Increase in circulating NT-proBNP in hypertension: An effect of left ventricular mass or pump dysfunction?

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Background: Hypertension is a risk factor for heart failure. Hypertensive heart failure could be a consequence of abnormalities of diastolic or systolic function. Brain natriuretic peptide (BNP), is recognised as an indicator of the presence and severity of heart failure. However, as a consequence of the strong relationship between BNP and left ventricular index (LVMI) the diagnostic value of BNP in hypertensive patients with a reduced ejection fraction is unclear. Therefore, the aim of our study is to determine whether plasma NT-pro-BNP is associated ejection fraction (EF) independently of LVMI in patients with hypertension (HT).

Methods: Echocardiography was performed on 175 hypertensive patients with average daytime ambulatory blood pressures (ABPM) >140/95mmHg, 31 of whom had a left ventricular (LV) ejection fraction (EF) <50%. Plasma NT-pro-BNP was measured using an electrochemi-luminescence type immunoassay. Multiple linear regression was performed to identify predictors of NT-pro-BNP adjusting for age and sex.

Results: Left ventricular mass index ($p<0.001$) and either systolic wall stress ($p=0.001$), LV EF (<0.0001), LV end diastolic diameter (LV EDD) ($p<0.001$), LV end systolic diameter (LV ESD) ($p<0.0001$) or systolic BP ($p<0.001$) were independently associated with plasma pro NT-BNP concentrations. As compared to controls hypertensive patients with an LV EF=50% had increased plasma pro NT-BNP concentrations. In addition as compared to both control and hypertensives with LV EF=50% hypertensives with an LV EF<50% had increased plasma pro NT-BNP concentrations.

Conclusions: Plasma pro NT-BNP concentrations are independently associated with LVMI, LV pump dysfunction and LV dilatation. Plasma pro NT-BNP concentrations may be useful to identify cardiac dilatation and pump dysfunction in patients with hypertension and LV hypertrophy.

Is diastolic dysfunction in hypertension closely related to left ventricular hypertrophy in patients of African ancestry?

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Background: In hypertension, left ventricular (LV) hypertrophy (LVH) in particularly concentric LVH is thought to be a critical cause of a reduced diastolic function of the LV chamber. This effect is thought to be a precursor of LV failure with a preserved systolic function (diastolic heart failure). A major goal of therapy in hypertension is therefore to regress LVH and hence return diastolic function to normal values. However, whether diastolic LV chamber dysfunction is caused by LVH, geometric LV remodelling or alternative associated myocardial changes is uncertain.

Methods: Echocardiography was performed on 175 hypertensive patients with average daytime ambulatory blood pressures (ABPM) >140/95mmHg, 84 (47%) of whom had concentric LVH, 33 (19%) of whom had concentric LV remodelling, and 31 (18%) of whom had a left

ventricular (LV) ejection fraction (EF) <50%. Pulse wave Doppler was employed to measure transmitral velocity during early (E-wave) and late/atrial (A-wave) LV filling. Factors associated with E, A and E/A were determined using multiple linear regression analysis with adjustments for age, sex and body mass index.

Results: Left ventricular mass indexed to body surface area (LVMI) was only modestly related to E/A, with decreases in the E-wave accounting for these relationships. Geometric remodelling, as determined from relative wall thickness (RWT) was not independently related to either E/A, E or A. LV EF was independently associated with the A-wave.

Conclusions: LV diastolic chamber dysfunction in hypertension is only modestly related to LVMI, and is unrelated to LV remodelling. Alternative myocardial changes are likely to be more important than LVM or LV remodelling in contributing to diastolic dysfunction in hypertension.

Pump dysfunction in hypertensive hypertrophy: Relative role of myocardial dysfunction versus adverse chamber remodelling in patients of African ancestry

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Background: Hypertensive heart failure in developing communities may be associated with a reduced pump function. Whether myocardial dysfunction and/or cardiac dilatation (adverse chamber remodelling) are important in mediating pump dysfunction produced by hypertension is controversial. We therefore evaluated the relative roles of myocardial dysfunction versus cardiac chamber enlargement in contributing toward pump dysfunction associated with hypertension in an urban, developing community in Gauteng.

Methods: Echocardiography was performed on 175 hypertensive patients with average daytime ambulatory blood pressures (ABPM) >140/95mmHg, 31 of whom had a left ventricular (LV) ejection fraction (EF) <50%. Systolic stress-corrected endocardial midwall fractional shortening (MFS) was employed to evaluate myocardial systolic function and cardiac dilatation was determined from chamber dimensions and relative wall thickness values (RWT). Comparisons were age, sex and body mass index (BMI) adjusted (ANCOVA) and values were compared to data obtained from 28 apparently healthy controls.

Results: As compared to controls, in hypertensives with a reduced EF, LV end diastolic diameter (EDD) was increased, RWT was unchanged, despite the presence of marked LV hypertrophy (LVH) and systolic-stress-corrected LV MFS was markedly reduced.

Conclusions: Left ventricular pump dysfunction in hypertensive hypertrophy is associated with both adverse LV chamber remodelling and a reduced LV stress-corrected myocardial systolic function.

Left atrial appendage closure with Amplatzer Cardiac Plug in atrial fibrillation: Initial South African experience

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Background: In approximately 90% of patients with atrial fibrillation (AF) and stroke, the source of the thrombotic embolism is the left atrial appendage (LAA).[1] Many patients are unable to take long term oral anticoagulation. Percutaneous closure of the LAA is an alternative form

of treatment for these patients. The Protect AF Trial showed non-inferiority of LAA closure compared with warfarin in 707 patients with non-valvular AF at average follow up of 21 ± 11 months.[2,3] This study details the initial experience in South Africa with the Amplatzer Cardiac Plug (ACP).

Methods and results: In 7 patients, the ACP was placed in the LAA under guidance of an experienced proctor. All 7 were males, average age 72.4 yrs (55-82 years), all permanent AF. Mean CHADS2 score = 3.1.[2-3] Five patients had massive gastro-intestinal bleeds requiring urgent blood transfusions, 1 had recurrent severe epistaxis requiring blood transfusions and 1 had 2 small strokes despite therapeutic INR and no other cause found. All devices were successfully placed via right femoral vein and transeptal puncture using trans-oesophageal and radiographic guidance. There were no intra-operative complications – specifically no pericardial effusions seen on post-op and discharge echocardiograms. All patients were discharged the following day on 82mg aspirin as chronic medication and clopidogrel for 1 month only. All patients have been seen at follow up – 3 at 6 months post and 4 at 3 months post procedure. All remain on aspirin alone. None have had any embolic events. There has been no device shift seen on echocardiogram.

Conclusion: Percutaneous closure of the LAA with the ACP device is a reasonable treatment to consider in patients with non-valvular AF who are unable to take oral anticoagulation therapy.

