Resveratrol, an activator of SIRT1, upregulates AMPK and improves cardiac function in heart failure

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ABSTRACT. Reduced AMP-activated protein kinase (AMPK) expression has been shown to play a significant role in the cardiac dysfunction in heart failure. This study was designed to examine the effect of resveratrol, a potent activator of silent information regulator (SIRT1), on cardiac function and AMPK expression in heart failure. Adult male rat left anterior descending arteries were ligated, and they were fed with either a regular diet or a diet enriched with resveratrol. Heart failure was produced by myocardial infarction, and was associated with markedly increased AMPK and SIRT1 protein levels. Resveratrol treatment had a tremendous beneficial effect, both in terms of improving AMPK expression and on cardiac function. Decreased cardiac function and AMPK expression were also found in SIRT1 knockout (+/-) mice. In cultured cardiomyocytes, resveratrol increased AMPK and SIRT1 expressions, and overexpression of SIRT1 was found to be sufficient to activate AMPK in H9c2 cells. In contrast, pretreatment
of cardiomyocytes with an SIRT1 antagonist, nicotinamide, blocked these beneficial effects of resveratrol. Therefore, the protective effects of resveratrol were found to be dependent on its ability to activate SIRT1 and improve AMPK expression. These results demonstrated that in heart failure, the enzymatic activity of cardiac SIRT1 is increased, which contributes to increased expression of AMPK, and resveratrol enhances the expression of AMPK and improves cardiac function through the activation of SIRT1.

**Key words:** Heart failure; SIRT1; AMPK; Resveratrol