Cardioprotective Effect of LCZ696 (sacubitril/valsartan) After Experimental Acute Myocardial Infarction

Koichi Kaikita, MD, PhD, FJCC, FESC

Masanobu Ishii[1], Koichi Kaikita[1], Koji Sato[1], Daisuke Sueta[1], Koichiro Fujisue[1], Yu Oimatsu[1], Tatsuro Mitsuse[1], Seiji Hokimoto[1], Hisao Ogawa[2], Kenichi Tsujita[1]

[1] Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

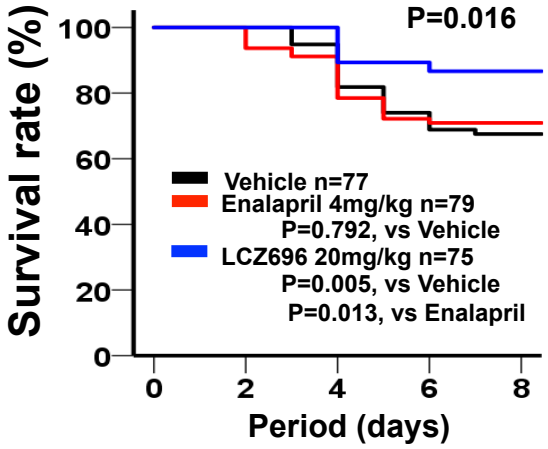
[2] Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Osaka, Japan

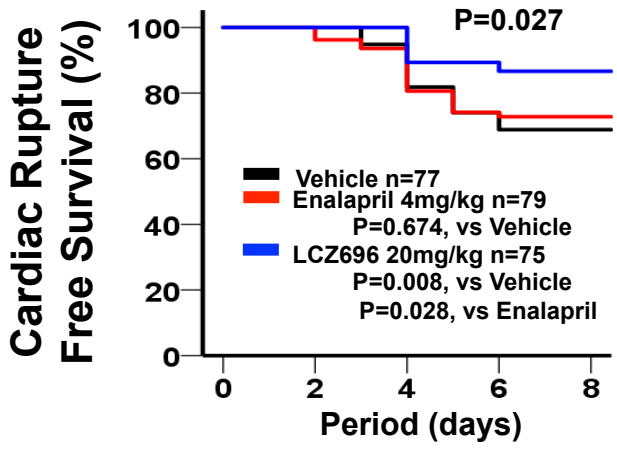
Objective

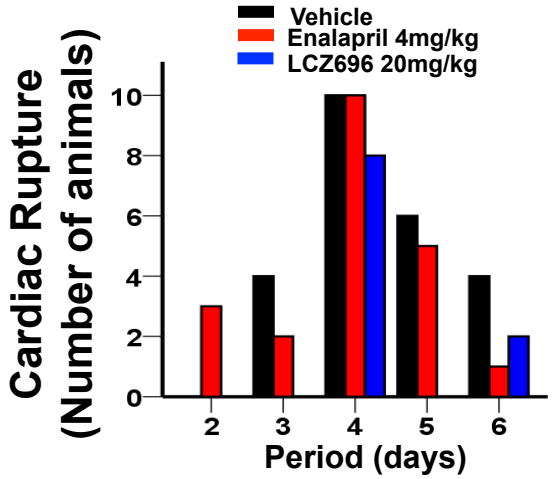
While the long-term benefits of LCZ696 on cardiac function and prognosis have been reported, it remains to be elucidated whether it can also ameliorate cardiac dysfunction on short-term.

The aim of the present study was to evaluate the effects of LCZ696 on cardiac remodeling at acute phase of experimental MI in mice.

