Basic Science: Cardiovascular Disease Basic Research

**e0001 THE EFFECTS OF TRANS FATTY ACIDS ON FATTY ACID CONSTITUTION RATIOS OF ERYTHROCYTE MEMBRANE IN RABBITS**

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**Objective** To investigate the influences of high trans fatty acids (TFA) intake on fatty-acid constitution ratios of erythrocyte membrane in rabbits.

**Method** 32 New Zealand white rabbits were randomly divided into four groups: control group with common feed; high TFA group with additional TFA 5.0 g/kg.d; high-fat (HF) group with high cholesterol feed and TFA+HF group. The erythrocyte membranes were prepared at 0, 4, 8, 12 weeks. Two kinds of saturated FA (C18:0 and C16:0), four kinds of unsaturated FA (C18:1, C18:2, C20:4, C20:5 and total ω-3) and two kinds of TFA (t-C18:1 and t-C16:1) in erythrocyte membrane were determined with gas chroma. Four constitution ratios of C18:1/C18:0, C18:1/t-C18:1, ω-3/∑TFA and ω-3/C18:0 were calculated.

**Results** Compared with the control group, TFA group showed not only obviously higher constitution ratios of TFA, but obviously higher ratios of saturated FA and lower ratios of polysaturated FA, especially ω-3 FA (2.38±0.35 vs 3.28±0.48, p<0.05), in erythrocyte membrane. The abnormality of constitution ratios of unsaturated FA and polysaturated FA in TFA were similar to that in HF group. More abnormal changes of erythrocyte membrane FA constitution ratios were showed in TFA+HF group.

**Conclusions** High TFA intake could increase the constitution ratios of TFA and saturated fatty acids, but decrease polysaturated fatty acids, especially ω-3 fatty acids, in erythrocyte membrane. These effects were equivalent with the effects of high cholesterol intake. Combined with TFA and high cholesterol intake had obviously synergistic effects.

**e0002 EFFECT OF TOLL-LIKE RECEPTOR-4 SIGNAL PATHWAY ON THE DYSFUNCTION OF CARDIAC MICROVASCULAR ENDOTHELIAL CELLS CAUSED BY HYPOXIA/REOXGENATION INJURY**

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**Aim** TLR-4 has been proved to take part in MIRI of heart. But the researches mostly focused on the relationship between TLR-4 and global heart dysfunction or cardiocyte apoptosis. The effect of TLR-4 on CMECs which are the most important component in MIRI is not clear. To explore the change of TLR-4 signal pathway during hypoxia–reoxygenation (H–R) of cardiac microvascular endothelial cells (CMECs) injury.

**Methods** The CMECs were isolated from the hearts of adult rats. The obtained CMECs were exposed to hypoxia (940 ml/l N2, 50 ml/l CO2 and 10 ml/l O2) for 6 h, following by reoxygenation (950 ml/l air, 50 ml/l CO2) for 2 h, 12 h or 24 h. The proliferation of CMECs was assessed by MTT colourimetry. TLR-4 and NF-κB expressions were analysed by Western blot. The levels of IL-6 and TNF-α were detected by ELISA.

**Results** The proliferation ability of CMECs was significantly inhibited by H–R injury (p<0.01). H–R injury increased TLR-4 expression after 2 h or 12 h reoxygenation (p<0.05). The level of NF-κB increased after 2 h and 24 h reoxygenation (p<0.05). H–R injury enhanced IL-6 and TNF-α secretion as compared with the control group (p<0.05).

**Conclusion** H–R injury increases TLR-4 and NF-κB expressions in CMECs and enhances the secretions of IL-6 and TNF-α. The activation of TLR-4 signal pathway on CMECs may participate in the H–R induced of CMECs injury.

**e0003 CARDIAC-SPECIFIC EXPRESSION OF E3 LIGASE NRDP1 INCREASES ISCHAEMIA AND REPERFUSION-INDUCED CARDIAC INJURY IN TRANSGENIC MICE**

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**Objective** Neuregulin receptor degradation protein-1 (Nrdp1) is an E3 ubiquitin ligase that regulates the proteasomal degradation and activity of proteins involved in cell growth, inflammation and apoptosis, including ErbB3, BRUCE, MyD88 and Tbk1. However, the effect of Nrdp1 on cardiac ischaemia/reperfusion (I/R) injury in vivo has not yet been investigated.

