¹¹

Although the systemic use of UFH has been proven to be effective in free flap thromboprophylaxis, studies using LMWH showed that subcutaneous injection of these products is safer with similar efficacy.¹³⁻¹⁵

Flap loss is a devastating complication of microsurgical procedures that leads to detrimental outcomes. Thrombosis of the microvascular pedicle may be secondary to either technical issues (poor anastomosis suture, bent vessels, intima damage) or systemic

influences (e.g., genetic coagulation disorders or hyper coagulate states).¹⁶⁻¹⁹ In medical interventions that subject the patient to the risk of macrovascular thrombosis, anticoagulation therapy is deemed an appropriate form of prophylaxis. Prevention of deep venous thrombosis or pulmonary embolism postoperatively, especially in immobilized patients, has benefited from decades of extensive research including clinical trials and numerous protocols.²⁰⁻²³ This topic naturally receives the attention of microsurgeons, who often face the same problems of thrombosis, just inside the smaller arterial and venous pedicle vessels. To reduce the rates of these perioperative complications, such as total flap loss, numerous suggestions have been proposed in microsurgical literature. These range from postoperative anticoagulation using aspirin, UFH, or LMWH to intravascular catheters that continuously deliver UFH locally into flap veins, reducing its systemic side effects.²⁴⁻²⁸

CASE REPORT

A 32-year-old male patient, basketball player weighing 100 kilograms, has a ruptured calcaneal tendon when performing sports training. He went to the Emergency Department where open tenorrhage surgery was scheduled 24 hours after the accident, a splint was placed for 2 months and when he started walking, he presented wound dehiscence with exposure of the calcaneal tendon. He underwent 5 surgical cleanings with multiple failed sequential attempts at wound closure. Interconsultation was requested to the traumatology department in its microsurgery division where it is proposed to perform neo-tendon with graft of palmaris longus of the right thoracic extremity and radial antebachial microvascular flap.

The neo tendon (with palmaris longus tendon graft) was performed in addition to the micro surgical coverage with the radial antebachial flap (right), anesthetic management with sedation and right supraclavicular block with peridural block. When having vascular control with micro-clamps, 6000 U of unfractionated heparin was initiated, approximately 20 minutes after the end of the microvascular anastomosis, there was incoercible bleeding, which is initially treated with spray fibrin. Continuous monitoring in Intensive Care Unit (ICU), hemodynamically stable, with good doppler flow of the flap, but continued bleeding after 3 hours, so it was decided to reverse the effect of heparin with transfusion of fresh frozen plasma, 10 mg of vitamin K and fibrinogen. The effect of heparin was reversed without having thrombotic complications of microvascular anastomoses. The flap was examined for colour (pink, pale, bluish), temperature (normal, cold), turgidity (normal, reduced), and capillary refill (normal, sluggish, brisk) etc. The flap was not reexplored since they showed no signs of vascular compromise.

The patient was discharged after 7 days, without the need for transfusion of globular packages.

