EXCESS ISCHEMIC ARRHYTHMIAS MAY PROTECT AGAINST MYOCARDIAL INFARCTION

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C-reactive protein (CRP) is not only an inflammation marker, but it also exerts direct cardiovascular actions. Here we analyzed the effects of CRP overexpression on cardiac susceptibility to ischemia/reperfusion (I/R) injury in adult spontaneously hypertensive rats (SHR) expressing human CRP transgene (SHR-CRP). Using an in vivo model of coronary artery occlusion, we found that transgenic expression of CRP predisposed SHR-CRP to prolonged ventricular tachyarrhythmias. The proarrhythmic phenotype in SHR-CRP was associated with altered heart and plasma eicosanoids, myocardial composition of fatty acids in phospholipids, and autonomic nervous system imbalance. Interestingly, excess ischemic arrhythmias in SHR-CRP led to a significant reduction in infarct size (IS) compared with progenitor SHR. To explain this unexpected finding, we performed metabolomic analysis of plasma before and after ischemia. Acute ischemia in SHR-CRP markedly increased plasma levels of multiple potent cardioprotective molecules that could reduce IS at reperfusion. We also determined cardiac ischemic tolerance in hearts subjected to remote ischemic conditioning (repeated occlusions of both hind legs during ischemia) which provided IS-limiting effect in SHR that was comparable with myocardial infarction observed in naïve SHR-CRP. In hearts ex vivo, IS did not differ between the strains, suggesting that extra-cardiac factors play a crucial role in cardioprotection. Our study shows that transgenic expression of human CRP predisposes SHR-CRP to excess ischemic ventricular tachyarrhythmias associated with a drop of pump function that triggers myocardial salvage against lethal I/R injury likely mediated by protective substances released to blood from hypoxic body tissues.

Keywords: C-reactive protein; metabolomics; myocardial infarction; remote ischemic conditioning; ventricular arrhythmias.