



Results: Although slope and offset of the baroreflex peripheral arc (linear relation) were similar, the neural arc response (inverted sigmoid curve) range was attenuated in SHR ($71 \pm 2\%$ vs. $91 \pm 3\%$, $P < 0.01$). The operating-point AP was higher in SHR than in WKY (144 ± 6 mm Hg vs. 109 ± 5 mm Hg, $P < 0.01$).

Although NE was higher in SHR at baseline condition (403.1 pg/ml vs. 203.2 pg/ml, $P < 0.01$), AP response to phenylephrine was similar (linear relation), suggesting preserved peripheral response to sympathetic activity.

Conclusion: The baroreflex equilibrium diagram indicates that baroreflex regulation of SNA rather than the cardiovascular response to SNA plays a critical role in the development of hypertension in SHR.

doi:10.1016/j.hlc.2011.05.023

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A Novel Recombinant CD39 Targeting Activated Platelets via a Fused Single-chain Antibody: Achieving Efficient Anti-coagulation While Minimising Bleeding Side Effects by Clot Directed Enrichment

J. Hohmann^{1,*}, S. Krajewski^{1,2}, F. Jia¹, H. Nandurkar³, A. Straub^{1,2}, K. Peter¹

¹ Baker IDI Heart and Diabetes Institute, Australia

² University of Tübingen, Germany

³ Medicine - St Vincent's Hospital, Australia

Introduction: CD39, an NTPDase with strong antithrombotic properties, has previously been shown to be protective in models of stroke, transplantations, pulmonary embolism and myocardial infarctions by hydrolysing/removing the platelet agonist ADP. However CD39's high potency comes at the cost of an increased bleeding risk. We hypothesise that targeting CD39 to activated platelets allows localised enrichment at the growing thrombus despite a low and safe systemic concentration.

Methods and results: CD39 was recombinantly fused to a single-chain antibody specific to activated platelets via selective binding to the active conformation of GPIIb/IIIa. The fusion construct was produced in Hek293 and purified using a His-tag chromatography step. Targeted-CD39 was significantly more effective at preventing platelet activation (flow cytometry) and platelet aggregation (aggregometry) with ADP and collagen as agonist than

its non-targeted control (CD39 fused to a non-functional mutated single-chain antibody). Most importantly in a mouse model of ferric chloride-induced carotid artery thrombosis, targeted-CD39 was protective against vessel occlusion at a concentration at which the non-targeted-CD39 was ineffective ($p < 0.005$). At the same concentration no tail bleeding prolongation was observed for the targeted-CD39 while the ineffective non-targeted-CD39 showed a bleeding tendency ($p < 0.01$).

Conclusion: Targeting CD39 to its desired site of action enables administration of such a low concentration as to avoid the previously observed bleeding tendencies while still being a highly effective antithrombotic drug. Thus, enriching CD39 to activated platelets at growing thrombi prevents the previously limiting bleeding side effects and advances CD39 towards potential clinical use.

doi:10.1016/j.hlc.2011.05.024

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Acute Pulmonary Embolism (PE)—Is Echocardiography Underutilised in Regional Australia

V. Tyagi^{1,*}, N. Kutaiba², M. Yates²

¹ Logan Hospital, Australia

² Ballarat Base Hospital, Ballarat, Australia

Background: Echocardiography is recommended after acute pulmonary embolisms (PE) to risk stratify patients at risk of developing chronic thromboembolic pulmonary hypertension (CTEPH) and then at six to eight weeks if elevated pulmonary artery systolic pressure (PASP) is found initially. The true incidence of CTEPH is unknown but ranges from 0.01% to 3%. PASP >50 mm Hg and age >70 years are risk factors for CTEPH. CTEPH is insidious in onset and missed in many patients. It is potentially curable if diagnosed early.

Methods: A retrospective one year case note review was undertaken of all confirmed (CT pulmonary angiography proven) PE cases (66 patients) admitted in Ballarat Base Hospital. Clinical variables, management and echocardiography reports were reviewed.

Results: Mean age was 59 years. Forty-seven percent of patients had troponin measured at diagnosis (Males 48%, females 44%) those with elevated troponin I (>0.04 ng/L) had prolonged hospital stay compared to normal result (10 days versus 5.4 days). Sinus tachycardia was most common ECG finding (30.3%). S1Q3T3 pattern on ECG was found in six patients. Deep venous thrombosis (DVT) accompanying PE was confirmed in 33% (22) patients. Echocardiogram was done in 45% (30) patients, with three patients (10%) all aged <70 years having pulmonary artery systolic pressure >50 mm Hg. Thus 33 eligible patients did not have echocardiogram.

