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Canstatin, a C-terminal fragment of type IV collagen α2 chain, prevents ischemia/reperfusion-induced ventricular arrhythmia in rats

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Ischemia/reperfusion (I/R) injury causes ventricular arrhythmia through inducing reactive oxygen species (ROS) and Ca^{2+} overload. We examined the effects of canstatin, a C-terminal fragment of type IV collagen $\alpha 2$ chain, on I/R-induced ventricular arrhythmia. I/R was induced by ligating left anterior descending artery for 10 min. Canstatin (20 μg/kg *i.v.*) was injected 5 min before the ligation. Ventricular arrhythmia within 10 min after reperfusion was recorded using an electrocardiogram. Neonatal rat cardiomyocytes (NRCMs) or adult rat ventricular myocytes (ARVMs) was subjected to oxygen and glucose deprivation/reoxygenation (OGD/R) in the presence or absence of canstatin (250 ng/ml). ROS production was detected by 2', 7'-dichlorofluorescin diacetate staining. Phosphorylation of Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) was determined by Western blotting. Canstatin significantly decreased duration of I/R-induced ventricular arrythmia without suppressing the incidence. Canstatin significantly inhibited OGD/R-induced ROS production in NRCMs and tended to inhibit OGD/R-induced phosphorylation of CaMKII in ARVMs. This study for the first time demonstrated that canstatin prevents I/R-induced ventricular arrhythmia in part through inhibiting ROS production and CaMKII activation.