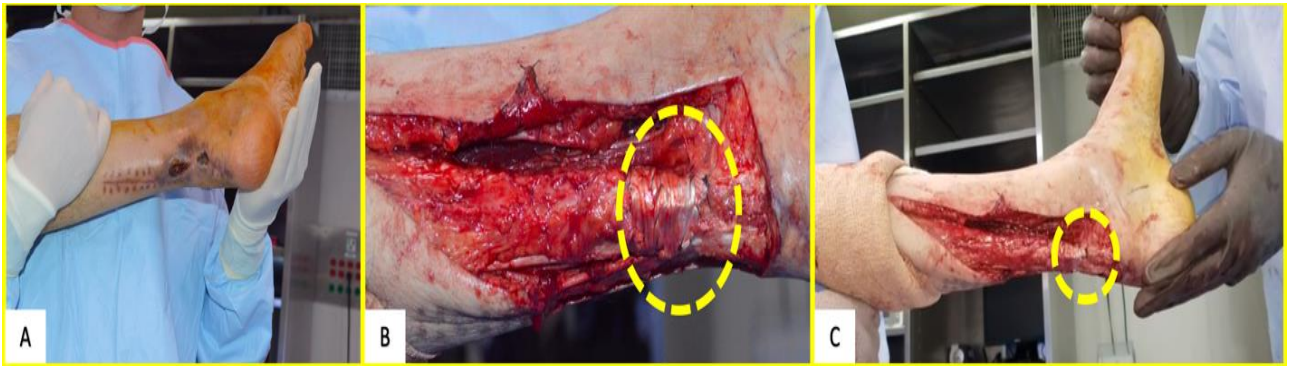


Figure 1: (A). Cutaneous defect, calcaneal tendon with necrosis due to chronic exposure. (B). Neo tendon performed with palmaris longus tendon graft (yellow circle). (C). Neo tendon dynamic resistance test.

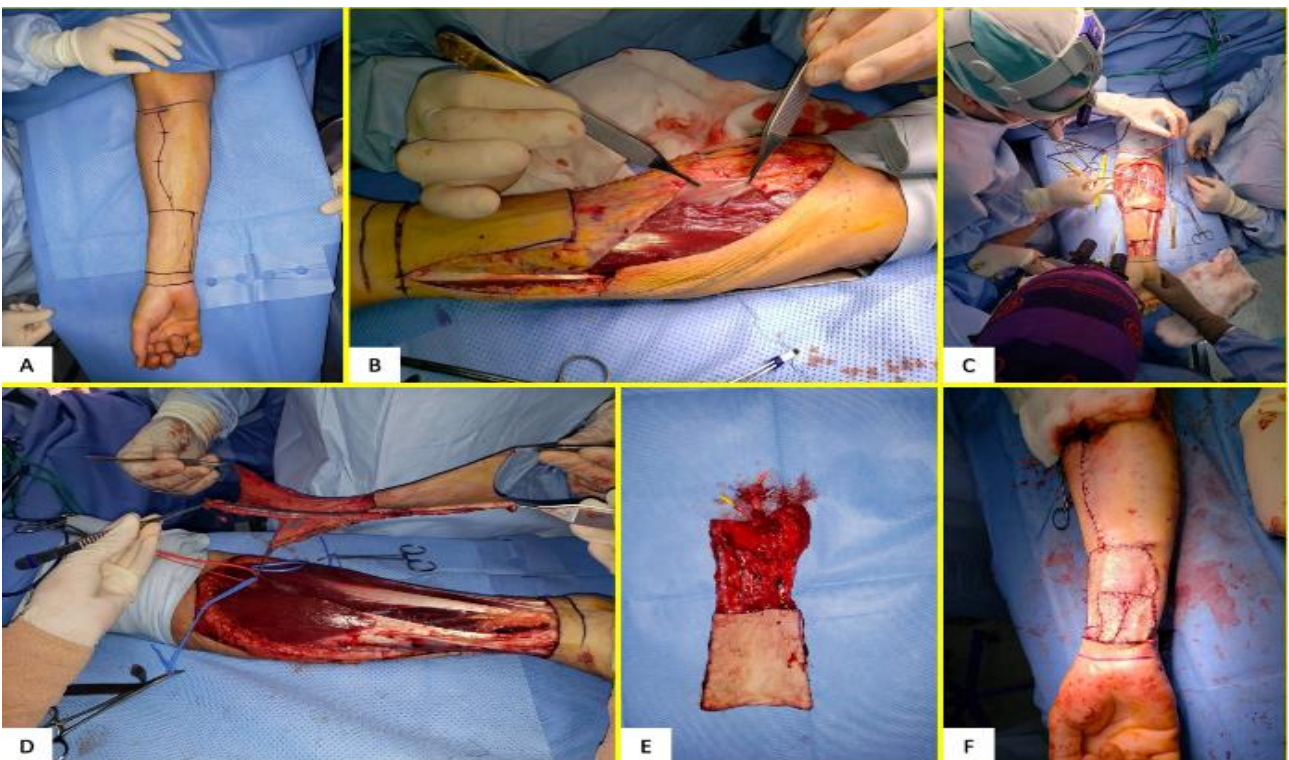


Figure 2: (A). Radial antebraclial flap cutaneous marking. (B). Location of the flap vein system. (C). Harvested flap pedicle. (D and E). Radial antebraclial flap (autonomized). (F). Reconstruction of the donor zone.