Reference: 1. Alberg H. Atrial Fibrillation: a study of atrial thrombus and systemic embolism in a necropsy material. Acta Med Scand 1969;185:373-379. 2. Holmes D R, Reddy V Y, Doshi S K, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet 2009;374:534-542. 3. Holmes D. R. Protect AF Trial – Intermediate Term Outcome. J Am Coll Cardiol. 2010;55:A181.

Two-year clinical outcomes after Sirolimus-eluting stent implantation for the treatment of coronary artery disease in a sample of South African patients

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Background: Coronary artery stents are known to reduce rates of restenosis after coronary stenting, but it is uncertain how long this benefit is maintained. Clinical data has raised concerns that drug-eluting stents are associated with increased rates of late stent thrombosis, death or myocardial infarction.

Objectives: To evaluate the safety and reliability of Sirolimus-eluting stents after 2 years of implantation.

Methods: From January 2008 to June 2008, 30 patients were enrolled in the study after implantation of 1 or more Sirolimus-eluting stents. We evaluated clinical follow-up information for up to 2 years after the implantation of Cypher® Select stents in 30 patients with 35 lesions.

Results: Mean patient age was 62.33 ± 10.99 years, 7% were diabetic and 30% presented with acute myocardial infarctions. The procedure's success rate was 100% for the Sirolimus-eluting stent implantation, and follow-up rates were 100%. Mean total stent length was 22.32 ± 6.63mm, with 13% receiving more than 1 stent. Two-year freedom from mortality, myocardial infarction, target vessel revascularisation and stent thrombosis was 100%. Dual anti-platelet therapy was taken by 100% at 1 month, 53% at 6 months, 40% at 1 year and 0% of patients at 2 years. The rate of survival free of myocardial infarction, bypass surgery and repeated angioplasty for stented lesions was 100% at 2 years.

Conclusions: Treatment of lesions with Sirolimus-eluting stents is associated with a sustained clinical benefit 2 years after device implantation.

Red or white wine: Which one should you drink to protect your heart?

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The red wine hypothesis suggests that moderate, regular consumption of red wine at meals is cardioprotective due, in part, to its content in the polyphenol resveratrol which is absent in white wine. Recently, we have shown that other components found in both red and white wine

(i.e. melatonin) may also contribute to the cardioprotective effect of red wine. Here, we compared the cardioprotective effect of a white South African wine versus a red South African wine of the same producer and of the same vintage (2010) against myocardial infarction.
Methods: The drinking water of Long Evans male rats was supplemented with a Pinot Noir or a Sauvignon Blanc (1 part of wine to 7 parts of water). After 2 weeks of treatment, hearts were isolated on a Langendorff system and subjected to 30 minute global ischaemia and 1 hour of reperfusion (I/R) (n=4 per group).
Results: Control hearts subjected to I/R presented a rate pressure product (RPP = heart rate x left ventricular developed pressure expressed as a percentage of baseline value) of 23.7 ± 1.7%. Pre-treatment with red wine improved the RPP to 42.2 ± 3.8% ($p<0.05$ vs. control). Moderate consumption of white wine protected the isolated heart to a similar extent to the red wine (36.0 ± 5.6, n.s. vs. red wine). Chemical analysis of the composition of both wines used in this study revealed that the white wine contained no resveratrol (2.11 µg/ml in red wine versus 0 in white wine) and that melatonin was absent in the red wine (0.34 ng/ml in white wine versus 0 in red wine).
Conclusion: Chronic and moderate consumption of South African red and white wines protected the isolated rat heart against myocardial infarction to a similar manner. The cardio protection of the white wine may be partly attributed to its content of melatonin.

Baseline characteristics and demographic differences of patients implanted with an Implantable Cardioverter Defibrillator in PANORAMA-Gulf observational study

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Background: PANORAMA is an observational study to construct a database of national profiles and epidemiological data on patients receiving Medtronic implantable cardioverter defibrillators (ICD) without and with cardiac resynchronisation therapy (CRT-D).
Objective: To assess the differences between baseline characteristics of patients implanted with ICDs and CRT-D devices in the Gulf region and in the rest of the world in routine clinical practice.
Methods: PANORAMA is a multi-centre, prospective, long-term study. Between May 2005 and November 2010, 610 patients were implanted (age 58.7 ±14.6 years, 79.7% male) in 1 centre in Kuwait and 6 centres in Saudi Arabia. These data are compared with 1 205 patients in the rest of the world (age 59.1 ±15.0 yrs, 82.3% male).
Results: PANORAMA results show the following: compared to the rest of the world the patients in the Gulf region more often receive a device for primary prevention indication, receive more often a dual chamber device and the RV lead is more often placed in the septal region. The population in the Gulf region less often has myocardial infarction, atrial fibrillation, and more frequent suffers from diabetes mellitus, hypertension and hypercholesterolemia. In general the Gulf population is in better NYHA functional class.
Conclusions: PANORAMA shows that the population from the Gulf region has some specific characteristics and that patient treatment is different from from the rest of the world. More often patients are treated for primary prevention and the RV lead is more often placed in the septal areas to mimic more physiological ventricular activation.

Cardiac hypertrophy modified: The modulating effect of a TPM1 gene variant on hypertrophy in a hypertrophic cardiomyopathy cohort

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Hypertrophic cardiomyopathy (HCM) is clinically defined by unexplained left ventricular hypertrophy (LVH) which is predictive of cardiovascular morbidity and all-cause mortality. The LVH may exhibit extreme variability in both degree and location even in individuals who carry the same

HCM-causing mutation, indicating that additional modifying factors may affect the severity of the cardiac phenotype. Various studies have shown that the presence of multiple functional sarcomeric variants is associated with an increased disease severity as well as increased risk of sudden cardiac death (SCD). Thus, sarcomeric genes are also candidate LVH modifiers.

An HCM-causing gene, Tropomyosin 1 (TPM1), encodes a-Tropomyosin (TM), which is an actin-binding sarcomeric protein that stabilises the thin filament as well as regulates muscle contraction via its association with the troponin (Tn) complex. Moreover, Ca^{2+}-binding to the Tn complex results in the repositioning of TM on actin, thereby exposing the myosin cross bridge binding sites on actin and allowing for muscle contraction. It is thus plausible that variants in TPM1 may affect force production within the sarcomere, potentially affecting sarcomeric function, and therefore modulating hypertrophy development in HCM. This study thus aimed to investigate TPM1 as a plausible modifier candidate in a familial HCM-cohort in which founder mutations in other sarcomeric genes segregate.

A total of 388 individuals, belonging to 27 HCM families in which 1 of 3 known founder HCM-causing mutations ($R92W_{TNNT2}$, $R403W_{MYH7}$, and $A797T_{MYH7}$) segregate, were genotyped by validated Taqman SNP genotyping assays. These data were compared to various hypertrophy traits using family-based association analysis with adjustment for known hypertrophy covariates, including the founder mutations.

