

# ABSTRACTS

## SA HEART CONGRESS 2009

### Risk factors associated with six-month mortality following vascular surgery

**Jamila Khatoon Adam, Bruce Biccard, Sumansha Nepaul and Wafaa N.S. Rmah**

Durban University of Technology, Department of Biomedical and Clinical Technology, Durban, KwaZulu-Natal, South Africa

**Introduction:** Every day a large number of patients undergo vascular surgery, but not all of these patients survive surgery. By looking at risk factors identified in previous studies the outcome of some patients' surgery may be predicted. However, there is a limited number of studies on South African patients with regards to risk factors associated with post-operative vascular surgical survival. The aim of this study was to identify risk factors associated with six-month mortality following vascular surgery.

**Methods:** Patients selected (>39y) for this study were scheduled for both elective and emergency vascular surgery at Inkosi Albert Luthuli Central Hospital, between June 2003 and July 2007. Demographic data from the hospital computerised data base was extracted, as well as patients' date of surgery and their inpatient and outpatient visit dates. The patients' hospital visits following surgery were analysed. 283 patients were included. The risk factors examined in this study were; male sex, history of smoking, ischaemic heart disease, congestive cardiac failure; cerebrovascular accident, diabetes, hypertension, creatinine  $>180 \mu\text{mol.L}^{-1}$ , chronic beta-blockade, major vascular surgery, mean daily heart rate (HR) the day before surgery; mean daily HR on the third postoperative day and mean daily systolic blood pressure (SBP)  $< 100$  or  $> 179\text{mmHg}$ .

These factors were entered into a bivariate cox regression analysis. Risk factors with a  $p < 0.1$  were entered into a multivariate analysis. We defined mortality as those patients that did not survive six months post surgery.

**Results:** There were 21 intermediate-term non-survivors and 262 survivors. Two risk factors, hypertension and diabetes were entered into a multivariate analysis. Hypertension had a hazard ratio of 3.59 (95% Confidence Interval (CI) 0.83-15.4,  $p=0.09$ ) and diabetes had a hazard ratio of 2.28 (95% Confidence Interval (CI) 0.94-5.52,  $p=0.07$ ).

**Conclusion:** Diabetes and hypertension were bivariate predictors of intermediate term mortality following vascular surgery.

### The anti-aging factor Sirtuin I: a possible role in cardioprotection?

**T. Adam, L.H. Opie and S. Lecour**

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Introduction:** Ischaemic preconditioning (IPC) is a process whereby brief episodes of alternating ischaemia and reperfusion prior to a prolonged lethal episode of ischaemia-reperfusion can reduce myocardial damage. However, the mechanisms mediating this cardioprotective effect remain unclear. Sirtuin I (SirtI) is a nicotinamide adenine dinucleotide-dependent class III histone deacetylase which regulates a myriad of cellular processes including anti-aging. Sirtuins can protect the heart by enhancing cardiomyocyte survival and oxidative stress resistance, as well as by preventing increases in cardiac hypertrophy, fibrosis and ventricular dysfunction associated with aging. We propose that SirtI activation plays a role in IPC-mediated cardioprotection.

**Methods:** Cultured C2C12 mouse skeletal muscle myotubes were preconditioned for 30 mins by exposure to hypoxia, or by pretreatment with the potent sirtuin activator resveratrol (RSV). Subsequent to a 1 hour washout period, cells were subjected to a simulated ischaemic insult for 8 hours. To investigate whether SirtI is involved in IPC, 50 M or 50 mM of nicotinamide (NAM), a sirtuin inhibitor, was given during the IPC stimulus. Cell viability was assessed at the end of sustained simulated ischaemia using the trypan blue exclusion test. In addition, SirtI deacetylase activity was measured after 30 mins of IPC.

**Results:** IPC increased cell viability to 61.91.7% ( $p < 0.001$  compared to the simulated ischaemic control: 47.11.9%). Similarly, RSV treatment mimicked IPC, improving cell viability to 69.32.9%. Incubation of C2C12 myotubes with both concentrations of NAM did not abolish the protective effect of IPC. Sirt1 deacetylase activity measured after IPC was similar to control cells (0.390.09 AU for IPC versus 0.420.08 AU for control cells).

**Conclusion:** These data suggest that cardioprotection by IPC is independent of Sirt1 activation.

## An unusual case of endomyocardial fibrosis in a 2 year old child

**P.E. Adams, G. Dumani, H. Ntsinjana and A.M. Cilliers**

Division of Paediatric Cardiology, Department of Paediatrics and Child Health, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

**Introduction:** Endomyocardial fibrosis accounts for a significant proportion of cardiovascular presentations of children in endemic areas. The cause of this cardiomyopathy remains elusive. However, this case strongly suggests a genetic aetiology.

**Case description:** We present a one year nine month old male child who was admitted with a cough and generalised body swelling for two days. He was described as previously well, with a single previous admission for pneumonia. He was born in South Africa of a Mozambican father and a South African mother. He has never travelled to Mozambique. On admission to Chris Hani Baragwanath Hospital he was diagnosed with a large pericardial effusion and anasarca.

Emergency treatment included pericardial drainage and institution of TB treatment. The effusion persisted despite TB treatment. Initial results were not suggestive of TB. Investigations for other possible causes of the effusion were unhelpful. Of note, there was no eosinophilia. The echocardiogram showed markedly dilated atria, an aneurysm arising from the RV and features of restrictive cardiomyopathy. A cardiac catheterisation was undertaken. The haemodynamic data showed restrictive physiology of both ventricles and a myocardial biopsy confirmed the diagnosis of endomyocardial fibrosis.

**Discussion:** Endomyocardial fibrosis is the most common cause of restrictive cardiomyopathy. In endemic areas of Africa such as Mozambique it has been associated with 20% of all heart failure (Mocumbi et al). The aetiology remains unknown. The study patient is most unusual in presenting at such a young age. The only apparent connection to an endemic area is a possible genetic link by virtue of his father being Mozambican.

**Conclusion:** The diagnosis of endomyocardial fibrosis should be excluded in all age groups presenting with a restrictive cardiomyopathy. A genetic aetiology is likely but needs further elucidation.

## A review of Takotsubo cardiomyopathy in Johannesburg

**G. Angel, P. Manga, N. Patel, M. Allison and R. Lamparelli**

Division of Cardiology, CM Johannesburg Academic Hospital, University of Witwatersrand and Milpark & Sunninghill Hospitals, Johannesburg, South Africa

**Background & aims:** Takotsubo cardiomyopathy mimics acute coronary syndrome and is accompanied by reversible left ventricular apical ballooning in the absence of angiographically significant coronary artery disease. Takotsubo cardiomyopathy is relatively uncommon but increasingly recognised. The aims of this study was to assess the patient demographics, precipitating events and outcomes in a series of patients diagnosed with Takotsubo cardiomyopathy in the Johannesburg metropolitan area, and to compare them to other reported series with the same condition.

**Methods:** We retrospectively studied seven patients diagnosed with Takotsubo cardiomyopathy from 2005-2009. Cardiac biomarkers, ECGs, transthoracic echocardiography and coronary and left ventricular angiography was performed in all the patients.

**Results:** The mean age of the patients was 60 years. All 7 (100%) patients had a specific precipitating stressful event just prior to the episode of chest pain. All patients were female, with equal representation across all the racial groups. All were found to have normal coronary arteries. 6 patients had the classic apical ballooning on left ventriculography, whilst one had sparing of the apex but ballooning of the base. Follow up examinations as well as echocardiography or LV angiography confirmed full resolution of the LV dysfunction in 85% (6/7) of the patients as well as full clinical recovery. One patient died of complications secondary to cancer prior to follow up echocardiography or LV angiography. 14% (1/7) of patients had residual cardiac pathology in the form of new onset Atrial Fibrillation. 42% (3/7) of the patients required intubation and inotropic support during initial presentation.

**Conclusion:** Our patients diagnosed with Takotsubo cardiomyopathy follow a similar clinical course and have similar precipitating stressors, such as the death of a relative, as reported in other case series. This unusual form of transient cardiomyopathy is more prevalent in middle aged females. Full recovery tends to be the norm. However, the acute period of the disease is not benign with up to 42% of patients requiring ventilation and or inotropic support.

## Platelet resistance pharmacogenomics and drug interaction: new thoughts for everyday practice

**John Benjamin**

Morningside Medi-clinic, Sandton, South Africa

The association between CYP2C19 genotype and Clopidogrel treatment outcome has been evaluated so far in two post hoc clinical trial analyses (sub studies of CLARITY-TIMI 28 and TRITON-TIMI 38) and five cohort studies. The CYP450 enzyme system is reviewed and simplified with relevance to the role of CYP2C19 in converting the prodrug Clopidogrel to its active metabolite. Only 15% of administered Clopidogrel is converted to its active form. The CYP2C19\*1 allele corresponds to fully functional metabolism, while the CYP2C19\*2 and CYP2C19\*3 alleles correspond to reduced metabolism. The \*2 variant of the CYP2C19 gene encodes a defective enzyme that fails to adequately convert Clopidogrel to its active metabolite, leading to lesser inhibition of platelet function and diminished cardiovascular protection. There appears to be a relationship between the incidence of polymorphisms of CYP2C19 and stent thrombosis. The \*2 allele of the CYP2C19 occurs in 30% of the population, with minor difference between races. As a result of these observations the US labeling for Clopidogrel has recently been updated to include additional information on factors affecting patients' responses to the drug; this includes a large new section on pharmacogenetics and new advice that concomitant use of drugs that inhibit the CYP2C19 enzyme should be discouraged. Point-of-care platelet-function tests are available, and some centers are now performing such tests on their PCI patients. Fast genotype tests however are not yet available but are in development. The current management of patients at risk is challenging and controversial and is being addressed by ongoing trials.

## Histological comparison of the effects of warm ischaemic times on harvested homografts

**D. Bester, F.E. Smit, L. Botes and J.J. van den Heever**

Department of Cardiothoracic Surgery, University of the Free State, Bloemfontein, South Africa

**Introduction:** Homografts in cardiac surgery are well established but availability remains the main limiting factor in their clinical application. Homografts are procured from beating heart donors and cadavers with a limited ischaemic time of 12-24 h post mortem. However, this time limitation has not been established scientifically. Several publications suggest that it would be acceptable to extend the harvesting times. Homograft availability is an international problem and the purpose of the study is to extend the harvesting time beyond 24 h, benefiting all cadaver donor based programs.

**Methods:** The study focused on three groups: (a) Group A (n=5), which contained homograft valves subjected to < 6 h ischaemic time, stored at 4C; (b) Group B (n=15), subjected to 24 h, 48 h and 72 h ischaemic times, stored at 4C, after which the valves were processed and cryopreserved; (c) Group C (n=15), subjected to 24 h, 48 h and 72 h ischaemic times, stored for 6 h at room temperature (23C), followed by 18 h, 42 h and 66 h at 4C, after which the valves were processed and cryopreserved.

Tissue strength was determined by thermal denaturation temperature (Td) and tensile strength. Tissue morphology was assessed by Scanning Electron Microscopy (SEM) and Haematoxylin and Eosin stain.

**Results:** No statistically significant difference ( $p>0.05$ ) in tensile strength could be demonstrated between Group A, B and C with no differences between the three ischaemic time intervals. The results were confirmed by Td analysis. Tissue strength did not decrease as a result of prolonged ischaemic times or elevated temperatures.

Autolysis were only observed in the 48 h (40%) and 72 h (100%) tissue of Group C but was not sufficient to affect tissue strength.

The reduction of endothelial cells over time in both Group B and Group C did not influence tissue strength up to 72 h.

**Conclusion:** Based on scientific evidence regarding tissue strength it seems acceptable to extend harvesting time to 72 h.

However, animal studies need to be performed to substantiate these results, as the in vivo graft host interactions might produce results that are not consistent with these findings.

## Predictors of outcome in 176 patients with peripartum cardiomyopathy

**Lori A. Blauwet\*, Elena Libhaber#, Olaf Forster#, Kemi Tibazarwa\*† and Karen Sliwa#**

\*Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota, USA

#Soweto Cardiovascular Research Unit, Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

†Groote Schuur Hospital, University of Cape Town, South Africa

**Background:** Peripartum cardiomyopathy (PPCM) is a rare, potentially devastating heart disease that occurs in previously healthy women. Factors predicting poor outcome in smaller cases series include left ventricular ejection fraction (LVEF) <30%, left ventricular end diastolic dimension > 55mm, and left ventricular thrombus on presentation. The identification of additional prognostic factors for poor outcome would be beneficial in order to provide optimal care for PPCM patients.

**Methods:** This was a single centre prospective study of 176 women with newly diagnosed PPCM in South Africa. Clinical assessment, echocardiography, and laboratory study results including complete blood count, liver function tests, and renal function performed at baseline and at 6 months were reviewed. Poor outcome was defined as the combined endpoint of death, LVEF <35%, or remaining in New York Heart Association functional class III/IV at 6 months. Improved left ventricular systolic function was defined as an increase in LVEF by a relative increment of >10 absolute units at 6 months.

**Findings:** Low systolic blood pressure ( $p=0.045$ ,  $OR=0.98$ ) and decreased LVEF ( $p=0.028$ ,  $OR=0.95$ ) at baseline were predictors of poor outcome. Normal range creatinine ( $p=0.0367$ ) at baseline predicted improved left ventricular systolic function at 6 months. Neither left ventricular dimensions or function, hemoglobin, or liver function tests were predictors of the combined endpoint of poor outcome, mortality, or improved left ventricular systolic function.

**Conclusion:** This large prospective study of patients with newly diagnosed PPCM confirmed that decreased systolic blood pressure and LVEF at baseline predict poor outcome in patients with PPCM, while lower plasma creatinine is a predictor of left ventricular systolic improvement at 6 months. No additional prognostic markers could be identified.

## Sarcomeric modifiers of hypertrophy in hypertrophic cardiomyopathy

**L.M. Bloem, L. van der Merwe, M. Revera, M. Herandien, A. Goosen, P. Brink and J.C. Moolman-Smook**

US/MRC Centre for Molecular and Cellular Biology, Department of Biomedical Sciences, University of Stellenbosch, South Africa

Hypertrophic cardiomyopathy (HCM) is an autosomal dominantly inherited cardiac disorder characterised by myocyte disarray, an increased risk of sudden cardiac death (SCD) and left ventricular hypertrophy (LVH). HCM thus serves as a model for the investigation of LVH, a symptom that is the strongest predictor of cardiac morbidity and mortality after age itself. Interestingly, the extent and pattern of LVH in HCM patients shows a large degree of variation even in homogenous patients with the same HCM-causing mutation, indicating that additional modifying factors may affect the severity of the cardiac phenotype.

The development of HCM has been ascribed to mutations in genes that encode primarily constituents of the cardiac muscle contractile unit known as the sarcomere. One such gene is TNNT2, which encodes Troponin T, a protein that regulates cardiac contractility in a calcium dependent manner via its interaction with tropomyosin. The latter competes with myosin for binding sites upon the actin molecules, and in doing so determines binding site availability, the state of which ultimately reflects the contraction status. Previous studies suggest that compound heterozygote individuals for sequence variants in sarcomeric genes are more severely clinically affected compared to simple heterozygous disease-causing mutation-carriers. Therefore this study aimed to investigate TNNT2 as a plausible modifier candidate to potentially identify variants in addition to the already documented HCM-causing founder mutations found to be present within our patient group.

The total study population of 227 individuals, belonging to 22 HCM families, carrying one of three known founder HCM-causing mutations (R92WTNNT2, R403WMYH7, and A797TMYH7), was genotyped.

Three of the TNNT2 SNPs investigated indicated association with a heritable hypertrophic trait, independent of known hypertrophy covariates ( $p=0.011$  indicated association of SNP rs2365652 with maximal interventricular septum thickness (mIVST)). The possibility that these findings resulted from linkage disequilibrium between the genotyped SNPs and the R92WTNNT2 founder mutation, was excluded by means of Haploview analysis. These data suggest that TNNT2 plays a role as modifier of the extent of hypertrophy in HCM. This study thus contributes to previous hypertrophy research by offering insight into modifiers of cardiac hypertrophy and highlights the potential for future therapeutic intervention studies.

## Hybrid rescue of a severely hypoplastic pulmonary artery

**Stephen Brown\*, Derize Boshoff# and Marc Gewillig#**

\*Department of Pediatric Cardiology, University of the Free State, Bloemfontein, South Africa

#Pediatric and Congenital Cardiology, University Hospitals Leuven, Belgium

Management of pulmonary atresia with ventricular septal defect remains difficult and challenging. Pulmonary arteries are usually hypoplastic and presents difficulties due to size-mismatch when systemic connection is required. This case report describes the successful novel use of a covered stent to facilitate vascular graft connection to a diminutive pulmonary artery during a hybrid procedure.

## Premature fetal closure of the arterial duct: clinical presentations and outcome

M. Gewillig\*, S. Brown#, L. de Catte†, A. de Beer\*\*, B. Eyskens\*, V. Cossey\*\*, D. van Schoubroeck\*\*, C. van Hole\*\* and R. de Vlieger†

\*Pediatric and Congenital Cardiology, University Hospitals Leuven, Belgium

#Department of Pediatric Cardiology, University of the Free State, Bloemfontein, South Africa

†Prenatal Ultrasound, University Hospitals Leuven, Belgium

\*\*Neonatology, University Hospitals Leuven, Belgium

**Introduction:** The prevalence of intra-uterine ductal dysfunction is unknown and the clinical consequences are poorly understood. The aim of this study was to investigate the echocardiographic abnormalities and outcomes of this rare phenomenon.

**Patients and methods:** Retrospective analysis of foetal (n=602) and neonatal echocardiographic databases (n=1477) between 1998 and 2007. Clinical and imaging studies were reviewed for pathology due to or associated with premature closure of the duct.

**Results:** Twelve cases were identified. Eight (1.3%) were diagnosed prenatally at a median gestational age of 29.0 weeks (range: 20.037.5 w). Four neonates (0.3%) with significant cyanosis and absence of the arterial duct were also included. The most common echocardiographic features were: excessive right ventricular hypertrophy (100%), more than expected tricuspid and pulmonary regurgitation (100% and 92%, respectively), and right atrial dilation (75%). Premature induction of delivery was advised for 5 patients. Neonatal therapy consisted of observation and oxygen administration (n = 7), ventilation with pulmonary vasodilators (n = 5); one required extracorporeal membrane oxygenation (ECMO). There were three deaths due to respiratory failure with severe pulmonary hypertension. During follow-up two children required additional right heart procedures and one developed a non-compaction cardiomyopathy.

**Conclusion:** The prevalence of prenatal ductal dysfunction is most likely grossly underestimated. Foetal premature closure of the arterial duct causes stress at different foetal ages and many different levels of the right heart and pulmonary circulation, resulting in a wide range of secondary pathology. Disproportionate right ventricular hypertrophy is the most common finding. Clinical outcomes range from mild symptomatology to lethal respiratory insufficiency.

## Stent expansion of stretch Gore-Tex grafts in children with congenital heart lesions

Stephen Brown\*, Derize Boshoff# and Marc Gewillig#

\*Department of Pediatric Cardiology, University of the Free State, Bloemfontein, South Africa

#Pediatric and Congenital Cardiology, University Hospitals Leuven, Belgium

**Objective:** This study evaluated the efficacy and safety of using stents to enlarge previously placed vascular shunt grafts in children with desaturation and congenital heart lesions.

**Methods:** Bench testing confirmed the expandability of 3.5 and 4mm vascular grafts up to 6mm. Eleven patients with desaturation where stretch grafts were placed for systemic to pulmonary artery shunts were identified. Stents were selected to be at least 1mm larger in diameter than nominal diameter of the implanted graft.

**Results:** Fifteen stents were implanted in 11 stretch grafts a median of 18.9 (range: 0.9-62.1) months after shunt surgery. There was a median increase in diameter of 136% (97-228) from nominal to final stented diameter of the shunts ( $p = 0.008$ ; 95% CI 0.5 to 2.8). Saturations improved from a median of 73% (62-82) to 87% (79-89) [ $p = 0.003$ ; 95% CI 6.5 to 20.1]. No severe complications were experienced during the procedures.

**Conclusion:** In our limited experience, stretch Gore-Tex vascular grafts can be safely expanded beyond nominal diameters using high pressure vascular stents. This leads to improvement pulmonary blood flow and saturations. It may potentially allow the clinician to tailor pulmonary flow to somatic growth.

## Temporary use of small stents to delay surgery in children with cardiac disease

**D.G. Buys\***, **S.C. Brown\***, **F. Smit<sup>#</sup>**, **M. Long<sup>#</sup>** and **A.D. Bruwer\***

\*Department of Pediatric Cardiology, University of the Free State, Bloemfontein, South Africa

<sup>#</sup>Department of Cardiothoracic Surgery, University of the Free State, Bloemfontein, South Africa

**Introduction and aim:** Critical obstruction of the aorta in small, critically ill neonates and infants is difficult to treat. These sick infants present significant surgical risk for mortality and the surgical repair itself is challenging. Primary stent implantation is an attractive alternative. The aim of this study was to determine the efficacy, safety and outcome of primary stenting in certain critical obstructive lesions in infants.

**Methodology:** Retrospective analysis of infants with cardiac disease who needed temporary small stents to delay surgery.

**Results:** Small stents were implanted in five infants with a median age of 2.0 months (range: 2.2-5.0). The median weight was 3.9 kg (range 2.2-5.1), all were severely symptomatic and surgery considered risky. Pre-implantation gradient was reduced from a median of 59.4 mmHg pre-implantation to 13.0 mmHg post-implantation ( $p < 0.001$ ). All coarctation stents were coronary stents and 4F sheaths were inserted in the femoral artery. All children could be weaned off ventilation and 3 were subsequently successfully repaired. In one child the stent was replaced with a second larger stent and noteworthy weight gain was achieved. There were no deaths.

**Conclusion:** Small stents are effective, safe and results in postponement of surgery. This approach is however, recommended only for very sick, small infants where surgical risk is high.

## Genetic variation in Na<sup>+</sup>/K<sup>+</sup>-ATPase gene isoforms are associated with extent of left ventricular hypertrophy in hypertrophic cardiomyopathy

**N. Carstens\***, **L. van der Merwe<sup>#</sup>**, **M. Revera<sup>†</sup>**, **M. Heradien\*\***, **A. Goosen\*\***, **P.A. Brink\*\*** and **J.C. Moolman-Smook\***

\*US/MRC Centre for Molecular and Cellular Biology, Department of Biomedical Sciences, University of Stellenbosch, South Africa

<sup>#</sup>Biostatistics Unit, Medical Research Council of South Africa, Tygerberg, South Africa

<sup>†</sup>Department of Cardiology, IRCCS San Matteo Hospital, Pavia, Italy

\*\*Department of Medicine, University of Stellenbosch Health Sciences Faculty, Tygerberg, South Africa

Hypertrophic cardiomyopathy (HCM) serves as a model to investigate left ventricular hypertrophy (LVH) development as this primary cardiac disease is characterised by LVH in the absence of increased external loading conditions. HCM is mostly caused by mutations in genes encoding sarcomeric proteins, but manifests extreme variability in the degree and pattern of LVH, even in HCM patients with the same causal mutation, which suggests the involvement of additional genetic modifiers. Previous studies identified genes encoding renin-angiotensin-aldosterone system (RAAS) components as modifiers of the hypertrophic phenotype of HCM. However, most of these investigations were centred on a set of so-called pro-LVH polymorphisms in only five genes encoding proteins with roles in the proximal part of the RAAS.