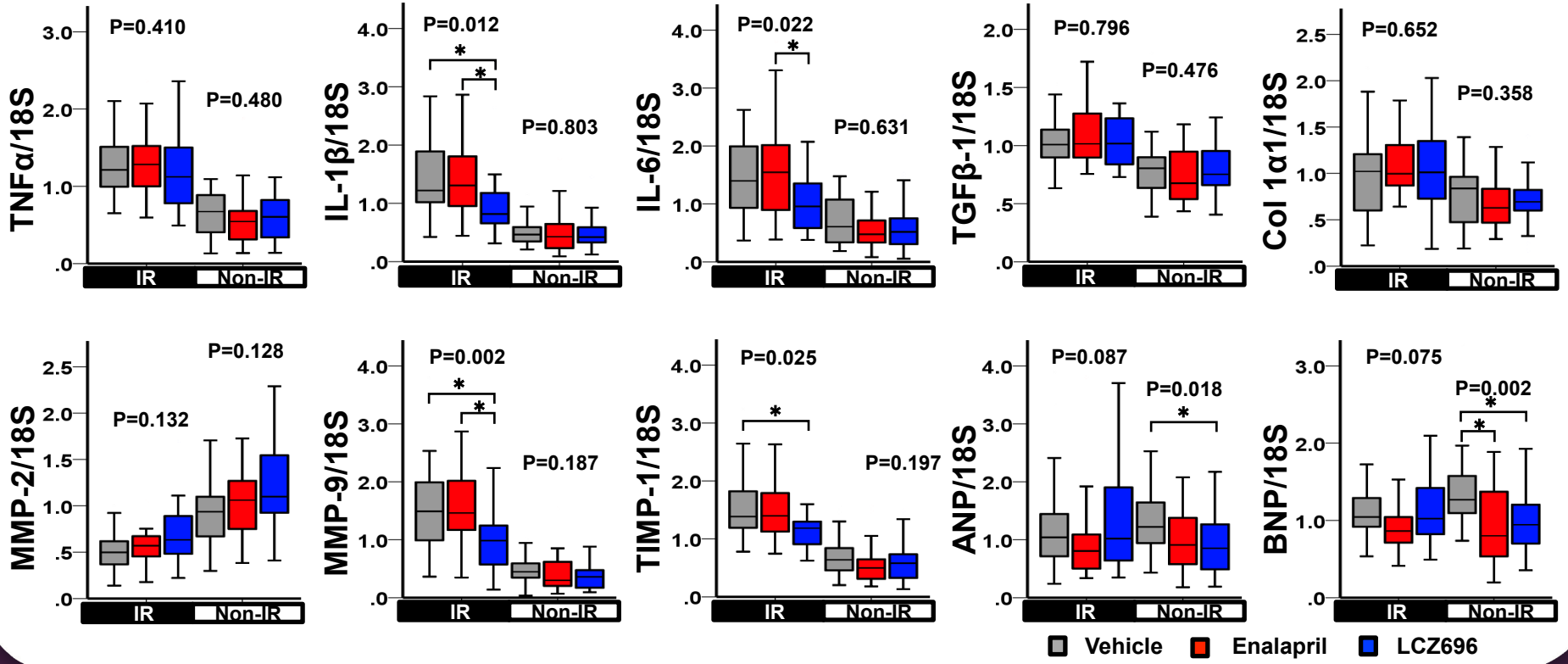
Survival and Cardiac Rupture Rate Post-MI