A TPM1 SNP, rs1071646, was associated with a number of heritable hypertrophic traits, independent of known hypertrophy covariates (echocardiographically determined left ventricular mass (LVMecho), p=0.0057; maximal interventricular septum thickness (mIVST), p=0.0016; maximal left ventricular wall thickness (mlvwt), p=0.0049; cumulative wall thickness (CWT) score, p=0.0004; principle component 1 (PC1) score, p=0.0002). The effect size of the variant was similar in all mutation groups.

We have thus identified a role for TPM1 as modifier of cardiac hypertrophy in HCM, irrespective of the causal mutation. These findings may contribute to improved patient risk stratification.

Left ventricular diverticulum presenting as a pulsating umbilical mass

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Introduction: Congenital ventricular diverticulae and aneurysms are rare cardiac malformations. Little is known about the natural history and pathogenesis. Patients may be asymptomatic or present with serious complications including sudden cardiac death. Congenital ventricular diverticulae are often associated with midline thoracoabdominal defects, which include cardiac, sternal, diaphragmatic, pericardial, and abdominal wall anomalies. However, 30% are isolated and have no other associated cardiac anomalies. We present a child with a large congenital left ventricular diverticulum, diaphragmatic hernia and double outlet right ventricle, which presented with a pulsatile umbilical mass. Left ventricular function was preserved despite a large and elongated apical diverticulum.

Conclusion: Congenital diverticulae and aneurysms are rare cardiac malformations. The size of this left ventricular diverticulum makes our patient unique. Left ventricle function is preserved despite the presence of a large left ventricle diverticulum. Repair of the lesion is straight forward with low complication rate.

Association of renin gene haplotype with hypertrophy in hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM), an inherited primary cardiac disorder mostly caused by defective sarcomeric proteins, serves as a model to investigate left ventricular hypertrophy (LVH). The disease manifests extreme variability in the degree and pattern of LVH, even in HCM

patients with the same causal mutation. Previous studies identified renin-angiotensin-aldosterone system (RAAS) components as hypertrophy modifiers in HCM; however, investigations of the renin section of the RAAS pathway in HCM are extremely limited.
We investigated 6 single nucleotide polymorphisms (SNPs) within the renin (REN) gene for association with heritable cardiac hypertrophy traits in a cohort of families that each harbour 1 of 3 HCM founder mutations.
After adjustment for the primary HCM-causal mutation, blood pressure and other known hypertrophy confounders, we identified a five-SNP haplotype that significantly decreased left ventricular mass (LVM) by 34.3g (p=0.005) and interventricular septal thickness by 2.79mm (p=0.0451).
We demonstrate that REN gene variations play a role in modulating hypertrophy in HCM, independent of the primary HCM-causal mutation and blood pressure. Given the efficacy of the direct renin inhibitor in promoting LVH regression in hypertensive patients, this study informs on potential anti-hypertrophic therapy targets for HCM.

A case of idiopathic right ventricular tachycardia arising from the body of the right ventricle

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Introduction: Ventricular tachycardia (VT) and premature ventricular complexes (PVCs) that arise from the right ventricle (RV) can be caused by arrhythmogenic right ventricular cardiomyopathy (ARVC). Idiopathic RV VT/PVCs usually arise from the RV outflow tract. Idiopathic RV VT/PVCs not arising from the RV outflow tract is uncommon. This case highlights a rare case of idiopathic VT/PVCs arising from the RV body (apex) which was successfully ablated.
Methods and results: A 48-year-old man with no medical comorbidity presented with a 6-month history of palpitations associated with light-headedness. There was no family history of heart disease or sudden cardiac death. Clinical examination was normal. A Holter monitor recorded 24 000 unifocal PVCs and a short run of monomorphic, non-sustained VT during a 24-hour period. A 12 lead ECG of the PVCs showed no features of ARVC. The ECG features of the PVCs suggested a RV apical origin (left bundle branch block morphology, R-wave in lead I, PVC axis -75 degrees, late precordial R-wave transition in lead V5). A signal-averaged ECG and MRI showed no features of ARVC. An echocardiogram confirmed normal left ventricular function. Coronary angiography showed normal coronary arteries.
At electrophysiological study, unifocal clinical PVCs were present to allow activation mapping. Sustained VT could not be induced by programmed ventricular extra- stimulation. An endocardial bipolar voltage map showed normal RV voltages with no evidence of scar. Using activation mapping and the CARTO 3 system, the PVCs were mapped to the region of the RV apex. Serial radiofrequency ablation burns were applied here with suppression of the PVCs. At 3-month follow-up the patient is asymptomatic with no recurrence of PVCs.
Conclusion: Idiopathic VT/PVCs arising from the body of the RV is an uncommon entity. The genesis and long-term outcome appears to be similar to idiopathic right ventricular outflow tract VT/PVCs. ARVC needs to be considered and excluded in all cases of VT/PVCs arising from the body and outflow tract of the RV.

Intracardiac thrombi in children with dilated cardiomyopathy

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Introduction: Intracardiac thrombosis (ICT) in patients with dilated cardiomyopathy (DCMO) is a serious complication and potential source of significant morbidity and mortality. Very few studies examine ICT in children with DCMO. In this study, we carried out a retrospective review of children presenting with ICT, all of whom had DCMO, to assess possible risk factors and outcome in children at a single tertiary care centre over a course of 17 years.

Methods: A retrospective review of a paediatric cardiology database was performed. All paediatric patients between 0-14 years diagnosed with DCMO from 1983 to 2010 at the Chris Hani Baragwanath Academic Hospital were assessed.
Results: 361 patients were found to have DCMO with an M:F=1.3:1 and an average age of 5.7 years. Of the 361 patients, 39 were found to have ICT (prevalence 11%) on echocardiography and 15 (38%) of these had thromboembolic events. More males than females are affected by DCMO and consequently more males are diagnosed with ICT and have embolic complications. The shortening fraction in patients does not differ statistically from those with ICT alone and those with ICT and embolic complications. Younger patients with DCMO and ICT are more likely to have thromboembolic complications (p=0.026). There is no statistical difference in the HIV status of the patients with DCMO alone or those with DCMO and ICT. The recorded mortality was unreliable and therefore could not be analysed with accuracy statistically.
Conclusion: The prevalence of ICT is 11% in children presenting with DCMO at the Chris Hani Baragwanath Academic Hospital and more than a third (38%) of these patients develop thromboembolic complications, with younger patients being more at risk. All children with DCMO should be screened for the presence of ICT and anticoagulation treatment instituted to prevent thromboembolic complications.

