e0013 MATRIX METALLOPROTEINASES-9—A BIOMARKER IN AORTIC DISSECTION

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Aortic dissection (AD) is a life threatening emergency. Early diagnosis and treatment are pivotal for patients with AD. Matrix metalloproteinases (MMPs), through degradation of extracellular matrix, may play an important role in these processes. Elevation of MMPs might represent an opportunity to diagnostically characterise acute aortic processes. We examined the potential diagnostic role of MMP-9 in AD.

Methods Between February 2009 and November 2009, 86 consecutive patients affected by acute AD who were admitted to our emergency department for evaluation were enrolled in this study (Traumatic AD, Marfan Syndrome were excluded). Blood samples were obtained from venipuncture in EDTA tubes from fasting patients at the time of hospital admission. Plasma levels of MMPs were evaluated by ELISA in 86 patients affected by AD (28 type A, 58 type B). 30 healthy subjects were used as controls. Aortic tissue samples obtained during surgery were evaluated by immunohistochemistry and western blot for MMP-9 expression. In addition, control tissue was obtained from subjects who underwent heart transplantation (2 male and 1 female). Data were analysed by SPSS statistical software (version 13.0). All data were presented as mean±SEM. A two-tailed unpaired Student t test was used to assess differences in MMP levels. $p<0.05$ was considered statistically significant.

Results Mean plasma values for MMP-9 were higher in patients affected by AD compared to control group at the time of hospital admission (22.78±1.28 ng/ml vs 17.45±1.36 ng/ml $p<0.05$). Moderate/strong expression (++/++++) of MMP-9 was present in both the intima and media layers at the entry site in AD compared to control aortas, Western blot analysis confirmed the expression of MMP-9 in AD whereas no/low (−/+) expression was present in control aortas.

Conclusions This pilot study suggests that MMPs play an important role in the pathophysiology of AD and that the acute phase of AD is characterised by an increase of MMP-9 plasma levels. In this setting, the detection of aortic dissection using biochemical techniques would represent an attractive, rapid, non-invasive and easy to perform diagnostic tool. Future investigation of MMPs and their inhibitors in AD will likely lead to advancements in the diagnosis, prognosis, and treatment of this deadly disease.

e0014 THE ROLE OF PEROXISOME PROLIFERATORACTIVATED RECEPTOR COACTIVATOR 1 IN MYOCARDIAL ISCHAEMIC PRECONDITIONING AND DIAZOXIDE PRECONDITIONING

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Objective Ischemic preconditioning (IPC) is an important endogenous protective mechanism for ischaemia-reperfusion (I/R) injury. Currently, it is believed that opening of the mitochondrial ATP-sensitive potassium channel (mitoKATP channel) plays an important role in IPC. Diazoxide is considered as a mitoKATP agonist that is capable of activating endogenous protective mechanism of the myocardium to antagonise myocardial ischaemic and hypoxic injury. In this study, we applied a rat isolated perfused heart model to observe the expression characteristics of peroxisome proliferator-activated receptor γ coactivator-1 -1α (PGC-1α) and ultrastructural changes of mitochondria after IPC and diazoxide preconditioning (DPC), in order to explore the protective role and mechanism of IPC and DPC during IR injury of the heart.

Methods 30 Wistar rats were used to establish Langendorff isolated perfused heart model. Rats were randomly divided into five groups, six in each group: (1) I/R group: after 30 min of equilibration perfusion, heart was subjected to 30 min of ischaemia and 1 h of reperfusion. (2) IPC group: after 10 min of equilibration perfusion, heart was subjected to two times of 5 min ischaemia and 5 min reperfusion, followed by a 30 min of ischaemia and 1 h of reperfusion. (3) DPC group: after 10 min of equilibration perfusion, heart was given two times of K-H perfusion solution containing diazoxide (100 μmol/l) for 5 min then non-diazoxide K-H perfusion solution for 5 min, followed by 30 min of ischaemia and 1 h of reperfusion. (4) Blank control group: equal amount of saline was used instead of diazoxide. Perfusion procedure was the same as the DPC group. (5) Dimethyl sulfoxide (DMSO) group: DMSO was applied instead of diazoxide, and perfusion procedure was the same as the DPC group. Cardiac apex muscle was cut for frozen section. Immunohistochemistry staining of PGC-1α was performed and average absorbance was calculated. Electron microscope was used for Flameng scoring of the myocardial mitochondria.

