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Flap preconditioning by pressure-controlled cupping in a rat model

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ABSTRACT

Background: Flap survival is essential for the success of soft-tissue reconstruction. Accordingly, various surgical and medical methods aim to increase flap survival. Because flap survival is affected by the innate vascular supply, traditional preconditioning methods mainly target vasodilatation or vascular reorientation to increase blood flow to the tissue. External stress on the skin, such as an external volume expander or cupping, induces vascular remodeling, and these approaches have been used in the fat grafting field and in traditional Asian medicine.

Materials and Methods: In the present study, we used a rat random-pattern dorsal flap model to study the effectiveness of preconditioning with an externally applied device (cupping) at the flap site that directly applied negative pressure to the skin. The device, the pressure-controlled cupping, is connected to negative pressure vacuum device providing accurate pressure control from 0 mm Hg to −200 mm Hg. Flap surgery was performed after preconditioning under −25 mm Hg suction pressure for 30 min a day for 5 d, followed by 9 d of postoperative observation. Flap survival was assessed as the area of viable tissue and was compared between the preconditioned group and a control group.

Results: The preconditioned group showed absolute percentage increase of flap viability relative to the entire flap by 19.0± 7.6% (average 70.1% *versus* 51.0%). Tissue perfusion of entire flap, evaluated by laser Doppler imaging system, was improved with absolute percentage increase by 24.2± 10.4% (average 77.4% *versus* 53.1%). Histologic analysis of hematoxylin and eosin, CD31, and Masson-trichrome staining showed increased vascular density in the subdermal plexus and more organized collagen production with hypertrophy of the attached muscle.

Conclusions: Our study suggests that flap preconditioning caused by controlled noninvasive suction induces vascular remodeling that increases tissue perfusion and improves flap survival in a rat model.

Introduction

Recent advances in angiography and topographic visualization of superficial vessel networks have increased our understanding of flap physiology.[1] Surgeons can now preoperatively evaluate the anatomy of arteries and veins in individual patients by computed tomography angiography. Furthermore, flap survival can be predicted in the operating

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room by various tissue perfusion assessment techniques.[2,3] In addition to preoperative evaluation of vessel anatomy, which can help surgeons to avoid flap necrosis with precise flap design, surgeons have sought new ways to improve flap viability. Many attempts have been made to increase flap survival using surgical, pharmaceutical, and mechanical methods. Although some of these methods have proven effective in preventing flap loss, none have been widely adopted owing to inconsistent effectiveness or procedure invasiveness.[4-8]

Recently, mechanical stimulation using a negative pressure device has become widely used, in addition to various forms of mechanotransductors.[9-11] External volume expansion devices have been especially adopted in breast augmentation with implants because these devices increase skin cell proliferation and vascular remodeling, eventually facilitating tissue adaptation to fat grafting.[12-14] Furthermore, cupping therapy in traditional Asian medicine adopts a "vacuum mechanism" that forms a suction pressure inside a dome-shaped empty space. The efficacy of cupping therapy is still controversial, but its mechanical stimulation involving suction pressure on the skin has been well studied in previous experimental reports.[15,16]

Previous studies of mechanical triggers using negative pressure suggest that the benefits of such therapy are mainly attributable to the induction of vascular remodeling and epithelial proliferation, which increases tissue resistance to stress.[12-16] This physiological adaptation may be applied to flap physiology to improve flap survival against ischemic insult, which is unavoidable in the immediate postoperative period. In our present experimental animal study, we used a well-established rat random-pattern dorsal flap model with external volume expansion activated by negative pressure as a preflap elevation treatment.[17,18] We hypothesized that precise mechanical stress induced by controlled noninvasive suction would stimulate tissue proliferation and vascular remodeling and eventually improve overall flap survival.

Methods

Animal models

Fourteen Sprague–Dawley rats, aged 9∼10 wk and weighing between 300 and 350 g, were caged with free access to standard hamster food and water, at room temperature (23 ± 1°C) and at a humidity of 55± 5%, with 12:12 h dark:light cycles under controlled light (150∼300 lux). All procedures were conducted in accordance with the Guide for the Care and Use of Laboratory Animals of the Asan Life Science Research Center animal review board. The 14 rats were randomly assigned to two groups. The rats of the control group ($n = 7$) were not preconditioned before the dorsal random flap elevation was performed. The rats of the preconditioned group ($n = 7$) were preconditioned with a negative pressure-controlled cupping device with occlusive dressing (Duoderm CGF, ConvaTec, NY) before flap elevation.

A dome-shaped plastic device with a diameter of 3.25 cm and internal volume of 25 mL (Hansol Bu-Hang, Hasol, Paju, Gyeonggi-do, Korea) was connected to a suction pump (CuraVAC system; Daewoong Pharmaceutical Company, Seoul, Korea) at a pressure of −25 mm Hg. Negative pressure was delivered through the dome-shaped device directly to the skin. The device was applied to the dorsal skin at the same position in each rat according to a 2 × 8–cm random-pattern dorsal flap design. The center of the dome-shaped device was placed at the midline spine at 1 cm from the distal margin of the flap in all rats, which were approximately 12-cm long from the cephalad to tail. Approximately 35% of the surface area of the flap at the distal end was under negative pressure during preconditioning. All animals were anesthetized with an intraperitoneal injection of 20 mg/kg Zoletil (zolazepam + tiletamine; Virbac Laboratories, Carros, France) during preconditioning.

Preconditioning: pressure-controlled cupping

Preconditioning was performed for 30 min at −25 mm Hg continuous suction pressure daily for 5 consecutive days. A pilot study conducted before the present study showed that pressure of −25 mm Hg was adequate for the rat skin flap. Suction pressure weaker than −25 mm Hg was too weak to maintain the cupping device in the proper position. On the other hand, a suction pressure stronger than −25 mm Hg induced skin irritation with microrupture of small vessels causing petechiae in the applied skin. The controlled pressure used in this study is in accordance with a previous study that used external volume expansion in a murine model.[12] At the time of preconditioning, the adequate delivery of −25 mm Hg pressure was measured continuously by a suction pump (CuraVAC system; Fig. 1). Preconditioning longevity and duration were chosen based on the results of a pilot study.

Surgical procedure

All animals were anesthetized using an intraperitoneal injection of 40 mg/kg Zoletil. The dorsal skin of the rats was shaved with electric clippers and then prepared with betadine. Caudally based 2 × 8–cm–sized dorsal flaps were raised under sterile conditions. The palpable hip joints were used as anatomical landmarks to define the base of the flap. The flap was dissected and detached with its panniculus carnosus and replaced in the native position with continuous sutures. The rats were carefully observed for 9 d after flap elevation. On postoperative day 9, the animals were killed by CO_2 inhalation.

Macroscopic evaluation

Digital photographs (Sony A57; Sony, Tokyo, Japan) of the whole flap were taken every other day in all rats. Necrotic and viable areas were calculated by digital evaluation of the photographs (IMT i-Solution, Vancouver, British Columbia, Canada). Three observers separately measured necrotic skin (defined by a dark color with eschar formation) and total flap (defined by a 2 × 8–cm surgical border) areas.