Metabolic and clinical changes in patients with acute coronary syndrome undergoing on-pump and off-pump coronary artery bypass surgery

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Background: Despite improvements in cardiac surgical and anaesthetic techniques, alterations in tissue perfusion during surgery results in various pathophysiological changes. This could result in decreased tissue oxygenation with increased lactate production. Furthermore, an augmented endocrine response, increasing catabolic hormones, resulting in hyperglycaemia is associated with the systemic inflammatory response associated with surgery and exposure to extracorporeal circulation.
Objective: Assessing the relationship of metabolic changes on the clinical outcomes and inflammatory marker response in acute coronary artery syndrome patients presenting for on- and off-pump coronary artery bypass surgery.
Methods: An observational cross sectional study was conducted. 60 patients diagnosed with ACS undergoing CABG surgery were recruited (30 in the on-pump and 30 in the OPCAB group). Arterial blood gasses were used to assess the metabolic changes during and after surgery and correlated with the patient's clinical outcomes and the inflammatory marker response.
Results: Intra-operative results indicated a marked difference ($p<0.05$) in lactate production, with lower lactate concentrations in the off-pump CABG group. Postoperative results indicated a marked difference ($p<0.05$) in lactate production, with lower lactate concentrations in the off-pump CABG group. However, glucose concentrations indicated no significant difference between on- and off-pump CABG patients. The study indicated, compared with the on-pump group, IL-6 was elevated in the off-pump surgical group (96 - 120hrs). The TNF-a values were higher in the off-pump CABG group, but without any significance between the on-pump and off-pump CABG groups at 24hrs (p=0.40147), 48hrs (p=0.31438), 72hrs (p=0.70912), 96hrs (p=0.40561) or 120hrs (p=0.48907) postoperatively. Despite 43% of the patient population in a high-risk group (lactate >5mmol/L) it had no correlation to the clinical outcomes (length of hospital or ICU stay, re-operations, gastro-intestinal complications, atrial fibrillation and septicaemia).
Conclusion: The metabolic changes observed indicated higher lactate concentrations in the off-pump group with no variation for glucose concentrations between on-pump CABG and off-pump CABG groups. Clinical outcomes proved similar for both on-pump and off-pump groups. Lactate concentrations of >5mmol/L could not be associated with clinical outcomes for this pilot group. Despite the elevated IL-6 and TNF-a concentrations in the off-pump group, no correlation with clinical outcomes was observed.

Myocardial infarction: injection of a biomaterial after 1 week is superior to immediate treatment

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Background: Remodelling following myocardial infarction can result in a progressive decline in left ventricular performance leading to heart failure in up to 1 third of patients. The potential of the delivery of hydrogels to the infarcted heart as a therapy has begun to receive attention.

Results indicate a reduction in remodelling after infarction by limiting the increase in wall stress and this may prevent progression to heart failure. In the present literature, there is no consensus on the optimal time point of delivery after infarction. The aim of this study was to directly compare the effect of injecting an enzymatically degradable polyethylene glycol (PEG) gel immediately or 7 days post-MI on pathological remodelling of the infarcted rat heart.

Methods: Following permanent ligation of the left anterior descending artery in male Wistar rats, PEG gel monomers were injected into the infarcted area and polymerised in situ. The gel was delivered either immediately or 1 week after infarct induction. Echocardiography was used for functional assessment while infarct size and scar thickness were quantified by histomorphometric analysis. The study was blinded and randomised. Distribution of the gel was determined by 3-D reconstruction from histology of sectioned hearts. The inflammatory cell response was characterised at various time points.

Results: Fractional shortening was significantly higher in the group that received treatment delayed by 7 days relative to immediate treatment at both 2 and 4 weeks post-MI ($p<0.05$). At 4 weeks, left ventricular end-systolic dimensions were significantly reduced ($p<0.05$). Treatment after 7 days resulted in significantly thicker scars ($p<0.05$). Gel distribution for immediate injection was intricately striated and temporary whilst 7-day delivery resulted in a cohesive mass that persisted for 4 weeks. The inflammatory response was similar.

Conclusions: The injection of a synthetic gel into a one-week-old infarct was effective in ameliorating pathological remodelling and was superior to immediate treatment. We believe this resulted in part from a gel distribution that limited degradation, an important consideration for further studies. These findings are of potential clinical relevance as delayed treatment may be applicable to myocardial infarction patients who have not received timely treatment such as reperfusion.

Sphingosine-1-Phosphate (S-1-P) and glucose: A new therapeutic approach to acute heart failure (AHF)

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Purpose: In our model of AHF, we propose that (1) increased circulating glucose improves contractile dysfunction (2) S-1-P, improves post ischaemic recovery could also improve contractile dysfunction.

Methods: AHF was induced by (1) increasing the levels of circulating FFA (1.3mM); (2) lowering the glucose levels (2.5mM); and (3) by lowering the perfusion pressure to 20cm H_2O, followed by recovery phase at 100cm H_2O. In separate experiments, S-1-P (10nM) was added during the AHF phase and recovery phase.

Results: In recovery phase, with high glucose (n=8), heart rate (BPM) improved $204.1 \pm 21.2^{\#}$ vs. 106.5 ± 37.3 compared to low glucose, while diastolic pressure fell from 42.2 ± 7.2 to $14.9 \pm 6.5^{\#\#}$. There was no difference in LVDP in either group. For the S-1-P treated group, we found significant elevation only in heart rate $182.5 \pm 25.2^{**}$ vs. 91.1 ± 25.7 non S-1-P treated. There was no change in the diastolic pressure or LVDP. When given together, only improvement in HR was significant 92.7 ± 28.6 (high glucose) vs. $179.7 \pm 18.2\$$ (high glucose + S-1-P) BPM. There was no significant change in diastolic pressure or LVDP.

Conclusion: Our model demonstrates that high glucose in the recovery phase helps recovery by enhancing both contractility and heart rate. S-1-P only improves recovery heart rate but not the LVDP when given in either phase. We suggest that in this particular model, metabolic therapy by glucose is better than molecular therapy by S-1-P. However, when given together, they improve heart rate rather than LVDP.

$^{\#}p<0.05$ vs. Rec Low glucose; $^{\#\#}p<0.01$ vs. Rec low glucose; BPM- Beats per minute; LVDP- Left ventricular developed pressure;
$^{**}p<0.01$ vs. without S-1-P; (ns) vs. S-1-P); $\$p<0.05$ vs. high glucose+S-1-P)

Transcatheter based aortic valve implantation at 5 years. What happened to our initial patients?

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Background: Short-term results of transcatheter valve implantations, for aortic valve stenosis, have been encouraging, with potential for reducing perioperative risk and hospital length of stay. However, little is known about mid-term efficacy of this approach. This report analyses a single institution's results, of the initial series of patients, over 5 years with transapical aortic valve implantations.

Methods: The first series of 100 patients had transapical aortic valve implantations at our institution starting in January 2005. The mean age was 85 ± 6 years. All patients had a high perioperative risk for aortic valve replacement, with a mean logistic Euroscore of 36 ± 12. Clinical and echocardiographic variables were entered prospectively into a database. Follow up was complete for all patients.
Results: After a mean follow up of 5.1 ± 2 years, overall mortality was 13% (n=13/100), 30 day mortality was 8% (n=8/100) and late mortality was 5% (n=5/100). The causes of late mortality were cardiac failure (n=2), respiratory failure, renal failure and cancer. There were 2 peri-operative rethoracotomies for bleeding, 2 intraoperative conversions, 1 prosthesis embolisation, and 2 impairments of coronaries. There were 2 late conversions.
One for aortic valve thrombosis and 1 for acute type A dissection. Valve thrombosis occurred after discontinuing Clopidogrel at 6 months. One patient developed late atrio-ventricular block and needed the implantation of a pacemaker. There were no cases of endocarditis or stroke in any of the patients. None of the valves showed structural valve degeneration. NYHA functional class at 5 years ranged between 1 and 3. Four patients did not improve their functional class. All others improved by 1 or 2 steps.
Conclusion: Mid-term outcomes after transcatheter aortic valve implantations, in high-risk patients at our institution, show an improvement in quality of life, with a good survival rate. Valve degeneration is not an issue at mid-term.

