tissue, while non-invasively tracking stem cells in vivo is a hurdle for its clinical application. Our group has addressed this concern by developing a bioluminescence tomography (BLT) prototype system with micro-CT (MicroCT) registration approach. In this subsequent study, we aimed to assess the mesenchymal stem cells (MSCs) as well as statins by this multimodality imaging platform and other strategies in the model of peripheral arterial disease (PAD).

Methods MSCs were isolated from adipose tissue of the transgenic mice carrying double-fusion reporter genes: firefly luciferase and enhanced green fluorescent protein (Fluc-eGFP). After eGFP flow sorting, 1×10^7 of Fluc-eGFP positive MSCs were injected into the ischaemic hindlimb, created by routine ligation, of the adult nude mice (n=20) with/without rosuvastatin pretreatment. Then we imaged the animals by our 3D BLT and MicroCT modalities as well as a 2D bioluminescence imaging (BLI). Detailed quantitative reconstruction were performed within the mice by adaptive hp finite element method (hp-FEM). Histological and molecular analysis are used to confirm MSCs' location and angiogenesis.

Results 1 week after engraftment, reconstructed BLT total power in MSCs group was 22.4±3.1 nW, while the 2D BLI data was $1.7\times10^6\pm2.1\times10^5$ photons/s/cm^2/sr. The total power decreased gradually from week 1 to week 6, from mean 22.4 nW to 1.9 nW, demonstrating MSCs' survival and proliferation. The combined treat by MSCs and rosuvastatin exhibited longer signal and higher power of the MSCs ($p<0.01$), which is also confirmed by 2D BLI with robust correlation ($r^2=0.93$). Moreover, BLT with MicroCT provided detailed 3D images of MSCs and angiogenesis in the hindlimbs. Immunohistology, RT-PCR and Western Blot showed that MSCs with/without rosuvastatin recovered vessel density in contrast to the control and its signal pathway.

Conclusions Versatile 3D molecular imaging modalities facilitate the super spatiotemporal visualisation and quantification of the MSCs in the ischaemic hindlimb, while MSCs hold beneficial potential for treating PAD and its survival environment in vivo may be promoted by rosuvastatin.

e0190 STUDY ON THE ROLE OF CD4CD25TREG ON ATHEROSCLEROSIS IN APOE MICE

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Objective To evaluate the effectiveness of right ventricular septum (RVS) pacing for the treatment of arrhythmia.

Methods We searched the electronic bibliographic databases, including Cochrane Central Register of Controlled Trials (Issue 1, 2010), PubMed (1994～2010.5). EMBASE (1994～2010.5), CNKI (1994～2010.5), VIP (1994～2010.5), Wanfang database (1994～2010.5) to assemble the randomised controlled trials (RCTs) of RVS Pacing compared with right ventricular apical (RVA) pacing. Two reviewers evaluated the quality of included studies based on the Handbook 5.0.2 and extracted data independently. Meta-analysis was performed by RevMan 5.0 software.

Results 35 RCTs involving 2054 patients were included. The results of meta-analysis showed: compared with the RVA pacing, RVS pacing could significantly reduce the QRS wave duration (MD=−0.05, 95% CI −0.07 to −0.02), significantly increase the left ventricular ejection fraction of 3 months and 18 months after operation (MD=7.10, 95% CI 3.03 to 11.17); (MD=7.44, 95% CI 5.46 to 9.42). 3 months later, there was no significant difference between the two groups with regard to pacing threshold (MD=−13.88, 95% CI −29.75 to 2.00), Compared with RVA, RVS was associated with a significant reduction in threshold perception current (MD=−0.73, 95% CI −29.75 to −0.12) and impedance (MD=−75.12, 95% CI −35.53 to −14.71).

Conclusion RVS pacing can give patients a good physiological state which is more consistent with biventricular electric conduction, and lead to haemodynamic improvement. RVS pacing might be expected to become a preferred site of ventricular pacing.

e0191 FREE FATTY ACIDS INHIBIT THE EXPRESSION OF ANTICOAGULANT THROMBOMODULIN PROTEIN C SYSTEM AN IMPLICATION FOR THE DEVELOPMENT OF THE PROTHROMBOTIC STATE IN METABOLIC SYNDROME

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Background Metabolic syndrome displays a significant prothrombotic state which renders patients highly susceptible to myocardial infarction, ischaemic stroke and peripheral vascular diseases. Although many clinical studies showed that the prothrombotic state is a key feature of metabolic syndrome, the pathogenesis and mechanisms involved are not completely understood. Metabolic syndrome is often characterised by obesity and subsequent high circulating concentrations of free fatty acids (FFAs). Thrombomodulin (TM)- protein C system is a key endogenous anticoagulant system. We therefore examined the effects of FFAs on the expression of TM- protein C system and the mechanisms involved.

