Letter to the Editor

'Transient Left Ventricular Hypocontraction Induced by Emotional Stress With Immobilization: An Animal Model of tako-tsubo Cardiomyopathy in Humans?'

To the Editor:

I read with great interest the article by Ueyama et al. in the Circulation Journal in which they demonstrated that emotional stress with immobilization in the rat induced reversible left ventricular apical ballooning that was normalized by pretreatment with adrenoceptor blockade. They had previously demonstrated the same stress-induced ST-segment elevation, which returned to pre-stress basal levels after removal of the stress. From those studies, they proposed activation of cardiac adrenoceptors in the absence of ischemia–reperfusion as the primary cause of tako-tsubo cardiomyopathy. Because this study was published as a Rapid Communication and therefore limited in length, I would like more detailed information about their study.

Recent clinical studies, including a multicenter study and my group's study, have demonstrated the predominance of female and elderly patients with tako-tsubo cardiomyopathy, and its precise mechanism remains to be investigated. In addition, few people develop tako-tsubo cardiomyopathy when undergoing mental stress in the clinical setting, suggesting that there are individual differences in the development of this condition. The authors need to state what proportion of rats generally develop left ventricular dysfunction associated with emotional stress with immobilization, and whether there is a predominance of female and elderly subjects, even in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model. In addition, the recent clinical study by my group demonstrated that the circulating norepinephrine concentration was normal or slightly elevated in this model.

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References

Author's Reply
Animal Model of ‘Tako-Tsubo’ Cardiomyopathy – Update

I thank Dr Kurisu for his thoughtful comments and appreciate his great interest in our study! Several important questions were raised. First, we have additional data regarding the high incidence of tako-tsubo cardiomyopathy in the elderly (postmenopausal) female. We compared left ventriculography performed under immobilization stress between ovariectomized (animal model of postmenopause) rats and estradiol-supplemented ovariectomized rats. The left ventricular wall motion under stress was significantly improved by increasing the estradiol concentration (unpublished observation) and we consider that estradiol may suppress the sympathetic nervous activity via several mechanisms. It has been reported that local injection of estradiol into several central autonomic nuclei inhibits sympathetic nervous activity, and estrogen decreased uterine sympathetic innervation via an estrogen receptor-mediated mechanism. We observed that this effect of estrogen also occurs in cardiac tissues (unpublished observation). Second, individual differences in reactivity to stress are generally observed; in fact, 20% of the rats were unaffected, as previously demonstrated! Third, the circulating norepinephrine concentrations were not as high in human patients with tako-tsubo cardiomyopathy, but prominent increases of norepinephrine and epinephrine in response to immobilization stress in rats have been reported. I think the discrepancy may lie in the sampling delay in clinical cases. The initial output of norepinephrine and epinephrine from sympathetic nerve endings and the adrenal medulla might be very high immediately after the attack, but might have subsided on arrival at hospital. I propose that measurement of the metabolites, such as dihydroxyphenyglycol, formed from oxidative deamination of cytoplasmic norepinephrine by monoamine oxidase, or of the urinary excretion of catecholamines and their metabolites will clarify this hypothesis. An increased plasma concentration of norepinephrine is associated with decreased sympathetic innervation, as well as decreased amounts of nerve growth factor and trkA, the neurotrophic factor for sympathetic neurons, and its high affinity receptor. In fact, Owa et al. reported that on cardiac imaging with MIBG, functional sympathetic nerve density showed a long-lasting defect in tako-tsubo (ampulla) cardiomyopathy suggesting that sympathetic dysfunction does occur in this syndrome.

Further studies based on clinical cases as well as animal experiments are required for the better understanding of the pathogenesis of tako-tsubo cardiomyopathy.

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References


