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Extracorporal shock wave may enhance skin flap survival in an animal model

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Summary Several methods have been used in an attempt to increase blood supply and tissue perfusion in ischemic tissues. The authors investigated the effect of extracorporal shock wave (ESW) treatment on compromised skin flaps. For this purpose, the epigastric skin flap model in rats, based solely on the right inferior epigastric vessels was used.

Twenty male Sprague-Dawley rats were divided into two groups (ESW-group, Control group) of 10 rats each. The ESW-group was administered 2500 impulses at 0.15 mJ/mm^2 immediately after surgery, whereas, the control group received no treatment. Flap viability was evaluated on day 7 after the operation. Standardised digital pictures of the flaps were taken and transferred to the computer, and necrotic zones relative to total flap surface area were measured and expressed as percentages. Overall, there was a significant reduction in the surface area of the necrotic zones of the flaps in the ESW group compared to the control group (ESW group: 2.2 ± 1.9% versus control: 17.4 ± 4.4% ($p < 0.01$)).

In this study, the authors demonstrated that treatment with ESW enhanced epigastric skin flap survival, as confirmed by the significant reduction of necrotic flap zones. ESW treatment seems to represent a feasible and cost effective method to improve blood supply in ischemic tissue.

Partial skin flap necrosis caused by inadequate arterial inflow or insufficient venous outflow remains a significant problem in reconstructive surgery.[1] If flap necrosis occurs, subsequent management often includes time-consuming and repetitive dressing changes aimed at promoting healing by secondary intention or even secondary reconstructive procedures. Several methods, for instance, treatment with hyperbaric oxygen, have been used in an attempt to increase blood supply and tissue perfusion in compromised tissues.[2] The potential of therapeutic agents, including a variety of growth factors, to stimulate the development of angiogenesis in ischemic skin flaps has aroused considerable interest.[3,4] However, the need for high initial doses and daily applications as well as short half-life of these growth factors suggests that

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an important aspect of their efficacy is the means of delivery. For this reason, recent investigations on therapeutic angiogenesis have mainly focused on the use of various gene therapy techniques for growth factor delivery[5-7]. Although, considerably effective potential side effects, and the cost intensiveness of these techniques represent some of the drawbacks of this approach.

Recent studies describe an until now unknown potential of extracorporal shock wave (ESW) to promote cell differentiation and neovascularisation.[8,9] On the basis of these experimental data, we investigated the feasibility of enhancing epigastric skin flap survival with ESW treatment.

Materials and methods

Twenty male Sprague-Dawley rats weighing 300-500 g were used in this study and were divided into two groups (ESW-group, Control group) of 10 rats each. The animals were maintained according to the National Research Council guidelines. The rats were anaesthetised with intraperitoneal injection of sodium pentobarbital (50 mg/kg).

The epigastric skin flap model

The previously described epigastric skin flap model was used in this study with some modification 123f the flap design.[10,11] Based solely on the right inferior epigastric vessels, the contralateral distal corner of the flap represents the random portion which predictably undergoes necrosis, amounting to about 30% of the total flap area. The flap is designed in such a way that the lateral branch of the right epigastric artery is excluded and the flap is supplied by the medial arterial branch alone.[12]

Operative technique

The rats were first anaesthetised and the epigastric flap measuring 8×8 cm^2 was outlined on abdominal skin extending from the xiphoid process proximally and the pubic region distally, to the anterior axillary lines bilaterally. The flap was elevated as a skin island flap pedicled on the right inferior epigastric vessels, whereas the left inferior epigastric vessels were ligated. Then, the flap was sutured back to its native configuration by using interrupted 4/0 nonabsorbable sutures.

ESW treatment

Immediately after the surgical intervention the anaesthetised rats were placed in a right lateral position. Ultrasound transmission gel (Pharmaceutical Innovations Inc., NJ, USA) was used as contact medium between the ESW apparatus and skin. Based on unpublished data from a pilot study, where we tried to find the optimal ESW strength, ESW treatment with 2500 impulses at 0.15 mJ/mm^2 (Epos Fluoro Dornier MedTech Gmbh, Wesslingen, Germany) was given to the left upper corner of the flap. This area represents the random portion of the flap, which according to literature predictably undergoes necrosis (Figs. 2 and 3).