The Na<sup>+</sup>/K<sup>+</sup>-ATPase is one of the downstream effectors of the RAAS and is responsible for maintaining transmembrane gradients of Na<sup>+</sup> and K<sup>+</sup>. The cardiac expression of Na<sup>+</sup>/K<sup>+</sup>-ATPase isoforms is altered in heart failure and hypertrophy. This study was therefore aimed at investigating the effect of three single nucleotide polymorphisms (SNPs) within the genes encoding the Na<sup>+</sup>/K<sup>+</sup>-ATPase  $\beta$ 1,  $\alpha$ 1 and  $\alpha$ 2-subunits on heritable hypertrophy traits in a HCM cohort of 22 families, each harbouring one of three HCM founder mutations.

One SNP in ATP1B1, rs1200130, was significantly associated with left ventricular mass (LVM) ( $p = 0.023$ ) and a hypertrophy score derived from principal component analysis, PC1, ( $p = 0.027$ ). Additionally rs7548116 in ATP1A2 was associated with LVM ( $p = 0.047$ ) and maximal left ventricular wall thickness (mLVWT) ( $p = 0.027$ ), while rs850609 in ATP1A1 was associated with mLVWT ( $p = 0.038$ ). These associations are independent of the primary HCM-causal mutation and other known hypertrophy covariates, such as age, sex and blood pressure.

This study is the first to implicate Na<sup>+</sup>/K<sup>+</sup>-ATPase isoforms in the development of hypertrophy within the context of HCM. Future studies should include downstream RAAS genes, particularly Na<sup>+</sup>/K<sup>+</sup>-ATPase isoforms, in hypertrophy modifier studies. The modest effect sizes reported for these variants are similar to those reported for other RAAS variants, which suggests that the hypertrophic phenotype of HCM may be the cumulative result of a number of modifier genes of modest effect.

## A case of tachycardia-induced cardiomyopathy

**Ashley Chin**

Cardiac Clinic, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** Tachycardia-induced cardiomyopathy (TIC) is an important reversible cause of left ventricular (LV) dysfunction that may complicate both supraventricular and ventricular arrhythmias. Although prior studies have shown that LV function can improve if the tachycardia is controlled by medication or ablation, LV function may not normalise and patients may be left with persistent LV dilatation and impaired LV function. One small study has also suggested that a recurrence of the arrhythmia may lead to a precipitous decline in LV function.

**Case report:** A 56 year old man presented to the cardiac clinic with a 3 month history of dyspnoea and frequent episodic palpitations in mild heart failure. An ECG of an episode revealed a supraventricular tachycardia (SVT) at 200bpm with no baseline pre-excitation in sinus rhythm. An echocardiogram showed a LV ejection fraction (LVEF) of 21%. He was started on metoprolol, enalapril and diuretics. At a 3 week follow-up visit, his symptoms had markedly improved with a repeat echocardiogram showing a LVEF of 51%, confirming a diagnosis of TIC. Unfortunately, he defaulted medical therapy and represented with an identical SVT 4 months later. He underwent an electrophysiological study which confirmed an orthodromic atrioventricular reentry tachycardia (AVRT) with successful ablation of multiple left lateral accessory pathways. An echocardiogram confirmed that his LV function had deteriorated to a LVEF of 35%. At a 2 year follow-up visit, he reported no recurrences of palpitations or SVT. His last follow-up echocardiogram showed a LVEF of 47%.

**Discussion:** This patient developed a TIC secondary to recurrent episodes of AVRT. Although medical therapy was successful in controlling the episodes of AVRT with a rapid improvement in LV function over a period of 3 weeks, recurrent episodes of AVRT resulted in a precipitous decline in LV function over a period of 3 months. Successful ablation of the AVRT resulted in improvement but not normalisation of LV function. This case report supports prior observations that LV function may not normalise and that recurrences of the arrhythmia may lead to a precipitous decline in LVEF in patients with TIC.

## A 10 year experience of endomyocardial biopsies at Groote Schuur Hospital, Cape Town

**Ashley Chin, D. Kapp, H. Wainwright, C. Russouw and A. Okreglicki**

Cardiac Clinic, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** The current role of endomyocardial biopsy (EMB) in the diagnosis and treatment of adult cardiovascular disease remains controversial resulting in wide variations in clinical practice. We report our experience of EMB at Groote Schuur Hospital over a 10 year period.

**Methods:** We reviewed the indications, histological reports and complications of all EMBs performed at Groote Schuur Hospital between 1999 and 2009 in non-posttransplanted hearts. All EMBs were performed by either a cardiology registrar or consultant using a flexible bioptone forceps with the aim of obtaining at least 3 samples in more than 1 region from the right ventricular septum via either the right internal jugular (predominantly), right subclavian or right femoral vein.

**Results:** We identified 67 patients who underwent EMB during the study period. The indications were myocarditis in 4, restrictive/infiltrative cardiomyopathy in 17, arrhythmogenic right ventricular cardiomyopathy (ARVC) in 21, and cardiomyopathy of unknown cause (majority dilated cardiomyopathy) in 25 patients. Histology did not support the clinical diagnosis of myocarditis in any of the 4 patients. A histological diagnosis was obtained in 5 patients (3 patients with sarcoidosis, amyloidosis, fibrotic stage of Loefflers syndrome respectively and 2 patients with ARVC) out of 17 with a diagnosis of restrictive or infiltrative cardiomyopathy. Histology did not identify a specific cause (amyloidosis, sarcoidosis or haemochromatosis) in all 25 cardiomyopathy patients. 13 out of 21 with suspected ARVC had histological features compatible with the diagnosis. Insufficient sampling occurred in 6 patients. Major complications occurred in 6 patients (3 patients required pericardiocentesis for cardiac tamponade and 3 patients had suspected RV perforation) with no deaths.

**Conclusion:** Our findings strongly support the use of EMB in the diagnosis of ARVC and suspected restrictive/infiltrative cardiomyopathies. The low diagnostic yield of EMB in myocarditis and dilated cardiomyopathy is compatible with previous studies. The 9% complication rate supports the need for careful risk/benefit assessment before performing an EMB.

## Radiofrequency ablation of accessory pathways: a 19 year experience of the Cardiac Clinic, Groote Schuur Hospital

**Ashley Chin, A. Okreglicki and M. Reid**

Cardiac Clinic, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** Radiofrequency ablation (RFA) is first-line therapy in the management of patients with symptomatic accessory pathways (APs). There is no published data on the experience of RFA of APs from Africa.

**Methods:** The aim of this study was to review the experience of RFA (1990-2008) at Groote Schuur Hospital in Cape Town and to evaluate the accuracy of the Arruda algorithm in predicting the location of APs in 110 patients with the Wolff-Parkinson-White syndrome.

**Results:** The study cohort comprised 194 patients with 205 APs who had undergone 230 RFA procedures. There were 98 males and 96 females, age 33.17 years (range: 1-84), with 25 patients (13%) of black African descent. Symptoms had been present for 8.5-9.9 years (median: 4.8 years, range: 1 month-60 years) before a RFA was performed. Atrial fibrillation had been documented in 34 patients (18%) before RFA. Only 5 patients (3%) had presented with an antidromic tachycardia. 92 APs (45%) were located on the left, 44 APs (21%) in the paraseptal space, 40 APs (20%) on the right, and 21 APs (10%) presented with a septal or parahisian location. 8 APs (4%) could not be classified. A single AP was found in 184 patients (98%) while multiple APs were noted in 10 patients (2%). 38 patients (20%) had concealed APs. RFA of all pathways were successful in 161 patients (83%). 14 patients (7%) required repeat RFAs. Serious complications occurred in 3 of 230 RFA procedures (1.3%). Although the Arruda algorithm had an overall sensitivity of 51% and a specificity of 97% in predicting the location of an AP, it was more useful in correctly localising left-sided (sensitivity 91%, specificity 96%) and paraseptal APs (sensitivity 82%, specificity 93%).

**Conclusion:** To our knowledge, this is the first reported series of RFA of APs from Africa. The most common APs were left-sided APs, followed by postero-septal and right APs. The Arruda algorithm was more useful in identifying left and paraseptal APs than right-sided APs. Similar to experience worldwide, RFA of APs at our institution, after an initial learning curve, is highly successful and safe.

## Radiofrequency ablation of a Mahaim accessory pathway in a patient with Ebsteins anomaly

**Ashley Chin and A. Okreglicki**

Cardiac Clinic, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** Mahaim accessory pathways are associated with Ebsteins anomaly. Antidromic atrioventricular reentry tachycardia (AVRT) over a Mahaim pathway is typically a left bundle branch block (LBBB) morphology tachycardia. We report an unusual case of Ebsteins anomaly with a right-sided Mahaim pathway associated with an antidromic AVRT without a typical LBBB morphology.

**Results:** A 20 year old man with Ebsteins anomaly presented with a 1 year history of episodic palpitations. A resting 12-lead ECG revealed sinus rhythm with no pre-excitation, atypical right bundle branch block (RBBB), and a QRS axis of +45 degrees. An ECG of one of the palpitations revealed a wide complex tachycardia at 192bpm, QRS duration 170ms, QRS axis 60 degrees, with a RBBB-like morphology in leads VI-V3 with different QRS morphologies compared to the resting 12-lead ECG. At electrophysiological study, a similar antidromic AVRT was easily induced with atrial and ventricular programmed electrical stimulation. Antegrade conduction over a decrementing accessory pathway (Mahaim pathway) was confirmed. Endocardial mapping localised this pathway to the posterior-septal (5 o'clock) tricuspid annulus which was successfully ablated.

**Conclusion:** Most studies have reported Mahaim pathways with antidromic AVRT to have a LBBB configuration with an rS pattern in lead VI with a precordial QRS transition  $\geq$  V5. We describe a patient with Ebsteins anomaly and a confirmed right-sided Mahaim pathway with an antidromic AVRT with a RBBB-like pattern in leads VI-3. We suggest that this patient has a long atrioventricular pathway because of no baseline pre-excitation, a QRS axis of -60 degrees and wide QRS complex antidromic tachycardia (170ms). The pathway probably inserts into the posterior wall of the right ventricle accounting for the positive concordant QRS morphologies in the right-sided chest leads (VI-V3). An alternative explanation is that the dilated right atrium and atrialised right ventricle has displaced the heart relative to the surface ECG electrodes with loss of the typical early activation and LBBB pattern in the right-sided chest leads. We hypothesize that Ebsteins anomaly with a right-sided posterior-septal Mahaim pathway may not display the typical LBBB pattern during antidromic AVRT as seen in structural normal hearts.

## Is dosage adjustment of low molecular weight heparin necessary and safe for pregnancies at greatest risk of thrombosis?

**R.S. Chitsike, P. Manga, H.A. Rhemtula and B.F. Jacobson**

Departments of Haematology, Cardiology and Obstetrics and Gynaecology, Johannesburg Hospital, University of the Witwatersrand and NHLS, South Africa

**Introduction:** Pregnancies at greatest risk of thrombosis include patients with mechanical prosthetic heart valves in the mitral position and patients with atrial fibrillation. Guidelines of the 7<sup>th</sup> American College of Chest Physician conference recommend the use of Low Molecular Weight Heparin (LMWH) as an option to attain adequate maternal thromboprophylaxis in these patients.

**Aim:** To determine whether dosage adjustment of LMWH in order to maintain an Anti-Xa of 1.0-1.2 IU/L is both necessary and safe for pregnancies at the highest risk of thrombosis.

**Methods:** This was a prospective study consisting of 6 pregnant patients with either mechanical prosthetic heart valves (n=5) or atrial fibrillation (n=1). Patients were started on LMWH at a dose of 1mg/kg twice daily and the dose adjusted to achieve an Anti-Xa of 1.0-1.2 IU/L. The LMWH dose was adjusted weekly or fortnightly throughout pregnancy and a monthly echocardiogram was performed to exclude the presence of valvular or atrial thrombosis.

**Results:** Marked inter-patient and intra-patient variation was noted in the dose required to maintain a therapeutic Anti-Xa as the pregnancy progressed, with one patient achieving over double the initial dose required. None of the patients developed bleeding or valvular/atrial thrombosis.

**Conclusion:** LMWH thromboprophylaxis with dosage adjustment appears both necessary and safe during pregnancy. However, a larger sample size would be required to test this hypothesis fully.

## Echocardiographical features of two infants with anomalous coronary arteries

**A.M. Cilliers, P. Adams and G. Dumani**

Department of Pediatric Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

**Introduction:** The echocardiographic diagnosis of anomalous coronary arteries requires a high index of suspicion in all cases of global myocardial dysfunction in children. The value of transthoracic echocardiography in making the diagnosis is highlighted.

**Case reports:** We present two infants, 4 months and 9 months of age who presented with dilated cardiomyopathy and heart failure. Echocardiography in both infants showed poor left ventricular function, hyperechoic changes of the endocardium and the papillary muscles suggestive of endocardial fibroelastosis, mitral incompetence, and abundant septal intramyocardial coronary flow signals. In each case an abnormal coronary was seen arising from the main pulmonary arterial trunk. The 4 month old child was found to have a typical anomalous left coronary artery from the main pulmonary artery (ALCAPA). The 9 month old child displayed the rare form of anomalous origin of the coronary artery where the right coronary artery was noted to be arising from the main pulmonary artery (ARCAPA). The diagnosis was confirmed angiographically and the patient underwent successful surgical reimplantation of the right coronary artery into the aorta.

**Discussion:** ALCAPA and even more so, ARCAPA, are very rare congenital abnormalities (0.0023 live births). They represent the most common causes of myocardial ischaemia and infarction in children and if left untreated results in a mortality rate of 90% within the first year of life. The clinical course and prognosis depends on the extent of collateralisation between the RCA and the LCA. Anomalous origin of the coronary arteries may be associated with other cardiac defects e.g. ventricular septal defect, coarctation of the aorta and tetralogy of Fallot. Echocardiography typically establishes the diagnosis by demonstrating the origin of the coronary artery from the pulmonary artery and characteristic Doppler flow patterns.

**Conclusion:** Echocardiography is a useful modality to screen for anomalous coronary artery disease. The combination of a dilated cardiomyopathy in the presence of endocardial fibroelastosis, mitral incompetence and should alert one to the possibility of abnormal coronary origins in infants. Colour flow Doppler abnormalities within the vessels and the myocardium may assist with the diagnosis. Angiography can be used to confirm the diagnosis.

## Assessing rheumatic mitral stenosis with the proximal isovelocity surface area (PISA) method: validation of the PISA method against the invasive gold standard (Gorlin formula)

**F.M. Claassen, A.L. Mbonambi, P.G. Herbst and A.F. Doubell**

Division of Cardiology, Department of Medicine, University of Stellenbosch and Tygerberg Hospital, South Africa

We have recently proposed the use of the proximal isovelocity surface area (PISA) technique to determine mitral valve area (MVA) in patients with mitral stenosis to overcome the weaknesses of the standard echocardiographic technique, 2-D planimetry (Herbst et al. SA Heart, 2008, 5; 224). The aim of this study was to validate the PISA method against the invasive gold standard, the Gorlin formula.

**Methods:** Patients diagnosed with mitral stenosis undergoing percutaneous mitral balloon valvuloplasty (PMBV) during an 18 month period were included. Transthoracic echocardiography was used to calculate MVA using the PISA method and 2-D planimetry. Hemodynamic data was captured during the PMBV procedure. The Gorlin formula was used to calculate valve area from the hemodynamic data.

**Results:** Eight patients were studied in this pilot phase. MVAs calculated using echocardiography varied between 0,4 cm<sup>2</sup> - 1,6 cm<sup>2</sup>. Three patients had mild aortic incompetence and all 8 patients had mild mitral incompetence. One patient had mildly impaired systolic function (EF=58%). MVAs calculated using the Gorlin formula varied between 0,4 cm<sup>2</sup> - 1,4 cm<sup>2</sup>. PISA correlated well with both the echocardiographic gold standard and the invasive gold standard including the patients with associated valve dysfunction.

**Conclusion:** The PISA method is a robust method to determine MVA in patients with mitral stenosis that ranges from mild to moderate. The PISA method correlates well with both the echocardiographic and the invasive gold standard for determining valve area.

## Phytosterol-enriched foods: evidence for their cholesterol-lowering efficacy and combination with other lipid-lowering approaches

**Isabelle Demonty**

Unilever R&D Vlaardingen, The Netherlands

The cholesterol-lowering properties of phytosterols (PS) are known since the 1950s. In the 1980s, the esterification of PS with fatty acids from vegetable oils eased their incorporation into fat-based foods. A meta-analysis of trials with fat-based foods enriched with PS esters showed a non-linear relationship between the daily dose of PS consumed and cholesterol-lowering efficacy. On average, 2.0-2.4 g/day PS lowered LDL-cholesterol (LDL-C) concentrations by 8.9%, with little additional benefit at intakes higher than 2.5 g/day (Katan et al., 2003). Several dietary recommendations include the daily consumption of 2 g of PS as a dietary option to lower elevated LDL-C concentrations. More recently, additional evidence became available for the cholesterol-lowering efficacy of PS incorporated in a wide variety of food formats, including low-fat or fat-free foods such as milk and yogurt, and single daily dose food formats such as yogurt drinks. Two recent meta-analyses including studies with these new food formats investigated the impact of food format on PS efficacy. AbuMweis et al. (2008) calculated an average effect for subgroups of PS doses. In our meta-analysis (Demonty et al. 2009) we established a continuous dose-response equation allowing predicting the LDL-C lowering effect of a given dose of PS in populations. We observed no significant differences between dose-response curves established for plant sterols vs. stanols, fat-based vs. non fat-based foods and dairy vs. non-dairy foods. Both single and multiple daily intakes of PS significantly lowered LDL-C, but there was a tendency towards a slightly lower efficacy of single vs. multiple daily intakes. PS-enriched foods are efficacious in subjects consuming a typical Western diet as well as a heart healthy diet and in subjects taking cholesterol-lowering medications such as statins or fibrates. The combination of PS with fish oil for a dual benefit on both LDL-C and triglycerides, either as fish oil fatty acid esters of PS or as a combination of PS-enriched foods and fish oil capsules has an overall beneficial effect on blood lipid profile. However, results on the nature of possible interactions between fish oil and PS on LDL-C and triglycerides are inconsistent, warranting further investigations.

## Mitral stenosis in pregnancy

**A.F. Doubell, U. Lalla, H. Weich and P. Herbst**

Division of Cardiology, Department of Medicine, University of Stellenbosch and Tygerberg Hospital, South Africa

The hemodynamic changes induced by pregnancy are poorly tolerated by patients with mitral stenosis (MS), often precipitating the onset of symptoms and the need for intervention. Percutaneous balloon mitral valvotomy (PBMV) is an effective intervention if the anatomy is suitable, but valve replacement (MVR) during pregnancy may be required in very diseased valves. Limited data is available for PBMV and MVR during pregnancy in the South Africa population. We review the management and outcome of MS in pregnancy at our institution to determine if the South African experience mirrors the experience recorded in other populations.

We review our experience with MS in pregnancy with emphasis on 31 patients who underwent PBMV and 10 patients who underwent valve replacement during pregnancy over a ten year period, comparing the outcomes with intervention in non-pregnant patients.

Patients undergoing interventions for MS are often diagnosed before pregnancy (55% of patients undergoing PBMV) indicating that opportunities are missed to address the valve lesion prior to conception. Conversely, patients in whom MS is identified for the first time in pregnancy (45% of patients undergoing PBMV) often present late in the second trimester. Beta blockers are the mainstay of medical treatment for MS but obstetricians are often reluctant to use beta blockers in pregnancy. A low threshold is required for PBMV during pregnancy in patients with severe MS and suitable valves as procedural success is high (97%) with significant improvement in mitral valve area ( $1.05 \pm 0.20$  cm to  $1.73 \pm 0.35$  cm [ $p < 0.001$ ]) and reduction in mean transmitral gradient ( $14.4 \pm 8.3$  mmHg to  $6.6 \pm 3.4$  mmHg [ $p < 0.001$ ]) in the pregnant group, mirroring the results in non-pregnant patients. Complications included mitral regurgitation (17%), anaphylaxis (3%), atrial fibrillation (6%) and TIAs (6%). The latter emphasises the hypercoagulable state of pregnancy. Favourable outcomes were maintained at follow-up (mean  $2.78 \pm 2.71$  years). No maternal deaths occurred in our patients undergoing PBMV or MVR during pregnancy. Perinatal loss was 25% for women undergoing MVR but fetal loss following PBMV was limited to a single patient in whom the procedure was performed as an emergency on a ventilator.

## Inter-sectoral and regional healthcare cooperation in southern Africa: The Namibian childrens heart project

**H. du Toit\*, S. Vosloo# and C. Hugo-Hamman†**

\*Panorama Medi-Clinic, Cape Town, South Africa

#Christiaan Barnard Memorial Hospital, Cape Town, South Africa

†Christiaan Barnard Memorial Hospital and Constantiaberg Medi-Clinic, Cape Town, South Africa

**Introduction:** Both public private sector and regional cooperation have been proposed as useful tools to alleviate critical shortages in health service provision in southern Africa. The aim of this project is the development of cardiac services for Namibian children and it was initiated at the request of the Ministry of Health of Namibia.

**Methods:** This is a review of a cohort of 60 patients with congenital or rheumatic heart disease referred for heart surgery over the period April 2007 to August 2009 (28 months). The majority of patients were recruited from the Paediatric Heart Clinic at Windhoek Central Hospital.

**Results:** Sixty (60) patients with age 7 days to 29 years received a total of 73 operations. Only 2 had surgery for rheumatic heart disease and there were 3 adults with congenital heart disease. There have been no deaths. There were 11 re-operations in 8 patients. Four (4) patients needed surgery for post-operative complications. Twenty-six (26) patients were on private health insurance. Of the 33 indigent state patients, 8 were paid for by a charitable trust and 25 by the Namibian Government. Eight operations were performed in state hospitals and the balance (65) in private hospitals in Cape Town.

**Conclusions:** With goodwill, political commitment and cooperation, this project provides strong evidence for supporting expansion of public private partnerships in the health sector in southern Africa.

## Assessment of warfarin control in patients with operated valvular heart disease in one hospital in Sudan

**Ahmed EISayed and Hanin Osama Mohammad**

AlShaab Teaching Hospital, Khartoum, Sudan

**Introduction:** Warfarin is one of the commonest causes of death related to prescription drugs. It's pharmacology is complicated and many factors need to be considered in the optimal management of each patient. In this study our aim is to study the control of warfarin in patients with operated valvular heart disease and to identify the factors that make it difficult to control and suggest improvements.

**Objectives:** To assess warfarin control in patients with operated valvular heart disease and to classify them as controlled or not. To determine the incidence of INR control complications. To try to determine factors that may influence poor control.

**Methods:** This is a retrospective hospital based study in valve replacement patients done by one surgeon in one hospital. After the patients were contacted and consented the data was collected by a questionnaire from the hospital computer database and further by reviewing the patient's files and interviewing them. It was then analysed using SPSS.

