

Multiorgan characterization of inflammasome expression in a surgical rat model of advanced heart failure

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Background: Targeting inflammasomes in heart failure (HF) might represent a novel therapeutic option. Nevertheless, previous studies focused only on myocardial inflammasome alterations, and data are scarce regarding their regulation and role in advanced HF-associated multiorgan dysfunction.

Aims: Therefore, we aimed to determine the myocardial, pulmonary, hepatic and renal expression of various inflammasome components in a surgical rat model of advanced HF.

Methods: Rats underwent transverse aortic constriction (TAC) surgery and were followed-up for 15 weeks. Utilizing a simple scoring method, animals featuring 2-3 clinical signs of advanced HF were included in the TAC-HF group. TAC rats with mild HF were also investigated (0-1 signs, TAC-M group). Sham-operated animals served as controls. The expressions of inflammasome component proteins in left ventricle (LV), right ventricle (RV), lung, liver and kidney tissue were measured with Western blot.

Results: Despite the differences between the clinical state of the TAC-HF and TAC-M groups, severe cardiac dysfunction of comparable degree developed in all TAC animals. Absent in melanoma 2 (AIM2) and NLR family CARD domain-containing protein 4 (NLRC4) inflammasome sensors were upregulated in both the LV and RV of the TAC-HF group compared to Sham. AIM2 and NLR family pyrin domain-containing protein 3 (NLRP3), but not NLRC4 expression were elevated in the lungs of the TAC-HF animals. Inflammasome components were downregulated in the liver and unchanged in kidney tissue in the TAC-HF group. Inflammasome changes were predominantly absent in TAC-M animals.

Conclusion: Inflammasome expression shows distinct patterns in specific organs in advanced HF.

Keywords: transverse aortic constriction, advanced heart failure; end-organ damage; multiorgan dysfunction; inflammasome

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