**Dipeptidyl Peptidase-4 Inhibitor Attenuated Ischemia-Reperfusion Injury Via Preventing Mitochondrial Dysfunction and Reducing Cellular Apoptosis**

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**Background:** Dipeptidyl peptidase (DPP)-4 inhibitor exerts cardioprotective effects. However, its benefits during cardiac ischemia-reperfusion (IR) injury are not clear. We hypothesized that 1) DPP-4 inhibitor reduces fatal arrhythmias, cardiac dysfunction, and infarct size during IR, and 2) this cardioprotection is via attenuating cardiac mitochondrial dysfunction and cellular apoptosis.

**Methods:** Rats were randomized to receive either DPP-4 inhibitor (vildagliptin, Vil) 2.0 mg/kg or normal saline solution (NSS) intravenously (n=5/group) prior to a 30-min left anterior descending coronary artery occlusion, followed by a 120-min reperfusion. Arrhythmia scores, cardiac functions, and the infarct size were evaluated. Cardiac tissues were harvested for mitochondria and immunoblot study.

**Results:** Compared to control, DPP-4 inhibitor significantly reduced infarct size (44% reduction, Figure) and preserved systolic function, while arrhythmia scores were not different. Vildagliptin significantly increased Bcl-2 and pro-caspase3 expression, whereas p-connexin43/total connexin43 ratio was not different. In cardiac mitochondria, DPP-4 inhibitor significantly reduced the reactive oxygen species (ROS) production, mitochondrial swelling, and mitochondrial depolarization (Figure).

**Conclusions:** DPP-4 inhibitor provides cardioprotection during IR by reducing infarct size and improving systolic dysfunction by attenuating cardiac mitochondrial dysfunction and apoptosis.