**Results:** 70 patients (40 males) were enrolled. Age range is 15-75. The majority are from the west but 75% live in Khartoum or nearby. MVR was the commonest operation (38 patients with AVR 17 and DVR 15). Mean warfarin dose was 5.3 (range 1-13). Of all 70 patients only 10 patients had good INR control. 68.6% of patients test INR at irregular intervals. The 31.4% who follow up regularly do it at different intervals {4.3% twice a month, 14.3% monthly, 4.3% 2 monthly, 5.7% 3 monthly and 2.9% 6 monthly}.

The most common complication was bleeding which happened to 45.7% during the course of their treatment, it was however mainly minor bleeding (which will be further explained). Only one patient developed severe retroperitoneal bleeding required hospitalisation. The other noted complaints were nausea in 8 and priapism in 2 patients.

**Conclusions:** Warfarin control as it now stands in Sudan Heart Center is very unsatisfactory. Reasons for this and possible solutions will be presented. The proposed solutions are the subject of ongoing studies now.

## More than 10 years of open heart surgery in Sudan: a presentation and suggestions for the future

**Ahmed EISayed and Alamin Alawad**

AlShaab Teaching Hospital, Khartoum, Sudan

**Introduction:** Open heart surgery has come a long way globally since its foundations were first laid in the 1950s. Today about 1 million cases are done annually globally with a global average of 167 open heart cases/million of population. In Africa however, only 29 open heart cases/million population are done annually giving a total of 25 000 cases per year in the whole of Africa. So it is obvious that Africa is very much behind the global average. This situation is more bleak when one realises that the European average is 3 times and the North American average is 5 times the global average. Sudan is doing relatively better than most of Africa but we are faced with a really uphill struggle to reach the global average. In this paper we present the open heart cases done in Sudan since it restarted in 1998 and present the case for expansion in this specialty in a developing world setting.

**Objectives:** To review all the cases done in Sudan since it restarted in 1998 till December 2008.

**Methods:** This is a retrospective and prospective hospital based study in the period from 01/01/1998 to 31/12/2008. The data was from the hospital computer database and further by reviewing the patient's files. The data was analysed using SPS package.

**Results:** Nearly 5 000 patients had open heart surgery in the period of the study. These varied between rheumatic heart disease patients, ischaemic surgery patients, congenital heart disease patients and other patients. The trends in the numbers and variety of these cases over the years is detailed in the presentation.

**Conclusions:** Sudan has in a short while reached a good standard in the numbers of open heart procedures being done and there are a large number of cases of different variety being done. Complications (including mortality) are high but reasonable when patient profile is considered. This is only the beginning for the country as a whole and the need for more centres and more international cooperation is evident. This could also serve as a regional nucleus for the surrounding countries.

## Development of a hand-held device for automated paediatric cardiac auscultation

**P.R. Fourie\***, **J. Lawrenson#**, **R. de Decker†**, **A. van Niekerk\*\***, **Joan Hunter\***, **M.L. Cronje\***, **O.M. Strydom\*** and **E. Pretorius\***

\*Diacoustic Medical Devices, Stellenbosch, South Africa

#Red Cross Children's Hospital and Stellenbosch University, South Africa

†Red Cross Children's Hospital, Cape Town, South Africa

\*\*Mowbray Maternity Hospital, Cape Town, South Africa

\*Louis Leipoldt Medi-Clinic Hospital, Bellville, South Africa

**Background:** Most of the heart murmurs detected in children are innocent. The skills of the first examiner are in most cases not adequate to distinguish between innocent and pathological murmurs, resulting in a large percentage of unnecessary referrals. The aim of this project was to develop a hand-held medical electronic device that could record heart sounds digitally, analyse the recording and aid the examiner in distinguishing between innocent and pathological murmurs.

**Methods:** Heart sound recordings of more than 400 patients were obtained, recorded at four positions on the chest, resulting in more than 1 600 recordings. The dataset contains recordings of 222 pathological and 45 functional murmurs, as well as recordings of 133 normal hearts without any murmurs. All pathological and functional murmurs were correlated to the presence or absence of cardiac abnormalities by echocardiogram. These recordings were used to develop the decision support algorithm. A touch screen hand-held device was developed using a three lead ECG and electronic stethoscope as input.

**Results:** Heart sound recordings of the most common innocent and pathological murmurs are presented as examples of the recorded data. The device functions well and the heart sound analysis methods are discussed with the possible advantages to the medical examiner. A screening sensitivity and specificity of respectively 90% and 96.5% were achieved in the initial tests conducted.

**Conclusions:** The accuracy by which medical examiners could distinguish between innocent and pathological murmurs could be improved by using a simple hand-held device. The device will be able to save, display, analyse and transmit the heart sound recording as well as the patient information. It is anticipated that this would reduce unnecessary referrals and improve the quality of referrals to cardiologists, while also reducing the financial and emotional impact that further referrals have on parents and their children.

## Native and reconstituted HDL protect cardiomyocytes from doxorubicin-induced apoptosis: roles of sphingosine-1-phosphate, ERK1/2 and Stat3

**Miguel Frias**, **Ursula Lang**, **Christine Gerber-Wicht** and **Richard W. James**

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Aims:** We analysed the impact of native and reconstituted (artificial) high density lipoproteins (HDL) on doxorubicin induced cardiomyocyte apoptosis. Whilst an effective anti-cancer agent, doxorubicin has serious, cardiotoxic side effects. Conversely, HDL has been shown to protect cardiomyocytes notably against oxidative stress.

**Methods:** Cultured neonatal rat ventricular cardiomyocytes were subjected to doxorubicin-induced stress, monitored as caspase3 activation and apoptotic DNA fragmentation. The protective effects of HDL and sphingosine-1-phosphate were investigated using native HDL isolated from human serum, reconstituted HDL of varied composition and agonists and antagonists of sphingosine-1-phosphate (SIP) receptors. Anti-apoptotic signaling pathways were identified with specific inhibitors.

**Results:** Native and reconstituted HDL significantly decreased doxorubicin-induced cardiomyocyte apoptosis. It was essentially attributable to the sphingosine-1-phosphate component of HDL. The effect of the latter was mediated by the SIP2 receptor; but not the SIP1 or SIP3 receptors. The ERK1/2 signaling pathway was required for the anti-apoptotic effects of HDL and sphingosine-1-phosphate. The transcription factor, Stat3, also played an important role as inhibition of its activity compromised the protective effects of native HDL and sphingosine-1-phosphate on doxorubicin-induced apoptosis.

**Conclusions:** HDL and its sphingosine-1-phosphate component can protect cardiomyocytes against doxorubicin toxicity and may offer one means of reducing cardiotoxic side effects during doxorubicin therapy. The study identified anti-apoptotic pathways that could be exploited to improve cardiomyocyte survival.

## A novel model of Endothelial Dysfunction (ED) in cultured Cardiac Microvascular Endothelial Cells (CMECs)

**Amanda Genis, Eva Madau, Amanda Lochner and Hans Strijdom**

Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

**Introduction & objectives:** ED occurs when the endothelium, in the presence of exposure to harmful circulating stimuli, associated with cardiovascular risk factors, produces reduced amounts of nitric oxide (NO), a potent vasodilator. ED is now recognised as the earliest, independent predictor of atherosclerosis and therefore has promising therapeutic value in prevention of ischaemic heart disease. Most studies focus on macrovascular ECs and the aim of this study was to establish a model for ED in CMECs and investigate possible cellular mechanisms. To achieve this, several cardiovascular risk factors were simulated in vitro to induce ED, which was defined as reduced intracellular NO-production.

**Experimental approach:** Rat CMEC cultures (4th 10th generations) were incubated with:

1. Glucose (25mM for 24h; 30mM for 72h)
2. Angiotensin II (Ang II) (100nM for 24h)
3. TNF- $\alpha$  (5ng/ml for 24h)

The following investigations were performed:

1. Cell viability: propidium iodide fluorescence.
2. NO production: DAF-2/DA fluorescence.
3. Total and activated eNOS expression in TNF- $\alpha$  groups (Western blot analysis)
4. Total and activated PKB expression in TNF- $\alpha$  groups (Western blot analysis)

**Results:** (1) 25mM glucose had no significant effect on NO levels. (2) 30mM glucose increased NO levels significantly. (3) Ang II had no effect on NO-production. (4) In TNF- $\alpha$  groups, a modest, but significant reduction in NO production was found in all three parameters assessed (91.133.22%, 94.252.58% and 93.421.95% respectively vs. 100% for control,  $p < 0.05$ ). Furthermore, a reduction in activated eNOS (0.600.27 vs. 1 for control) and a significant reduction in activated PKB (0.310.13 vs. 1 for control,  $p < 0.05$ ), were observed in TNF- $\alpha$  treated groups. None of these interventions had significant effects on cell viability.

**Discussion & conclusion:** An in vitro model of ED has for the first time been described in CMECs using TNF- $\alpha$  as the ED-inducing factor. It appears as if the model is associated with increased inactivation of PKB and eNOS, which could help explain the reduced NO-production observed. This can lead to possible further exploration of the mechanisms and signaling involved in ED in CMECs.

## Infective endocarditis in a HIV positive population

**R. Goncalves, J. Vorster, R. Garda, G. Angel, L. Mkhwanazi, N. Lester, N. Ruhmya and P. Manga**

Department of Cardiology, CM Johannesburg Academic Hospital, University of Witwatersrand, Johannesburg, South Africa

**Aims:** The association between HIV and infective endocarditis remains poorly defined. The aim of this study was to compare HIV positive to HIV negative patients with infective endocarditis admitted to CM Johannesburg Academic Hospital in terms of patient demographics and outcomes.

**Methods:** The study was a prospective observational study over a 3.5 year period. The modified Duke criteria were used to classify patients as having a definite, possible or rejected case of IE.

**Results:** 56 patients were identified as definite or possible IE. Of these 17 (30%) were HIV positive; definite (11) and possible (6). The remaining 39 patients were HIV negative. In the HIV positive cohort a female preponderance (1.4:1) was noted with a mean age of 35.3 years (range 22 - 67 years) as compared to a male preponderance (1.78:1) in the HIV negative patients with a mean age of 43.2 years

(range 16 - 76 years). Nine (53%) HIV positive patients had chronic rheumatic heart disease, based on standard clinical and echocardiographic criteria, compared to 25 (64%) in the HIV negative group. Five (29%) HIV positive patients and four (10%) HIV negative patients were intravenous drug abusers. No HIV positive patient had degenerative heart disease but five HIV negative patients had degenerative valvular disease (aortic stenosis and myxomatous mitral degeneration).

A positive blood culture was confirmed in 41% of patients among HIV positive patients versus 51% in HIV negative patients.

The mortality rate was 29% (5 deaths) and the same percentage underwent valve replacement in the HIV positive group. In the HIV negative group the mortality rate was 38.5% (15 deaths) and 46% (18 patients) underwent valve replacement.

**Conclusion:** As compared to HIV negative patients with IE, HIV positive patients with IE tend to be younger and female. Similar predisposing factors are present in both groups. Our study suggests that HIV is not a risk factor for infective endocarditis per se. Contrary to popular belief the prognosis is not worse in the HIV positive group as compared to the HIV negative group. Thus both groups should be treated similarly, medically and surgically.

## Infective endocarditis at CM Johannesburg Hospital: a prospective review

**R. Goncalves, J. Vorster, R. Garda, L. Mkhwanazi, G. Angel, N. Lester, N. Ruhmya and P. Manga**

Department of Cardiology, CM Johannesburg Academic Hospital, University of Witwatersrand, Johannesburg, South Africa

**Aims:** The epidemiology of infective endocarditis (IE) throughout the world continues to evolve. The aim of this study was to evaluate the demographics and patient outcomes of patients admitted to CM Johannesburg hospital with a presumed diagnosis of infective endocarditis.

**Methods:** The study was a prospective observational study. Patients referred with probable IE were prospectively enrolled over a three and a half year period. The study collected only in-hospital data during the index admission. The modified Duke criteria were used to classify patients as having a definite, possible or rejected case of IE.

**Results:** A total of 65 patients were identified with a presumptive diagnosis of IE. 31 (48%) had a definite diagnosis of IE. In 25 patients (38%) the diagnosis was possible and in 9 it was rejected. Of the 56 patients with a definite or possible diagnosis of IE a male predominance (1.3:1) was found with a mean age of 40.8 years (range 16-76 years). Thirty four patients (61%) had chronic rheumatic heart disease, based on clinical and echocardiographic findings. Five patients had degenerative valvular disease (aortic stenosis and myxomatous mitral degeneration). Nine patients had a history of intravenous drug abuse, 1 had a prosthetic cardiac valve and 2 had intravascular haemodialysis catheters. The aetiological agent was confirmed on blood culture in 27 patients (48%), with *Streptococcus Viridans* and *Staphylococcus Aureus* being the most common isolates. Cultures were negative in 52% of patients. Heart failure was very common (82%) as was renal failure (43%). 30% of the patients were found to be HIV positive. 41% of patients required valve replacement. The overall in-hospital mortality for this cohort of patients was 35%.

**Conclusion:** Patients with infective endocarditis tend to be young. The most common predisposing risk factor is chronic rheumatic valvular disease followed by degenerative valve disease. A high culture negative rate was noted possibly due to prior treatment with antibiotics or collection of insufficient samples. The prevalence of HIV in this study was high, probably a reflection of the burden of this disease in the community. The in-hospital mortality for IE remains very high.

## Percutaneous closure of a subclavian artery to Innominate vein fistula in a neonate

**K. Govendrageloo and J. Harrisberg**

Sunninghill Clinic, Sandton, South Africa

**Introduction:** Congenital Arteriovenous fistulae are fairly uncommon. Congestive cardiac failure may be a presenting feature dependent on the size of the communication from the high pressure arterial bed to the low-pressure venous circuit.

**Case report:** Dilated right heart chambers were detected antenatally by ultrasound. Term female neonate born by C/S weighing 3.24kg. No immediate problems. Prominent continuous murmur and radiological cardiomegaly noted immediately after birth. Normal vital signs.

**ECG:** SR. 146/min. Axis: +240. RA +. RV +.

**CXR:** Increased CTR - 73%. Clear lung fields.

**ECHO:** Normal venous return to RA and LA. PFO with L->R flow. Dilated RA, RV, MPA. Mild TI with mild + PHT. Very dilated Innominate vein and RSVC. Abnormal flow from LSA to Innominate vein via a short fistulous connection .

**CTA:** Small PDA. Short fistula from LSA -> Innominate vein. Mild Isthmal hypoplasia.

**INTERVENTIONAL PROCEDURE:** Successful percutaneous occlusion of the fistula with a 6:4 Type I Amplatzer PDA occluder.

**Conclusion:** An uncommon congenital arteriovenous fistula was found in a neonate -> right heart volume overload and the potential for CCF. Following preliminary investigations, successful percutaneous occlusion of the fistula was undertaken.

## Hybrid procedures to the aortic arch

**D.G. Harris, A. Saaiman, D. du Toit and G. Rossouw**

Kuilsriver Hospital, Kuilsriver, South Africa

**Objective:** Traditional repair of aortic arch aneurysms requires cardiopulmonary bypass and a period of profound hypothermia and circulatory arrest - allowing detachment of the head vessels off the aneurysm, and their anastomosis onto the graft. The procedure is safe and reproducible, however complications include air embolism, stroke, excessive bleeding, and acidosis. In addition the procedures are time consuming, and cardioplegic arrest is also necessary, resulting in the potential for low cardiac output.

With improving techniques of descending aortic repair with stent grafts, hybrid techniques (which involve aortic arch debranching followed by stenting over the aortic arch) are becoming popular.

**Methods:** Four cases are presented. The technique involves initial sternotomy or upper sternal split, detachment of the innominate and left common carotid arteries, and their re-attachment (transposition) to the ascending aorta by separate grafts (debranching procedure). The left subclavian is usually left intact for technical reasons – this is safe as the shoulder has adequate collateral circulation, and therefore stenting over this vessel is well tolerated. The aortic arch is then completely covered with a stent graft which is inserted via the femoral artery.

**Results: Case 1:** Repair of traumatic aortic dissection involving the arch.

A 33 year old male patient involved in an MVA sustained traumatic dissection of the descending aorta with retrograde extension into the arch. Repair would require clamping over the carotid artery and its re-attachment onto the graft with or without circulatory arrest – a technically difficult and risky procedure. Upper sternal split was performed, and a side clamp placed on the ascending aorta while a bifurcated graft was sewn in place. The innominate and left carotid arteries were transected and grafted to the graft. The left subclavian artery was left intact. After closure the patient was immediately transferred to the cath lab where the aortic arch was successfully stented. Follow up angiogram shows no endoleak. At 4 year follow up he remains well, with no claudication in the left arm. CT has been repeated and shows good position of the prosthesis.

**Case 2:** Off pump repair of saccular arch aneurysm.

This 65 year old male presents with a saccular aneurysm of the aortic arch, involving the innominate and left carotid arteries. Sternotomy was performed, a side clamp placed on ascending aorta, and a bifurcated graft attached. The innominate and left carotid arteries were

sequentially transected and attached to the graft. Stenting had originally been planned, but the aneurysm was amenable to surgical closure: a long clamp was placed across the arch, below the aneurysm, and it was excised and oversewn.

**Case 3:** Repair of left subclavian aneurysm with dissection into the descending aorta.

This 75 year old male patient presents with chest pain. Cardiac catheterisation confirms triple vessel disease, as well as a saccular aneurysm of the left subclavian artery. This has caused a dissection which extends into the descending aorta. CABG was performed, with vein grafts to LAD, circumflex and right coronary, and at the same time the left carotid and subclavian arteries were detached and grafted to a bifurcated graft from the ascending aorta. One month later a stent graft was placed over the arch from the innominate artery and over the aneurysm.

**Case 4:** Staged replacement of entire thoracic aorta.

A 58 year old female patient presents for repair of ascending aortic aneurysm. This measures 55mm, the arch 35mm, and descending aorta 42mm. The aneurysm extends up to and involves the innominate artery. Cardiac cath shows proximal LAD disease. Stage 1 involved vein graft to LAD, transection of the innominate artery, graft replacement of ascending aorta up to level of left carotid, and attachment of innominate lower down on graft via a 10 mm graft. Stage 2 was performed when the patient (lost to follow up) presented after 5 years with symptomatic 7cm aneurysm of distal descending aorta. Two 45mm x 15cm stent grafts were inserted from proximal aorta to the level of the coeliac artery. Stage 3 is available if arch replacement is indicated in future (presently measures 40mm). This would involve a stent across the arch after performing carotid-carotid grafting from right carotid.

**Conclusions:** Endovascular repair of the descending thoracic aorta, initially reserved for inoperable patients, is now becoming the accepted initial management. With improved technology and grafts it is now the safest option, especially for traumatic dissection. With debranching techniques available, stenting over the aortic arch, as a hybrid procedure is yielding gratifying results. Good pre-operative planning is necessary to make the procedure feasible.

## Repeat coronary artery bypass grafting: the role of the off pump left thoracotomy approach

**D.G. Harris and J.A. Saaiman**

Kuilsriver Hospital, Kuilsriver, South Africa

**Objective:** Repeat CABG has increased risks, including injury to patent grafts. We have evaluated the thoracotomy procedure, using the off pump technique in all patients. The procedure is well documented but reported data is limited to case reports and small series.

**Methods:** There were 55 patients over an 8 year period. Mean age was 63.2 years (41-82), and age at previous operation was 51.7 years (31-69). Predicted mortality was 14.1% (logistic EuroSCORE).

**Results:** Forty three patients had intact LIMA grafts. The LIMA was used in 7 patients, where it had not been used before. Stenting, as a hybrid procedure was performed in 13 patients (23.6%) during the same admission. There were 91 distal grafts (including 4 sequential). We performed 54 venous, and 26 radial artery grafts. 21 patients had 1 distal graft, 32 had 2 distals, and 2 had 3 distals performed (average 1.6 grafts per patient). It was possible to graft the distal right coronary branches (PDA or RPL) in 10 patients. Mean blood loss (24 hours) was 380mls, mean ventilation time 4.8 hrs (0-12), icu stay 2.7 days(2-8), and hospital stay 6.3 days (5-20). There was one postoperative death (1.8% mortality).

**Conclusion:** The procedure is safe, especially with patent LIMA-LAD grafts, and risks are decreased. Multislice CT scanning allows better preoperative planning, especially regarding sites of proximal graft implantation, allowing a less invasive incision. The procedure is now considered to be the method of choice for patients requiring redo surgery for lateral wall grafting especially when there is an intact LIMA to LAD graft.

Pre-operative data		
Number of patients	55	%
Mean age	63	41-82
Age at previous op	51.7	31-69
Congestive failure	7	2.7
Diabetes	25	45.5
EF 30-50%	21	38.2
EF<30%	4	7.3
Pre-op IABP	9	16.4
Pre-op inotropes	5	9.0
Previous stents	15	27.3
Peripheral vascular disease	11	20.0
Carotid disease	4	7.3
Calcified aorta	9	16.4
Unstable angina	25	45.5
2nd redo	4	7.3

Vessels stented (as hybrid procedure)	
Right coronary artery	6
LAD	3
Circumflex	1
Large septal perforator	2
Mainstem	1
<b>Total</b>	<b>13</b>

Post-operative data		
24 hour blood loss	380 (mls)	125-1100
Ventilation time	4.8 (hrs)	0-12
ICU stay	2.7 (days)	2-8
Hospital stay	6.5 days	5-20
Early death	1 patient	1.8%
Late death (1 year postop)	1 patient	1.8%
Re-angiogram (all grafts intact)	4 patients	7.3%

## Percutaneous management of a complex coarctation, PDA and mycotic aortic aneurysm: case report

**J.R. Harrisberg and K. Govendrageloo**

Sunninghill Clinic, Sandton, South Africa

**Introduction:** Complex coarctation with added pathology such as acquired mycotic aneurysms in the region of the coarctation may present as difficult and challenging surgical cases. These patients may often be better managed percutaneously with a variety of new stents which have recently become available.

**Case Study:** A 27year old male with Down Syndrome was born with an Atrio-Ventricular Septal Defect (AVSD), left ventricular outflow tract obstruction and a mild coarctation of the aorta. At the age of 4 months he underwent a successful surgical repair of the AVSD. At the age of 7 years he had a resection of a progressing subaortic membrane. He was then followed up for many years and was relatively asymptomatic. He developed Staph Aureus infective carditis at the age of 18 years which was successfully managed with antibiotics. This was followed by a diagnosis of spinal osteitis at the age of 26 years which again was treated with a prolonged course of antibiotics.

Over the more recent years, he had developed a severe long tunnel subaortic stenosis as well as a progressive severe coarctation of his native aorta associated with upper limb hypertension. At the age of 27 years, a CT angiogram to demonstrate the anatomy of the coarctation of the aorta, revealed a surprise finding of a large mycotic false aneurysm beneath the coarctation of the aorta and a long small PDA. He was turned down for surgery and percutaneous stenting of the coarctation and the aneurysm was attempted.

**Procedure:** In the cath lab, the patient underwent a successful percutaneous closure of the PDA with an Amplatzer Duct II device, complete relief of the coarctation of the aorta with a covered CP stent and then isolation of the mycotic aneurysm with a Relay stent graft. He now awaits surgery of his left ventricular outflow tract.

**Conclusion:** Complex coarctations of the aorta with added pathology such as mycotic aneurysms may be readily managed in the cath lab with a variety of new stents available to the cardiologists.