**Methods and results** We generated transgenic mice with cardiac-specific overexpression of Nrdp1 using α-myosin heavy chain promoter. Echocardiography demonstrated that cardiac-specific Nrdp1 expression resulted in depression of cardiac contractile function under basal condition (TG6 mice, EF, 62.74±4.40%, FS, 35.85±5.17%, WT mice, EF, 67.52±11.07%, FS, 37.64±5.64%). When subjected to 30 min of left coronary artery ischaemia and 24 h of reperfusion, the infarct size, expressed as the ratio of infarct/AAR and infarct/IV, was significantly increased in Nrdp1 TG6 mice (23.6% vs 17.0%) compared with that of WT mice (18.4% vs 11.4%, p<0.05). Furthermore, the survival rate after I/R in Nrdp1 TG6 mice (75.9%, 22/29) was significantly lower than that of WT mice (84.6%, 22/26). Moreover, the numbers of TUNEL-positive nuclei (22.83% vs 15.78%) neutrophil and macrophage infiltration after I/R were significantly higher in Nrdp1 transgenic mice than in WT mice (p<0.05). Additionally, the activation of ErbB3, AKT, ERK1/2 and STAT3 after I/R were markedly suppressed in Nrdp1 transgenic mice compared with WT mice (p<0.01).

**Conclusion** These data provide the first in vivo evidence that over-expression of Nrdp1 enhances cardiac I/R injury, this effect is mediated by inhibition of ErbB3-dependent signalling pathways.

**e0004 HYDROGEN SULFIDE INHIBITS NEURONS APOTOPSIS IN RATS AFTER CARDIOPULMONARY RESUSCITATION**

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**Objective** To investigate the effects of hydrogen sulfide (H2S) on brain injury after cardiopulmonary resuscitation (CPR) in rats by examining neurons apoptosis.

**Methods** The 40 male SD rats were randomly divided into experimental and control groups equally. In control group, CPR was performed with Utstein mode at 6 min after CA. On this basis, sodium hydrosulfide was administrated to the rats after restoration
of spontaneous circulation in experimental group. On seventh day after CPR, neurons apoptosis was examined using terminal deoxy-
ucleotidyl transferase mediated dUTP nick end labeling (TUNEL) staining and the expression of caspase-3 was detected by 
the immunohistochemical strepto avidin biotin peroxidase complex (SABC) method in cortex, hippocampus CA1 region and cerebellum 
of the rats.

Results 1. There were 12 and 10 rats completed the experiment in 
the experimental and control group respectively. Their fate between 
the two groups was no significant difference (χ²=0.404, p=0.576). 2. 
On seventh day after CPR, The serum concentrations of H2S was 
9.12±3.17 μmol/l in the experimental group and the contrast was 
3.72±1.05 μmol/l, the difference between the two groups had 
statistic significance (t=5.136, p=0.000). 3. Compared with the 
control group, the experimental group’s neurons apoptosis index 
and the sum of integrated optical density (IOD) of caspase-3 in 
cortex, hippocampus CA1 region and cerebellum were obviously 
reduced (p<0.05).

Conclusion After CPR, H2S can inhibit neurons apoptosis and 
its mechanism may be through caspase-3 pathway. It may play a role in 
the treatment of the brain injury after CA.

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**e0005 MODEL OF CARDIAC ARREST IN RATS BY 
TRANSCUTANEOUS ELECTRICAL EPICARDIUM 
STIMULATION**

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Objective To establish a new model of Cardiac Arrest (CA) in rats by 
transcutaneous electrical epicardium stimulation.

Methods Two acupuncture needles connected to the anode and 
cathode of a stimulator were transcutaneously inserted into the 
epicardium as electrodes. The stimulating current was steered to the 
epicardium and the stimulation was maintained for 3 min to induce 
CA. Cardiopulmonary resuscitation (CPR) was performed at 6 min after 
a period of nonintervention.

Results The success rate of induction was 12/20 at the current 
intensity of 1 mA; and reached 20/20 when the current intensity 
was increased to 2 mA. The average time from the electrical stim-
ulation to CA induction was 5.10 (±2.81) s. When the electrical 
stimulation stopped, 18/20 rats had ventricular 
brillation and 2/20 rats had pulseless electrical activity. CPR was performed for aver-
gage 207.4 (±148.8) s. The restoration of spontaneous circulation 
was 20/20. The death rate within 4 h after CA was 5/20, and the 
72-h survival rate was 10/20. There were only two cases of compli-
cations, a minor muscle contraction and a minor lung lobe injury.

Conclusion The model of CA in rats induced by transcutaneous 
electrical epicardium stimulation is a stable model that requires low-
intensity current and has fewer complications.