Follow-up

Follow-up evaluation was performed on postoperative day 7. The animals were anaesthetised and after standardised digital pictures of the flaps were taken and transferred to the computer, they were killed with an overdose of intraperitoneal pentobarbital (100 mg/kg). The following flap zones were defined for surface area measurement: necrotic zone and total flap area (defined by surgical borders). Surface area of these defined zones was measured by using Image Pro Plus Software (version 4.1, Media Cybernetics LP, Silver Spring, MD). The results were expressed as percentage relative to total flap surface area.

Statistical analysis

The statistical analysis was conducted by the Department of Biostatistics of the University of Innsbruck. A paired student's t-test was used. No correction was made for multiple testing. Results were expressed as mean $\pm$ SD and considered significant when $p < 0.05$.

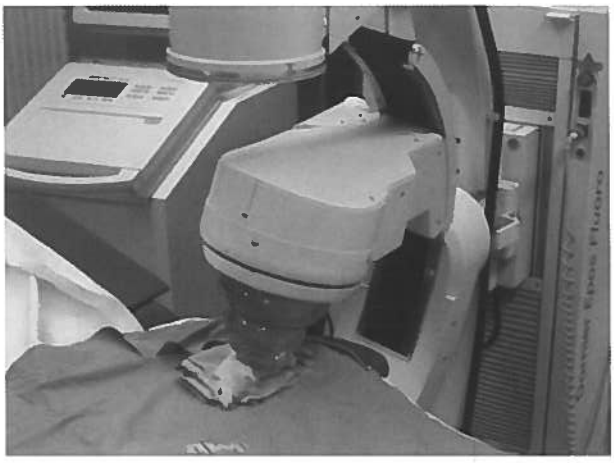

Figure 1 Experimental setting: ESW treatment was given to the left upper corner of the flap.

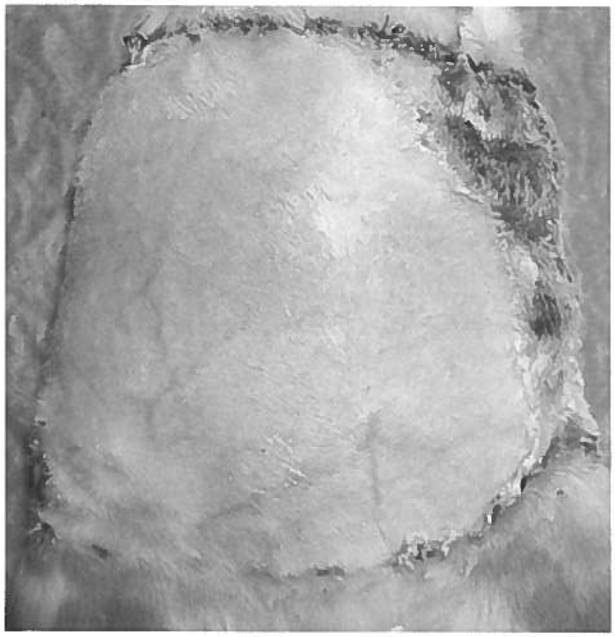

Figure 2 Characteristic sample of the control group at day 7 after surgery showing a necrotic area in the left upper corner of the flap.

Results

None of the epigastric flaps showed any signs of infection, seroma, or hematoma formation. Overall, there was a highly significant reduction in the surface area of the necrotic zones of the flaps in the ESW group (Fig. 3) compared to the control group (Fig. 2) (area of the necrotic zone described as a percentage of the total flap area: ESW group: 2.2 ± 1.9% versus control: 17.4 ± 4.4% ($p < 0.01$)) (Table 1 and Fig. 4).

Discussion

In an attempt to understand skin flap viability and necrosis, the effects of a number of growth factors on flap survival have been examined. Several factors, most notably vascular endothelial growth factor,[13,14] fibroblast growth factor[15] and endothelial growth factor[16] have demonstrated marked abilities to improve skin flap survival. Induction of neovascularisation was thought to be the major

Table 1 Exact values of medians and standard deviations in the ESW and the control group

	Median	Standard deviation
ESW group ($N = 10$)	2.246	1.94957
Control group ($N = 10$)	17.36	4.40081

