Acute and high-dose therapy of urinary trypsin inhibitor could inhibit vascular endothelial cell disorders in critical illness

during and after CPB. The levels of iNOS and COX-2 were detected during and after CPB but without any difference between groups. Phosphorylation of p38 MAP and ERK1/2 MAP kinases and of IκB was detected before, during and after CPB. Levels of phospho-p38 MAP kinase but not of ERK1/2 MAP kinase and IκB tended to be lower in animals on hypothermia than in the others ($P < 0.1$).

Conclusion This study shows for the first time that cardiac surgery induces the expression of TNF-α in the myocardium as soon as 30 min after institution of CPB, before aortic clamping. This is associated with the activation of p38 MAP and ERK1/2 MAP kinases and NF-κB pathway. The inhibition of TNF-α expression by hypothermia is related to the inhibition of p38 MAP kinase.

P199 Acute and high-dose therapy of urinary trypsin inhibitor could inhibit vascular endothelial cell disorders in critical illness

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Introduction Urinary trypsin inhibitor (UTI) (MIRACLID®, Mochida Corp., Tokyo, Japan), an elastase inhibitor extracted from human urine, has been used to treat for patients with acute pancreatitis or acute circulatory failure since more than 15 years ago in Japan.

Objective The current study was performed in order to evaluate the efficacy of UTI for vascular endothelial disorders in critical illness.

Materials and methods Thirteen severe patients, who had an APACHE II score above 20 at transportation to our emegency room, were elected and randomly assigned to either a treated group or a control group. The number of patients in the treated group was five and eight patients were in the untreated group. Maximum dose of UTI (30,000 U/ml) were administrated to patients in the treated group at the emergency room. After admission in the ICU, the neutrophil elastase level, IL-6 level, thrombomodulin (TM) level, protein C level and UTI level in plasma were examined daily until the 7th day after hospitalization. Values are expressed as mean ± SD. An unpaired Student's *t* test was used and $P < 0.05$ was considered statistically significant.

Results In the untreated group, the UTI level in plasma at the 7th day after hospitalization was siginificantly higher than that in the treated group (96.9 ± 44.4 vs 15.6 ± 6.5 U/ml, $P < 0.05$). Also, the TM level was also significantly different between the untreated group and the treated group (6.0 ± 2.4 vs 3.6 ± 1.4 FU/l, $P < 0.05$) at the 7th day. Other examination values showed no significant differences between the two groups during their clinical courses.

Conclusion The half-time of UTI is very short (about 40 min) and the plasma level linear decreases until 3 hours after its administration. The difference of UTI level on the 7th day was considered as spontaneous UTI. And vascular endothelial disorders were recognized in the higer UTI level group at the same day, but this group was the untreated group. This study proposes it i important for high-dose administration of UTI at a very acute phase in critical illness to inhibit the vascular endothelial disorders.

P200 Effects of urinary trypsin inhibitor for trauma patients

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We investigated the effect of urinary trypsin inhibitor (UTI) on the output of plasma mean neutrophil elastase (PMNE) and cytokine.

The participants of this study are 15 trauma patients with shock on arrival at our insutitution. We divide them in two groups: one group is administrated 300,000 U (intravenous) UTI, and the other is the control group. At 0, 1, 3, 5, and 7 days after hospitalization of each group, we measured the serum levels of IL-6, IL-8, UTI, PMNE, thrombomodulin, protein C, and the SIRS score and SOFA score as an index of severity.

The PMNE levels in the UTI-administered group were observed to be significantly lower than those in the control group at 1 and 3 days after hospitalization.

These data suggest that. UTI can suppress vascular endothelial cell disorders by inhibiting the production of PMNE and by direct inhibition of PMNE.

P201 Exosomes derived from plasma of septic patients induce myocardial dysfunction

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Background Exosomes are small vesicles (50–100 nm) released from cells after activation. We have previously shown that exosomes derived from platelets of septic patients induce apoptosis of endothelial and vascular smooth muscle cells through a redox-dependent pathway. Since reactive oxygen species may be involved in myocardial dysfunction of sepsis, the aim of this study was to investigate a possible role of exosomes in sepsis-induced myocardial dysfunction.

Methods Exosomes were separated by filtration and ultracentrifugation of plasma from 26 septic shock patients (SSP) and from 10 healthy volunteers. After separation, exosomes were infused at a 0.5-fold plasma concentration in Langendorff-perfused hearts from 22 New Zealand rabbits. In other experiments, 12 isolated rat papillary muscles were exposed to a 0.5-fold plasma concentration of exosomes from septic patients and healthy controls.