

## **Vascular Inflammation and Endothelial Dysfunction in Fracture Healing**

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Several in vitro studies showed that angiogenesis is involved in the first stages of bone healing but it has not been demonstrated in vivo.

Methods: 20 young healthy patients that were admitted with traumatic long bone fractures were studied for vascular responsiveness and markers of inflammation (osteopontin, E-selectin and vascular endothelial growth factor) in the first week of the study and after 1 month.

Results: Patients (13 men, 7 women, mean age of  $40.63 \pm 11.13$  years old) had severe endothelial dysfunction [FMD% of  $-2.5\% \pm 7.5\%$ ]. Neither of them was smoking, had diabetes mellitus, hypertension, or hypercholesterolemia, and their fractures were caused by a traumatic event. Healthy volunteers (10 men and 10 women, mean age of  $41.86 \pm 11.34$  years old) that had no risk factors for cardiovascular disease served as the control group. Their endothelial function was normal [FMD% of  $+15.0 \pm 6.5\%$ ] with a significant difference ( $p=0.0001$ ) compared with the patients' FMD%. High osteopontin levels were found in the first week, but after 1 month levels decreased towards normal [from  $77.19 \pm 52.10$  ng/ml to  $30.73 \pm 17.49$  ng/ml;  $p=0.001$ ]. E-selectin levels were high in the first week, then decreased [from  $28.15 \pm 14.88$  ng/ml to  $21.50 \pm 10.75$  ng/ml;  $p=0.01$ ]. VEGF levels were high in the first week of the fracture and stayed high without change during the first month [from  $449.81 \pm 191.38$  pg/ml to  $400.81 \pm 323.19$  pg/ml;  $p=0.5$ ].

Conclusions: Long bones' fractures caused intense vascular and inflammatory responses represented by high levels of osteopontin, E-selectin, and VEGF. In vivo measurements have demonstrated severe endothelial dysfunction that could support the idea of recruitment of the vascular system to build new blood vessels that will support bone regeneration.