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Shock wave therapy promotes survival of cardiac stem cells in end-stage heart failure

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Chronic ischemic heart disease is characterized by an imbalance between cardiac cell death and regeneration. The local non-invasive activation of cardiac stem cells offers the possibility to influence the course of cardiomyopathy and to inhibit or reverse the pathological remodelling. In patients with coronary artery disease, low energy shock wave (SW) therapy was found to improve symptoms and ameliorate ischemia.

The aim of our study was to evaluate the effects of SW on cardiac resident primitive cells in vitro. CD117(+) cells were isolated from the atria of adult human normal (n=7, males, mean age 51±5.6 years) and pathological hearts with ischemic cardiomyopathy (n=11, males, mean age 55±3.2 years), and treated with 800 shots of SW at the energy flux density of 0.05mJ/mm². Phospho-MAPK protein expression was assayed with proteome profiler array after 1 hour and total mRNA was examined by signal transduction-specific PCR-based array 72 hours after the treatment.

Gene expression profiling revealed in CD117(+) cells from pathological heart the down-regulation of genes relevant to the hedgehog pathway (EN1, BMP4, FOXA2), that is active in the early stages of the developmental process, or belonging to the induction and positive regulation of programmed cell death functional groups (CDKN2A, CDKN2B, CDKN1A, TP53I3, TNF), while the transcriptionally up-regulated genes included CSF2, CCL20, BIRC3, IL8, and IL1A that are involved in NFκB survival pathway and CEBPB, HK2, LEP involved in insulin pathway and myogenesis. Although SW treatment resulted in the significant increase in phospho-ERK1/2 in both cell populations, the phosphorylation of its downstream substrate RSK1 increased only in the normal cells. Similarly, in the normal cells the phosphorylation of p38-MAPKα, β and γ increased 4, 4-, 1, 2- and 4,2-fold, respectively, while only 1,3- and 2,2-fold increase in phosphorylated p38α and γ was observed in pathological cells. Moreover, the pro-survival kinase Akt1 resulted activated only in the normal cells.

We conclude that the application of SW activates survival pathways and protects from apoptosis, although different signal transduction pathways can be responsible for these effects in cardiac primitive cells from normal and pathological heart with ischemic cardiomyopathy.

Key words
Cardiac stem cells, ischemic cardiomyopathy, shock waves