Results The average absorbance values of PGC-1α were respectively: I/R group (3.88±1.72), IPC group (10.94±5.23), DPC group (8.40±3.64), blank control group (3.55±1.56) and DMSO group (4.16±0.52). The expression of PGC-1α was significantly increased in IPC and DPC groups and the differences were statistically significant compared to the I/R, blank control and DMSO groups, that is, $p<0.01$ for IPC group and $p<0.05$ for DPC group. However, there was no significant difference between the IPC and DPC groups ($p>0.05$). Flameng score: IPC group (0.44±0.13), DPC group (0.47±0.10), I/R group (1.78±0.14), blank control group (1.70±0.03) and DMSO group (1.68±0.06). Flameng score of the IPC and DPC groups had statistically significant difference as compared to the I/R group, blank control group and DMSO group ($p<0.01$), but no significant difference was detected between the IPC and DPC groups ($p>0.05$).

Conclusion IPC and DPC have a protective effect on myocardial mitochondria, and their mechanism in action may be related to activation and over-expression of PGC-1α.

e0015 EFFECT OF THE ISCHAEMIC PRECONDITIONING ON ISCHAEMIC REPERFUSED MYOCARDIUM OF ELDERLY RAT HEART

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Objective To explore the effect of ischaemic preconditioning (IPC) on ischaemic-reperfused (I/R) myocardium of elderly rat.

Methods 56 male Wistar rats were divided into seven groups of eight rats each: adult control group, adult I/R group, adult IPC group, elderly control group, elderly I/R group, elderly IPC group and elderly enhanced IPC group.

The Langendorff isolated heart perfusion models were established. The control group had a 90-min perfusion without any intervention. The I/R group had a 30-min equilibration period and a 30-min ischaemia and a 30-min reperfusion. The IPC group had a 10-min equilibration, then was elicited by two cycles of 5 min of ischaemia interspersed with 5 min reperfusion prior to 30 min ischaemia and a 30-min reperfusion. The enhanced IPC group had a 10-min equilibration, then was elicited by four cycles of 5 min of ischaemia interspersed with 5 min reperfusion prior to 30 min ischaemia and a 30-min reperfusion. The recovery rate of the left ventricular function, such as cardic output (CO), left ventricular

developed pressure (LVDP), the maximum change rate of left ventricular pressure rise and fall (±dp/dtmax) were recorded. The activity of creatine kinase (CK) in coronary outflow, the activity of malonyldialdehyde (MDA) and superoxide dismutase (SOD) in myocardium were dectected. The percentage of necrotic area were observed.

Results In adult rats, the content of CK (89.48±18.72 U/l vs 115.76±16.72U/l, p<0.01) and MDA (9.53±3.44 nmol/mg vs 16.84±2.29 nmol/mg, p<0.01) were significantly less in IPC group than those in I/R group. In IPC group, the activity of SOD (584.7±122.62 U/mg vs 429.46±85.24 U/mg), the recovery rate of the left ventricular function, including CO, LVDP and±dp/dtmax, were much higher than those in I/R group (78.69±9.68% vs 65.10±8.63%, 83.61±8.46% vs 67.23±8.68%, 81.68±8.68% vs 67.89±6.89%, 89.79±7.78% vs 66.79±8.46%, p<0.01). And the percentage of necrotic area were lower in adult IPC group than in I/R group (5.25±4.33 vs 14.75±8.02, p<0.01). But there were no significant changes between IPC group and I/R group in elderly rats (p>0.05). However, there were great significant changes between enhanced IPC group and IR group in elderly rats, the content of CK (88.60±28.32 U/l vs 105.76±9.64 U/l, p<0.01) and MDA (8.38±3.36 nmol/mg vs 16.80±3.06 nmol/mg, p<0.05), the activity of SOD (558.87±78.66 U/mg vs 433.75±86.65 U/mg, p<0.01), the recovery rate of the left ventricular function, such as CO, LVDP and±dp/dtmax, were much higher than those in I/R group (77.99±10.02% vs 66.26±9.78%, 85.59±6.67% vs 73.90±6.66%, 83.87±9.98% vs 68.90±8.68%, 86.01±7.66% vs 70.39±7.98%, p<0.01). The percentage of necrotic area were lower in elderly IPC group than in I/R group (7.95±6.32% vs 15.68±10.36%, p<0.01).

Conclusion The effect of IPC on ischaemic reperfused myocardium of elderly rats was weaken. Prolonged ischaemia was able to resume the protective effect of IPC on elderly rat hearts.

e0016 TONGXINLUO REDUCES MYOCARDIAL ISCHAEMIA-REPERFUSION INJURY AND NO-REFLOW BY STIMULATING THE EXPRESSION AND PHOSPHORYLATION OF ENOS VIA PKA PATHWAY

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Objective To investigate whether oral administration of Tongxinluo (TXL), a traditional Chinese medicine, at a single low loading dose 1 h before myocardial ischaemia can attenuate ischaemia-reperfusion injury by regulating endothelial nitric oxide synthase (eNOS) via protein kinase A (PKA) pathway.