Methods 8 to10 weeks of male wide-type mice were divided into two groups. One group of mice (n=15) were fed a chow diet, while the other group of mice (n=15) were fed a high-fat diet for 20 weeks. Tail-bleeding time and the occlusion time induced by $FeCl_3$ were recorded. Circulating free fatty acids were measured. Primary human aortic endothelial cells (HAECs) were cultured and treated with different dose of palmitic acid (PA). TM expression and protein C activation were measured with western blot and RT-PCR. The effects of JNK, p38 stress pathways and transcriptional factor Foxo1 involved in PA-inhibited TM expression were elucidated with siRNA-induced gene silencing and DNA plasmids-induced gene over-expression.

Results Mice fed a high-fat diet showed notably higher blood level of FFAs ($p<0.05$), and a shortened tail-bleeding time and a shortened occlusion time induced by $FeCl_3$ ($p<0.01$). Furthermore, TM was down-regulated in obese mice ($p<0.001$). PA significantly decreased the expression of TM and protein C activation in a dose-dependent fashion ($p<0.01$). Silencing JNK and p38 with specific siRNAs decreased PA-induced thrombomodulin suppression ($p<0.01$), while wide type of JNK plasmid can enhance PA's inhibitory effect on TM expression ($p<0.05$). When endothelial cells were transiently transfected with Foxo1−specific siRNAs, PA-induced inhibition of TM expression was significantly decreased ($p<0.001$). Furthermore, wide type and constitutively active of Foxo1 plasmids enhanced PA's inhibitory effect of TM expression ($p<0.05$).

Conclusion In summary, a high-fat diet induced high elevated circulating FFAs level, and the prothrombotic state in mice. PA inhibited the expression of TM and the activation of protein C in endothelial cells. JNK, p38/Foxo1 pathway mediated free fat acids' inhibitory effect of TM expression, which may be a new therapeutic target in treating and reducing cardiovascular and cerebrovascular complications of the metabolic syndrome.

e0192 A METAANALYSIS OF RIGHT VENTRICULAR SEPTUM PACING

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Yulong Zhang, Feng Bai, Xiaowei Zhang, Hui Pan.

Objective To evaluate the effectiveness of right ventricular septum (RVS) pacing for the treatment of arrhythmia.

Methods We searched the electronic bibliographic databases, including Cochrane Central Register of Controlled Trials (Issue 1, 2010), PubMed (1994～2010.5). EMBASE (1994～2010.5), CNKI (1994～2010.5), VIP (1994～2010.5), Wanfang database (1994～2010.5) to assemble the randomised controlled trials (RCTs) of RVS Pacing compared with right ventricular apical (RVA) pacing. Two reviewers evaluated the quality of included studies based on the Handbook 5.0.2 and extracted data independently. Meta-analysis was performed by RevMan 5.0 software.

Results 35 RCTs involving 2054 patients were included. The results of meta-analysis showed: compared with the RVA pacing, RVS pacing could significantly reduce the QRS wave duration (MD=−0.05, 95% CI −0.07 to −0.02), significantly increase the left ventricular ejection fraction of 3 months and 18 months after operation (MD=7.10, 95% CI 3.03 to 11.17); (MD=7.44, 95% CI 5.46 to 9.42). 3 months later, there was no significant difference between the two groups with regard to pacing threshold (MD=−13.88, 95% CI −29.75 to 2.00), Compared with RVA, RVS was associated with a significant reduction in threshold perception current (MD=−0.73, 95% CI −29.75 to −0.12) and impedance (MD=−75.12, 95% CI −35.53 to −14.71).

Conclusion RVS pacing can give patients a good physiological state which is more consistent with biventricular electric conduction, and lead to haemodynamic improvement. RVS pacing might be expected to become a preferred site of ventricular pacing.