## 10 year single centre experience with percutaneous ASD occlusion and surgical closure

**J.R. Harrisberg, K. Govendrageloo, R. Kinsley, P. Colsen, H. Mamorare and G. Martin**

Sunninghill Clinic, Sandton, South Africa

**Introduction:** Amplatzer ASD occluders were introduced to South Africa in October 1999. Since then the number of percutaneous closures of secundum ASD's has steadily risen. At the same time, the surgical cases have not diminished much.

**Method:** This study is a non-randomised, retrospective observational analysis looking at both the percutaneous closure group and the surgical repairs over a 10 year period in a single centre.

**Percutaneous group:** 153 patients were taken to the cath lab with intention to close the secundum defects. 19 were rejected based on unsuitable anatomy with transoesophageal echocardiography (TEE) and were subsequently sent for surgery. 132 patients had 135 devices successfully implanted. There were 2 failures (wire entangled in chiari network and one case of temporary heart block). Both were sent for surgery.

**Surgical group:** Together with the 21 cases referred from the percutaneous group, a total of 143 cases were closed surgically over the 10 year period.

**Follow up:** Immediate and short term complications in both groups will be discussed in detail. In addition, the medium to long term follow up will be presented.

**Conclusions:** Percutaneous closure of selected secundum ASD's is a very effective and successful alternative with distinct advantages over surgical repair. Follow up has shown these cases to be free from medium to long term complications.

## PCI in diabetics: real world data: a comparison to the CARDia trial

**Peter Haworth, Sue Ellery, Miles Behan, Mrinal Saha, Anna Stubbs, Stephen Holmberg, David Hildick-Smith and Adam de Belder**

Cardiology Research Unit, Sussex Cardiac Centre, Brighton, UK

**Introduction:** 1 year mortality in diabetic patients with multivessel disease randomised to PCI in the CARDia trial showed no statistical difference to those randomised to CABG. Slow recruitment and failure to meet target numbers may have lead to selection bias. To assess whether the CARDia PCI is relevant to day-to-day practice, we analysed diabetic patients treated with PCI in our centre to assess 1 year mortality.

**Methods:** Baseline details were recorded peri-procedurally. 1 year follow up was performed by questionnaire. Mortality data was collected by analysis of the NHS strategic tracking system. Patients older than 80, with left main stem disease and patients with cardiogenic shock were excluded.

**Results:** 1 217 patients who met the CARDia admission criteria were included for analysis. There was no difference in age (65 years vs 64 years  $p=ns$ ), gender (male 71% in each group  $p=0.5$ ) or pre intervention EF < 50% (43% vs 45%  $p=0.7$ ). In our group there was a lower incidence of DES use (23% vs 71%  $p<0.001$ ), glycoprotein IIb/IIIa inhibitor use (4.3% vs 95%  $p<0.001$ ) and hypertension (62% vs 76%  $p<0.001$ ) along with a much higher incidence of acute patients (50% vs 22%  $p<0.001$ ) and a history of smoking (46% vs 37%  $p=0.01$ ). Insulin use was higher in the CARDia patients but not statistically significant (25% vs 31%  $p=0.06$ ). Mortality at 1 year was 3.2% in the CARDia group vs 4.8% in our group ( $p=0.37$ ).

**Conclusion:** Despite a higher incidence of PCI for acute coronary syndromes in our group, 1 year mortality is statistically no different than that of CARDia. We argue that our group more closely represents real world practice in PCI in diabetics. These results are a significant improvement on 1 year outcome seen in the BARI trial and support the use of PCI in diabetic patients.

## Syncope and sustained ventricular tachycardia predict mortality in Arrhythmogenic Right Ventricular Cardiomyopathy: evidence from the ARVC registry of South Africa

**Neil Hendricks, David A. Watkins, Z. Brian Vezi, Francesca Little, Motasim Badri, Andrzej Okreglicki and Bongani M. Mayosi**

The Cardiac Clinic, Groote Schuur Hospital, Observatory, Cape Town, South Africa

**Background:** Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a progressive heart muscle disorder that manifests with ventricular arrhythmias, heart failure and sudden death. Little is known about the outcome of patients with ARVC in South Africa.

**Methods:** Subjects were recruited to the ARVC Registry of South Africa from 2004 to 2009. Fifty unrelated cases were confirmed to have ARVC according to published criteria. Details on presenting symptoms, family history and annual follow-up were collected. Kaplan-Meier survival analysis was performed, and cohort survival was compared to the general South African population using the Chi-square test. Coxs proportional hazards regression models were fitted to identify risk factors associated with mortality.

**Results:** All major South African racial groups and both genders were represented in the cohort, though there was a preponderance of Caucasians (80%) and males (66%). Presenting characteristics were similar to cohorts in Europe and North America. Nine individuals (18%) died over a median follow-up of 4.55 [1.29-8.89] years. The mean age at death was 36.9 ± 14.7 years, annual mortality rate was 2.82%, and five-year cumulative mortality rate was 10%. Overall survival was similar to the general South African population ( $p=0.99$ ). Implantable cardioverter-defibrillators (ICDs) were placed in 20 subjects (40%). No subjects with an ICD died over the follow-up period, compared with 9/30 (30%) deaths in those without an ICD (Chi-square test  $p=0.007$ ). In univariate analysis, history of syncope and sustained ventricular tachycardia were the only two parameters associated with death ( $p=0.017$  and  $p=0.020$ , respectively); these remained significant in multivariate analysis (HR 10.73, 95% CI 1.88-61.18,  $p=0.008$  and HR=22.97, 95%CI 2.33-226.18,  $p=0.007$ , respectively).

**Conclusions:** The mean age of death (36.9 ± 14.7 years) of South Africans with ARVC is lower than elsewhere (54 ± 19 years). Survival is however comparable to the overall South African population, which is experiencing an increase in mortality due to the colliding epidemics of HIV/AIDS and non-communicable diseases. Presentation with syncope or sustained ventricular tachycardia are poor prognostic factors and mandate consideration for ICD implantation.

## Lucky to be alive: complex mediastinal AV fistula and false aneurysm case report

**K.M. Hossain, R.F. Chauke, P.S. Ramoroko and S.M. Mazibuko**

Department of Cardiothoracic Surgery, University of Limpopo, South Africa

Penetrating injury of the thoracic aorta is uncommon but mostly fatal, and more so are mediastinal arteriovenous(A-V) fistulae. Very few patients survive long enough to need surgical treatment and a minority of them develop chronic aorto-venous fistula. Chronic post traumatic aortovenous fistula patients present with features of congestive cardiac failure and need a specialised imaging procedures for precise anatomical diagnosis and well planned surgical intervention sometimes with cardiopulmonary bypass and hypothermic circulatory arrest. We report a case of a 19 year old patient with chronic aortic arch-left brachiocephalic vein fistula and aneurysm. The patient presented about 2 years after a stab to the left parasternal area with neck swelling, distended left sided neck and chest veins and in heart failure. Investigations undertaken were: Chest x-ray, echocardiogram, arch angiogram and thoracic CT angiogram. Chest x-ray revealed widened mediastinum and cardiomegally. Arch angiogram showed ill-sited mediastinal arteriovenous fistula and aneurysm with rapid venous runoff. CT-angio improved localisation of the fistula and also revealed multiple aneurysms. Intra-operative findings were through and through injuries of distal brachiocephalic vein, the aortic arch at the origin of the bovine trunk and under surface of the arch with multiple aneurysms. Successful repair of the pathology was done using cardiopulmonary bypass, hypothermic circulatory arrest and selective antegrade cerebral perfusion. Patient was discharged home without major neurological deficit but had developed delayed post-pericardiotomy pericardial effusion which resolved with drainage. Successful repair of chronic mediastinal A-V fistula with minimal neurological complications can be achieved with multidisciplinary cooperation and a well planned surgical approach.

## Pre-treatment with a DPP-4 inhibitor is cardioprotective in insulin resistant rats

**B. Huisamen, A. Genis and A. Lochner**

Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

Therapy based on the incretin hormone, glucagon-like peptide-1 (GLP-1) is currently hailed as one of the most promising treatments for type 2 diabetes, also because GLP-1 is cardioprotective in animals as well as humans. Because GLP-1 is rapidly degraded by depeptidyl-peptidase IV (DPP4), some research has focused on inhibitors of this enzyme to raise levels of GLP-1, the latter being attenuated in type 2 diabetes. We have tested whether pre-treatment of obese, insulin resistant rats, known to present with cardiovascular pathology, with a DPP4 inhibitor, is cardioprotective.

Obesity was induced by hyperphagia in Wistar rats (DIO) for a period of 12 weeks whereafter control fed and DIO animals were treated with 10mg/kg/day of the DPP4 inhibitor PFK275-055 (Novartis) given orally set in a gelatine/jelly cube. After 4 weeks of treatment, animals were sacrificed in a non-fasting state, trunk blood collected for biochemistry, body weight and intra peritoneal (IP) fat weight recorded, pancreases harvested for histology and the isolated hearts perfused (Langendorff with regional ischaemia to determine infarct development). Ventricular myocytes were prepared via standard collagenase perfusion techniques to determine insulin stimulated glucose uptake.

**Results:** GLP-1 levels were attenuated in DIO and restored by treatment while glucagon levels were 56.7% lower in DIO animals coupled to 49% higher insulin levels. These were not affected by treatment. No effects were found on weight, IP fat or blood glucose levels. DIO animals presented with 43.44.6% infarct of area at risk vs control = 30.73.7 and DIO treated = 30.113.1;  $P < 0.05$ ,  $n = 6$ . Coronary flow was enhanced from 16.80.7 to 200.6 ml/min,  $p = 0.008$ ,  $n = 6$  in control hearts but no effect found in DIO hearts. No sensitisation of cardiomyocytes towards insulin could be detected in cells from DIO animals while controls cells presented with a higher fold increase in glucose uptake after treatment. No effects on beta-cell neogenesis were found.

**Conclusions:** Pretreatment with the DPP4 inhibitor PFK275-055 is cardioprotective in obese animals but did not alleviate insulin resistance over a 4 week treatment period.

## 2-D echocardiographic evaluation of neonates with respiratory distress

**Rakesh Jalota and S.S. Sarkar**

Vivekanad Polyclinic and Institute of Medical Sciences, Lucknow, India and Sarkar Medical Diagnostic Centre Pvt Ltd, India

**Purpose:** To evaluate significance of 2-D echocardiography in neonates with respiratory distress in 1st week of life due to congenital cardiac defects (CCD).

**Method:** Total 240 neonates with respiratory distress were echocardiographed in detail were reassessed six weeks later and data was analysed.

**Results:** Total infants: 240 (135 males, 105 females), Normal 82 (34.16%), with CCD 158 (65.85%), FTND-118, FTCS-97, PMND-18, PMCS-7. It was found that the most common defect among the neonates having CCD was Patent Ductus Arteriosus (43%), Atrial Septal Defect (11.39%), Patent foramina ovale (10.75%), PDA+ASD/PFO (11.35%) and 25.9% were associated with mild to significant Pulmonary Arterial Hypertension, PAH ranged from 32.11mmHg to 64.17mmHg (Avg 43.22mmHg) Total percentile of CCD among the type of birth viz. FTND, FTCS, PMND & PMCS were almost the same. After six weeks, reassessment by 2D echo it was found that all PDA, ASD, PFO & VSD were closed except two large ASD and one subcostal VSD, PAH was reversed to normal in all neonates and they were also clinically stable.

**Conclusion:** In neonates with respiratory distress apart from primary lung problem another major contributory factor is the congenital cardiac defects with PAH (25.94%) which probably due to the left to right shunt from congenital cardiac defects. Within six weeks majority of the neonates improved, CCD closed and PAH was also normalised.

It is therefore concluded that all the neonates with respiratory distress, if found to have CCD with left to right shunt and PAH should be deferred from active intervention and should be managed medically up to 6 to 8 weeks as there is significant chance of their improvement due to spontaneous closure of left to right shunt and resolution of PAH.

## Percutaneous pericardioscopy in tuberculous pericarditis: improving the diagnostic yield

**C.G. Kyriakakis, H. Weich and A.F. Doubell**

Division of Cardiology, Department of Medicine, University of Stellenbosch and Tygerberg Hospital, South Africa

**Introduction:** Tuberculous pericarditis remains an important cause of morbidity and mortality in the developing world with an increasing prevalence due to the HIV pandemic. Definitive diagnosis via direct identification of the mycobacterium bacillus is challenging and not always possible via conventional investigations. Previous studies have demonstrated a low yield of acid fast bacilli or Mycobacterium tuberculosis culture on pericardial fluid alone.

**Objective:** To evaluate the potential advantage of percutaneous pericardioscopic biopsy of the pericardium in tuberculous pericarditis.

**Methods:** All patients presenting to the Division of Cardiology, Stellenbosch University and Tygerberg hospital, with a large non-traumatic pericardial effusion (epicardial separation distance > 10mm) were offered participation. Each patient underwent pericardiocentesis via a standard procedure followed by percutaneous pericardioscopy and pericardial biopsy via a flexible fibre optic pericardioscope. Pericardial fluid evaluation included: biochemistry including adenosine deaminase level, cell count, acid fast bacilli (AFB) and tuberculosis (TB) culture. Pericardial biopsy specimens were evaluated for AFBs, TB culture and histologically for granulomas.

**Results:** Sixteen patients agreed to participate. Pericardial biopsy could be obtained in 11 patients, all of which were uncomplicated. Mean age was 35. Six (54,5%) had associated HIV disease and 2 (18,2%) presented in clinical tamponade. Six (54,5%) had macroscopic evidence of pericardial inflammation with an exudative surface visualised at pericardioscopy. Seven patients (63,6%) were found to have definite pericardial TB. Three of the remaining 4 had an alternative diagnosis. Six of the 7 patients with proven TB were AFB positive on pericardial biopsy. In none of these patients could AFBs be seen on fluid and only five fluid samples subsequently cultured TB within 42 days (mean time 23,2 days).

**Conclusion:** In contrast to the assessment of pericardial fluid where a definite diagnosis of TB is dependant on culture, biopsy enabled a more rapid diagnosis via demonstration of acid fast bacilli.

## Innate immunity and protection against reperfusion injury via the SAFE pathway

**Lydia Lacerda, Sarin Somers, Lionel Opie and Sandrine Lecour**

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Introduction:** Although the cytokine, tumour necrosis factor alpha (TNF $\alpha$ ), is considered to have mainly detrimental effects, brief perfusion of TNF $\alpha$ , at the onset of reperfusion, confers protection against lethal reperfusion injuries. We hypothesised that TNF $\alpha$  confers protection via the activation of STAT-3, a pathway recently described as the survivor activating factor enhancement (SAFE) pathway.

**Methods:** Hearts from wildtype (WT), TNF $^{-/-}$ , or cardiac specific STAT-3 deficient (STAT-3 $^{-/-}$ ) mice were isolated, mounted on a Langendorff perfusion system and subjected to 35 min global ischaemia (I) followed by 45 min of reperfusion (R) (CTL). Ischaemic postconditioning (IPostC) was performed by 6 alternative cycles of 10 sec reperfusion, 10 sec ischaemia. In a separate group, pharmacological postconditioning with TNF $\alpha$  was performed by 6 cycles of alternative perfusion with/without 0.5ng/ml TNF for 10 sec (TNF-PostC). AG 490, a STAT-3 inhibitor; wortmannin, an Akt inhibitor; or PD98059, an inhibitor of Erk1/2, were given during the first 15 min of reperfusion with either postconditioning protocol. Infarct size (IS) was evaluated at the end of the protocol. In a separate set of experiments, hearts were collected after 15 min of reperfusion for Western blot analysis.

**Results:** Both IPostC and TNF-PostC reduced infarct size in WT hearts compared to their CTL group (182% and 181%, respectively,  $p < 0.05$  vs 483% for their respective CTL) but failed to protect the TNF $^{-/-}$  and STAT-3 $^{-/-}$  mice. Similarly, the infarct sparing effect of TNF-PostC was abolished in the presence of AG-490 but remained unchanged in the presence of wortmannin or PD98059. Phosphorylated levels of

STAT-3, were increased after TNF-PostC stimulus in the nucleus from 182 arbitrary units (AU) for I/R,  $p < 0.05$  to 546 AU. Similarly Erk1/2 phosphorylation was increased from 91 AU for I/R to 262 AU while Akt phosphorylation was decreased after the TNF stimulus from 182 AU for I/R  $p < 0.05$  to 61 AU.

**Conclusion:** Ischaemic postconditioning protects against reperfusion injury via the activation of the SAFE pathway which involves the activation of the innate immune system and the transcription factor, STAT-3. Our data provide a novel therapeutic target to limit the lethal effects of reperfusion injury.

## Melatonin found in red wine: just a sleep away from cardioprotection

**Kim Lamont, Lionel Opie and Sandrine Lecour**

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Introduction:** Moderate chronic consumption of red wine (2-3 glasses/day) can protect against cardiovascular disease. However, the exact components found in the wine, which can account for this protective effect, still need to be delineated. Recently, the presence of melatonin, a hormone that regulates circadian rhythms, has been detected in red wine. Interestingly, melatonin also protects against experimental ischaemia reperfusion injury. Therefore, we hypothesized that the presence of melatonin in red wine contributes to the cardioprotective effect of chronic red wine consumption. In addition, we propose that the protective effect of melatonin occurs via the activation of the transcription factor signal transducer and activator of transcription 3 (STAT3), known to protect against ischaemia reperfusion injury.

**Methods:** The drinking water of male Wistar rats was supplemented with red wine (equivalent of 2 glasses per day) or melatonin (0.075g/day). After 10 days of treatment, hearts were perfused on the Langendorff system and subjected to 30min global ischaemia (I) followed by 60min of reperfusion (R). Functional parameters were recorded throughout the experiments and infarct size was measured at the end of the protocol. Rate pressure product (RPP) measured at 60min of reperfusion was expressed as a percentage of baseline value.

**Results:** Control hearts subjected to I/R presented a rate RPP of (16.4%  $\pm$  2.7). A chronic treatment of red wine or melatonin improved RPP to a similar level (28.5%  $\pm$  2.7 and 27.4%  $\pm$  2.9, respectively,  $p < 0.001$  vs control). Interestingly, pretreatment with red wine or melatonin were associated with an increase in STAT3 phosphorylation compared with the control groups (70% for red wine and 79% for melatonin). Furthermore, experiments conducted in the presence of AG490, a STAT3 inhibitor abolished the protective effect of melatonin or red wine.

**Conclusion:** Our data strongly suggest that melatonin may account for the protective effect of chronic moderate consumption of red wine and that this protective effect is mediated via the activation of STAT3 activation.

## Cardiac abnormalities in thoracopagus conjoined twins. The Red Cross Children's Hospital experience

**John Lawrenson, John Hewitson, Jenny Thomas, Richard Pitcher and Alastair Millar**

Department of Paediatrics and Child Health, University of Stellenbosch and School of Adolescent and Child Health, University of Cape Town, Red Cross Children's Hospital, Cape Town, South Africa

During the past 4 decades, the surgical unit at the Red Cross Children's hospital has become an expert centre in the evaluation and treatment of conjoined twins. In thoracopagus twins, the extent of cardiac sharing may determine whether separation is possible. In this brief review, the evaluation of cardiac abnormalities in the 24 sets of thoracopagus twins will be discussed. The author will highlight the technical difficulties and ethical dilemmas which characterise the management of these patients.

## HIV cardiomyopathy is associated with a low body mass index: evidence from a case-comparison study

**C.E. Lemmer, M. Badri, M. Visser and B.M Mayosi**

Department of Medicine, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** The cause of cardiomyopathy in patients infected with human immunodeficiency virus (HIV) remains largely unknown, although a number of predisposing factors have been identified. Malnutrition has been postulated as a contributory factor but the association of malnutrition with HIV-associated cardiomyopathy has not been established in prospective studies.

**Method:** We prospectively investigated the association between nutritional state measured by anthropometric measures of lean body mass and HIV positive individuals with and without cardiomyopathy.

**Results:** 17 cases of HIV-associated cardiomyopathy (HIVAC) and a comparison group of 18 HIV positive patients without heart disease were recruited. There were no significant differences in age, CD4 cell count, HIV RNA viral load and WHO clinical stage of HIV disease between the two groups. HIVAC cases had evidence of malnutrition compared to those without cardiomyopathy: a significantly lower Body Mass Index (cases: 20.9kg/m<sup>2</sup>; controls: 27.0kg/m<sup>2</sup>; P=0.02), Mid-Upper Arm Circumference (cases: 26.2cm; controls: 27.3cm; P=0.02), and Bone Free Arm Muscle Area (cases: 26.7cm<sup>2</sup>; controls: 32.8cm<sup>2</sup>; P=0.02). However, in a multi-variate step-wise logistic regression model, body mass index (BMI) was the only independent anthropometric risk factor for cardiomyopathy (odds ratio = 0.73 95%CI 0.64-0.97, p=0.02).

**Conclusion:** Cardiomyopathy is associated with a lower BMI in people who are living with HIV.

## Mechanism of melatonin-induced cardioprotection: let me count the ways...

**Amanda Lochner**

Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

Melatonin (N-acetyl-5-methoxytryptamine) is synthesized mainly by the pineal gland and regulates mammalian and circadian rhythms. It is a highly conserved molecule found in organisms from unicells to vertebrates. Melatonin is a potent free radical scavenger and an anti-oxidant and is highly effective against oxidative stress. For example, melatonin is 5 and 14 times more effective at scavenging the highly toxic hydroxyl radical than is either glutathione and mannitol respectively. Melatonin is involved in many physiological systems including the cardiovascular system. Melatonin effectively protects the heart against ischaemia-reperfusion damage, having both acute and long-term effects. Although these effects were initially attributed to its free radical scavenging abilities and anti-oxidant activity, recent evidence suggested a role for the melatonin receptor, since its beneficial effects are abolished by luzindole, a melatonin receptor blocker. In addition, melatonin has potent anti-adrenergic actions, involving nitric oxide, guanylyl cyclase and PKC, which have been shown to participate in melatonin-induced cardioprotection. Simultaneous administration of melatonin and inhibitors of nitric oxide synthase or guanylyl cyclase abolished cardioprotection. Recent studies showed that melatonin also protected the mitochondrial integrity and functional capacity by virtue of its free radical scavenging actions and it was suggested that it may directly interact with the mitochondrial permeability transition pore, keeping it in a closed confirmation.

There is continued interest in discovering new cardioprotective agents of high potency and low toxicity. Melatonin fulfills most of these criteria and the virtual absence of toxicity renders it a good candidate for long-term use. However, all studies thus far have been done on animals and only one clinical trial is currently in progress where melatonin is used as an adjunct in patients with acute myocardial infarction undergoing angioplasty. Clearly the outcome of such a study may play a pivotal role in the decision to use melatonin in patients with ischaemic heart disease or to use the drug prophylactically.

## Cell death in ischaemic injury: a dynamic response concept

**Ben Loos and Anna-Mart Engelbrecht**

Department of Physiological Sciences, University of Stellenbosch, South Africa

Autophagy, apoptosis and necrosis have previously been described as distinct static processes that induce and execute cell death. Due to an increased use of novel techniques in mapping cellular death the existence of grey zones between cell death modes have been revealed. Therefore, we aim to dissect out the molecular overlap between the cell death modes and to place them into clear context of autophagic activity, the intracellular metabolic environment and kinetics of the cell death modes. It is hypothesized, that cell death is a dynamic response scheme with autophagy as a central role player in providing cellular adaptability and ensuring highest likelihood for cell survival.

