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CARDIAC FUNCTION AND HEART FAILURE

HYDROGEN SULFIDE THERAPY ATTENUATES ISCHEMIA-INDUCED HEART FAILURE VIA NRF2 AND NRF1 SIGNALING

ACC Poster Contributions
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Background: Hydrogen sulfide (H2S) is an endogenously produced gaseous signaling molecule that induces cardioprotection via induction of antioxidant and anti-apoptotic defenses. We investigated H2S-mediated signaling in an in vivo murine model of heart failure (HF).

Methods: HF was induced by subjecting mice (C57BL6/J) to 60 minutes of myocardial ischemia (MI) followed by reperfusion (R) for 4 weeks at which time 2-D echocardiography was performed to evaluate left ventricular (LV) dimensions and ejection fraction (EF). H2S (Na2S; 100 µg/kg), or saline was administered at the time of R (intracardiac) and then daily (i.v.) for the first 7 days following MI. In separate studies, mice were treated with H2S for 7 days and myocardial tissue was collected to evaluate potential cellular targets of H2S.

Results: At 4 weeks of R, H2S therapy ameliorated LV dilatation and preserved ejection fraction compared to saline vehicle. Additional studies revealed that 7 days of H2S treatment increased the nuclear localization of both Nrf2 ($p = 0.04$ vs. vehicle) and nuclear respiratory factor 1 (NRF1; $p=0.03$), a transcription factor that is activated by Nrf2 and that regulates the mitochondrial genome. H2S also increased the phosphorylation of Akt ($p = 0.04$ vs. vehicle).

Conclusions: Our results indicate that the transcription factors Nrf2 and NRF1 play a role in mediating the cardioprotective effects of H2S in the setting of HF.