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Combined therapy with shock wave and autologous bone marrow-derived mesenchymal stem cells alleviates left ventricular dysfunction and remodeling through inhibiting inflammatory stimuli, oxidative stress & enhancing angiogenesis in a swine myocardial infarction model

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ABSTRACT

Background: We hypothesized that combined therapy with shock wave (SW) and autologous bone marrow-derived mesenchymal stem cells (BMDMSCs) is superior to either therapy alone for alleviating left ventricular (LV) dysfunction.

Methods and results: Male mini-pigs (n = 30) equally divided into group 1 (sham control), group 2 [acute myocardial infarction (AMI) by left coronary artery ligation], group 3 (AMI-SW), group 4 (AMI-BMDMSC), and group 5 (AMI-SW-BMDMSC) were sacrificed by day 60 and the hearts were collected for studies. Baseline LV injection fraction [LVEF (%)] and LV chamber size did not differ among the five groups ($p > 0.5$). By day 60, LVEF was highest in group 1 and lowest in group 2, significantly higher in group 5 than that in groups 3 and 4, and significantly higher in group 4 than that in group 3 ($p < 0.001$). Cellular and protein levels of VEGF, CXCR4, and SDF-1α were significantly increased progressively from groups 1 to 5 (all $p < 0.05$). Small vessel number and protein expressions of CD31 and eNOS were highest in groups 1 and 5, lowest in group 2, and significantly higher in group 4 than those in group 3 ($p < 0.001$). Protein (MMP-9, TNF-1α and NF-κB) and cellular (CD14+, CD40+) levels of inflammatory biomarkers, protein expressions of oxidative stress (oxidized protein, NOX-1, NOX-2), apoptosis (Bax, caspase-3, PARP), infarct size, and LV dimensions showed a pattern opposite to that of LVEF among all groups (all $p < 0.001$).

Conclusions: Combined SW-BMDMSC therapy is superior to either therapy alone for improving LVEF, reducing infarct size, and inhibiting LV remodeling.

1. Introduction

Despite state-of-the-art treatment strategies, including advanced pharmacomodulation and early reperfusion therapy using thrombolysis or primary coronary intervention, acute myocardial infarction (AMI) is still the leading cause of death in patients hospitalized for cardiovascular diseases [1–4]. Pump failure, which is the crucial cause of both short-term and long-term mortalities after AMI [1,3–7], is attributable to the

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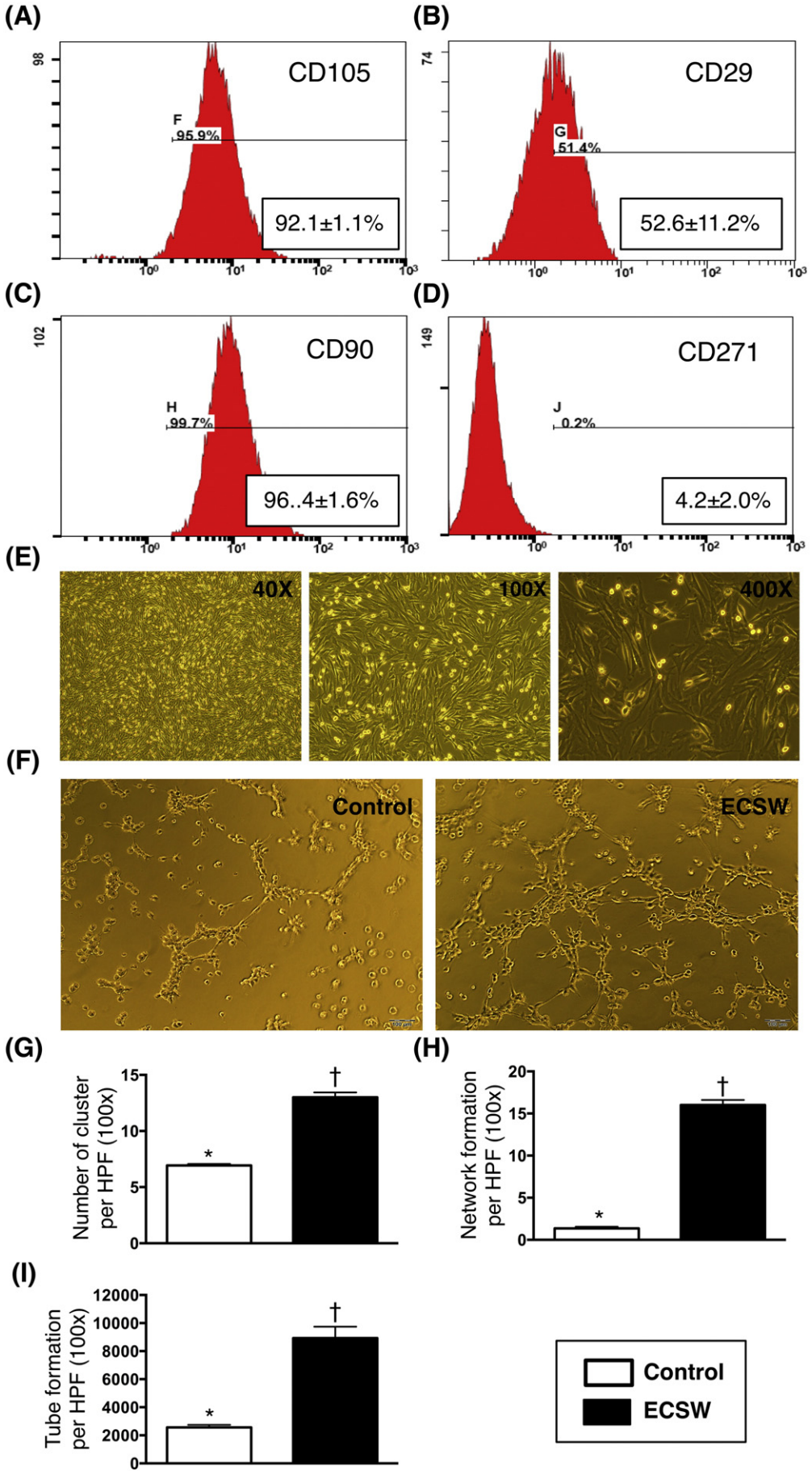
(A)
CD105
F
95.9%
92.1±1.1%
(B)
CD29
G
51.4%
52.6±11.2%
(C)
CD90
H
99.7%
96..4±1.6%
(D)
CD271
J
0.2%
4.2±2.0%
(E)
40X
100X
400X
(F)
Control
ECSW
(G)
Number of cluster per HPF (100x)
(H)
Network formation per HPF (100x)
(I)
Tube formation per HPF (100x)
Control
ECSW