premature ventricular beats of ex vivo heart, under the acute adrenergic challenge, they significantly enhanced the frequency of premature ventricular beats.
Conclusions BPA promotes arrhythmogenesis in female rat heart by induced DADs, and effects of BPA and E_2 are synergistic instead of additive.

e0181 RENALASE DEFICIENCY IN HEART FAILURE—A NOVEL MECHANISM UNDERLYING CIRCULATING NOREPINEPHRINE ACCUMULATION

doi:10.1136/hrt.2010.208967.181

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Background Sympathetic overactivity and catecholamine accumulation are important characteristic findings in heart failure, which contribute to its pathophysiology. However, the mechanism underlying circulating catecholamine accumulation remains largely unclear.
Objective To identify a novel mechanism underlying norepinephrine accumulation in a rat model of heart failure.
Methods and results Initially, we constructed a rat model of unilateral renal artery stenosis and found that the expression of renalase, a previously identified secreted amine oxidase, was markedly reduced in the ischaemic compared to the non-ischaemic kidney. Subsequently, we utilised an isolated perfused rat kidney model to demonstrate that the clearance rate of norepinephrine decreased with reduction of either perfusion flow or pressure. On the basis of these findings, we hypothesised that the reduced renal blood supply which occurs in heart failure would result in impaired synthesis of renalase by the kidney and consequently reduced degradation of circulating norepinephrine. To verify this, we used a rat model of infarction-induced heart failure caused by ligation of the left anterior descending coronary artery. In these rats, renal expression of renalase, when measured at 4 weeks, was reduced, and this was associated with an increase in circulating norepinephrine.
Conclusions We conclude that impaired synthesis of renalase by the kidney may represent a novel mechanism underlying circulating norepinephrine accumulation in heart failure.

e0182 ELECTROPHYSIOLOGICAL SUBATRATE FOR CANINE ATRIUM

doi:10.1136/hrt.2010.208967.182

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Objective Hypertension is frequently complicated by atrial fibrillation (AF). However, the atrial substrate for AF is not known. This study investigated the electrophysiological properties of atrial repolarisation by monophasic action potential (MAP) in order to explore the mechanism of paroxysmal AF initiation and maintenance.
Methods MAP were recorded from left and right atrium in 14 canine. action potential duration (APD) at 90% repolarisation (APD_{90}), Repetitive atrial firing (RAF, the occurrence of two or more successive premature atrial activations with return cycle of 250 msec or less following atrial stimulation) and APD alternans (the difference in APD between two consecutive beats, were induced by overdrive pacing at LA and RA) were induced by use of programmed stimulation at LA and RA. In the study, episodes of PAF were recorded and analysed.
Results APD_{90} were significantly shorter in the left atrium compared to the right atrium ((157.4±43.5) vs (170.9±37.9), $p<0.05$)). The mean S_1S_2 interval induced RAF was (130±32) ms. 15 RAF were induced in 14 dogs. RAF induced in LA were more than in RA (11 vs 4, $p<0.05$). Alternans of APD were induced at CL of (162±25) ms. 13 APD alternans were induced at LA (8) and RA (5) of 14 dogs. In total, 61 episodes of PAF were induced in 14 canines. 38 episodes of PAF were induced in the left atrium, more than in the right atrium (23, $p<0.05$).
Conclusions The incidence of RAF and alternans was significantly higher in LA than in RA. Heterogeneity between LA and RA repolarisation creates subatrate for re-entrant arrhythmias and vulnerability to atrial fibrillation.