Morbidity and mortality associated with anomalous origin of pulmonary artery from aorta; review of case seen at Chris Hani Baragwanath Academic Hospital

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Introduction: Anomalous origin of 1 pulmonary artery from the ascending aorta with separate aortic and pulmonary valves is a rare congenital cardiac anomaly associated with early onset of pulmonary hypertension and irreversible pulmonary vascular disease.
Methods: Retrospective clinical review of 13 cases between June 1991 and August 2011 presenting to the Division of Paediatric Cardiology at the Chris Hani Baragwanath Academic Hospital. Data related to clinical features, diagnosis, operative procedures, preoperative and post-operative follow up was collected.
Results: Twelve infants and 1 adult (6 males and 7 females) were diagnosed. The most common presenting features were dyspnoea, tachypnoea, a cardiac murmur and congestive cardiac failure. Median age at presentation was 70 days. Initial diagnosis was made with echocardiography in 9 patients and angiography in 4 patients. Median time to diagnosis was 3 days.
The right pulmonary artery in 11 patients and left pulmonary artery in 2 patients originated from the aorta. Patients were divided into 3 categories: 3 patients had isolated lesions; 9 patients had simple lesions with patent ductus arteriosus and 1 patient with anomalous LPA origin and associated CATCH 22 syndrome had a complex lesion (pulmonary atresia, ventricular septal defect, patent ductus arteriosus and large collaterals arising from the descending aorta). The second patient with anomalous origin of left pulmonary artery also had Mckusick- Kaufman syndrome.
Two patients had successful direct re-implantation of the right pulmonary artery to the main pulmonary artery. One patient died on day 20 post repair with sepsis and the second patient is well with no complications on follow up. Three patients were deemed inoperable including the adult patient. The majority viz. 8 patients died early before further investigations or surgery could be undertaken.
Conclusion: Early diagnosis with good preoperative care is essential to reduce morbidity and mortality. Excellent results are achieved with early repair and good postoperative follow up even in newborn and premature babies. Early repair prevents irreversible pulmonary vascular disease and leads to complete resolution of pulmonary hypertension.

A prospective study based on a cohort from the PANORAMA study evaluating CRT non-responders, hyper-responders and super-responders

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Introduction: Improvement of left ventricular ejection fraction (LVEF) following CRT implantation is known to range between 3-5%. Some patients present with dramatic increase in LVEF of up to 20% or more or a final post CRT implantation EF of=45%, known as "super-

responders". Patients whose LVEF normalise with CRT are labelled "hyper-responders". The objective of this study was to assess the number of super, hyper, normal and non-responders in our cohort of patients from the Panorama study.

Methods: Panorama is a multi-centre, prospective, long-term study. 22 patients (age 65.1 years, 81.8% male, EF= 35%, (NYHA II-IV) implanted with a CRT-P/D device at Unitas Hospital were analysed. Pre- and post-measurements were collected on QRS-duration, NYHA class, LVEF and cardiac dimension, and were compared using a paired T-test. An improvement of more than 20% in EF, were termed super-responders and normalisation of EF, were termed hyper-responders.

Results: Mean baseline EF 25.3%, LVIDd 65mm and LVIDs 56.4mm. Mean pre-implantation QRS duration 141.4ms. Post-implantation Mean improvement in QRS-duration was 19ms and Mean improvement of EF was 41% (P <0.0001). Improvement in LVIDs and LVIDs was observed. There were 1 (4.5%) non-responder, 14 (727%) normal responders, 3 (13.6%) hyper-responders and 4 (18.1%) super-responders. No major implant complications occurred.

Conclusion: There was a significant improvement in EF in patients who received CRT. The majority were normal responders. Percentage of super- and hyper-responders was higher than previously described. This may be due to the highly selective population and the broad QRS-duration pre-implantation with a mean of 141.4ms.

Evaluation of QT interval in ß thalassemia major and intermedia patients compared with control group

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Introduction: Cardiac complications are major cause of death in patients with ß thalassemia. Corrected QT (QTc) interval is a marker variability of ventricular repolarisation and is elevated in various high-risk groups of patients. The aim of this study was to investigate QTc interval in ß thalassemia major and intermedia compared with control group.

Patients and methods: Sixty ß thalassemia major and/or intermadia patients (40 thalassaemia major and 20 intermadia) consisted of 28 males and 32 females and 62 healthy controls (30 males and 32 females) were investigated in this analytical cross-sectional study. Thalassaemia patients with no clinical symptoms of cardiac disease underwent echocardiographic and stress tests. QTc interval , blood pressure and heart rate and average serum ferritin levels were measured. Statistical analysis was performed using version 15 SPSS (Chicago, USA). Values were defined as significant when values for P were defined as P <.05.

Results: Mean age of ß thalassemia and control group were 25.2 ± 5.9 and 25.4 ± 3.1 years old, respectively. It was shown no significant differences in age and gender between groups. Serum ferritin level was 2 640 ± 1 510 g/L. Electrocardiographic and echocardiographic findings were normal in all patients with no evidence of cardiac failure or arrhythmia. The systolic and diastolic blood pressure values were lower in ß thalassemia group (p=0.001), while the heart rate was higher in ß thalassemia compared with control group (105.1 ± 15.1vs 89.7 ± 12.3, p=0.001), respectively. QTc interval values before and during of exercise test revealed that resting QTc interval was slightly longer in ß thalassemia group with no statistical significance (419.7 ± 30.1 vs. 410 ± 26.2, p=0.06). However, during exercise QTc interval significantly prolonged in ß thalassemia patients compared with control group (452.6 ± 29.4 vs. 414.2 ± 24.5, p=0.001). There was no correlation between serum ferritin levels and QTc interval among ß thalassemia patients.

Conclusion: Increased QTc intervals have been found in this group of thalassemia patients who have neither clinical nor electrocardiographic and gross echocardiographic signs of cardiac disease. Because of its high reproducibility as a non-invasive method, QTc interval can be used in the cardiac care of thalassemia major patients.

The use of echocardiography in predicting left ventricle thrombus in patients with idiopathic dilated cardiomyopathy at Chris Hani Baragwanath Academic Hospital

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Background: Idiopathic dilated cardiomyopathy (IDCMO) is the second most important cause of heart failure (HF) in Soweto. This disorder is characterised by impaired myocardial contractility, left ventricular (LV) dilatation and intracavitatory stasis of blood. Left ventricular thrombus

is a recognised complication, which causes considerable morbidity and mortality resulting from cardio embolism. There is a paucity of data relating to the prevalence and predictors of LV thrombus in subjects with IDCMO in South Africa. This information may be useful to guide use of warfarin in patients with IDCMO.