Methods and results In 90-min ischaemia and 3-h reperfusion model, Minipigs were randomly assigned to four groups (n=8 in each group): (1) Sham; (2) Control; (3) TXL: 0.05 $g \cdot kg^{-1}$ of TXL was gavaged 1 h prior myocardial ischaemia; (4) TXL+H-89 (1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$, an inhibitor of PKA). TXL significantly decreased creatine kinase (CK) activity, reduced the infarct size from 78.5% to 59.2% and no-reflow area from 48.6% to 9.5% (p<0.05), while H-89 completely abolished the reduction of CK activity and necrosis size, and partially diminished the reduction of no-reflow size. TXL enhanced the PKA activity in ischaemic myocardium, increased the expression of PKA, Thr 198 p-PKA and Ser 635 p-eNOS in no-reflow area, and upregulated the expression of eNOS and Ser 1179 p-eNOS in reflow area. H-89 repressed the enhancement of PKA activity and the upregulation of eNOS and Ser 635 p-eNOS, but without great inhibition on the expression of PKA and Thr 198 p-PKA in no-reflow area, and even stimulated the expression of Ser 635 p-eNOS in reflow area.

Conclusion Pretreatment with single low loading dose of TXL 1 h before myocardial ischaemia reduces myocardial no-reflow and ischaemia-reperfusion injury by upregulating the expression of eNOS and p-eNOS (Ser 1179 and Ser 635), and this effect is partially mediated by PKA pathway.

e0017 EFFECTS OF EXTRACORPOREAL CARDIAC SHOCK WAVE THERAPY ON ANGIOGENESIS AND EXPRESSION OF VEGF IN ACUTE MYOCARDIAL INFRACTION PIGS

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Objective To investigate the effect of different methods of extracorporeal cardiac shock wave therapy on angiogenesis and expression of VEGF in acute myocardial infraction pigs, and optimise that of methodology.

Methods 25 miniature swine were randomly divided into three groups: group of cardiac shock wave therapy (n=15), positive control group (n=5), negative control group (n=5). According to the method, the animals of cardiac shock wave therapy were divided three subgroups: standard, prolonged course of treatment and extend area. The number of capillary density, mRNA of VEGF were evaluated and compared between with every group.

Results Compared with control positive group, the number of capillary density (837±54 vs 1856±78, p<0.0001) and expression mRNA of VEGF (20.52±4.94 vs 28.56±6.84) increased in the group of cardiac shock wave therapy, especially, in group of prolonged course of treatment. Whereas, there was no significance in the difference of between standard group and extend area group in capillary density (1633±24 vs 1695±32/mm^2, p>0.05) and mRNA of VEGF (26.31±7.24 vs 27.44±3.59, p>0.05).

Conclusions Successive extracorporeal cardiac shock wave therapy at early stage of acute myocardial infarction could improve myocardial micro-vascular circulation. It will be a new and non-invasive angiogenic therapy.

e0018 VAGUS NERVE-MEDIATED ELECTRICAL REMODELLING OF PULMONARY VEINS IN CHRONIC ATRIAL PACING DOGS WITH OR WITHOUT SUPERIOR VENA CAVA AND AORTIC ROOT FAT PAD

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Xiong Rixin.

Objectives We aim to elucidate the relationship between vagus nerve and the electrical remodelling of pulmonary veins in vagus nerve-mediated atrial fibrillation dogs.

Methods 24 adult mongrel dogs weighing 15–20 Kg were randomly divided into sham operation group (S group, n=8), SVC-Ao fat pad removal group (R group, n=8) and SVC-Ao fat pad reserved group (Re group, n=8). After exposure of superior vena cava and aortic root fat pad, SVC-Ao fat pad was excised in R group dogs, and sewed epicardial pacing lead into high right atrium and successively paced for 6 weeks; for Re group dogs, suture of epicardial pacing leads and pace for 6 weeks, take the sham operation dogs as control. To detect the Left Superior Pulmonary Vein, Right Superior Pulmonary Vein, Left Inferior Pulmonary Vein, Right Inferior Pulmonary Vein respectively, including Sinus Cycle Length (SCL), Effective Refractory Period (ERP), dispersion of ERP (dERP), and the expression of Cx40 and Cx43 by Western Blot, observed the distribution of gap junctions at pulmonary vein sleeves by immunofluorescence and electron microscope.