e0183 LIVIN PROTECTS AGAINST CARDIOMYOCYTE APOPTOSIS IN ANOXIA/REOXYGENATION INJURY VIA P38-MEDIATED SIGNAL PATHWAY

doi:10.1136/hrt.2010.208967.183

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Introduction Although anoxic preconditioning (APC) in the myocardium has been investigated for many years, its physiological mechanism is still not completely understood. Increasing evidence indicates that transiently increased resistance to ischaemic damage following APC is dependent on de novo protein synthesis. However, the key effector pathway(s) associated with APC still remains unclear. Livin, a member of the inhibitor of apoptosis protein (IAP) family, since IAP-mediated activation of JNK1, as well as protection against TNF-β and ICE-induced apoptosis. The detailed mechanism underlying its antiapoptotic function in cardiomyocytes has not yet been fully characterised.
Objective To investigate whether Livin expression might be aberrantly induced in cardiomyocytes that were subjected to anoxia/reoxygenation (A/R) injury and to investigate whether Livin might also contribute to cardio-protection after APC.
Methods We cloned a Livin expression vector, transfected it into rat cardiomyocytes, and examined Livin expression in rat cardiomyocytes that were subjected to A/R injury. Moreover, we studied the role of three major MAPK pathways, for example, p38 MAPK, JNK, and ERK1/2, in order to evaluate the molecular mechanism underlying Livin up-regulation and A/R induced cardiomyocyte injury.
Results APC induced an up-regulation of Livin and the transfection of Livin gene into the cardiomyocytes attenuated A/R injury. The inhibition of p38 MAPK by SB203580 abolished both the Livin up-regulation and the cardio-protection provided by APC.
Conclusion APC could act to protect the heart from A/R injury with cooperation from the Livin in addition, it up-regulates Livin expression through a p38 MAPK signalling pathway.

e0184 THE PROTECTION EFFECTS OF TRIMETAZIDINE ON RATS MYOCARDIAL INFRACTION

doi:10.1136/hrt.2010.208967.184

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Objective To observe the myocardial protection effects of trimetazidine on Sprague-Dawley (SD) rats with myocardial infarctions (MI).
Methods 90 SD rats were randomly assigned to normal control group (NL, n=30), Trimetazidine group (T, n=30) and sham-operated group

(S, n=30). The MI model was set up in SD rats by permanent ligation of the left anterior descending coronary artery. In S group suture was through the left anterior descending coronary artery without ligation. Before and after MI, in NL group/S group and T group normal saline and Trimetazidine (0.3 mg/kg) were separately given by gavage. The changes of serum cTnI were observed at 8, 24, 48 h after MI. The changes of serum cTnI in S group was only observed at 24th hour after operations. In 1 week, 2 weeks and 4 weeks after treatment, the areas of myocardial infarction were analysed, and isovolumic systolic left ventricular maximum rate of pressure rise ($+dp/dt_{max}$) and isovolumic diastolic left ventricular maximum rate of pressure drop ($-dp/dt_{min}$) were measured to evaluate the myocardial protection effects of STV-1Na. The groups were compared with one-way analysis of variance (ANOVA) test. A value of p 0.05 between NL group and T group. But the serum cTnI level at 24 h after MI decreased in T group (22.7±5.3 ng/ml, $p<0.05$) compared with NL group (42.3±5.4 ng/ml). The serum cTnI level at 24 h in NL group and T group was significantly increased compared with S group (1.59±1.42 ng/ml) ($p<0.01$). Trimetazidine (0.248±0.021, $p<0.01$) decreased significantly the myocardial infarction area compared with NL group (0.362±0.027). The infarction areas in NL group (0.362±0.027) and T group (0.248±0.021) increased significantly compared with S group (0.072±0.1445) ($p<0.01$). In 1 week after MI, the $+dp/dt_{max}$ in T group (7535±265) was not significantly different ($p>0.05$) compared with NL group (6702±329), and the $-dp/dt_{min}$ in T group (−5511±400) was no significant difference ($p>0.05$) compared with NL group (−5400±339). In 2 weeks after MI, the $+dp/dt_{max}$ in T group (8101±313) increased significantly compared with NL group (5868±412) ($p<0.01$), and the $-dp/dt_{min}$ in T group (−6514±493) decreased significantly compared with NL group (−4750±463) ($p<0.05$). In 4 weeks after MI, in T group (7629±374) the $+dp/dt_{max}$ increased significantly compared with NL group (5876±200) ($p<0.01$,), and the $-dp/dt_{min}$ in T group (−5883±436) decreased significantly compared with NL group (−4546±279) ($p<0.05$). The $-dp/dt_{max}$ in T group and NL group were significantly decreased ($p<0.05$) compared with S group in 1 week, 2 weeks and 4 weeks after the operation. The $+dp/dt_{min}$ in T group and NL group were increased ($p<0.05$) compared to S group in 1 week, 2 weeks and 4 weeks after the operation.