A model of simulated ischaemia (SI) is employed using the cardiac myoblast cell line H9c-2. Cells were submitted to a protocol of 2, 4 and 8 hours of SI followed by 1 hour reperfusion. To modulate SI severity, 2-deoxy-glucose, sodium dithionate and a combination thereof are employed. We evaluated the contribution of the cell death modes using viability- and ATP assays. LC3, Beclin-1, Cyt-c and HMGB-1 were evaluated using 3-dimensional fluorescence and live cell-imaging techniques, Western blot analysis and flow cytometry.

Our results indicate a differential induction of cell death, which is dependent on the duration, severity of SI and the metabolic state of the cell. The inhibition of glycolysis leads to the induction of autophagy, to significantly increased ATP generation and pyknosis. The inhibition of mitochondrial respiration fails to induce an autophagic response but rather induces loss of membrane integrity. An onset delay of apoptosis and necrosis is suggested, when the autophagic machinery is induced in time. These findings indicate the urgent need to address the cell's metabolic capacity in context with cell death parameters from a dynamic perspective.

## Recognition of cardiac abnormalities with the aid of a precordial auscultation device

**W.W.Lubbe\*, J.S.F.Botha#, H.S.Weich†, P.G.Herbst†, I.B.Louw†, H.L.Koekemoer\*\*, C.Scheffer# and A.F.Doubell†**

\*Division of Internal Medicine, University of Stellenbosch and Tygeberg Hospital, South Africa

#Department of Mechanical and Megatronic Engineering, University of Stellenbosch, South Africa

†Division of Cardiology, Department of Medicine, University of Stellenbosch and Tygerberg Hospital, South Africa

\*\*Geoaxon Holdings (Pty) Ltd., South Africa

**Introduction:** A precordial auscultation device (PAD) has been developed with the aim of screening for cardiac disease by differentiating between normal and abnormal heart sounds and recording an ECG. The use of the PAD as a screening tool to assess the auscultation data of a patient might prove useful for healthcare workers in rural communities by improving the detection of cardiac abnormalities and preventing inappropriate referrals. Our aim was to determine the sensitivity and specificity of the PAD to detect cardiac disease.

**Methods:** Sixty people were recruited of which 30 had normal hearts and 30 had abnormal hearts, as determined by echocardiography. All participants were examined by a cardiologist and had PAD auscultatory and ECG recordings performed. The cardiologist and PAD findings were separately used to classify participants as normal or abnormal. This was then compared to the echocardiographic diagnosis and sensitivities and specificities calculated. An ECG using the PAD was recorded which was categorised by the cardiologist as normal, abnormal or quality insufficient to comment.

**Results:** Seven of the 60 PAD recordings could not be analysed due to technical difficulties (data not included in this analysis). The PAD correctly identified 16 of the 28 abnormal participants (sensitivity 57%) and 21 of the 25 normal participants (specificity 84%) with a positive predictive value of 80% and a negative predictive value of 63%. The ability to detect abnormality was enhanced by using the PAD ECG together with the PAD recordings, resulting in a sensitivity of 86% and a specificity of 71%. The positive and negative predictive values were 75% and 83% respectively. The PAD accuracy was unaffected by weight, height, BMI or chest circumference.

**Conclusions:** The PAD when used together with the information supplied by the PAD ECG is a sensitive and specific tool to screen for cardiac disease.

## Comparison of PCI and CABG in shortening the QTc interval, and correlation with the incidence of sudden cardiac death

**K. Majola, M. Heradien, A. Goosen, P. van der Bijl, P. Brink and A. Doubell**

Department of Medicine, Faculty of Health Sciences, University of Stellenbosch and Tygerberg Hospital, South Africa

**Objectives:** To compare the effect on shortening of the QTc interval obtained via Percutaneous Coronary Intervention (PCI) or Coronary Artery Bypass Grafting (CABG) and by extrapolation, the incidence of sudden cardiac death after abovementioned procedures.

**Methods:** All patients admitted to Tygerberg Academic Hospital (TAH) for angiography, and subsequently progressing to a revascularisation procedure (either PCI or CABG, according to standard indications) during 2009, were included. Bazetts formula was employed to manually calculate QTc-intervals prior to and immediately after revascularisation, as well as one day prior to or upon hospital discharge. The mean, nett, difference in QTc-intervals (prior to and immediately after revascularisation) between the two groups (PCI vs. CABG) were compared.

**Results:** In the PCI group, 41 patients have been entered thus far; 32 males (78% of the population). The mean, pre-PCI QTc was 435 ms, and the mean, post-PCI QTc was 412 ms. This translates to a mean, nett difference of 23 ms. In the CABG group, 20 patients have been entered thus far; 16 males (80% of the population). The mean, pre-CABG QTc was 444 ms, and the mean, post-CABG QTc was 404 ms. This translates to a mean, nett difference of 40 ms. CABG appears to shorten QTc more than PCI.

**Conclusions:** It has been proven that both procedures improve coronary perfusion and cardiac systolic function, but CABG has a more dramatic effect on mortality. In this preliminary study, CABG also appears to shorten the QTc more than PCI, which would suggest that the difference in QTc is a potential, surrogate marker for mortality in this context. If a clear correlation can be proven between QTc shortening and sudden cardiac death, even more credibility will be added to using QTc as an index for mortality in the setting of ischaemic heart disease and revascularisation procedures.

## Life threatening chronic traumatic broncho-pulmonary arterial fistula

**M.R. Manganyi, R.F. Chauke and P.S. Ramoroko**

Department of Cardiothoracic Surgery, Medunsa Campus, University of Limpopo, South Africa

Bronchovascular fistula occurs rarely following pulmonary resection occurring in 3% of patients who have undergone bronchoplastic procedure. Other cases of bronchopulmonary fistula were reported after tracheobronchial stents, lung transplantation and CABG. Its occurrence is even rarer following gunshot wounds to the chest. Literature search for penetrating traumatic bronchovascular fistula are very hard to come by. No article could be found that addresses bronchial – pulmonary arterial fistula following penetrating injuries to the chest. We report an unusually presentation of major haemoptysis in a 37 year old male patient presenting 17 years after gunshot to the chest with bullet in-situ. The patient was transferred to our institution after presenting at the local hospital with massive haemoptysis. Investigation undertaken included chest X-ray and CT scan of the chest which revealed right upper lobe consolidation with foreign body in the perihilar region. The patient was taken to theatre for emergency right upper lobectomy. During dissection the fistula was discovered between the pulmonary artery and the right upper lobe, where the patient was bleeding into the pulmonary parenchyma, hence the haemoptysis. The lobectomy and the fistula were successfully repaired and the bullet retrieved. The patient was well at sixth months follow-up. High index of suspicion is therefore needed for management and good outcome.

## Mutations in plakophilin 2 gene are a common cause of Arrhythmogenic Right Ventricular Cardiomyopathy in South Africa: evidence from the ARVC Registry of South Africa

M. Mbele, G. Shaboodien, M. Parker, N. Hendricks, D. Watkins, A. Okreglicki, H. Moolman-Smook and B.M. Mayosi

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Background:** Genetic mutations in the plakophilin-2 (PKP2) gene cause 10-43% (average 26%) of cases of inherited arrhythmogenic right ventricular cardiomyopathy (ARVC) in Europe and North America. The prevalence of PKP2 mutations in South African patients with ARVC is not known. The aim of the study was to determine the prevalence of PKP2 mutations in patients with ARVC in South Africa.

**Method:** Thirty-six DNA samples from unrelated probands with ARVC were screened for variants in 14 exons of PKP2 using denaturing high-performance liquid chromatography and sequencing. Population frequencies of novel PKP2 variants were determined in control individuals by SNaPshot and restriction enzyme digestion. As a rare novel variant recurred in three apparently unrelated ARVC probands, determination of common ancestral haplotype was done by means of microsatellite marker genotyping across a 300kb region on chromosome 12 (NC\_000012.10) in which PKP2 resides.

**Results:** Seven PKP2 gene mutations, 5 of which were novel, were found in 8/36 (22%) unrelated participants. The novel C1162T mutation occurred in 3 persons of Afrikaner ancestry who shared a common haplotype, suggesting a founder effect. Compound heterozygotes exhibited a severe phenotype, in keeping with an allele-dosage effect.

**Conclusion:** PKP2 gene mutations are common in South African individuals with ARVC. Additionally, we describe for the first time an allele-dosage effect and a novel founder mutation in Afrikaners in this gene.

## Reperfusion injury and PKC: two new kids on the block

J. McCarthy\*, A. Lochner#, S. Genade# and L.H. Opie\*

\*Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

#Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

Cardiovascular diseases are predicted to become the major cause of mortality world wide by 2020.

During or shortly after myocardial infarction (MI), the optimal treatment is rapid restoration of myocardial blood flow on the assumption that this will limit infarction damage. However, clinical studies during PCI for acute myocardial infarction suggest that up to 45% of cardiac cells that should have been saved from ischaemic death rather undergo reperfusion-induced necrosis. This phenomenon is known as reperfusion injury. Intense research has pioneered three methods of cardioprotection to minimise this injury: ischaemic preconditioning, ischaemic post conditioning and remote preconditioning. These cardioprotective mechanisms all activate one or more of the protein kinase C family (PKCs) occurring in the cytosol. Only two PKCs are important in cardioprotection: PKCepsilon (PKCε) is cardioprotective and PKCdelta (PKCδ) is deleterious. Small and large animal trials illustrated the benefit of inhibiting PKCδ, leading to a small human trial (DELTA MI) which demonstrated preliminary clinical benefit from PKCδ inhibition at reperfusion after MI - ejection fraction increased to normal values, LV developed pressure improvement and decreased infarct size.

Our research focuses on the protective benefit of increased activated PKCε at the level of the mitochondrion. Mitochondria are more than just energy generators for the cell, but also regulate the life and death of the cell. To explore the contribution of activated PKCε to cardioprotection we have a transgenic mouse model overexpressing cardiac-specific PKCε. These mouse hearts are extremely resistant to acute or chronic oxidant stress, exhibiting dramatically reduced infarct size ( $p < 0.03$  vs WT) and a robust cardioprotective programme residing in part at the mitochondrion. Isolated PKCε mitochondria respire better (PKCε: 180.25 vs 116.12 in the WT,  $n=8, p < 0.02$ ) and produce more ATP after acute and chronic oxidant stress ( $p < 0.03$  vs WT).

Glucose as cardiac fuel source is cardioprotective, especially during reduced oxygen levels. PKCε hearts preferentially metabolise glucose, producing more cardiac work at lower oxygen consumption (1.78 0.1 vs 1.25 1.2 mJ/min/g dry weight,  $p < 0.05$ ). We conclude therefore that activated PKCε-mediated preferential cardiac fuel selection might be the source of the robust cardioprotection seen in aPKCε animals.

## Are all the pulses present? An interesting presentation of aortic coarctation

**B.J. Mitchell, F.F. Takawira and J. Joshi**

Department of Paediatric Cardiology, Steve Biko Academic Hospital and University of Pretoria, South Africa

**Introduction:** This case of neonatal coarctation re-emphasises the importance of evaluating the neonates pulses and blood pressures (BPs) in all four limbs.

**Case study:** A 2.5kg male infant was born normally to a 37yr G5P5 mother at 8 months gestation. He was admitted on day 2 of life with oedema and respiratory distress with saturations of 85%. He had minor dysmorphic features - a diagnosis of Noonan syndrome was considered. Pulses and BPs were equivalent in all four limbs: 65/35 mmHg. He was intubated and ventilated with improved saturations of 99%.

Cardiac echo showed normal intra-cardiac anatomy, a dilated right heart and severe pulmonary hypertension (PAH), with estimated pulmonary pressures of 60/30mmHg and bidirectional shunting across the patent ductus arteriosus (PDA) and foramen ovale. The aortic arch anatomy was suspicious of coarctation in evolution with narrowing of the juxtaductal aorta. No coarctation gradient was present however due to the large PDA. In addition, an aberrant subclavian artery arising distal to the narrowing was seen.

The next morning he had no pulses palpable in the right arm and legs with BP in these three limbs significantly lower: 48/28 (mean 36) mmHg than that of the left arm 63/32 (mean 50) mmHg. The repeat echo showed a small PDA with clear coarctation of the aorta. The PAH had resolved. Due to the clinical findings, the right subclavian artery was thought to be aberrant and arise distal to the site of coarctation. This was confirmed with CT angiography and at surgery. An end-to-end anastomosis was performed with satisfactory results.

**Discussion:** Aberrant right subclavian artery (ARSA) accompanies 3% of congenital cardiac defects and 1% of coarctations. Embryologically, the RSA develops proximally from the right 4th aortic arch, the right dorsal aorta and the right 7th intersegmental artery distally. In ARSA, only the latter remains, connected to the descending aorta. The ARSA can complicate coarctation repair: as the spinal artery arises from the subclavian arteries via the vertebral arteries, if both subclavian arteries are clamped, distal hypoperfusion and spinal cord ischaemia may occur. The diagnosis must thus be made pre-operatively to aid operative planning.

## Infantile Marfan syndrome: a short tale

**B.J. Mitchell, F.F. Takawira and J. Joshi**

Department of Paediatric Cardiology, Steve Biko Academic Hospital and University of Pretoria, South Africa

**Introduction:** Marfan Syndrome is readily diagnosed. A more severe form, termed infantile or congenital Marfan Syndrome, is associated with significant mortality at an early age. We present a case study of this rare disorder.

**Case study:** A one-year-old boy presented with a cardiac murmur, recurrent chest infections, failure to thrive and developmental delay. He had a worried old man appearance with frontal bossing, dolicocephaly, high arched palate, micrognathia and low-set ears. He had pronounced hypermobility of his joints, pectus carinatum, kyphoscoliosis, arachnodactyly and contractures of the metacarpo-phalangeal joints. Ophthalmological examination showed megalocornea and iridodonesis with lens subluxation. His vitals were normal for age. He had cardiomegaly with an associated apical systolic thrill. Auscultation confirmed a 4/6 pansystolic murmur over the apex. He had mild hepatomegaly and a small umbilical hernia. ECG showed mild LVH with LV strain. His cardiac ultrasound showed a markedly dilated aortic root of 30mm with no aortic regurgitation. Aorta annulus measured 14mm. There was mitral and tricuspid valve prolapse with moderate mitral and mild tricuspid regurgitation. On the basis of the clinical examination and sonar findings, a diagnosis of infantile Marfan syndrome was made.

**Discussion:** Marfan Syndrome is an inheritable connective tissue disorder involving especially the cardiovascular, musculoskeletal, and ocular systems. Autosomal dominantly-inherited or sporadic mutations in the fibrillin (FBN1) gene on chromosome 15 lead to disruption and disarray of collagen and elastic fibers with increased interstitial ground substance. Myxomatous thickening and redundancy of the mitral and tricuspid leaflets, and marked elongation of their chordae tendinae, lead to significant valvar insufficiency. Cardiac ultrasound demonstrates

the aortic root dilatation that occurs in 80% of cases and evaluates the degree of AV valve regurgitation. Sporadic cases tend to be more severe with mutations generally in exons 24-32. Children with these mutations usually die of cardiopulmonary failure in the first few years of life. This severe form has been termed neonatal, infantile or congenital Marfan syndrome. Hyperextensible joints and arachnodactyly are a reliable clinical marker of connective tissue disease and with the characteristic facial appearance, the diagnosis of infantile Marfan syndrome is readily apparent.

## The Atrial Switch: does it cut the mustard?

**B.J. Mitchell, F.F. Takawira, G. Sinyangwe and J.J. Joshi**

Department of Paediatric Cardiology, Steve Biko Academic Hospital and University of Pretoria, South Africa

**Introduction:** The Atrial Switch procedures remain an imperfect solution to a complex condition. We present a case of obstructed systemic venous return following Mustard operation.

**Case study:** A 2.6kg female patient presented at age 4 weeks with severe cyanosis and respiratory distress. She had dysmorphic features in keeping with Goldenhar syndrome. She was supported with Prostaglandin E<sub>1</sub> infusion and mechanical ventilation. Echocardiography diagnosed d-transposition of the great arteries with intact interventricular septum (TGA/IVS) and a restrictive foramen ovale. Coronary artery anatomy was normal. She underwent successful balloon atrial septostomy but developed protracted nosocomial sepsis in PICU. Due to her fragile state and relatively late presentation, she was not considered a candidate for early Arterial Switch Operation (ASO) and a Mustard operation was performed when she was 2yrs old.

Routine follow-up was uneventful until age 3yrs 3mths when she presented with anorexia, abdominal distension and ascites. Echocardiography showed marked right heart dilation and turbulence in the superior systemic venous baffle. Angiography confirmed narrowing of the SVC baffle, interrupted IVC with azygous continuation and unobstructed pulmonary venous return. Balloon dilation of the obstructed baffle provided only temporary relief and symptoms soon recurred. A balloon-expandable covered stent was therefore positioned across the narrowed area and dilated to provide relief of the obstruction. Her symptoms resolved satisfactorily and have not recurred.

**Discussion:** Correction of TGA/IVS by the Mustard or Senning operations is associated with significant complications and long-term morbidity. The right ventricle is anatomically unsuited to the role of systemic ventricle and becomes progressively less functional, with increasing tricuspid valve regurgitation and loss of sinus rhythm. Obstruction of the venous return baffles occurs in 5% of cases. Re-operation to relieve baffle obstruction carries an increased mortality risk especially in small, unstable patients such as ours, thus catheter intervention provides an attractive alternative. Serial dilation of the stent can be performed as interim palliation until re-do of the Mustard operation or conversion to an ASO is possible. While intra-cardiac stents may complicate baffle take-down at the time of the ASO conversion, they provide valuable time for growth and stabilisation in these patients.

## An evaluation of NT-proBNP blood levels in HIV positive patients with pericardial effusions

**T.J. Naicker, P. Manga and Y. Veriawa**

Department of Chemical Pathology, NHLS, Department of Cardiology, Johannesburg Hospital and University of the Witwatersrand, Johannesburg, South Africa

**Aim:** To determine the clinical utility of the biochemical marker NT-proBNP in the diagnosis and management of HIV positive patients with pericardial effusions.

**Methods:** 10 patients (all < 60 years of age) admitted to the Johannesburg Hospital with a presumptive diagnosis of pericardial effusion were recruited for the pilot study. The diagnosis was deduced from the history, symptoms, physical examination, ECG findings and confirmed with 2-dimensional echocardiography. Patients in renal failure, with diffuse myocardial disease, valvular disease and effusions secondary to cardiac failure were excluded. Blood for NT-proBNP was sampled on diagnosis and again approximately 48hrs after pericardiocentesis. NT-proBNP was measured with a chemiluminescence immunoassay on the Roche Elecsys 2010 analyser (Roche Diagnostics-Hitachi, Germany). Values < 125ng/L excluded cardiac dysfunction.

**Results:** All patients had raised NT-proBNP at presentation with levels ranging between 289 ng/L and 1976ng/L. The levels fell by 20 to 66% 48hrs post pericardiocentesis.

**Conclusions:** Echocardiography is a labour intensive procedure and may not be immediately available at regional hospitals. These results indicate that NT-proBNP could be a useful diagnostic marker in this setting aiding an earlier diagnosis and hence an improved patient outcome. Further investigation is warranted.

## Fasting plasma arginine concentrations and ambulatory blood pressures

**C. Naidoo\*, A.D. Cromarty#, J. Peters\* and G.P. Candy\***

\*Department of Surgery, Wits Medical School, University of the Witwatersrand, Johannesburg, South Africa

#Faculty of Health Sciences, School of Medicine, Department of Pharmacology, University of Pretoria, South Africa

Stroke, end stage renal failure and heart failure are the consequences of elevated blood pressures which afflict the African community far more than other racial groupings. Arginine is the precursor to the arterial vasodilator nitric oxide (NO), a key cellular messenger and mediator of a host of physiological functions. Although supplementation with arginine is known to reduce blood pressure, there have been several reports, including our own study, demonstrating elevated fasting plasma arginine concentrations in patients of African ancestry with hypertension. This suggests that arginine is available but is either not available for NO formation or the NO formed is degraded or cannot mediate vasodilation. There is little baseline data, both locally and internationally, of fasting plasma arginine concentrations and whether these affect ambulatory blood pressure profiles.

**Methods:** 24 hour ambulatory blood pressures (ABPM) were measured in consenting participants recruited from clinics in the Johannesburg area. Fasting blood samples were obtained and frozen until analysed by HPLC/mass-spectrometry.

**Results:** Arginine concentrations were elevated in subjects with hypertension and correlated with average diastolic pressures, particularly night time DBP ( $r=0.280$ ;  $p<0.05$ ). In males of  $BMI<30\text{kg/m}^2$ , arginine correlated with both night time diastolic ( $r=0.461$ ;  $p<0.005$ ) and systolic pressures ( $r=0.420$ ;  $p<0.005$ ). These data are similar to data reported in the literature. Re-analysis of the data, dichotomizing by the median arginine concentration ( $56\text{mol/L}$ ), showed differences in the ABPM profile pattern between the arginine groups.

**Conclusion:** Plasma concentrations of the NO precursor, arginine are elevated in black South Africans with hypertension and correlated with average night time blood pressure particularly in men of lower BMI. As fasting arginine concentrations were elevated in black South African subjects with hypertension, further studies are needed to determine whether decreased arginine uptake into endothelial cells or NO production/availability contributes toward the increased blood pressure in this high risk population. ABPM profile patterns differed between study participants with higher and lower arginine concentrations.

## An awareness programme to help reduce patient delays in acute myocardial infarction

**Raveen Naidoo\* and Karen Sliwa#**

\*Department of Emergency Medical Care and Rescue, Durban University of Technology, South Africa

#Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

**Introduction:** Definitive treatment for heart attack is early reperfusion by either primary angioplasty or thrombolytic therapy. The time elapsed from the onset of symptoms to reperfusion is directly related to patient outcomes as demonstrated in the GISSI trial more than 20 years ago. Reperfusion is a time-related intervention. There are three key components to prompt and effective reperfusion therapy: addressing patient delay, increasing utilisation of the ambulance service and addressing the prolonged in-hospital treatment delays would significantly reduce pain-to-needle times. The patient is most probably the most important factor involved in the delay between the onset of AMI and the start of reperfusion treatment. A number of factors, including the type of acute coronary syndrome, the nature and localisation of the symptoms, the place where the symptoms occurred, the patients interpretation of symptoms and knowledge were associated with the patients decision time (Herlitz, Thuresson et al. 2009). Various registries of patients with acute myocardial infarction have shown that the time from symptom onset to hospital presentation was  $\geq 4$  hours in 50%,  $> 6$  hours in 40% and  $> 12$  hours in 9 – 31%. A study in South Africa has shown that the patient took a mean time of  $3:32 \pm 5:26$  hours to call for help and that only 10% (12) patients utilised an ambulance service. This implies that for maximum effectiveness, the public should be trained to recognise symptoms early and activate the emergency medical services early through a health awareness program via mass media to reduce delay times. The purpose of this study was to develop a culturally sensitive and affordable chest pain education program.

**Methods:** A document study was undertaken on existing chest pain awareness programs in international settings that led to the development of a culturally sensitive and affordable chest pain awareness program.

**Ethics:** Ethical approval was granted by the Human Research Ethics Committee - University of Witwatersrand.

**Results:** A poster, an information booklet and a video on heart attack awareness were developed after studying documentation from United Kingdom, Canada, Australia and South Africa.