PE patients	Echo	No echo	PASP >50 mm Hg
66	30	33	3

Conclusion: Echocardiography is underutilised in acute PE in some regional hospitals in Australia. Elevated troponin levels are associated with increased short term morbidity in acute PE. There is a high proportion of accompanying DVT with acute PE.

doi:10.1016/j.hlc.2011.05.025

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Assessment of Optimal Cell Therapy for the Angiogenesis Response in a Murine Hindlimb Ischaemia Model using CD34⁺ cells and Endothelial Progenitor Cells

C. Hsu^{1,2,*}, R. Chow², L. Dunn², K. Chan^{1,2}, M. Guillou², D. Celermajer^{1,2}, M. Ng^{1,2}

¹ Royal Prince Alfred Hospital, Australia

² Heart Research Institute, Australia

Purpose: Therapeutic angiogenesis using stem/progenitor cells has been the focus of recent research. CD34⁺ cells and endothelial progenitor cells (EPCs) have been found to promote angiogenesis. This study aimed to assess the angiogenic potential of CD34⁺ cells and EPCs using different modes of delivery *in vivo*.

Methods: Human EPCs were isolated from cell cultures and CD34⁺ cells were purified from buffy coat using microbeads. Unilateral hindlimb ischaemia was introduced on BalbC nu/nu mice. At 24 hours post-surgery 2×10^5 CD34⁺ cells, EPCs, or PBS control were injected intravascularly (IV) to the tail vein, or intramuscularly (IM) into adductor muscle. Laser Doppler perfusion imaging (LDPI) was used to assess flow recovery. Adductor muscle was assessed for capillary density.

Results: By day 10 post-surgery mice injected IM showed better recovery in LDPI, compared with those mice injected IV (LDPI 0.30 ± 0.06 vs. 0.15 ± 0.05 ; $P < 0.05$). This was true for CD34⁺ cells, EPCs and PBS. Mice receiving CD34⁺ cells IM recovered better from day 10 to 21 when compared to mice injected IM with EPC or PBS (day 21 LDPI 0.45 ± 0.04 , 0.35 ± 0.05 and 0.28 ± 0.05 , respectively; $P < 0.05$). Immunohistochemical staining of adductor muscles revealed capillary density was highest in mice receiving CD34⁺ cells IM, compared with those mice receiving EPC IM, PBS IM, CD34⁺ IV, EPC IV, and PBS IV ($155 \pm 9\%$, $140 \pm 5\%$, $135 \pm 7\%$, $115 \pm 10\%$, $110 \pm 10\%$ vs. 100% for PBS IV, respectively; $P < 0.05$).

Conclusions: This study provides evidence that direct IM injection of CD34⁺ cells into the ischaemic hindlimb delivers the best angiogenesis outcome among various cell therapy techniques investigated in this study.

doi:10.1016/j.hlc.2011.05.026

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Association of Left Ventricular Motion and Central Blood Pressure Waveform Morphology

K. Cheng, J. Cameron, M. Tung, P. Mottram, I. Meredith, S. Hope*

MonashHEART and Monash Cardiovascular Research Centre, Southern Clinical School, Monash University, Melbourne, Australia

Background: Central blood pressure is a determinant of cardiovascular outcome however it can be described by parameters other than systolic and diastolic pressure with central augmentation index (AIx) often utilised. Although generally considered as determined by peripheral pressure wave reflection the not all data are consistent with this interpretation of AIx. We hypothesised that the velocity of the base of the heart during systole may influence central pressure waveform morphology, including the augmentation index.

Methods: We studied the carotid pressure waveform, aortic stiffness and endothelial function in 20 healthy young males (full data available in 19). Arterial stiffness was measured by carotid-femoral pulse wave velocity (cPWV), endothelial function by Peripheral Arterial Tonometry and central BP waveform by carotid applanation tonometry. Basal cardiac motion was assessed with pulsed wave tissue Doppler imaging of the anterior mitral annulus.

Results: Carotid AIx decreased after the administration of GTN by $11.3 \pm (\text{sem})4.6\%$ ($P = 0.02$) however time to the inflection point (Ti) did not change. During systolic contraction at both baseline and after GTN the time to peak annular systolic velocity was directly related to, and always preceded, carotid Ti ($R^2 = 0.81$; $p < 0.01$). Carotid Ti and AIx were not related to cPWV or endothelial function.

Conclusion: Rather than only being a consequence of arterial properties Ti, and therefore central AIx, may be substantially determined by left ventricular function. These findings question the interpretation of central AIx as a measure of pressure wave reflection and aortic stiffness and therefore impact on its interpretation in diagnosis and treatment of cardiovascular risk.

doi:10.1016/j.hlc.2011.05.027

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Augmentation Index (AIx) and Augmentation Pressure (AP) in a Cardiac Population

L. Wong^{1,2,*}, E. Shanehsaz^{1,2}, T. Hong¹, J. Chiha², P. Kovoor², P. Mitchell¹, A. Thiagalingam²

¹ Centre for Vision Research, Department of Ophthalmology and Westmead Millennium Institute, University of Sydney, Australia

² Department of Cardiology, Westmead Hospital, Sydney, Australia

Background: Arterial stiffness and pressure wave reflection are associated with cardiovascular risk. The AIx is