**e0006 EFFECTS OF NEOTYPE PERITONEAL COOLING ON 
THE INJURED OF INTESTINAL MUCOUS AFTER 
CARDIOPULMONARY RESUSCITATION IN RABBITS**

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Objective To explore whether the peritoneal cooling after cardio-
pulmonary resuscitation could improve the injured of intestinal 
mucous in rabbits.

Methods 36 adult New Zealand rabbits were induced ventricular 
fibrillation by AC current. After the restore of spontaneous 
circulation (ROSC), rabbits were randomly divided into three 
groups according to the way of body temperature controlling, that 
is, normothermia group (NT), surface cooling group (SC) and peri-
toneal cooling group (PC). The changing of tympanic temperature 
and peritoneal temperature were observed after ROSC. The animals 
were sacrificed by over anaesthesia after ROSC for 12 h, the end 
ileum was removed and fixed in formalin, the histological injured 
and the expression of TNF-a and VCAM-1 in ileum were observed 
by HE staining and immune chemical methods.

Results 12 animals in each group, 9 in group NT, 10 in group SC 
and 9 in group PC were successfully resuscitated; all animals were on 
mechanical ventilation for 2 to 4 h. 5, 6 and 8 animals in each group 
respectively survived to the end of the experiment. The temper-
atures of tympanic and peritoneal cavity of animals in group NT 
were maintained in normal range. The tympanic temperature of 
animals in group SC and PC was arrived target temperatures at 
29 ±6.55 min and 62 ±8.27 min. During the stage of maintenance 
of hypothermia, the tympanic and peritoneal temperatures of animals 
in group SC were in range 35 to 35°C, while the peritoneal 
temperature of animals in group PC were in range 31 to 34°C, 1 to 
2°C lower than the tympanic temperature. The scores of histological 
injured of ileum were 1.48 ±0.35 in group PC, 3.48 ±0.35 in group 
NT and 3.17 ±0.41 in group SC. The differences among them were 
significantly, PC versus SC, p<0.000; PC versus NT, p<0.000; while 
SC versus NT, p=0.30. The expression of TNF-a in ileum was 
9.98 ±1.79% in group NT, 5.87 ±1.4% in group SC and 3.78 ±0.53% 
in group PC, the differences among them were significantly. 
The phenomenon of the expression of VCAM-1 was little like the TNF-a, 
3.78 ±0.53% in group PC was significantly from the 8.55 ±1.53% in 
group NT and 5.92 ±1.06% in group SC.

Conclusion The neotype peritoneal cooling can improve the injured 
of ileum mucous beside quickly induce hypothermia after ROSC in 
rabbits.

**e0007 THE EFFECT OF OMEPRAZOLE ON THE OXIDATIVE STRESS 
AND ACUTE ATRIAL ELECTRICAL REMODELLING IN 
RABBITS**

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Objective To investigate the effect of omeprazole on the acute atrial 
electrical remodelling and oxidative stress status in rabbit atrial 
fibrillation (AF) model.

Methods 18 rabbits were randomly divided into atrial tachypacing 
(ATP) group, sham operating (SM) group, and atrial tachypacing 
with omeprazole therapy (A+O) group. In the ATP group and A+O 
group the right atrium was tachypaced at 500 e600 bpm to induce 
AF for 3 h. The A+O group were given intravenous administration 
of omeprazole treatment (4 mg/kg) 15 min before 
tachypacing. The ATP group were given intravenous 
administration of physiological saline 10 ml 15 min before pacing. The SM group 
were not paced. The atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). Oxidative stress 
markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing).

Results At baseline, the atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). Oxidative stress 
markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). 
ATP group and A+O group were given intravenous administration 
of omeprazole treatment (4 mg/kg) 15 min before 
tachypacing. The ATP group were given intravenous 
administration of physiological saline 10 ml 15 min before pacing. The SM group 
were not paced. The atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
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markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). 
The SM group were not paced. The atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). Oxidative stress 
markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). 
ATP group and A+O group were given intravenous administration 
of omeprazole treatment (4 mg/kg) 15 min before 
tachypacing. The ATP group were given intravenous 
administration of physiological saline 10 ml 15 min before pacing. The SM group 
were not paced. The atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). Oxidative stress 
markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). 
The SM group were not paced. The atrial electrophysiological indexes (AERP, Rate 
adaptive of ERP) were measured at different time point (baseline, 
0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). Oxidative stress 
markers (SOD, MDA, T-NOS) in serum were measured at different 
time point (baseline, 0.5 h, 1 h, 1.5 h, 2 h, 2.5 h and 3 h after pacing). 