Conclusions Trimetazidine has myocardial protection effects on myocardial infarction and improves myocardial systolic and diastolic function in SD rats with acute myocardial infarction.

e0185 THE EFFECT OF CLASSIC MAPKERK5 PATHWAY ON HYPERTHERMIA INDUCED VENTRICULAR CARDIOMYOCYTES DAMAGE

doi:10.1136/hrt.2010.208967.185

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Objective In China, the occurrence rule, mechanisms and prevention measures of diseases under extreme weather are few reported and which (del) only focused (focus) on pathophysiological manifestation rather than molecular mechanism level. So (del) (Thus,) further study in this work will be carried out from molecular cytological level. This study explored (del) the effect of hyperthermia on ventricular cardiomyocytes and the participative roles of classic MAPK - ERK5 pathways on hyperthermia induced cardiomyocytes damage.

Methods Neonatal rat ventricular cardiac myocytes (NRVM) were isolated from the hearts of 1- to 3-day-old Sprague Dawley rats. NRVM were exposed to a hyperthermia (42°C, 60 min) environment. The degree of cell damage was observed at 0, 4, 8, 12, 16, and 24 h after recovery. The effects of hyperthermia on myocardial cells were probed by evaluating lactate dehydrogenase (LDH) release, cells beating rate and rhythm and viability (assessed by MTS assay). Apoptosis was detected using an annexin V-FITC/propidium iodide (PI) staining binding assay. Using western blot semi-quantitating Bim and extracellular signal-related kinase (ERK5) /phosphorylated extracellular signal-related kinase (p-ERK)(??). Using PD98059 as an inhibitor of MAPK pathways, semi-quantitating Bim by western blot(??).

Results 1. The beating rate of myocardial cells was slightly decreased immediately after temperature recovery, (del)(and) gradually decreased with time prolonged, and the (del)(.) Cell viability was (del) decreased ($p<0.05$);(and) the activity of lactate dehydrogenase was (del) increased ($p<0.05$). 2. Based on western blot analysis, the elevation of Bim protein expression occurred at recovery time (8 h) and (del)(,) peaked at 12 h(,) then went down slowly at 24 h after hyperthermia ($p<0.05$); ERK5 pathway responding to hyperthermia treatment ($p<0.05$). 3. Levels of Bim slightly decreased at (in) PD98059 group compared with hyperthermia group ($p<0.05$).

Conclusions Hyperthermia induces myocardial cells damage with apoptosis as main type. ERK5 participated the injure process of hyperthermia and Bim played its role via a MAPK-ERK5 pathway.

e0186 STUDY ON THE MECHANISM OF INHIBITORY EFFECT OF CTLA-4IG FUSION PROTEIN ON ATHEROSCLEROSIS IN APOE DEFICIENT MICE

doi:10.1136/hrt.2010.208967.186

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Objective To investigate the mechanism of inhibitory effect of CTLA-4Ig fusion protein on atherosclerosis in mice with an apolipoprotein-E gene defect fed on cholesterol diet.

Methods 30 male 10-week-old apoE(-/-) mice were fed on cholesterol diet and divided into CTLA-4Ig treatment group, IgG1 group and PBS group at random, 10 in each. The three groups were given intraperitoneal injection of CTLA-4Ig (10 μg per time), Rat-IgG1 (10 μg per time), (and) PBS (100 μl per time) respectively, twice a week, for 12 weeks. Followed by a 12-week treatment, the whole aorta from the root to crotch of iliac artery was separated after anaesthesia with the intraperitoneal injection of 1% pentobarbital and the whole (total) blood was taken to obtain serum. Subsequently, the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, the lipid-soaking extent intra-plaque and the content of collagen fibrils and smooth muscle cells intra-plaque were analysed by image-processing soft. The serum concentration of total cholesterol, CRP, sICAM-1, IFN-γ, IL-10, and TGF-β1 were measured.

Results There were typical atherosclerotic plaque in apoE(-/-) mice fed on cholesterol diet after 12 weeks and it was light in the CTLA-4Ig group. There were statistical value of difference in the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, the lipid-soaking extent intra-plaque, and the content of collagen fibrils in three groups (p all<0.05). It was found that the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, and the lipid-soaking extent intra-plaque were significant lower and the content of collagen fibrils was higher in the CTLA-4Ig group than those in the IgG1 group and PBS group (p all<0.05), but there was no significant difference in those between the IgG1 group and PBS group (p all>0.05). There were no significant difference in content of smooth muscle cells in three groups ($p>0.05$). There were no significant difference in serum concentration of total cholesterol in three groups ($p>0.05$). There were statistical value of difference in the serum concentration of CRP,