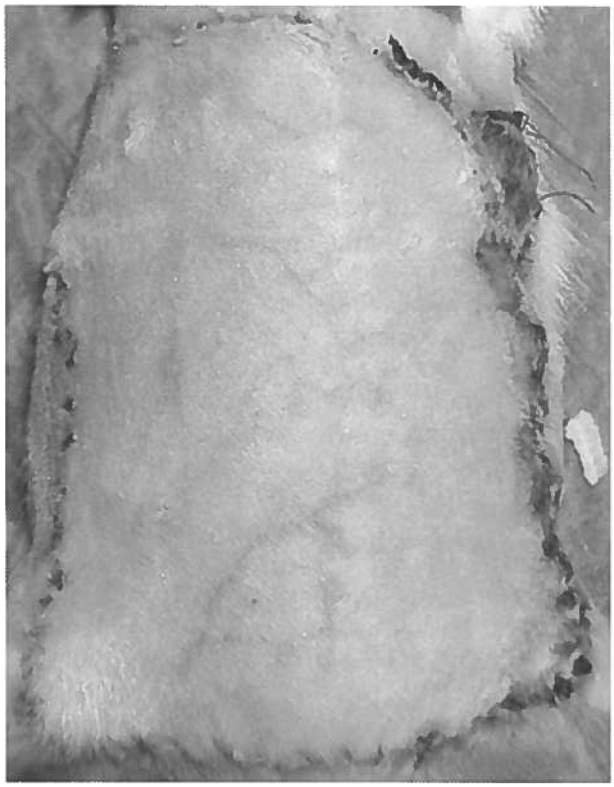

Figure 3 Characteristic sample of the ESW group showing a significant reduction in the surface area of the necrotic zone of the flap compared to the control group.

mechanism for the improvement of flap survival by these growth factors. However, application of these growth factors is based mainly on various gene therapy techniques, and both the cost intensiveness and associated undesirable side effects

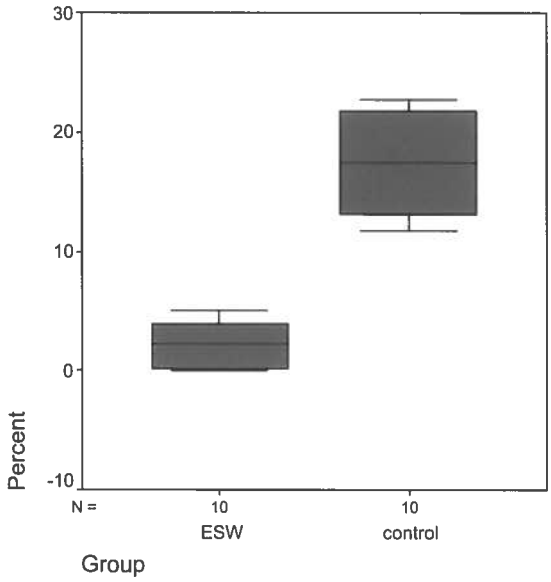

Figure 4 Diagram showing the distribution of the necrotic zones in the ESW group compared to the control group.

represent some of the major drawbacks of this approach.[17]

A recent result of an animal study suggests that ESW treatment stimulates the early expression of angiogenesis-related growth factors.[5] According to Wang, there is a significant rise of growth factors such as endothelial nitric oxide synthase, vascular endothelial growth factor and proliferating cell nuclear antigen inducing ingrowth of new vessels.[18] In further studies, Wang et al. demonstrated that shock wave treatment is effective in promoting the healing of fractures[19,20] probably by stimulated expression of the growth factors mentioned above and transforming growth factor-β1.[9] All of these studies mainly focused on orthopaedic problems. We wanted to investigate whether this approach was feasible and useful from a plastic surgical perspective. As loss of flap due to poor circulation is a major problem confronting plastic surgeons in reconstructive surgical procedures, we tried to assess the effectiveness of ESW treatment on skin flaps.

Despite success in the treatment of certain orthopaedic disorders,[21,22] the exact mechanism of shock wave therapy is not yet known. However, it was postulated that ESW treatment may have beneficial effect not just on bone and tendon healing but may also cause microtrauma or microfracture and hematoma formation. According to available literature the incidence of shock wave complications varied significantly with the location of treatment and the amount of shock wave energy.[23] As the ESW treatment we applied consisted of 2500 impulses at 0.15 mJ/mm^2, which represents a low-dose treatment, we did not encounter any complications like hematoma or seroma formation. On the contrary, we were able to achieve impressively small necrotic zones of epigastric skin flaps representing 2.2% of the total flap area. To our knowledge, this is the first time that such results have been described. One possible reason for this finding is that unlike in other studies where a single growth factor was used, ESW treatment probably stimulates a cascade of growth factors interacting in a complex and more efficient way than a single agent does. Although further studies have to be conducted to determine the exact level of growth factors after ESW treatment, this technique seems to represent a feasible and cost effective method to improve blood supply in ischemic tissue.

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