GW23-e0780  DYNAMIC ALTERATIONS OF CONNEXIN 43, MATRIX METALLOPROTEINASE-2 AND TISSUE INHIBITOR OF MATRIX METALLOPROTEINASE-2 DURING VENTRICULAR FIBRILLATION IN DOGS

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Objectives  We aimed to investigate the dynamic alterations of cardiac connexin 43 (Cx 43), matrix metalloproteinase-2 (MMP-2) and tissue inhibitor of metalloproteinase-2 (TIMP-2) in the setting of different ventricular fibrillation (VF) duration and try to reveal the possible initiation and/or persistence mechanisms of VF.

Methods  VF was electrically induced in 32 dogs. The animals were randomly divided into four groups (sham control group: n=8; 8-min VF group: n=8; 12-min VF group: n=8; 30-min VF group: n=8). Echocardiography measurement and hemodynamic variables were recorded before VF. Cx 43 and phosphorylated Cx 43 (p-Cx43) were analysed by western blot and immunofluorescence. MMP-2 and TIMP-2 were analysed by western blot and immunohistochemistry.

Results  There were no statistically significant differences among the animals in body weight, heart rate, LAD, LVDd, LVEF and hemodynamic variables at baseline. Compared with the sham control group, Cx 43 in other three VF groups were significantly decreased, and the amount of Cx 43 declined with the duration of VF (0.83±0.04 vs 0.71±0.06 vs 0.66±0.05 vs 0.52±0.07, p<0.05). p-Cx 43 in 12-min and 30-min VF group were significantly reduced (0.76±0.07 vs 0.56±0.05 vs 0.41±0.03, p<0.05) while there was no statistical distinction between the sham control group and 8-min VF group (0.76±0.07 vs 0.69±0.05, p>0.05). In addition, the same change tendency was observed in the ratio of p-Cx43/Cx43 (0.87±0.03 vs 0.85±0.04 vs 0.76±0.06 vs 0.64±0.04). Compared with sham controls, dogs under VF showed significantly decreased contents of TIMP-2, and the level of TIMP-2 declined by degrees with the duration of VF (0.86±0.08 vs 0.75±0.06 vs 0.68±0.04 vs 0.51±0.06, p<0.05). No significant difference was observed between the sham control group and 8-min VF group concerning levels of MMP-2 (0.51±0.03 vs 0.54±0.04, p>0.05), however, the MMP-2 increased in other two longer-duration VF groups (0.59±0.07 vs 0.71±0.05, p<0.05). The ratios of MMP-2/TIMP-2 were higher in VF groups, and rose up gradually with the duration of VF (0.64±0.08 vs 0.85±0.09 vs 1.12±0.07 vs 1.39±0.09, p<0.05). A remarkable correlation was observed between the ratio of p-Cx43/Cx43 and the ratio MMP-2/TIMP-2 (r=−0.93, p<0.01).

Conclusions  Dynamic alterations in total amount, distribution and phosphorylation status of Cx43 were observed within the 30 min duration of VF. Meanwhile, the present findings also demonstrated that the expression of TIMP-2 declined and MMP-2 increased with the duration of VF. A remarkable correlation was also observed between the ratio of p-Cx43/Cx43 and the ratio MMP-2/TIMP-2. These data are consistent with previously published data by our laboratory. In conclusion, the alteration of Cx43 and/or p-Cx43, the imbalance between MMP-2 and TIMP-2 may contribute to the initiation and/or persistence of VF. Therefore, manoeuvres managed to modify Cx43 or normalise the balance of MMP-2/TIMP-2 may be used to ameliorate prognosis of VF.