**Conclusion:** Attempts to change the actions of individuals experiencing AMI symptoms on an ongoing basis must and should continue. Structures to facilitate various approaches need to be established for coordination and implementation. Until reperfusion strategies are delivered effectively, the promise of reduced morbidity and mortality from AMI will not be realised.

## Impact of time to treatment with fibrinolytic drugs in patients presenting with ST- elevation myocardial infarction

**R. Naidoo\*, N. Ranjith#, D. Singh\* and N. Castle\***

\*Department of Emergency Medical Care and Rescue, Durban University of Technology, KwaZulu-Natal, South Africa

#Department of Medicine, Coronary Care Unit, R K Khan Hospital, Durban, KwaZulu-Natal, South Africa

**Aims:** The prompt restoration of myocardial blood flow is vital to myocardial salvage and mortality reduction after ST- elevation myocardial infarction [STEMI]. Reperfusion is achieved with primary percutaneous coronary intervention (PPCI) or fibrinolytic agents. Due to the limited availability of PPCI, fibrinolytic therapy still remains an important treatment modality in managing STEMI. The aims of this study were to address the time interval from first patient contact to initiation of fibrinolytic treatment, possible reasons for treatment delay, and complications arising in those with and without treatment.

**Methods:** The study population comprised 120 patients with STEMI presenting to 20 different hospitals in Durban and surrounding regions between August to December 2006. Demographic data, time to treatment, reasons for non-treatment, and complications encountered during hospital stay and at day 30 were obtained from hospital records and patient interviews.

**Results:** The median age of the study group was 58 years with a clear male preponderance [71%]. Sixty five percent received fibrinolytic treatment [Streptokinase (58%); Tenecteplase (42%)]. In patients who presented to hospital less than 2 hours from symptom onset [n=9 (8%)], 78% received fibrinolytic treatment; within 2-6 hours [n=46 (38%)], 63% were thrombolysed, while 65 patients [54%] presented greater than 6 hours of whom only 46% were given fibrinolytic drugs. The mean time from symptom onset to fibrinolytic treatment was 8.36 5.57 hours. The major reasons for patients not given fibrinolytic drugs were late presentation and inadequate facilities for fibrinolysis [88%] while 12% were excluded because of standard contraindications to fibrinolytic treatment. The commonest complications observed during hospital stay and at 30-day follow-up included cardiac failure [18%], death [14%], recurrence of angina [11%], and recurrent myocardial infarction [4%]. Significantly more patients developed cardiac failure [p = 0.05], if they presented to hospital after 6 hours from symptom onset, irrespective of whether they received fibrinolytic treatment or not.

**Conclusion:** Delay in the administration of fibrinolytic drugs for STEMI results in increased morbidity and mortality. Prompt recognition of STEMI and shortening the time interval from first patient contact to initiation of fibrinolytic drug infusion will greatly improve survival.

### Relationship between anatomical and electrical indices of left ventricular hypertrophy, derived from cardiac MRI and ECG

**Richard Nethononda<sup>\*,#,\*\*</sup>, Barbara Casadei<sup>#</sup>, Nicola Alder<sup>†</sup>, Polly Whitworth<sup>\*,#</sup>, Jane Francis<sup>\*,#</sup>, Steffen Pettersen<sup>\*,#</sup>, Hugh Watkins<sup>#</sup> and Stefan Neubauer<sup>\*,#</sup>**

\*Oxford Center for Cardiac Magnetic Resonance Imaging Research (OCMR), University of Oxford, United Kingdom

#Cardiovascular Medicine Department, University of Oxford, United Kingdom

†Center for Statistics in Medicine, University of Oxford, United Kingdom

\*\*Division of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

**Background:** ECG is commonly used to screen for left ventricular hypertrophy (LVH), but doubts exist about its accuracy for this purpose. Cardiac MRI (CMR) is the gold standard for measurement of LV mass (LVM) and other cardiac parameters.

**Objective:** To determine the relationship between anatomical and electrical indices of LVH, derived from ECG and CMR in a large cohort with high prevalence of this condition.

**Methods:** 430 subjects from the Oxford Family Blood Pressure cohort were recruited over a 2-year period. Medical history, demographic and anthropometric data, 24h ambulatory blood pressure (ABP) and 12-lead ECGs were obtained. CMR was used to measure LV parameters and chest dimensions. One blinded observer manually analysed ECGs to obtain the QRS duration, Sokolow-Lyon, Cornell, 12-lead sum of QRS voltages and LV mass. Genders were compared using chi-squared and t-tests for categorical and continuous data, respectively. Pearson correlation and the Bland-Altman methods were used to analyse the relationship between ECG indices and CMR-derived LV parameters.

**Results:** Age, BMI, prevalence of diabetes and hypertension, and the distance from the epicardium to skin surface position of lead VI were not significantly different between males and females, whereas height, weight, BSA, 24h ABP, all chest dimensions, all ECG indices, and CMR-derived LVM and wall thickness were larger in males. ECG-derived indices of LVH were moderately correlated with CMR LVM and wall thickness in males; in females, however, the strength of these correlations was weaker. Agreement between ECG- and CMR-derived LV mass was poor.

**Conclusion:** The ability of the ECG to estimate LV mass and detect anatomical LVH is limited, particularly in females. These findings have implications for current guidelines on management of hypertension, as risk stratification based on ECG indices of LVH only may be inappropriate for many, particularly females.

## The predictors of effusive constrictive pericarditis in patients with confirmed tuberculous pericarditis

**Mpiko Ntsekhe**

The Cardiac Clinic, Department of Medicine, Groote Schuur Hospital and University of Cape Town, South Africa

**Background:** Constrictive pericarditis is a frequent late complication of tuberculous [TB] pericarditis. Effusive constrictive pericarditis (ECP) is thought to be a precursor of constrictive pericarditis. It occurs when a hemodynamically significant pericardial effusion and visceral pericardial constriction co-exist. The diagnosis requires measuring the pre and post pericardiocentesis cardiac and intra-pericardial pressures; echocardiography is insensitive and non-specific. The syndrome remains unrecognised in many patients with pericardial effusion until they present later in their course with constriction and heart failure. Although ECP is a rare manifestation of idiopathic pericarditis, the Initiative for the Investigation and Management of Pericarditis In Africa (IMPI) registry has shown that it is a common presentation of TB pericarditis. We set out to determine the predictors of ECP in patients with TB pericardial effusions.

**Methods:** Between Dec '06 and July '08 consecutive patients with large TB pericardial effusions were enrolled in the IMPI registry. At baseline all patients had full clinical, CXR, ECG, full blood count, serum chemistry, HIV, CD4 count and pro-BNP. Pericardial fluid volume, cell count, chemistry and cultures were recorded. Pre and post pericardiocentesis right atrial and intra-pericardial pressures were measured and the presence or absence of tamponade was determined.

**Results:** 68 consecutive patients with confirmed tuberculosis and complete data were included in the analysis. Median [IQR] age was 31 [28-41], 56% were male, 74% were HIV infected and 50% were TB culture positive. The mean volume of fluid drained was 971 cc. 53% had ECP. By univariate logistic regression analysis age, opening RAP [ $>15\text{mmHg}$ ] and opening IPP were significantly associated with the risk of ECP. However only the opening RAP remained significant in the final multivariate model; odds ratio 15.4, 95% CI 2.4-99.6 [ $p=.004$ ].

**Conclusions:** In this first and largest study of its kind, we show that a very high right atrial pressure, in patients with a hemodynamically significant tuberculous pericardial effusion, is associated with co-existing constriction of the visceral pericardium or ECP. These findings may have implications for identifying patients who are at very high risk for developing constrictive pericarditis despite completion of anti-tuberculosis therapy.

## Myocardial rupture with left ventricular pseudoaneurysm formation complicating staphylococcal pericarditis

**A. Nzimela, E.G.M. Hoosen and N.J. Buckels**

Paediatric Cardiology, Inkosi Albert Luthuli Central Hospital, Durban, South Africa

A previously well 12 year old female presented to our cardiology unit with signs of congestive cardiac failure. She had been admitted to the referring hospital for 3 weeks prior to transfer and was managed for suspected septic arthritis of the right knee, for which she eventually had incision and drainage of a right thigh abscess from which staphylococcus aureus was cultured. She had been on intravenous cloxacillin for two weeks. On examination, she was ill, pyrexial and in respiratory distress. Pulses were small volume, jugular venous pressure was raised, a 12 cm tender hepatomegaly was palpated and the cardiac apex could not be localised. A large right pleural effusion and cardiomegaly were evident on chest radiography.

The echocardiogram demonstrated a massive pericardial effusion with signs of tamponade. Urgent pericardiocentesis was performed and a pyopericardium confirmed. This was followed by open drainage for pyopericardium, the pericardial space was washed out with saline and specimens sent for histology and culture from which cloxacillin sensitive staphylococcus aureus was again cultured. A pericardial drain was left in situ from which, three days later, bleeding was noted. A repeat echo showed on colour flow mapping flow from the left ventricular

posterior wall into a 30mm pseudoaneurysm. A CT angiogram confirmed the echocardiographic findings and an uneventful resection of the false aneurysm was performed on the same day.

The child made a complete recovery with complete resolution of the effusion on follow up.

A pseudoaneurysm of the ventricle is a contained myocardial rupture, its wall being lined by pericardium and mural thrombus. It is most commonly seen post myocardial infarction. Myocardial rupture following septic pericarditis is exceedingly unusual with few cases reported in the literature.

## Outcomes of off-pump Coronary Artery Bypass Grafting (CABG) and Coronary Artery Bypass Grafting (CABG) versus Cardiopulmonary Bypass (CPB) in a South African patient population

**C.K.P. Ofoegbu and J. Brink**

Chris Barnard Division of Cardiothoracic Surgery, University of Cape Town/Groote Schuur Hospital, South Africa

**Introduction:** Off-pump coronary artery bypass grafting (OPCAB) was developed to avoid the deleterious effects of CPB. Current literature reveals some peri-operative advantages of OPCAB, with few studies detailing these in Africa. We review our institutional experience with both approaches to determine pre-operative characteristics, short and mid-term outcomes in a developing country.

**Patients and methods:** A retrospective review of patients operated by the 2 surgeons in the department between January 2001 and December 2007. Fields determined include: pre-operative patient characteristics, intra-operative data and post-operative variables (intensive care unit (ICU) stay, blood loss, use of blood products, complications, death and follow-up).

**Results:** Records of 342 patients were reviewed. Of these, 199 had OPCAB and 143 had CABG-CPB. There were no significant differences between the 2 groups for age and CAD risk factors, with CAD family history commoner in OPCAB patients ( $p = 0.009$ ). There were no significant differences in incidence of co-morbidities, NYHA class, left ventricular ejection fraction (LVEF) and proportion of urgent/emergency surgery. The mean number of vessels grafted was 3.31 and 3.45 in OPCAB and CABG-CPB groups respectively ( $p = 0.145$ ). The intra-operative conversion rate from OPCAB to CABG-CPB was 2.5%. The mean ICU duration for OPCAB and CABG-CPB patients was 80.7 hours and 104.1 hours respectively ( $p = 0.181$ ). The mean mechanical ventilation duration in OPCAB and CABG-CPB patients was 22.3 hours and 38.3 hours respectively ( $p = 0.091$ ). The mean ICU blood loss in OPCAB and CABG-CPB patients was 808.5 mls and 988.2 mls respectively ( $p = 0.0029$ ). Mean red cell (RBC) transfusion was 1.72 units and 2.66 units in OPCAB and CABG-CPB patients respectively ( $p = 0.03$ ). The CABG-CPB patients had more post-operative ward stay than OPCAB patient (7.4 versus 5.5 days,  $p = 0.01$ ). The peri-operative mortality rate was 3% and 9% in OPCAB and CABG-CPB patients respectively ( $p = 0.016$ ). There was no significant difference in major adverse cardiac events (MACE) during the follow up period ( $p = 0.605$ ).

**Conclusion:** The pre-operative characteristics in both groups were similar. There was less ICU blood loss, less usage of RBCs and less hospital stay in the OPCAB group. Peri-operative mortality was significantly worse in the CABG-CPB group, but no difference in MACE during follow up.

## Prevalence of Asymptomatic Left Ventricular Systolic Dysfunction in Hypertensive Nigerians: Echocardiographic study of 832 subjects

**Okechukwu S. Ogah, Rufus O. Akinyemi, Gail D. Adegbite, Oscar I. Udofia, Sunday B. Udoh, Julius O. Adesina, Oluwaseun S. Ojo, Albert A. Alabi, Julius K.L. Osinfade, Roseline F. Ogundipe, Ayodele O. Falase**

Department of Medicine, Federal Medical Centre, Idi-Aba, Abeskuta, Ogun Stat, Nigeria

**Introduction:** We sought to determine the prevalence of echocardiographically determined left ventricular systolic dysfunction in asymptomatic hypertensive subjects seen in Abeokuta, Nigeria.

**Methods:** Echocardiography was performed in 832 consecutive hypertensive subjects referred for cardiac evaluation over a three-year period.

**Results:** Data was obtained in 832 subjects, (50.1% women), aged 56.012.7 years (men 56.913.3, women 55.012.0, (range 15-88 years). The prevalence of left ventricular systolic dysfunction was 18.1% in the study population (mild LVSD = 9.6%, moderate LVSD = 3.7%, and severe LVSD = 4.8%). In a multivariate analysis, male gender, body mass index, LV mass were the predictors of LVSD.

**Conclusion:** We conclude that screening for LVSD among hypertensive subjects who are at risk of heart failure is feasible and has substantial yield, even among patients without symptoms of heart failure. In light of the low cost of screening and the available therapies to prevent progression of LVSD to overt HF, we suggest limited echocardiography (where available) especially for patients with marked abnormalities on their 12 lead electrocardiographs. A controlled clinical trial of screening high-risk hypertensive patients appears to be justified.

## Pattern of prescription of anti-hypertensive medications in a tertiary health care facility in Abuja, Nigeria

**D.B. Ojji\*, A.A. Akor#, O.S. Omonua# and A.O. Falase†**

\*Cardiology Unit, Department of Medicine, University of Abuja Teaching Hospital, Gwagwalada, Abuja

#Department of Medicine, University of Abuja Teaching Hospital, Gwagwalada, Abuja

†Cardiology Unit, Department of Medicine, University College Hospital, Ibadan

**Introduction:** There have been marked changes in the pharmaco-therapy of hypertension over the years with a trend towards the use of calcium channel blockers, angiotensin converting enzymes, angiotensin receptor blockers and low dose thiazide diuretics. In Sub-Saharan Africa, there is the original belief that anti-hypertensive therapy still centres on thiazide diuretics, beta blockers and centrally acting medications with little or no use of newer medications like calcium channel blockers, angiotensin converting enzymes and angiotensin receptor blockers. We therefore decided to look at anti-hypertensive prescription pattern in a tertiary centre in Abuja, Nigeria, to see how it conforms to current trends.

**Methods:** Five-hundred and fifty-nine (559) hypertensive subjects presenting newly at the Cardiology Unit of University of Abuja Teaching Hospital over a three-year period were studied. Demographic, clinical and baseline blood analysis data were obtained.

**Result:** Male subjects constituted 49.7% of the study population while female constituted 50.3%. The mean age of the subjects was 49.7412.21 years, mean arterial blood pressure was 111.79 17.90 mmHg while the mean fasting blood sugar was 5.922.97 mmol/l.

Calcium channel blockers were the most frequently prescribed anti-hypertensives in 66.9% of the study population followed by low dose thiazides in 54%, angiotensin receptor inhibitors in 47.8% and beta blockers in 34.2% of cases. Centrally acting medications were prescribed in only 5.01% of cases. Single-pill combination either alone or in combination with other anti-hypertensive medications were prescribed in 55.3% of cases, with combination of low dose thiazide and potassium sparing diuretic (amiloride) in 35.2%, Lisinopril and low dose thiazide combination in 12.5% and angiotensin receptor blockers and low dose thiazide combination in 5.01% of cases. Calcium channel blockers (CCBS) based combinations constituted the most frequently used multiple drug combinations with CCBS and thiazides in 39.4% of cases,

CCBS and angiotensin receptor inhibitors in 18.2%, CCBS and beta blockers in 9.48% and CCBS and angiotensin receptor blockers in 5.72% of cases. 94.6% of the subjects required more than one medication.

**Conclusion:** Anti-hypertensive pharmacotherapy at the University of Abuja Teaching Hospital, Nigeria, compares favourably with the current trends in the prescription pattern of anti-hypertensive medications.

## Atropine in the EP lab: not a discarded drug; rather, a useful adjunct in difficult tachycardia induction in young patients with exercise related palpitations

**A. Okreglicki and A. Chin**

Cardiac Clinic, Groote Schuur Hospital, Cape Town, South Africa

**Introduction:** Electrophysiological studies (EPS) are occasionally indicated on the basis of history of palpitations alone without documentation tachycardias. Typically this occurs in young patients with infrequent episodes only during exercise. At EPS of such patients, tachycardia may remain non-inducible unless extra-ordinary measures are attempted including drugs such as catecholamines. Atropine, often relegated to dealing with bradycardia associated with vasovagal reactions, is a useful tool for initiating tachycardia in the EP laboratory.

**Aim:** To review the cases where atropine played a pivotal role during EPS for rapid palpitations.

**Methods and results:** Four athletes, with only exercise related paroxysmal palpitations and no documented tachycardia who had EPS were reviewed: 3 males, 1 female, aged 20, 22, 31 and 32, competitive extreme athletes, a professional cyclist and a squash player. In all, EST and prolonged ECG recordings had revealed no abnormal arrhythmias.

Baseline EPS, done unsedated, off medications for 1 week, showed no evidence of accessory pathways and no tachycardia with programmed stimulation. In none was dual AV nodal (AVN) physiology at baseline demonstrated. EPS and induction of tachycardia were repeated with increasing doses of catecholamine infusion. On intravenous adrenaline at 0.06 to 0.18 microgram/kg/min no sustained tachy-arrhythmia occurred. In 1 patient, dual AVN physiology was demonstrated. 1mg bolus of intravenous atropine sulphate was given to all. No spontaneous abnormal tachycardias occurred. In all 4, there was a significant shortening of the AVN effective refractory period. Rapid atrial pacing induced arrhythmias in all: AV nodal re-entry tachycardia (AVNRT) in 2, unifocal atrial tachycardia (AT) in 1 and multiple monomorphic atrial tachycardias in 1. Radiofrequency ablation was performed. At the end of the procedure, re-inducibility was again tested using the drugs.

**Conclusion:** In patients with exercise related palpitations, and non-inducibility at EPS, high dose catecholamine infusion may be insufficient to initiate tachyarrhythmia. Unless, parasympathetic withdrawal is achieved, which occurs at peak exercise, and simulated in the EP laboratory by administration of atropine, the tachycardias may remain non-inducible and the EPS inconclusive. Atropine, as demonstrated by significant improvement in baseline electrophysiological parameters, may abolish the rebound increased vagotonia during catecholamine infusion causing non-inducibility. Therefore, atropine should not be discarded but rather considered earlier in routine EP studies.

## The risk factor profile of a local community in KwaZulu-Natal: a preliminary analysis

**R. Prakashandra**

Department of Biomedical and Clinical Technology, Durban University of Technology, KwaZulu-Natal, South Africa

It is well documented that worldwide, immigrant Asian Indians are reported to have higher rates of coronary heart disease [CHD] than the native populations of their adopted countries. Furthermore, premature CHD is increasingly common in this group. The risk factor profile of this community in Phoenix, KwaZulu-Natal, has been poorly studied.

**Aims/objectives:** To determine the major risk factors for cardiovascular disease (CVD) in the Phoenix community. To determine the prevalence of metabolic syndrome (MS) in this community.

**Method:** A randomised sample was selected for study and stratified into gender and 6 age groups (15-24, 25-34, 35-44, 45-54, 55-64 and >65). The WHO STEPS questionnaire was administered to each subject, and demographic and behavioural information was recorded. Further physiological, biochemical and anthropometric measurements were done at the Lifestyle Centre at Inkosi Albert Luthuli Hospital. Descriptive statistics were performed for biochemical and anthropometric parameters. The presence of metabolic syndrome (MS) was determined using the National Cholesterol Education Programme Adult Treatment Panel III [NCEP ATP III] and International Diabetes Federation [IDF] criteria.

**Results:** A total of 1419 participants have been studied, of which 72% were women, and 28% were men. Impaired fasting glucose was present in 3% of the 15-24 age group, and increased to 19% in the 35-44 age group. Elevated total cholesterol (>5.18mmol/L) was observed in 41% of the 25-34 age group, with this group also comprising the highest percentage of subjects (20%) with abnormal HDL (< 1.0mmol/L). There was a 24% prevalence of MS in males and 44% in females when the NCEP criteria was applied; with an almost 10% increase with the IDF criteria. MS was present in 7% of the 15-24 age group, and 23% in the 25-34 year group. There was a steady rise after that to 57% in the 55-64 year old group.

**Conclusion:** There is a very high prevalence of MS in both men and women in this randomised sample. Age-related trends show that the risk factors starts as early as 15 years, with a sharp increase by the first quintile. The high prevalence of metabolic syndrome in our young participants does indeed herald the earlier onset of accelerated atherosclerotic disease in these subjects.

## Heart sound segmentation and classification using neural networks

**E. Pretorius\*, O.M. Strydom\*, W. Schoonbee#, M. Blanckenberg#, C. Scheffer#, P.R. Fourie\*, M.L. Cronje\* and J. Lawrenson†**

\*Diacoustic Medical Devices, Stellenbosch, South Africa

#Engineering Department, University of Stellenbosch, South Africa

†Red Cross Children's Hospital and University of Stellenbosch, South Africa

**Aim of study:** The aim of this study was to develop a heart murmur screening system that can aid non-specialists to make informed referrals and to decrease the number of unnecessary referrals, while also aiding specialists with less auscultation experience to make a diagnosis with higher confidence.

**Methods:** To evaluate the algorithms, both the heart-sounds and electrocardiograph (ECG) of 400 patients were recorded in a clinical environment at the four main auscultation locations, namely; aortic, pulmonic, tricuspid and mitral areas. The recordings were made using a WelchAllyn Meditron stethoscope. All the patients had an echo cardiograph done by a cardiologist to determine the correct diagnosis. The dataset contains 222 pathological, 45 functional and 133 normal (no murmur present) patient recordings.

Each heart signal was noise filtered and split into heartbeats using the ECG as reference and 5 representative beats were selected. These beats were segmented into s1, systole, s2 and diastole regions and feature vectors calculated. Features were chosen to include the signal

shape, time-frequency content and signal statistics. To evaluate the feature selections, a 2-layer neural network was used to classify signals as either normal or pathological. To determine the sensitivity and specificity of the system, the Jack-Knife method was used with a test set size of 1, 5 and 10 signals.

**Results:** Initial results, firstly considering VSD's, obtain performances of 82% sensitivity and 99% specificity ratings. Other pathologies need to be optimised since sensitivities were lower using the same type of features.

**Conclusion:** Normal heart-sounds have low frequency components with large amplitudes at s1 and s2 and less frequency information in the systole and diastole regions. Murmurs on the other hand, contain higher frequency components that usually have lower amplitudes, making it difficult for the human ear to detect. This and the fact that clinical conditions are rarely noiseless, makes a diagnosis much more difficult. The proposed system shows that automatic auscultation is possible and can perform well in real clinical conditions to aid both specialists and non-specialists to make improved confident decisions.