Figure 3: (A). Bleeding after 3 hours of administration of unfractionated heparin. (B). 1 hour after pharmacologically reversing the effect of heparin, less bleeding and adequate doppler flow. (C). Final result 7 days after surgery.

DISCUSSION

Thrombosis at the anastomotic site is not only the most common cause of failure of microsurgical operations, but it is also one of the factors resulting in circulatory failure in free flaps.^{11,29}

Surgery itself causes changes in hemostasis, leading to a hypercoagulable state that has been linked to both arterial and venous thrombotic complications.¹¹

In a large study of free flap surgery, the subcutaneous administration of heparin was associated with significant improvement in flap survival.²⁹ However, perioperative anticoagulation with intravenous heparin showed no clinical benefit.³⁰ Aspirin seems to be as effective as subcutaneous heparin in free flap surgery.³¹

Pre and post-operative treatment with antithrombotic drugs is associated with the risk of hemorrhagic complications. Ideally, local injection of a high concentration of antithrombotic drug has been suggested, which produces minimal systemic effects.²⁸ UFH is useful in local intravascular irrigation (100 U/ml) prior to vascular unclamping (50 to 100 U/kg) for preventing thrombosis and the ischemia-reperfusion cascade. After surgery, LMWH should be administered for prophylaxis of deep venous thrombosis. This prevention may have also a positive effect on the patency of the micro anastomosis.¹¹

Besides platelet aggregation inhibition, a certain degree of anticoagulation is mandatory. To act on the coagulation pathway, heparin has the double advantage to inhibit the coagulation pathway and to protect the tissue from the ischemia-reperfusion phenomenon. Perioperative use is safe in local infusion (50 to 100 U/ml). Comparison with other products (modulators of the fibrinolysis pathway, thrombin inhibitors like hirudin) offers no advantages in term of efficacy, and are associated with more hemostasis disorders, except for the human recombinant tissue factor pathway inhibitor (0.05 ng/ml).³² Classical systemic postoperative prevention of deep venous thrombosis (subcutaneous 40 mg/day of enoxaparin, 0.4 to 0.6 ml/day of dalteparin) is sufficient to protect the micro anastomoses, without increasing the bleeding risk.¹¹ Free flap surgery induces acute and subacute changes in coagulation, comparable to other major surgeries and severe injuries. This leads to an increase in platelet count and fibrinogen over the postoperative course. These changes do not differ significantly between patients with an uneventful course and patients that develop thrombosis of the microvascular pedicle. However, patients that developed bleeding requiring surgical re-exploration showed an insufficient increase in fibrinogen, resulting in significantly lower fibrinogen levels. Therefore, monitoring and correction of

fibrinogen levels might aid in preventing or treating bleeding complications following free flap surgery.³³

Also, an insufficient production or depletion of fibrinogen might lead to lower fibrinogen concentrations. Low levels of fibrinogen have been associated with bleeding in a variety of settings.³⁴⁻⁴²

CONCLUSION

Surveillance during the immediate postoperative period in the intensive or intermediate care unit may be beneficial in certain postoperative microsurgical transfer patients.

It is considered that if microvascular anastomoses are performed with expertise and by an expert group, the risk of thrombosis without the use of anticoagulants may be minimal. If anticoagulants have been used and an incoercible hemorrhage is found in microsurgical transfer, the effect of heparin must be reversed, considering the possibility of reoperation and / or thrombectomy.

In the transfer of tissues with microsurgery, the recommended and safe anticoagulation are prophylactic doses and not therapeutic doses.

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