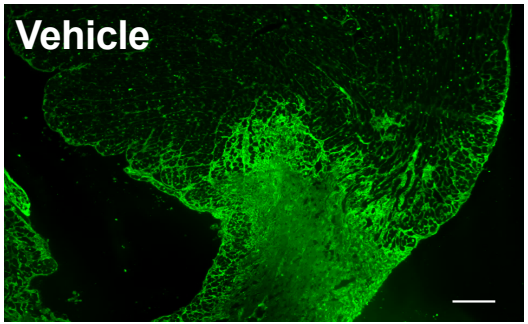


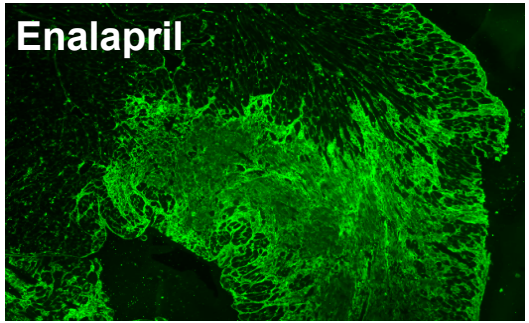


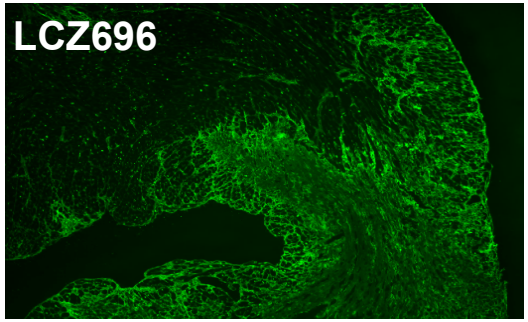
Gene Expression 3 Days Post-MI

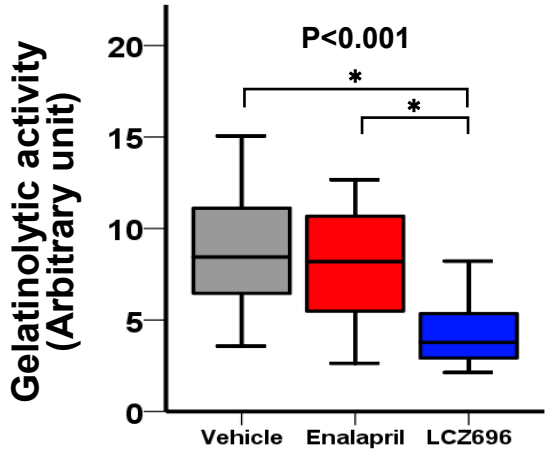


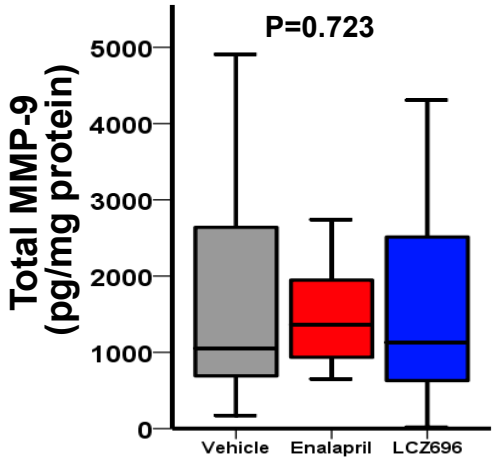
Gelatinolytic Activity 3 Days Post-MI

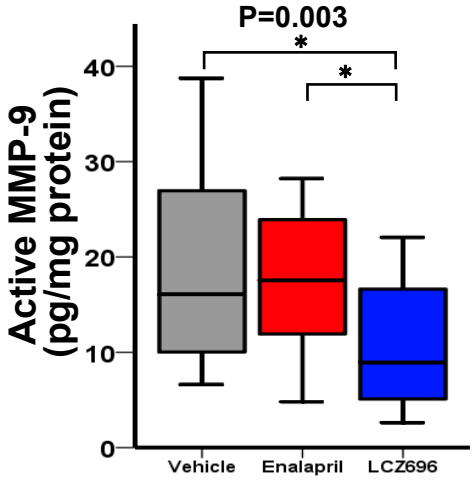




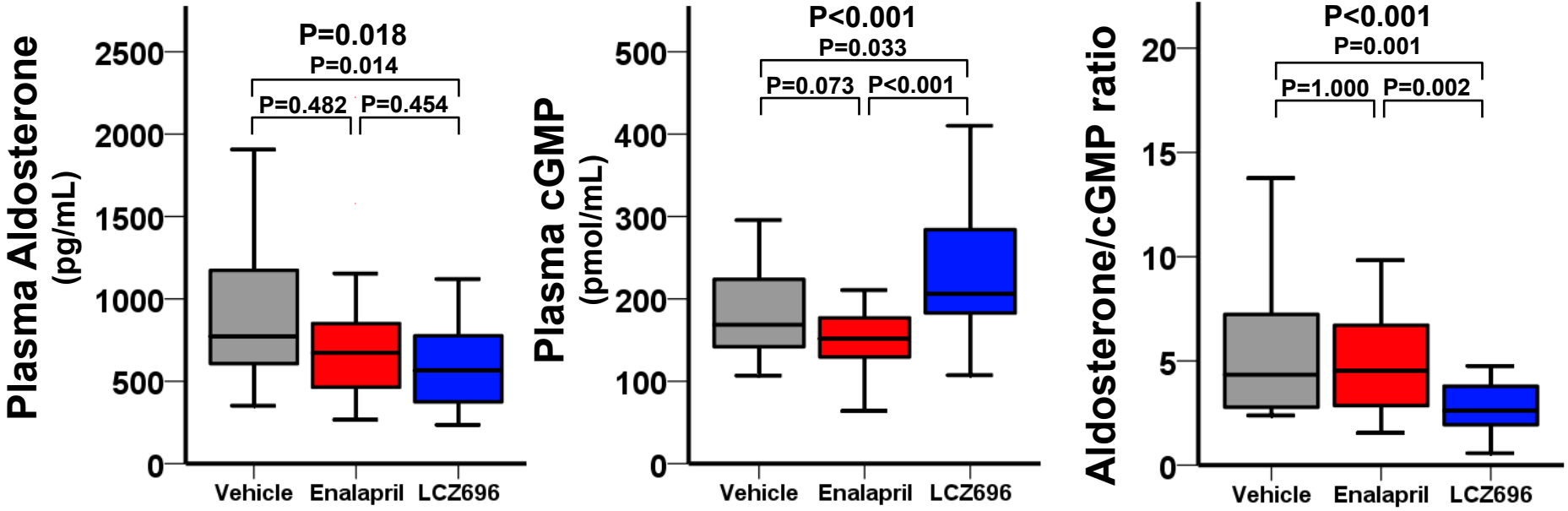








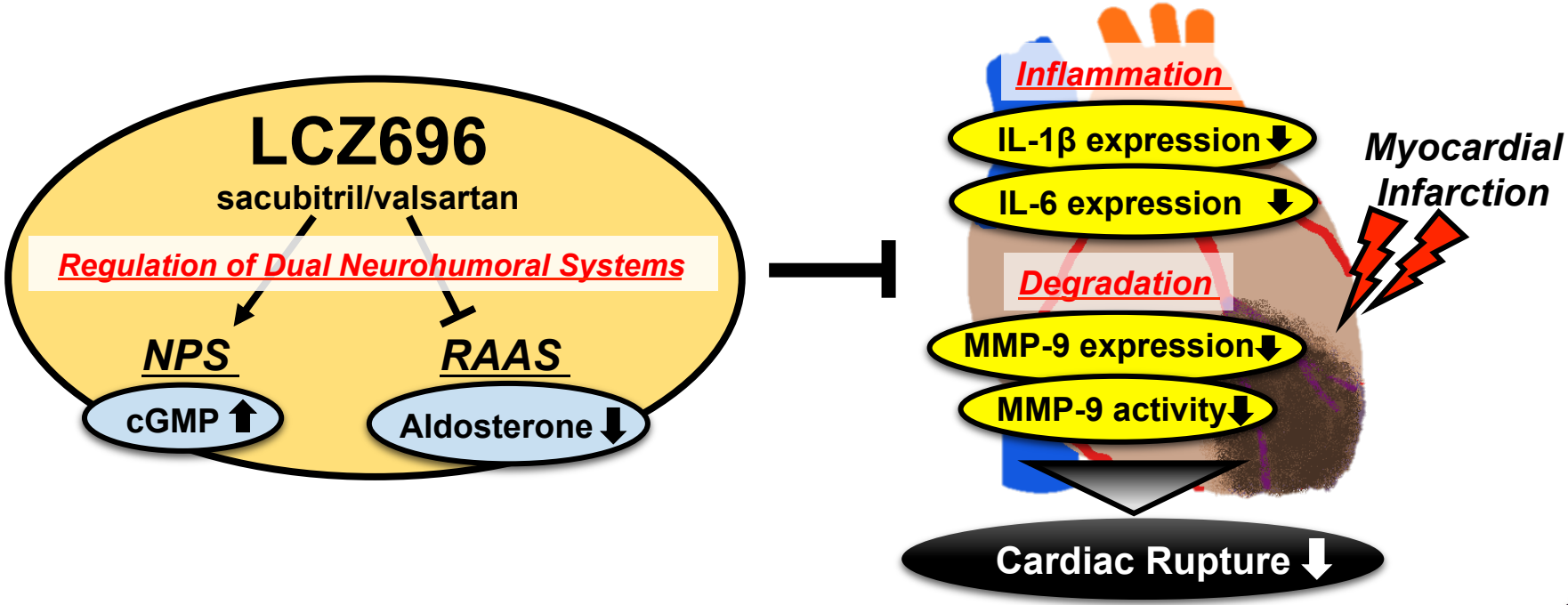
Plasma Aldosterone and cGMP Levels



Summary

1. LCZ696 significantly reduced death caused by cardiac rupture within 1 week after MI compared with vehicle and enalapril groups.
2. Echocardiography revealed that %FS was significantly improved in LCZ696 but not in enalapril, compared with that in vehicle group at 14 and 28 days after MI.
3. At 3 days after MI, expression of IL-1β, MMP-9 mRNA and MMP-9 activity in infarcted myocardium were significantly decreased in LCZ696 group compared with other two groups, and IL-6 mRNA were significantly decreased in LCZ696 compared with enalapril.
4. At 3 days after MI, plasma cGMP levels were significantly higher, and plasma aldosterone levels were significantly lower in the LCZ696 group than the other groups.

Schematic Diagram in Mechanism of Protective Effects of LCZ696 on Post-MI Cardiac Rupture



Conclusions

- LCZ696 modulated both RAAS and natriuretic peptides systems on acute phase of MI, and prevented the survival rate after MI via the suppression of inflammatory cytokines and MMP-9 activity.
- LCZ696 might be a novel medical treatment for improving the cardiac remodeling after acute phase of MI.