Methodology: Seventy patients with IDCMO who fulfilled the inclusion and exclusion criteria of this study were enrolled from a tertiary academic cardiomyopathy clinic into this prospective single centre study. All subjects were evaluated clinically prior to undergoing detailed systematic echocardiography.

Results: The mean age was 47.8 ± 13.8 years with 55.7% male. Previous cardio embolism was documented in 3 patients (4.3%). Sixteen patients (22.9%) were on warfarin. Mean left ventricular end diastolic diameter (LVEDD) was 62mm with the mean left ventricular ejection fraction (LVEF) 24.1%. Moderate or severe mitral regurgitation (MR) was documented in 40 subjects (57.2%). Spontaneous echo contrast (SEC) was observed in 20 patients (28.6%). Left ventricular (LV) thrombus was observed in 13 subjects (18.6%). The most common site was the apex – 11/13 subjects (84.6%). By using univariate logistic regression, the independent predictors of LV thrombus formation were LVEF (unadjusted odds ratio = 0.92, 95% CI 0.86-0.99; p=0.03) and age (unadjusted odds ratio = 0.92, 95% CI 0.86-0.98; p=0.006). Multivariate logistic regression analysis identified age (adjusted odds ratio = 0.92, 95% CI 0.86-0.98; p=0.01) as the sole predictor for LV thrombus formation when including LVEF, presence of MR and SEC into the model. However the association between LVEF and LV thrombus was borderline significant (p=0.05).

Conclusion: The prevalence of LV thrombus formation in this cohort was 18.6%. Echocardiographic parameters alone cannot predict which patients are more likely to develop thrombus formation.

Desmoplakin gene mutations: A common link between arrhythmogenic right ventricular cardiomyopathy and dilated cardiomyopathy

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Introduction: It has been shown that all forms of cardiomyopathy, including the dilated, hypertrophic, restrictive, and right ventricular arrhythmogenic forms, are found in African populations. Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare heart muscle disease characterised by fibro fatty replacement of the right ventricular myocardium, leading to electrical instability and eventually heart failure. Dilated cardiomyopathy (DCM) is a disease characterised by a reduction in ventricular wall thickness, which leads to reduced contractility, and impaired ventricular function. Mutations in the DSP gene, which encodes the desmosomal protein desmoplakin, have been shown to be causative of ARVC and DCM. Our aim was to determine whether DSP mutations are causative of ARVC and DCM in African patients.

Methods: In this study, 62 patients with ARVC and 150 patients with DCM (19 familial, 131 idiopathic) were screened for mutations in DSP by means of high-resolution melt analysis and DNA sequencing. Population screens were conducted on novel variants to determine the frequency of variants in a representative control population.

Results: The frequency of disease-causing mutations in DSP was 3% in cases of ARVC (2/62 probands), 5% in cases of familial DCM (1/19 probands) and 4% in apparently sporadic cases of DCM (5/131 probands). We also detected a number of variants of unknown significance, which require further study to determine their role in disease. We found mutations that were common to both the ARVC and DCM cohorts, and were determined to be causative of both these diseases.

Conclusion: This study has shown that mutations in DSP are causative of ARVC and/or DCM in African patients. This is the first study to demonstrate a large number of mutations in the DSP gene in cases of idiopathic DCM in Africans, and 1 of the first studies to implicate DSP in familial DCM. We have also shown that the same mutations can cause ARVC and DCM, which suggests that ARVC and DCM may form part of a common spectrum of cardiomyopathy.

A retrospective review of rheumatic mitral valve repair in a threshold country

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Study background and aim: Rheumatic heart disease predominates cardiac valvular surgery in threshold countries. We reviewed the role of mitral valve repairs as opposed to replacements in a 10-year cohort of rheumatic single mitral valve (MV) procedures.
Methods: Between 2000 and 2010, 560 consecutive adult (>13 yrs) patients had a primary, single mitral valve procedure. Of the 215 primary MV repairs, 69 were rheumatic (32%) as opposed to 281 out of 345 primary MV replacements (81%). From the 281 single MV replacements for rheumatic disease an equal number of 69 were propensity-matched with the repair group. Based on propensity score analysis, Kaplan-Meier actuarial analysis with log-rank testing was used to evaluate survival and morbidity.
Results: Follow-up was 100% complete (n=138) and ranged from 0.6 months to 132.5 months (Mean 53.32 ± 36.48). Of all rheumatic single MV procedures, 19.7% were repaired. Actuarial freedom from valve-related mortality was 95.6 ± 3.1% and 91.7 ± 3.6% at 5 years and 95.6 ± 3.1% and 80.2 ± 11.2% at 10 years for repairs and replacements, respectively (NS). Actuarial freedom from all valve related events (deaths, re-operations and morbidity) was 79.8 ± 5.8% and 85.6 ± 4.5% at 5 years and 69.8 ± 8.4% and 69.2 ± 10.7% at 10 years (NS). Actuarial freedom from all valve related events was 57.1 ± 11.1% and 95.5 ± 3.1% at 5 years (p=0.0008) and 41.6 ± 12.4% and 95.5 ± 3.1% at 10 years (p<0.001) for those mitral valve repairs with and without commissural fusion, respectively (p=0.0002 overall).
Conclusions: The long-term results for mitral valve replacement in an older, indigent, rheumatic heart disease population of a threshold country are distinctly better than generally perceived. Nevertheless, mitral valve repair has superior long-term outcomes in those patients who do not have commissural fusion at surgery.

LV diastolic function and filling pressure assessment using the time intervals changes on the mitral inflow and mitral annular velocities

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Background: The aim of our study was to evaluate the left ventricular (LV) function using the time intervals between mitral inflow and mitral annular velocities.
Methods: 40 patients (age from 31-68 years old, mean age: 42 yrs) with heart failure and 30 age-matched healthy controls (age from 30-65 yrs, mean age: 41yrs) were enrolled. Two-dimensional echocardiography, pulsed Doppler, and pulsed tissue Doppler were performed. Patients were classified into 2 groups according to the ratio of E/E': (1) group 1: E/E' from 8-15; (2) group 2: E/E' >15. The measurements were: the time intervals from the R-wave on the ECG to the peak E-wave on the transmitral flow (TMF) (R-pE), to the peak E'-wave on the LV septal wall of tissue Doppler imaging (TDI) (R-pE'); The time intervals from the onset of P-wave on the ECG to the peak A-wave on the TMF (P-pAA), and to the peak A'-wave on TDI (P-pA', P-onset A').
Results: The time intervals of P-pA' were significantly decreased in heart failure patients compared to the control group, and the P-pA' also significantly decreased in the group 2 compared to the group 1(91.6 ± 20.5, 121.1 ± 13.0 vs 1 57.2 ± 16.3, respectively p<0.001).
Conclusion: The time intervals of P-wave to A-wave on TDI changed earlier than on the pulsed Doppler when the LV filling pressure increased, and it may be a useful new method to evaluate the LV diastolic function in patients with heart diseases.