## Surgical decision making in patients with ischaemic mitral regurgitation undergoing CABG: more opinion than evidence? A systematic review

V. Pretorius, Y. Liang, R. Tsuyuki and D.B. Ross

Division of Cardiac Surgery, University of Alberta, Canada

**Objectives:** It is unclear if patients presenting for coronary artery bypass grafting (CABG) with ischaemic mitral regurgitation (MR) should undergo CABG only or be offered CABG and mitral valve (MV) surgery. We aimed to quantify the effects of CABG and MV surgery (repair or replacement) compared to CABG only by conducting a systematic review of the literature. Specific outcomes included: Overall survival, Thirty-day mortality, NYHA functional class.

**Methods:** To identify relevant studies, a medical librarian searched the following computerised bibliographic databases: MEDLINE, EMBASE, SCOPUS, PASCAL, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and Dissertation Abstracts. Studies were included if they compared the two groups, reported the outcomes of interest and provided primary data. Methodological quality was assessed using the Newcastle-Ottawa method. Studies were combined using the log Hazard Ratio (HR) for survival, the Risk Difference (RD) for 30-day mortality, and the Weighted Mean Difference (WMD) for the change in NYHA functional class.

**Results:** The search identified 1580 studies; 117 were examined for inclusion. Thirteen studies (2591 patients) were included. Study designs included retrospective cohort (n=11) and case-control (n=2) studies. The pooled unadjusted HR for overall survival was not significantly different between the two treatment groups (HR=1.13; 95%CI:0.93,1.37 I<sup>2</sup>=27%). Subgroup analysis by study design, quality or period failed to demonstrate a significant difference between treatment groups. Sensitivity analysis comparing only studies where the MR grade was the same in both groups prior to surgery found no significant difference in overall survival (HR=0.98; 95%CI:0.55,1.73).

For 30-day mortality no significant RD between the two groups was seen (RD=0.05; 95%CI:-0.01, 0.10; I<sup>2</sup>=64.9%). Subgroup analysis revealed that high quality studies favored CABG only with a Number Needed to Treat of 9.09 (95% CI 5.56, 33.33).

Change in NYHA functional class significantly favored CABG and MV surgery (WMD=0.66; 95%CI:0.05,1.27). Sensitivity analysis revealed that for studies where the MR grade was the same between the two treatment groups the pooled estimate (WMD=0.93; 95%CI:0.05,1.81) was in favor of CABG and MV surgery.

**Conclusions:** A systematic analysis of the existing literature cannot elicit the best treatment for patients with ischaemic MR undergoing CABG surgery. A randomised controlled trial is required.

## The role of b-adrenergic receptors and prosurvival kinases in the cardioprotective effects of Beta Preconditioning (BPC)

R. Salie\*, A. Lochner# and J.A. Moolman#

\*Medical Research Council of South Africa, South Africa

#Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

Transient pharmacological stimulation of beta-adrenergic receptors elicits cardiac protection against ischaemia (beta-adrenergic pre-conditioning) (BPC) by unknown mechanisms.

**Aim:** To determine the involvement of adrenergic receptors and signaling pathways in the mechanism of BPC.

**Methods:** Isolated perfused rat hearts were subjected to 35 min regional ischaemia / reperfusion and preconditioned with 5 min isoproterenol (Iso)  $10^{-7}$  M (BPC). Selective beta-1, -2, -3 AR blockers CGP 20712A (300 nM), ICI 118551 (50nM), SR 59230A (100 nM), or beta-2, -3 AR agonists, formoterol (1 nM), BRL 37344 (1uM), respectively were applied to BPC as well as non-preconditioned hearts (NPC). Inhibitors of ERK (PD 098,059; 10 M), PI3-K (Wortmannin; 100 nM), PKA (Rp-8cAMP; 16 M) or NOS (L-NAME, 50M) were administered prior to ischaemia / at reperfusion. Pertussis toxin (Ptx, 30 g/kg) was given ip 48h prior to experiments. Infarct size (IS) was determined using TTC staining. Hearts were freeze-clamped at reperfusion for Western blot determination of PKB / ERK.

**Results:** BPC or Beta-2 AR stimulation resulted in significantly smaller IS compared to NPC hearts (23.251.62; 20.70.9 vs 40.01.5,  $p < 0.001$ ). CGP 20712A and ICI 118551 abolished BPC completely (40.61.2 and 41.51.6, respectively), whereas beta-3 AR inhibition / stimulation or NOS inhibition had no effect. PKA inhibition abolished BPC (40.361.65 vs 23.351.62,  $p < 0.001$ ) while Ptx had no effect. Wortmannin or PD 098,059 abolished BPC (401.65% and 441.7%, respectively). Wortmannin significantly decreased activation of PKB (2.780.16 vs 0.71 0.17,  $p < 0.01$ ) and ERK p44 (3.550.32 vs 2.160.17,  $p < 0.05$ ) / p42 ERK (2.670.13 vs 1.56.09,  $p < 0.05$ ), whereas PD 098,059 decreased ERK p44 / p42 activation.

**Conclusion:** Cardioprotection of B-PC involves beta-1 and -2 AR but not beta-3 AR. Beta-2 AR stimulation indicated similar cardioprotective effects to that of BPC. PKA activation via Gs may play a role. PKB and ERK p44 / p42 activation during triggering and reperfusion is essential for cardioprotection.

## Crystal methamphetamine use and myocardial pathology

Lior Y. Sareli and Anton F. Doubell

Division of Cardiology, Department of Medicine, University of Stellenbosch and Tygerberg Hospital, South Africa

**Introduction:** Methamphetamines (MAP) use has been linked to tachyarrhythmias, myocardial injury due to coronary thrombosis and/or vasospasm, pulmonary hypertension, prolonged QTc and cardiomyopathy. Our aim was to assess the occurrence of myocardial pathology with MAP abuse in the acute and chronic setting.

**Methods:** Twenty eight study and 25 control participants younger than 45 with no prior history of cardiovascular pathology were recruited. Study participants had a positive MAP use history (chronic abuse) or a positive MAP urine sample (acutely intoxicated) and no previous cocaine use. Controls had ejection fractions  $> 55\%$ , no prior history of MAP and cocaine use and MAP/cocaine negative urine samples. A cardiovascular examination, electrocardiogram, echocardiogram, troponin I level (study group only), urine sample for cocaine and MAP and a questionnaire on previous drug use was obtained in all participants. The measured parameters in the study and control groups were compared.

**Results:** The measured parameters did not differ statistically between the study and control groups although there was a trend towards chamber enlargement and higher pulmonary pressures with MAP abuse. Three MAP abusers presented acutely, 1 with a dilated cardiomyopathy (DCMO) and 2 with ST elevation myocardial infarcts (STEMI). One of the STEMI occurred 3 days after a MAP binge. Angio-

graphy in the STEMI patients revealed unobstructed coronary arteries and the infarctions were attributed to vasospasm and/or thrombosis. There was no correlation between amounts of drug used (MAP use days) and changes in measured parameters.

**Conclusion:** MAP use may manifest with serious cardiovascular complications including STEMI and DCMO. Acute intoxication with MAP does not always present with identifiable electrocardiography, echocardiography and troponin I abnormalities and the cumulative dose of MAP use does not predict cardiovascular involvement. However, severe cardiovascular events may be related to MAP binges. Management of a STEMI in MAP abusers must address the underlying pathophysiology of vasospasm and/or thrombosis.

## Anthracycline-induced-cardiac-myopathy

**Balindiwe J.N. Sishi\***, Jacques van Rooyen<sup>#</sup> and Anna-Mart Engelbrecht\*

\*Department of Physiological Sciences, University of Stellenbosch, South Africa

<sup>#</sup>Cape Peninsula University of Technology, South Africa

Anthracyclines, in particular Doxorubicin (DXR), are some of the most effective anti-cancer treatments ever developed. Their clinical use however is limited due to their significant cardiotoxic effects, highly believed to be caused by the generation of ROS amongst others. Although the underlying biochemical mechanisms remain largely undefined, it has recently been shown that DXR stimulates ubiquitin-proteasome system (UPS)-mediated proteolysis by acting on the ubiquitination machinery and the proteasome. While the concept of muscle atrophy via the UPS is well established in skeletal muscle, we set out to determine whether the same is true in cardiac muscle under the context of DXR-induced cardiotoxicity.

**Material & methods:** Male Wistar rats (300g body weight) were injected with 2mg/ml/kg DXR solution for a period of 3 weeks. After 3 weeks of daily treatment, the animals were sacrificed, their hearts removed and frozen in liquid nitrogen for subsequent analysis through Western blotting using phospho-specific and total antibodies.

**Results & discussion:** The main findings of this study are that the ubiquitin E3 ligase protein expression for both MAFbx/Atrogin-1 and MuRF-1 were significantly increased when compared to the control counterparts. In addition, SAPK/JNK phosphorylation also appeared to increase. The FoxO subfamily of forkhead transcription regulates gene expression of MAFbx/Atrogin-1 and MuRF-1 thus suggesting a common regulatory pathway of both ligases. In contrast to our study, cardiac atrophy induced by heterotopic transplantation of the rat heart resulted in decreased levels of the ubiquitin ligases. Increased SAPK/JNK phosphorylation was expected, as DXR triggers ceramide production as well as apoptosis. This phenomenon has been observed by others proposing a dose-dependent increase.

**Conclusion:** The UPS is the major pathway of non-lysosomal degradation of intracellular proteins. From the very few studies conducted on the UPS in relation to cardiotoxicity, what can be gathered is that this system appears to be functionally active to a different extent in the initiation, progression and complication of cardiac myopathy.

## Bromocriptine promotes recovery of cardiac function and survival in patients with PPCM- proof of concept study

K. Sliwa\*, K. Tibazarwa†, L. Blauwet\*\*, E. Libhaber\*, J.P. Smedema‡, A. Becker\* and D. Hilfiker-Kleiner#

\*Soweto Cardiovascular Research Unit, Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand Johannesburg, South Africa

#Medizinische Hochschule Hannover, Department of Cardiology and Angiology, Hannover, Germany

‡Groote Schuur Hospital, University of Cape Town, South Africa

\*\*Department of Cardiovascular Disease, Mayo Clinic, Rochester, Minnesota, USA

\*Netcare NI City Hospital, Cape Town, South Africa

**Background:** Peripartum cardiomyopathy (PPCM) has a poor prognosis and a high mortality (9-30%). We demonstrated that mice with a cardiac specific knockout for the signal transducer and activator of transcription-3 (STAT-3) develop PPCM. Treatment with bromocriptine (BR), a dopamine-D2 receptor antagonist that inhibits prolactin secretion, completely prevented PPCM in these mice. A few case reports in humans suggest that BR may also have beneficial effects in PPCM patients.

**Aim:** To assess the efficacy of BR on the clinical parameters and recovery of left ventricular (LV) function in symptomatic patients with newly diagnosed PPCM presenting within the first month after child birth.

**Methods:** This was a proof-of-concept prospective single centre randomised study of women with newly diagnosed PPCM receiving standard care including ACE-inhibitors, beta-blockers, and diuretics (PPCM-Std, n=10) versus standard care plus BR 2.5 mg bid for 2 weeks and 2.5 daily for 4 weeks (PPCM-BR, n=10). The 6 month outcome of their offspring (n=21) was also studied, as mothers receiving BR could not breastfeed their children. Clinical assessment, echocardiography and measurement of prolactin were done at baseline and 6 months post diagnosis. Cardiac MRI was performed in PPCM-BR patients to identify thrombus formation due to BR therapy.

**Results:** There was no significant difference in baseline characteristics between the two study populations. PPCM-BR patients had significant recovery of LV systolic function ( $p=0.006$ ), reduction of mitral regurgitation, and improvement in parameters of LV diastolic function compared to PPCM Std patients (Table). Four patients in the PPCM-Std group died versus 1 patient in the PPCM-BR group. There was no significant difference between prolactin levels in the two groups either at baseline or at 6 months. No thromboembolic events were reported. There was no difference in outcome between the children of PPCM-BR mothers versus children of PPCM-Std mothers.

**Conclusions:** The addition of bromocriptine to standard heart failure therapy improved LV systolic and diastolic function as well as survival in patients with newly diagnosed PPCM. No detrimental effect on the children that could not be breastfed was observed in this cohort.

Comparing PPCM-BR (6 months) to PPCM-Std (6 months)					
	PPCM-BR Baseline*	PPCM-BR 6 months*	PPCM-Std Baseline*	PPCM -Std 6 months*	p value
EF, %	28 + 9	58 + 11	28 + 9	26 + 11	0.006
Mitral ERO, cm <sup>2</sup>	0.45 + 0.13	0.11 + 0.03	0.44 + 0.18	0.34 + 0.18	0.02
TDI E medial, m/sec	7.0 + 1.3	12.4 + 2.4	6.5 + 1.1	7.3 + 2.5	0.04
TDI E lateral, m/sec	7.2 + 1.1	12.4 + 2.5	6.6 + 1.0	7.3 + 2.5	0.02

\*Value = mean + 1 SD

## Incidence and characteristics of newly diagnosed rheumatic heart disease in urban African adults: Insight from the Heart of Soweto study

**K. Sliwa\***, **Melinda Carrington\*\***, **Bongani Mayosi†**, **Elias Zigiades\*\***, **Robert Mvungi\*\*** and **Simon Stewart#**

\*Soweto Cardiovascular Research Unit, Department of Cardiology, Chris Hani Baragwanath Hospital Soweto, University of the Witwatersrand Johannesburg, South Africa

#Preventative Cardiology, Baker Heart Research Institute, Melbourne, Australia

†Department of Medicine, Groote Schuur Hospital and University of Cape Town, South Africa

\*\*Division of Cardiothoracic Surgery, Johannesburg Hospital, South Africa

**Background:** Little is known on the incidence and clinical characteristics of newly diagnosed rheumatic heart disease (RHD) in adulthood from urban African communities in epidemiologic transition and their need for surgery.

**Methods:** Chris Hani Baragwanath Hospital services the black African community of 1.1 million people in Soweto, South Africa. A prospective, clinical registry captured data from all de novo cases of structural and functional valve disease (VD) presenting to the Cardiology Unit during 2006/2007. We describe in detail all cases with newly diagnosed RHD.

**Results:** There were 4005 de novo presentations in 2006/07 and 960 (24%) had a valvular abnormality. Of these, 344 cases (36%) were diagnosed with RHD. Estimated incidence of new cases of RHD for those aged > 14 years in the region was 23.5 cases/100,000 per annum. Most were black African females (n = 234 -68%) with a similar age profile to males (median 36 [interquartile range 26 50] years versus 37 [interquartile range 20 50] years. The predominant valvular lesion (n = 204 - 59%) was mitral regurgitation (MR), with 48 (14%) and 43 (13%) cases, respectively, having combination lesions of aortic plus MR and mixed mitral VHD. Impaired systolic function was found in 53/204 cases (26%) of predominant MR and in 35/126 cases (28%) with predominant aortic regurgitation. Elevated right ventricular systolic pressure > 35 mmHg (88 cases), atrial fibrillation (34 cases) anemia (27 cases) were found in 26%, 10% and 8% of all 344 RHD cases, respectively. Subsequent valve replacement/repair was performed in 75 patients (22%). Of these, 18 patients (24%) were readmitted for bacterial endocarditis within 30 months.

**Conclusion:** These data reveal a high incidence of newly diagnosed RHD within an adult urban African community. As the majority of cases were middle aged or older; these data suggest the burden of RHD extends well beyond childhood.

## Cardiac complications of Morquios syndrome

**H.D. Solomons**

Meiring and Partners Pathology Practice, Benoni, South Africa

Morquios syndrome is a rare type of mucopolysaccharidosis (type iv) which becomes evident when the affected infant starts to walk. The condition is marked by severe dwarfism especially of the torso, short neck, prominent sternum, dorsolumbar kyphosis, genu valgum, flat feet and waddling gait. In contrast to Hurlers syndrome the mental retardation is slight to normal. They get aortic valve disease, specifically aortic regurgitation. To make the diagnosis one picks up keratan sulfate in the urine. There is a type a and a type b form of the disorder. They also get cloudy cornea and spinal malalignment. Hypoplasia of the odontoid causes atlantoaxial subluxation, producing myelopathic changes.

In a nut-shell the internal organs continue to grow while the skeletal system stops growing. A good example of this was in the movie *The Mighty Freak*. Most die of congestive cardiac failure related to aortic regurgitation and compression of the heart! On auscultation they characteristically get early diastolic murmurs of aortic incompetence. All the other stigmata of a wide pulse pressure are picked up; Corrigan's pulse etc.

The only form of reversing the condition is by means of a cardiac transplant but the problem is that the skeletal changes are so severe.

Gene therapy may be of value as may stem cell therapy. Most patients are put onto anti-cardiac failure therapy which includes Lasix, Slow K Digoxin and an ace-inhibitor. Synonyms for the condition are; eccentro-osteochondroplasia, familial osteochondrodystrophy and osteochondrodystrophia deformans. It is also known as Morquio-Ullrich syndrome.

## How pliable is the bicuspid valve?

**H.D. Solomons**

Meiring and Partners Pathology Practice, Benoni, South Africa

The art of timing on auscultation to see how pliable the mitral valve is in mitral stenosis. By timing the interval between the opening snap and the start of the mid-diastolic murmur one can work out how pliable the mitral valve is. The normal time should be about 0,4 seconds. One has to be an experienced auscultationist to determine this.

This is useful in mitral stenosis but may also be of value in mixed mitral valve disease. This is best done on auscultation but can also be done by means of a phonocardiograph. The closer the interspace between the opening snap and the beginning of the mid-diastolic murmur the more pliable the valve.

This gives the cardiothoracic surgeon an indication of who to operate on and the nature of the valve.

Should it be a bjork-shalli, a homograft or a porcine valve? This will ultimately provide the prognosis for the patient and determine whether he can avoid cardiac failure or not. So timing is of vital importance in determining how pliable the valve is and the ultimate prognosis of the patient. This will determine the morbidity or mortality of the recipient.

## Signaling pathways activated in HDL-mediated cardioprotection: is it SAFE or at RISK?

**Sarin Somers, Lionel Opie and Sandrine Lecour**

Hatter Cardiovascular Research Institute, Faculty of Health Sciences, University of Cape Town, South Africa

**Introduction:** Sphingosine-1-Phosphate (SIP), a major component of High Density Lipoprotein (HDL), can protect against myocardial reperfusion injury but the exact signalling mechanism remains unclear. Recently, two powerful cardioprotective pathways have been described, as the RISK pathway (that involves the activation of Akt and FOXO-1) and the SAFE pathway (that involves the activation of Signal Transducer and Activator of Transcription-3 (STAT-3)). We propose that these two pathways are involved in SIP induced cardioprotection.

**Methods:** Control hearts from wildtype and cardiac deficient STAT-3 male mice were perfused on a Langendorff apparatus and subjected to 35min global ischaemia and 45min reperfusion. Alternatively, SIP (10nM) was given at the onset of reperfusion for the first 7min, with/without STAT-3 and Akt inhibitors, AG490 and Wortmannin (W), respectively. At the end of the experiment, myocardial infarct size was assessed. Additionally, phosphorylated levels of STAT-3, Akt and FOXO-1 were examined by Western Blot analysis after 15min of reperfusion in SIP-treated wildtype hearts.

**Results:** SIP significantly reduced the myocardial infarct size in the wildtype hearts (39.34.4% in control vs 17.33.1% in SIP-treated hearts;  $n \geq 6$ ;  $p < 0.05$ ) but not in the cardiac deficient STAT-3 mice (34.72.8% in control vs 34.24.3% in SIP-treated hearts;  $n \geq 6$ ;  $p = ns$ ). Both STAT-3 and Akt inhibitors abolished the protective effects of SIP (33.73.3% in SIP and AG490 and 36.64.9% in SIP and W;  $n = 6$ ;  $p < 0.05$ ). Levels of phosphorylated STAT-3, Akt and FOXO-1 were significantly increased following SIP administration in the wildtype mice (53% STAT-3, 47% Akt and 41% FOXO-1 greater than control).

**Conclusions:** SIP protects against reperfusion injury via the activation of both the SAFE and RISK pathways therefore suggesting a novel protective signalling mechanism in HDL induced cardioprotection. These findings may contribute to a better understanding of the cardioprotective action of HDL and present novel therapeutic opportunities against ischaemic heart disease.

## The value of cardiac MRI in the diagnosis of Loefflers endocarditis: a case report

**Johann Steyn\***, **Sulaiman Moosa#**, **Niel Hendricks†**, **Adrzej Okreglicki†**, **Ernesta Meintjes\***, **Bongani M. Mayosi†**

\*Medical Imaging Research Unit, Department of Biomedical Engineering, University of Cape Town, South Africa

#Department of Radiology, Groote Schuur Hospital and University of Cape Town, South Africa

†Division of Cardiology, Department of Medicine, Groote Schuur Hospital and University of Cape Town, South Africa

Hypereosinophilic Syndrome is a rare disorder characterised by a persistent eosinophilia of  $1,500/\text{mm}^3$  for at least 6 months. It is classified as a primary (idiopathic) disorder or secondary to allergies, parasitic infestation, autoimmune disorders, endocrinopathies (eg Addisons), myeloproliferative disorders and lymphoma. End organ damage is widespread and affect the heart, brain, bone marrow, skin, lungs, liver and gastrointestinal tract. Cardiovascular magnetic resonance can be used to evaluate the nature, extent and implications of hypereosinophilic associated myocardial disease.

A 37-year-old woman was admitted with palpitations and worsening dyspnoea. She is known with Graves disease with hypothyroidism secondary to radioactive iodine. ECGs showed diffuse subendocardial ischaemic changes and ventricular tachycardia. She was clinically diagnosed with non-ST elevation myocardial infarction. Cardiac Echography showed antero-septal hypokinesia with enhanced endocardial echogenicity. Cardiac MRI showed pericardial and pleural effusions, biatrial enlargement, mitral- and tricuspid incompetence and significant obliteration of both ventricular apices. The left ventricle had an end diastolic volume of 71,7ml (absol) and ejection fraction of 47%. The delayed enhancement showed global endocardial enhancement in a non-ischaemic pattern. Both apices revealed non-enhancing ventricular thrombus with associated subendocardial enhancement in the distribution of ventricular injury. The differential diagnosis of non-ischaemic global subendocardial delayed enhancement include Amyloidosis, Collagen Vascular disease (e.g. Scleroderma) and myocarditis. Associated with bi-apical thrombus, it is classic in hypereosinophilic syndrome and Loefflers endocarditis. Special investigations showed eosinophilia 3.08 (Normal: 0-0.45) that decreased to 0.06 over three weeks and platelet count 98 (Normal 178 400  $\times$  10<sup>9</sup>/l). Bone marrow biopsy revealed a focal increase in marrow eosinophils but no morphological evidence of a myeloproliferative disorder or lymphoma. Stools were negative for parasites, but Fasciola serology was positive. Endomyocardial biopsy showed mural thrombus, but no eosinophils. The patient received an orthotopic heart transplant. Ex vivo histology revealed subendocardial myocyte necrosis, organising endocardial thrombus, infiltrate of lymphocytes, plasma cells and haemosiderin as well as fibrosis and dystrophic calcification. These features support the diagnosis of Loefflers endocarditis.