e0193 A CRITICAL ROLE OF CKIT IN CXCR4-MEDIATED PROGENITOR CELL NICHE MAINTENANCE AND MOBILISATION

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Therapeutic mobilisation of bone marrow progenitor cells (BM PCs) is a novel strategy for cardiovascular repair. Both CXCR4 antagonism and c-kit blockade can rapidly and potently mobilise BM PCs; however, the functional interaction between CXCR4 and c-kit remains unclear. We treated c-kit-deficient (c-kit $^{W/W\text{-}V}$) and wild-type (WT) mice with CXCR4 antagonist AMD3100 and evaluated PCs in the peripheral blood (PB) with a colony-forming assay. AMD3100 treatment for 2 h dramatically increased the number of PCs in the PB in WT mice but not in c-kit $^{W/W\text{-}V}$ mice (c-kit$^{W/W\text{-}V}$ vs WT: 30 vs 194 colonies/ml blood, p<0.01). To confirm that c-kit deficiency impairs BM PC mobilisation by AMD3100, we developed an in vivo BM niche clearance/occupation assay. The c-kit $^{W/W\text{-}V}$ and WT mice were firstly treated with AMD3100 to remove PCs from the niche, and 2 h later, transplanted with eGFP transgenic BM cells to competitively occupy the niche. After 3 h, BM cells were isolated and analysed by FACS. Despite the total donor-derived (eGFP+) cells were similar between WT and c-kit $^{W/W\text{-}V}$ recipients, the donor-derived CXCR4-expressing PCs, including eGFP$^+$CXCR4$^+$Lin$^-$, eGFP$^+$CXCR4$^+$Lin$^-$Sca1$^+$, and eGFP$^+$CXCR4$^+$Lin$^-$ckit$^+$ cells, were much fewer in the c-kit $^{W/W\text{-}V}$ mice (c-kit$^{W/W\text{-}V}$ vs WT: 19.7% vs 30.6%, p<0.01; 20.3% vs 29.1%, p<0.05; and 6.7% vs 17.9%, p<0.001, respectively), indicating that c-kit deficiency specifically reduced the capacity of AMD3100 to clear the CXCR4$^+$ PC niche. To better understand the mechanisms, we designed an ex vivo adhesion assay. Mouse BM mononuclear cells were isolated and applied onto plates pre-coated with BM stromal protein VCAM-1, followed by addition of AMD3100. The adhesion of BM cells to VCAM-1 resulted in marked c-kit phosphorylation. Interestingly, AMD3100 significantly attenuated the c-kit phosphorylation. In vivo, AMD3100 treatment for 15 min significantly reduced the level of phospho-c-kit in the BM as assessed by Western blotting of the BM lysates. Consistently, immunofluorescence staining of BM niche demonstrated a significantly lower ratio of phospho-ckit$^+$/total ckit$^+$ PCs in AMD3100-treated mice as compared to PBS-treated mice. We conclude that c-kit plays a critical role in CXCR4-mediated BM PC niche maintenance and mobilisation.

e0194 SRC FAMILY KINASE SFK IS ESSENTIAL FOR RECRUITMENT OF BONEMARROW PROGENITOR CELLS TO THE ISCHAEMIC MYOCARDIUM

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Background The G protein-coupled receptor CXCR4 and its ligand stromal−cell derived factor 1 (SDF-1) play an important role in directing progenitor cells (PC) homing to ischaemic tissue. The Src family protein kinases (SFK) can be activated by, and serve as effectors of, G proteins. However, whether SFK play a role in SDF-1/CXCR4-mediated PC homing is unknown.

Methods and results To investigate whether SDF-1−CXCR4 signalling activates SFK, we isolated mouse bone marrow mononuclear cells (BM MNCs) and applied onto VCAM1-coated plates, followed by addition of CXCR4 agonist SDF-1 and/or antagonist AMD3100. SDF-1 rapidly (in 2 min) and dose-dependently increased phosphorylation (activation) of Lyn, a major SFK in the BM; AMD3100 attenuated the SDF-1−induced Lyn phosphorylation. Notably, SDF-1 treatment did not increase Lyn phosphorylation in the BM MNCs isolated from Mx1-cre$^+$CXCR4$^{fl/fl}$ mice in which the CXCR4 gene had been deleted. To investigate whether SFK play a role in SDF-1/CXCR4-mediated chemotaxis, we performed Boyden chamber migration assay; SU6656, a SFK inhibitor, significantly inhibited BM-MNC migration towards SDF-1 (p<0.001, n=4). To investigate whether SFK play a role in SDF-1/CXCR4-mediated BM-MNC homing to ischaemic heart tissue, we isolated BM MNCs from CXCR4$_{BAC}$:eGFP transgenic mice and injected 1×10^6 cells into WT and SDF-1$_{BAC}$:SDF1-RFP transgenic mice (in which the expression of SDF1-RFP fusion protein is driven by the SDF-1 genomic regulatory sequence and the level of total SDF-1 protein is doubled) that had undergone surgical myocardial infarction 8 h earlier. Some recipient mice also received two i.p. injections of SU6656 (6 mg/kg) at the time of cell injection and again 4 h later. We found a significantly greater amount of eGFP+ cells (1.6-fold, p<0.01, n=5) and eGFP+c-kit+ cells (1.9-fold, p<0.01, n=5) recruited in the infarct border area of the SDF-1$_{BAC}$: SDF1-RFP recipients than in WT recipients. SU6656 treatments significantly reduced the amount of eGFP+ cells and eGFP+c-kit+ cells (p<0.01, n=5) in both WT and SDF-1$_{BAC}$: RFP recipients and abrogate the difference between the two groups.

Conclusions SFK play a critical role in SDF-1/CXCR4−mediated BM PC homing to the ischaemic cardiac tissue thus may provide a target for modulation of tissue repair.

e0195 RESEARCH ON THE EVALUATION OF OCT ON ATHEROSCLEROTIC PLAQUES OF CAROTID ARTERY IN RABBITS WITH INSULIN RESISTANCE

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Objective The purpose was to analyse the feasibility and repeatability of OCT to evaluate atherosclerotic plaque diagnosed by pathologic examination of common carotid artery in rabbits with insulin resistance.

Methods There were 26 male China White rabbits. 20 rabbits were made atherosclerotic with a high-cholesterol diet after injury of the