Cardioprotective effects of DPP4 inhibition in obese, insulin resistant rats

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Therapy based on GLP-1 is currently 1 of the most promising treatments for T2 diabetes, because GLP-1 (1) is attenuated in T2 diabetes; (2) has pancreatic protective and (3) cardioprotective effects. Since GLP-1 is rapidly degraded by dipeptidylpeptidase IV (DPP4), research

focused on either DPP4 inhibitors or GLP-1-mimetics. We tested whether treatment of obese, pre-diabetic rats with cardiovascular pathology, with a DPP4 inhibitor (PFK275-055) is cardioprotective.

Obesity was induced in Wistar rats (DIO) for 12 weeks where after half of control-fed & DIO rats were treated orally with 10mg/kg/day PFK275-055. After 4 weeks animals were sacrificed, blood collected, body weight and intra peritoneal (IP) fat weight recorded, pancreatic harvested and isolated hearts perfused (Langendorff: regional ischaemia, infarct development and recovery after low-flow ischaemia and kinase profile on reperfusion). Ventricular myocytes were isolated (standard collagenase perfusion) to determine insulin sensitivity via [3H]-2-deoxyglucose accumulation.

GLP-1 levels: attenuated in DIO and restored by treatment. Insulin levels: 49% higher in DIO and lowered by treatment. DIO suppressed pancreatic beta:alpha cell ratio and treatment partially corrected this. No effects on weight, IP fat or blood glucose levels. DIO animals: 47.7 ± 4.6% infarct of area at risk vs. control = 30.0 ± 3.7 and DIO treated = 29.8 ± 3.1; $p<0.05$, $n=6$. The ratio of phospho/total PKB/Akt and ERK42 was attenuated in DIO and improved after treatment. Cardiomyocytes did not show insulin sensitisation.

DPP4 inhibition in prediabetic animals (1) restored GLP-1 levels, (2) was cardioprotective, (3) improved pancreatic cell composition and (4) improved glucose homeostasis.

Changes in RAAS (renin angiotensin aldosterone system) biomarkers in stable chronic heart failure (HF) patients following short-term angiotensin receptor neprilysin inhibitor (ARNI) treatment

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Background: Treatment of HF patients with RAAS blockade (ACEi, ARB and aldosterone antagonists) decreases mortality and morbidity. Treatment with dual angiotensin II and neutral endopeptidase (neprilysin) inhibition may offer additional therapeutic benefit. LCZ696, an ARNI (angiotensin receptor neprilysin inhibitor) delivers concomitant angiotensin II receptor and neprilysin inhibition and was thus tested in patients with HF.

Objective: To assess the effects of short-term treatment with LCZ696 on RAAS and other biomarkers in patients with stable chronic HF.

Methods: Patients with stable chronic HF (NYHA II-III and LVEF <40%) entered an open-label, 2-dose phase study. After brief washout of their ACEi or ARB agent, the patients received LCZ696 100mg bid for 7 days and were subsequently up titrated to 200mg bid for 14 days while maintaining their background therapy. Plasma levels of aldosterone, active renin concentration (ARC), plasma renin activity (PRA), and endothelin-1 were determined at baseline, and on Day 7 and Day 21 at the end of each dose treatment period.

Results: No serious adverse events occurred and LCZ696 100mg and 200 mg BID were well tolerated. The serum biomarker results are presented as geometric means and 95% confidential intervals:

Summary and conclusion: Short-term treatment of HF patients with LCZ696 100mg and 200mg bid significantly increased PRA and PRC consistent with AT1 blockade, and, LCZ696 200mg bid significantly decreased plasma aldosterone and endothelin 1. These results indicate a significant impact on multiple components of the RAAS in NHHA II-III patients and support the development of LCZ696 in HF.

Serum markers	Baseline	7 day	21 day
Aldosterone (pg/mL)	237.2 (200.5 - 280.5)	220.0 (184.7 - 262.5)	189.7 (159.2 - 226.1)#
PRA (ng/mL/h)	0.69 (0.42 - 1.13)	2.7 (1.4 - 5.18)*	1.64 (0.71 - 3.8)#
ARC (pg/mL)	9.92 (8.15 - 12.08)	42.64 (25.66 - 70.85)*	34.11 (17.5 - 66.49)*
Endothelin-1 (pg/ml)	2.43 (2.06 - 2.86)	2.18 (1.87 - 2.53)	1.99 (1.75 - 2.26)*

*#p<0.05; *p<0.001 (Values compared to pre-dose baseline)*

Study of markers of inflammation as predictors and prognosticators of Acute Coronary Syndrome (ACS) in patients with acute chest pain

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Background: The role of inflammation in the pathogenesis of acute coronary syndrome (ACS) is well established. Little is known however, regarding the use of inflammatory markers as predictors of future short-term cardiovascular events in patients of acute coronary syndrome.
Objective: To assess whether inflammatory markers (hs-CRP, TLC and serum albumin) can correlate with the diagnosis of acute coronary syndrome (ACS) in patients with acute chest pain and to see whether these markers can be used to predict short-term cardiovascular events in patients of ACS.
Material and Methods: Patients presenting within 12 hours of the onset of central non-traumatic chest pain were enrolled if the inclusion criteria were fulfilled. All patients were investigated and the diagnosis of ACS was made as per JACC 2004 guidelines for ST –elevation MI, unstable angina and non-ST elevation MI as per ACC 2002 guidelines. Diagnosis of non-ischaemic chest pain was made if it did not meet any of the above criteria. All patients received routine institutional care and treatment as per diagnosis blinded to CRP, Albumin and Leukocyte count. The independent predictors of ACS and predictors of adverse events in 30 days was evaluated using multivariate analysis.
Results: 149 patients of = 18 years (88 male & 61 female) were included in the study. Final hospital diagnosis were non-ischaemic chest pain in 30 (20%) and ACS in 119 (80%) patients. Leukocyte count and hs-CRP levels were higher (11 576 ± 3 083, 14.04 ± 6.17) in patients with ACS compared to NICP (5596 ± 1370, 2.39 ± 1.55) with significant p=value (<0.001). High hs-CRP level (19.95 ± 6.46, 7.87 ± 2.14), TLC (15 630 ± 3 522, 10 278 ± 1 503) and low serum albumin (3.45 ± 0.31, 3.93 ± 0.39) were there in patients in whom adverse cardiovascular events occurred with significant p-value (<0.001). They had also significantly high neutrophil count (p<0.001) and low lymphocyte count (p=0.032).
Conclusion: Leukocyte count and hs-CRP level are the independent predictors of ACS in patients presenting to the ED with chest pain suggestive of ACS. High hs-CRP, TLC, neutrophil count and low serum Albumin, lymphocyte count are independent predictors of adverse short–term cardiovascular events.