## COMMD4: a novel link between cMYBPC-associated HCM, protein trafficking and turnover?

**C.C. Swanepoel**, **A. Ramburan** and **J.C. Moolman-Smook**

US/MRC Centre for Molecular and Cellular Biology, Department of Biomedical Sciences, University of Stellenbosch, South Africa

Cardiac myosin binding protein C (cMyBPC) mutations are the second most common cause of hypertrophic cardiomyopathy (HCM), which is viewed as a model disease for studying cardiac hypertrophy development. cMyBPC is involved in sarcomeric structure and function and also modulates cardiac contractility in a phosphorylation-dependent manner of the MyBPC-motif. In a previous yeast two-hybrid (Y2H) library screen, the Copper metabolism MURRI-domain containing protein 4 (COMMD4) was found to bind to the N-terminal of cMyBPC, in an interaction similarly dependent on phosphorylation of the MyBPC-motif. Although the functions of COMMD proteins are still unclear, it has been linked to copper metabolism as well as the ubiquitin-proteasome pathway (UPS). Interestingly, recent studies have shown that the UPS have been implicated in at least MyBPC-derived HCM, whereas dietary copper-depletion has been shown to cause cardiac hypertrophy. We therefore set out to investigate the function of COMMD4 by identifying its protein binding partners by Y2H analysis and confirming these interactions via various verification assays.

A COMMD4 Y2H bait construct was generated and used to screen a cardiac cDNA-library. Putative interactors were identified by direct sequencing and analysed using bioinformatics tools. Eight plausible positive interactors were verified via in vitro and in vivo co-immunoprecipitations analysis and 3D live cell fluorescent colocalisation. The effect of RNAi-mediated COMMD4 knock-down on cMyBPC turnover was also investigated.

These plausible interactors yielded novel insights into the role of COMMD4, implicating it in protein trafficking and turn-over and providing support for the link between cMyBPC-related HCM and protein degradation. Therefore, the results to date may shed light on the functioning of cMyBPC and also present a greater understanding of its role in the pathogenesis of HCM.

## Endovascular covered stent treatment for descending aorta pseudoaneurysm following coarctation of the aorta repair in an infant

**FF Takawira\***, **G Sinyangwe\***, **L Mitchell\***, **R Mooloo#**

\*Department of Paediatric Cardiology, Steve Biko Academic Hospital and University of Pretoria, South Africa

#Department of Cardiothoracic Surgery, Steve Biko Academic Hospital and University of Pretoria, South Africa

**Introduction:** Aneurysm development following coarctation of the aorta repair is a rare, but recognised complication. Surgical management of these patients is usually associated with a high morbidity and mortality. We describe successful endovascular deployment of a covered stent in an infant with a descending aorta pseudoaneurysm.

**Case Report:** The infant is one year old and has Downs syndrome. At six months old he was found to have a complete atrio-ventricular septal defect, coarctation of the aorta and transverse arch hypoplasia for which he had surgical repair. A Gore-Tex graft was used to widen the hypoplastic arch and isthmus.

The patient had done well until 12 months of age when he presented in respiratory distress. On examination he weighed 5 kg and appeared pale with a haemoglobin of 6 g/dl. He had a right mediastinal shift. There were no signs of congestive cardiac failure. The left lung was dull to percussion with decreased air entry. Chest radiography confirmed complete white out of the left chest and right mediastinal shift with the trachea deviated to the right. Echocardiography demonstrated a large extra-cardiac mass in the left chest, with compression of the LPA. The mass was fluid filled with evidence of swirling. A CT angiogram demonstrated a large pseudoaneurysm of the descending aorta just below the origin of the left subclavian artery. At cardiac catheterisation the large pseudoaneurysm was demonstrated. A 5 mm x 19 mm pre-mounted covered stent was deployed through a 7F sheath and 7F guiding catheter in the descending aorta, straddling the lumen into the aneurysm. Surgical evacuation of the aneurysm, which was then a bag of clot was undertaken five days later. The lung re-expanded and the infant was discharged from hospital 2 weeks later.

**Discussion:** Early or late development of an aortic pseudoaneurysm is a recognised complication following coarctation of the aorta repair. It is more common after patch augmentation of the aorta than after end to end anastomosis. It is often seen in patients with aortic arch hypoplasia. It has also been described more often following balloon dilatation of native coarctation of the AO. Surgical intervention has traditionally been used to manage these patients. Endovascular treatment with stents has been performed in adults and older children, but has not been described in infants. This approach was selected as the least risky in our patient and proved a major success. The challenges include the large femoral artery sheath required to deploy the stent in a small infant. There is also a limit to the size of stent one can deploy, leaving the need for future intervention as the patient grows.

## Clinical characteristics and outcome of lone atrial fibrillation: the Groote Schuur Hospital experience

V. Thomas, S. Schulein, V. Khanyi, A. Okreglicki, R.N. Scott Millar and B.M. Mayosi

Cardiac Clinic, Department of Internal Medicine, Groote Schuur Hospital and University of Cape Town, South Africa

**Introduction:** Atrial fibrillation (AF) is a common arrhythmia. The classical risk factors are well known. When AF represents an electro-physiological phenomenon in structurally normal hearts, it is termed lone AF. There are currently no studies to describe the clinical characteristics and outcomes of patients with lone AF in Africa.

**Methods:** A retrospective descriptive study in which 300 medical records of patients with AF at the GSH Cardiac Clinic were reviewed (1992-2006). Clinical data was interrogated to exclude identifiable causes of AF. Information on clinical characteristics and outcomes were entered into a data-entry form. Baseline descriptive statistics were expressed as means and range for continuous variables, and counts with percentages for categorical variables.

**Results:** Fifty three patients had lone AF, with a mean follow-up time of 5.8 years. Males comprised 58% (n=31) and females 42% (n=22). The mean age for males was 45; no males being older than 65 at diagnosis. The mean age of females was 58.6. Fifty seven percent (n=30) were white, 30% (n=16) were mixed race, 7% (n=4) were black and 6% (n=3) were unspecified. Forty seven percent (n=25) had normal weight, 36% (n=19) were overweight and 17% (n=9) were unspecified. Sixty two percent (n=33) had paroxysmal AF, 38% (n=20) had chronic AF and 13% (n=7) progressed from paroxysmal to chronic AF. Subsets of lone AF included concomitant atrial flutter (15%) (n=8) and sick sinus syndrome (13%) (n=7). Presenting complaints were palpitations (73%), dizziness (66%), dyspnoea (46%), near blackouts (41%), chest pain (22%) and fatigue (22%). Triggers included exercise (27%) and alcohol (17%). Complications included stroke (9%) (n=5), tachycardia-related cardiomyopathy (24.5%) (n=13). No mortalities were recorded. Fifty seven percent (n=30) were on betablockers, 23% (n=12) progressed onto amiodorone, 13% (n=7) had radiofrequency ablations. Nine percent (n=5) had atrioventricular nodal ablations with permanent pacemaker insertion. Sixty four percent (n=34) were on warfarin and 23% (n=12) on aspirin for prevention of thromboembolism. Nine percent (n=3) had bleeding complications while on Warfarin.

**Conclusion:** Lone AF is a relatively common condition with a preponderance to white, thin, middle-aged males. There are subsets of lone AF. The symptoms can be debilitating. Complications include tachycardia-related cardiomyopathy and thromboembolism. No mortality was recorded. Rate control and appropriate anticoagulation are the cornerstones of patient management.

## Delayed mortality in peripartum cardiomyopathy indicates need for long-term follow up

K. Tibazarwa<sup>†</sup>, K. Sliwa<sup>\*</sup>, O. Forster<sup>\*</sup>, E. Libhaber<sup>\*</sup>, A. Becker<sup>\*</sup>, A. Yip<sup>\*</sup> and D. Hilfiker-Kleiner<sup>#</sup>

<sup>\*</sup>Soweto Cardiovascular Research Unit, Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

<sup>#</sup>Medizinische Hochschule Hannover, Department of Cardiology and Angiology, Hannover, Germany

<sup>†</sup>Groote Schuur Hospital, University of Cape Town, South Africa

**Background:** Peripartum cardiomyopathy (PPCM) is a rare form of cardiomyopathy with heterogeneous presentation around the world occurring in women between 1 month antepartum and 5 months postpartum. It carries a substantial risk of mortality within the first 6 months after diagnosis but few studies have outlined prospective long-term morbidity and mortality. The aim of this study is to assess long-term clinical outcome and mortality over a 2-year period in an African cohort.

**Methods:** Prospective, single centre study of eighty consecutive women with PPCM enrolled at diagnosis over a period of 2 years. Patients were started on standard heart failure therapy (ACE-inhibitors, beta-blockers, diuretics) and detailed assessments, including echocardiography, were made at 6-month intervals for 24 months in surviving cases.

**Results:** At baseline, the mean age of this cohort was 29.9 ± 7.4 years, 38% were in their first pregnancy and 34% of patients were co-infected with HIV. Overall, 89% patients presented in NYHA functional class III-IV at baseline and mean left ventricular ejection fraction (LVEF) was 30%. During the 2-year study period, 4 patients were lost to follow-up, 9 moved to remote areas, and 7 had a subsequent pregnancy, predisposing them to additional myocardial risk. Within the entire 2 year period, 24 women (30%) died. The mortality rate at 6 months was 10% (8 of 80), beyond 6 months additional 16 of 69 (23%) patients died despite apparent recovery of left ventricular function. In the remaining cases, mean LVEF was: 44 ± 11% at 6 months, 46 ± 13% at 12 months and 50 ± 14% at 24 months follow up, respectively. No difference in cardiac function and mortality were observed between PPCM patients with or without HIV co-infection.

**Conclusion:** Overall the prognosis in this African cohort was poor confirming the high mortality rate of PPCM. A novel and somehow unexpected finding of this study is the high mortality rate in PPCM occurring beyond 6 months, which seems independent from HIV infection. This finding strongly suggests the need for long-term clinical follow-up including risk assessment of arrhythmic death.

## Using protein-protein interactions to identify modifier genes of cardiac disease

**G.M. Uys\*, A. Ramburan\*, B. Loos#, M. Revera†, A. Goosen\*\*, P.A. Brink\*\* and J.C. Moolman-Smook\***

\*US/MRC Centre for Molecular and Cellular Biology, Department of Biomedical Sciences, University of Stellenbosch, South Africa

#Central Analytical Facility, Department of Physiology, University of Stellenbosch, South Africa

†Department of Cardiology, IRCCS San Matteo Hospital, Pavia, Italy

\*\*Department of Medicine, Faculty of Health Sciences, University of Stellenbosch, South Africa

In order to identify novel modifier genes of cardiac disease, our laboratory uses a protein-protein interaction approach to define components of molecular pathways involved in these conditions. Using yeast-two-hybrid (Y2H) library screening, novel interactors of a protein known to be involved in the particular disease can be identified, and these proteins themselves can then be further tested at a genetic level to determine their role as potential modifier genes.

Cardiac contractility is regulated by dynamic phosphorylation of sarcomeric proteins by kinases such as cAMP-activated protein kinase A (PKA) which is anchored close to its targets by A-kinase anchoring proteins (AKAPs) to control phosphorylation. Cardiac Myosin Binding Protein-C (cMyBPC) and cardiac troponin I (cTNI) are hypertrophic cardiomyopathy (HCM)-causing sarcomeric proteins which regulate contractility in response to PKA phosphorylation. We identified a phosphodiesterase4D-interacting protein-like ligand of the N-terminal of cMyBPC via Y2H. This protein is also known as myomegalin. Because AKAPs sometimes anchor both PKA and phosphodiesterases, we hypothesized that myomegalin acts as an AKAP, and tested this by Y2H analyses.

The myomegalin cDNA was cloned into a bait vector, which was directly assessed for interaction with two distinct PKA regulatory-subunit preys. This bait was also used to screen a cardiac cDNA library for novel myomegalin interactors, and the prey clones sequenced to determine their identity.

Myomegalin bound both PKA regulatory subunits as well as with other cardiac proteins that are PKA targets, including cTNI. Thus, myomegalin acts as an AKAP in the phosphorylation of sarcomeric proteins involved in the regulation of cardiac contractility.

The myomegalin (MMGL) and both PKA regulatory subunit genes (PRKARIA and PRKAR2A) were then tested as potential modifier genes by screening a panel of 353 individuals including genetically and clinically affected plus unaffected HCM individuals for the presence or absence of all three HCM founder mutations. Individuals genotypes were determined by subjecting the DNA samples to TaqMan allelic discrimination technology using ABI TaqMan Validated SNP Genotyping Assays. Statistical analysis using quantitative transmission disequilibrium testing (QTDT) was performed to see whether the difference in genotype have an effect on HCM phenotype. One variant in MMGL (rs1664005) showed strong association with clinical hypertrophy traits, including left ventricular mass, maximal interventricular septum thickness, maximal posterior wall thickness as well as composite scores. Two variants in PRKARIA (rs11651687 and rs3785906) also showed strong association with numerous clinical hypertrophy traits. This study therefore gave statistical evidence that these three variants in these two genes may act as modifiers of the HCM phenotype.

## Protective effect of red palm oil against ischaemia/ reperfusion in isolated perfused rat heart

**J. van Rooyen, D. Bester, A.J. Esterhuysen, E.F. du Toit, T. Csont, K. Kupai, P. Ferdinandy and A.M. Engelbrecht**

Department of Biomedical Sciences, Cape Peninsula University of Technology, South Africa

**Purpose:** The formation of harmful reactive oxygen species (ROS) is associated with several pathological conditions and contributes to ischaemia/reperfusion injury. We have previously shown that red palm oil protects against the consequences of ischaemia/reperfusion injury. The detailed mechanism of this protection is still unresolved. We investigated whether RPO supplementation could protect against ischaemia/reperfusion injury in the isolated perfused rat heart and to elucidate a possible regulatory mechanism associated with the regulators of the protective Akt pathway.

**Methods:** Wistar rats were fed a standard rat chow diet for 4 weeks with or without RPO. Hearts were excised and mounted on a Langendorff perfusion apparatus. Reperfusion mechanical function recovery was measured after 25 min of global ischaemia. Hearts were freeze clamped at 10 min into reperfusion to investigate Akt and its regulators. In a second protocol wortmannin was added to the perfusion fluid to inhibit PI-3 Kinase.

**Results:** Hearts supplemented with RPO showed significantly improved rate pressure product recoveries independent of the presence of wortmannin (93.46 ± 5.24% vs 65.50 ± 6.25%,  $p < 0.05$ ). Biochemical results showed that wortmannin successfully inhibited PI-3 Kinase. However, Akt was significantly phosphorylated despite the inhibition of PI-3-kinase. RPO also caused significant increases in ERK 44 and phospho-ERK 44 in RPO groups, with or without wortmannin.

**Conclusions:** Our results show that RPO protected successfully against the consequences of ischaemia/reperfusion. Akt was phosphorylated despite the inhibition of PI-3 Kinase. This argues for and PI-3 Kinase independent phosphorylation of the pro-survival Akt pathway. Both the Akt and ERK pathways may be involved in protection.

## Protein phosphatase 2A is not involved in myocardial ischaemia/reperfusion injury... or is it?

**Derick van Vuuren, Corli Westcott and Amanda Lochner**

Division of Medical Physiology, Department of Biomedical Sciences, Faculty of Health Sciences, University of Stellenbosch, South Africa

Research into cardio-protective interventions (such as postconditioning) has emphatically demonstrated the involvement of phosphorylation-mediated signalling pathways in myocardial ischaemia/reperfusion (I/R) injury. Although the kinases have received much attention, the dephosphorylation modulation of these pathways (regulated by the phosphatases) are under-explored. We aimed to investigate the participation of a major serine/threonine phosphatase, Protein Phosphatase 2A (PP2A), in the events associated with I/R.

The isolated working rat heart model was used to determine the effects of the administration of a PP2A inhibitor (okadaic acid (OA); 10 nM a PP2A specific concentration), or activator (the A1 agonist 2-chloro-N6-cyclopentyladenosine (CCPA); 0.5 M), or a combination of the two for 10 minutes directly prior to an index ischaemia, or in the final 5 minutes of ischaemia and the first 10 minutes of reperfusion. An index ischaemia of 35 minutes regional ischaemia (RI; at 36.5 C) was applied to determine infarct size (IFS; expressed as percentage of area at risk), while 20 minutes global ischaemia (GI; 36.5 C) was used to investigate functional recovery. Hearts were freeze-clamped at different time-intervals in the last half of GI and the first 10 minutes of reperfusion to assess the cellular distribution and modification of the PP2A A (scaffolding)- and C (catalytic)-subunits, using Western blotting techniques.

Inhibition of PP2A with OA either before and/or after RI failed to elicit any effect on IFS relative to control. CCPA administration as a pretreatment however reduced I/R injury, while reperfusion administration abrogated damage (pretreatment: 29.833.06%; reperfusion treatment: 57.573.95 vs control: 40.242.33%;  $P < 0.05$ ). Co-administration with OA did not abolish these effects (pretreatment: 32.476.91%,

and reperfusion treatment: 44.226.29%). Preliminary Western blotting data however indicate that both the C- and A-subunits translocate between cellular fractions, while the C-subunit is modified during ischaemia and initial reperfusion.

Although AI-stimulation influenced the extent of I/R injury, PP2A inhibition failed to implicate PP2A in the events associated with I/R. In contrast to this, assessment of PP2A location and modification revealed that PP2A undergoes cellular translocation and modification during I/R. It is however still unknown whether these cellular changes are the consequence of I/R injury, or actively mediating I/R response.

## Organ donation and paediatric cardiac transplantation in South Africa

**Susan Vosloo**

Christiaan Barnard Memorial Hospital, Cape Town, South Africa

South Africa has one of the lowest rates of successful organ donation compared to other countries offering transplantation. In addition, significant diversity exists between different regions in SA regarding population composition, mortality rates, causes of death, life-expectancy and donor referrals, as well as the reasons for non-procurement of potential donors.

The last 2 decades saw transplant services reducing in State institutions, with increased delivery of such needs being provided in the private sector. Despite this, only 40% of patients referred had the procedure.

Worldwide and locally, paediatric patients constitute up to 20% of all cardiac transplantation procedures done annually. Operative mortality, as reported by the ISHLT is around 10%, with 1 year survival of over 80% and 5 year survival 70%.

At Christiaan Barnard Memorial Hospital to date over 150 cardiac transplantation procedures had been done. Operative mortality is <5%, with 1 and 5 year survival rates comparing favorably with worldwide figures.

Details on the paediatric / congenital group, consisting of 20 patients, will be presented. Of those, half underwent surgery for congenital heart defects, not amenable to conventional surgical correction.

## Review of our approach in mediastinal abscess caused by oesopharyngeal infections

**F.S. Vural, M. Olusoji, A.R. Patel, E. Zigiriadis and F.C. Cardio**

Division of Cardiothoracic Surgery, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa

We studied 8 patients with mediastinal abscess caused by oesopharyngeal infections between April 2008 and 2009.

All the patients were operated on after Maxillofacial and ENT surgeons treated the primary source and neck extensions and if necessary tracheostomy was performed. CT chest was obligatory for delineation of extent of disease.

Two of the patients required right thoracotomy for posterior mediastinal collections of which one of them also had an anterior mediastinal collection. Others were treated by parasternal small mediastinotomy (Chamberlain) incisions. Two of them required bilateral anterior mediastinal incisions.

After CT control three patients required repeat drainage procedures for new collections. There was no mortality. Our conclusion early gravity drainage at the most dependent point for mediastinal abscess with good antibiotic cover and repeat CT chest after 3 days in an effective approach in highly mortal disease.

## The quattro valve in rheumatic mitral valve disease: a 10 year follow up

**M. Wasiak, P. Manga and A. Patel**

Department of Cardiology & Cardiothoracic Surgery, CM Johannesburg Academic Hospital, University of Witwatersrand, Johannesburg, South Africa

**Background & aims:** There remains a need for durable bioprosthetic valves in developing countries where monitoring of anticoagulation is still problematic. The study aim was to assess the long term outcome of mitral valve replacement with a stentless bovine pericardial quadricuspid (Quattro) valve, which maintains mitral annular-papillary continuity. The study was conducted in relatively young patients with isolated severe rheumatic heart disease.

**Methods:** Since 1996 the Quattro valve had been implanted in 48 patients. The mean age was 34-13 yrs (34% aged < 25 yrs). All had significant rheumatic mitral valve disease and all patients were symptomatic with the majority (40) in NYHA class III or IV. Patients were followed-up at 6 monthly to yearly intervals. At follow-up visits, clinical and echocardiographic evaluations were done in each patient.

**Results:** At a mean follow up of 10 0.5 years, the overall mortality was 20.8% (10 deaths). 14 patients have been lost to follow up. Of the remaining patients who returned for regular follow-up, 6 patients have had repeat mitral valve replacement for severe valve degeneration at a mean interval of 7.3 years after the initial Quattro valve implantation. Five of the 6 patients had rupture of anterior leaflet resulting in severe mitral regurgitation. There have been 2 patients with infective endocarditis both requiring valve replacement. Thromboembolism or clinically overt haemolysis has not occurred. Serial echocardiographic data were available in 18 patients at the mean 10 year follow-up interval. Fourteen of these patients have developed moderate to severe valve degeneration. Six have moderate valve degeneration. Eight patients have severe valve degeneration and require repeat valve replacement. Only 4 patients remain asymptomatic with mild valve degeneration.

**Conclusion:** Long term results after Quattro valve implantation in a relatively young population has shown poor long term durability. There remains a need for more durable bioprosthetic valve types in a younger age group with rheumatic mitral valve disease.

## Rheumatic heart disease: the quest for new answers to age-old questions

**Liesl Zühlke**

Western Cape Pediatrics Cardiac Services, Red Cross and Tygerberg Hospitals, Cape Town, South Africa

At the beginning of the twentieth century, Rheumatic Heart Disease (RHD) was a huge public health burden worldwide. In fact until the 1960s, it remained a leading cause of death in children. Although the disease has waned significantly in the developed world, it continues to reign rampant in the developing world. Conservative estimates report 470 000 new cases of rheumatic fever and 233 000 deaths attributable to rheumatic fever or rheumatic heart disease each year, almost all of which are occurring in developing countries. These numbers demand a new approach to this disease.

The advent of screening for asymptomatic disease ushered in by the development of sensitive hand-held echo machines has raised an important issue: that of the significance of subclinical disease. Screening criteria have to address the minor changes representing rheumatic valve damage in its earliest stages. Screening criteria defined in a surveillance study conducted in Cape Town separate these into possible, probable and definite with only definites referred for secondary prophylaxis. All participants in the study are undergoing careful follow-up to determine the long-term course of asymptomatic disease.

Confirmed cases of RHD in children aged 5-15 years represents only 15-20% of all the cases in a population. Focusing on this vulnerable group especially in the developing world is of value in assessing the burden of disease. The most effective way to manage this disease is delivering secondary prophylaxis within a strictly controlled register. The soon-to-be-launched Global Registry Initiative provides a unique opportunity to both assess the burden of disease while simultaneously managing patients with established disease.

It is 33 years since the remarkable study by Barlow et al highlighted in this conference yet critical questions still remain regarding this age-old disease. We present our quest for answers using new approaches and strongly invite all practitioners dealing with this disease to join the Global registry Initiative.