

Shock wave therapy causes increased macrophage recruitment and enhances M2 polarization

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Objective:

Shock wave therapy (SWT) has been shown to induce angiogenesis in ischemic muscle. However, the mechanism of action remains unknown. Macrophages are crucial for angiogenic responses after ischemia. Proinflammatory M1 macrophages phagocytose necrotic tissue. M2 macrophages create a milieu of regeneration and enable angiogenesis. We hypothesized that the angiogenic effects of SWT are caused by enhanced macrophage recruitment.

Methods:

C57BL/6 mice were subjected to unilateral hind limb ischemia with subsequent SWT (0,1mJ/mm², 500 Impulses, 5 Hz) or sham treatment. Successful limb ischemia was confirmed via Laser Doppler perfusion imaging. Gastrocnemius muscle was harvested 72h and 28d after ischemia induction and further processed for immunofluorescence staining and RT-PCR analysis.

Results:

Treated muscles show increased expression of the pivotal recruiting factor monocyte chemoattractant protein 1 (MCP-1) ($217,9 \pm 30,18$ vs. $102,7 \pm 14,08$, $p=0,0016$). Indeed, an increase of the macrophage marker CD14 could be observed after SWT ($118,1 \pm 20,9$ vs. $22,16 \pm 2,874$, $p=0,0001$). The higher numbers of macrophages could be confirmed in immunofluorescence stainings. The expression of the M2 polarization promoting chemokine IL-13 was significantly increased in the treatment group ($517.7 \pm 81,83$ vs. 3087 ± 1043 , $p=0,0138$). Increased levels of the M2 scavenger receptor CD163 could be found after SWT compared to untreated controls ($172,4 \pm 35,84$ vs. $40,56 \pm 6,266$, $p=0,0008$). We found higher numbers of capillaries (CTR 8.18 ± 1.9 vs. SWT 16.25 ± 2.09 , $p=0.009$) and arterioles (CTR 1.11 ± 0.26 vs. SWT 3.78 ± 0.52 , $p=0.0003$) after SWT. Treated animals showed significantly improved limb perfusion (CTR 0.45 ± 0.67 vs. SWT 0.76 ± 0.09 , $p=0.027$).

Conclusion:

SWT causes increased macrophage recruitment and enhanced polarization towards reparative M2 macrophages in ischemic muscle. It could therefore become a promising tool for the regeneration of ischemic myocardium.