Telomere dynamics in premature coronary artery disease

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Introduction: Atherosclerosis is an age-related disorder that is clinically silent until the manifestation of full-blown disease. Telomere length (TL) is considered a marker of biological ageing and may predict the susceptibility to, and onset of, age-related disorders such as coronary artery disease (CAD) and type 2 diabetes mellitus.
Aim: To establish the relationship, if any, between telomere length and CAD in patients with premature CAD and matched controls in a high-prevalence population.
Method: 100 symptomatic patients with angiographically proven CAD were compared to 100 age-matched controls. The anatomy and severity of coronary artery disease was profiled using the syntax score. Clinically overt atherosclerotic vascular disease was excluded in controls by standard symptom-based questionnaires, clinical examination, and exercise stress test to maximum heart rate. The presence of risk factors such as family history, smoking, obesity, metabolic syndrome, dyslipidaemia, hypertension, insulin resistance and diabetes were recorded. Markers of oxidative stress, inflammation and apoptosis assays were measured. Telomere length in circulating white blood cells was determined by quantitative PCR and defined as the T/S ratio. All chronic medications were documented.
Results: The mean age of subjects in both groups was 37.5 years. Preliminary analysis shows that there was no difference in the prevalence of current smokers or the blood pressure, cholesterol, insulin resistance and hsCRP levels between the groups. Cases had significantly higher BMIs and a higher prevalence of type 2 diabetes. 85% of cases and 3% of controls were receiving HMG CoA Reductase Inhibitors. Telomere length was significantly longer in cases versus controls (0.70 vs. 0.66, p=0.001).

Conclusion: Telomere length was significantly increased in this cohort of patients with premature CAD, possibly due to medication. HMG CoA Reductase Inhibitor therapy has been shown to increase the production of a telomere capping protein called TRF2 (telomere repeat binding protein 2). Shorter telomere length in control subjects suggests that this population is inherently at high risk of coronary artery disease.

Evaluation of the AMPK alpha 1 gene (PRKAA1) as a possible modifier of cardiac hypertrophy in hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is an autosomal dominantly inherited cardiac muscle disorder characterised by left ventricular hypertrophy (LVH) and increased risk of sudden cardiac death. LVH is the strongest predictor of morbidity and mortality after age and is a feature of complex disorders such as hypertension and diabetes. Understanding the molecular mechanisms involved in the development of LVH is therefore very important, however, investigating these mechanisms in such complex disorders is challenging. Since LVH is a primary feature of HCM, this disease is considered a good model to investigate these elusive molecular mechanisms.

Over 1 000 HCM-causing mutations in 14 genes have been described thus far. One feature that all these HCM-causing mutations share is inefficiency in ATP utilisation. Therefore, genes encoding proteins involved in energy homeostasis could be considered plausible HCM-modifying genes.

The present study investigated 3 single nucleotide polymorphisms (SNPs) in PRKAA1, which encodes the alpha 1 subunit of AMPK. AMPK is a heterotrimeric protein that functions to protect cells from critical ATP depletion by activating glycolysis and fatty acid uptake during extreme metabolic demand or hypoxic stress. A total of 227 phenotypically well-characterised individuals belonging to 22 HCM families with known HCM-causing mutations were genotyped using validated TaqmanTM genotyping assays.

Following adjustments for known hypertrophy confounders, 1 SNP (rs466108) was found to be associated with an increase in maximum left ventricular wall thickness (p=0.041). The data presented here provides evidence for the involvement of PRKAA1 in the development of LVH in patients with HCM.

Percutaneous pericardioscopy in tuberculous pericarditis: improving the diagnostic yield

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Purpose: 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 (AFB) or mycobacterium tuberculosis culture on pericardial fluid alone. We set out to evaluate the potential advantage of percutaneous pericardioscopic biopsy of the pericardium in tuberculous (TB) pericarditis.

Methods: All patients presenting to our Division of Cardiology 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, AFB's and TB culture. Pericardial biopsy specimens were evaluated for AFB's, TB culture and histologically for granulomas.

Results: Thirty-one patients agreed to participate. Pericardial biopsy could be obtained in 27 patients all of which were uncomplicated. Mean age was 33. Thirteen patients (48.1%) had associated HIV disease and 16 (59.2%) presented in clinical tamponade. Fifteen patients (55.5%)

were found to have definite pericardial TB. An alternative diagnosis was made in 4 of the remaining 12 patients and the remainder were classified as idiopathic. A definite diagnosis of pericardial tuberculosis was made in all 15 patients by means of pericardial biopsy whilst fluid evaluation alone missed the diagnosis in 3 (20%) patients. Nine (60%) of the 15 patients with proven TB were AFB positive on pericardial biopsy and 2 (13.3%) had histological evidence of granulomas. All patients with pericardial TB were fluid AFB negative and only 12 fluid samples subsequently cultured TB within 31 days (mean time 22.6 days).

Conclusion: In contrast to the assessment of pericardial fluid where a definite diagnosis of TB is dependent on culture, biopsy enables a more reliable and rapid diagnosis.

Ischaemic post conditioning confers protection via TNFalpha: Identifying the cellular origin of TNFalpha

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Purpose: Ischaemic post conditioning (IPostC) is a powerful tool used to protect against lethal reperfusion injuries. We have recently demonstrated that IPostC-induced cardio protection requires the activation of tumour necrosis factor alpha (TNFa) at the onset of reperfusion. In stress conditions, TNFa can be activated from multiple cell sources, including cardiomyocytes and inflammatory cells. Using macrophage/neutrophil TNFa deficient mice and creating cardiomyocyte-specific TNF knock out mice using the Cre-Lox system, we proposed to investigate the cellular origin of TNFa production required for the cardio protection induced by IPostC.

Methods: Wild type (WT), TNFa deficient (TNFa-/-), macrophage/neutrophil TNFa deficient (mnTNFa-/-) or cardiomyocyte-specific TNF knock out (cmTNF-/-) mouse hearts were subjected to an ischaemic-reperfusion insult using a Langendorff perfusion system (n=6 per group). IPostC was initiated with 6 alternating 10-second cycles of ischaemia and reperfusion at the onset of reperfusion. Infarct size was evaluated by triphenyltetrazolium chloride staining and computer planimetry.

Results: IPostC reduced infarct size from 49 ± 3% to 16 ± 3%, in WT hearts ($p<0.001$ versus control) and from 50 ± 1% to 23 ± 1% in mnTNF-/- hearts, ($p<0.001$ versus control). In contrast, IPostC failed to protect TNF-/- hearts (infarct size of 34 ± 3% in IPostC versus 38 ± 4% for the control; p=not significant). Similarly, hearts from the cardiomyocyte-specific TNF-/- mice could not be protected with IPostC (56 ± 2%) versus their wild type littermate controls (28 ± 3%)

Conclusion: Our novel findings strongly suggest that the production of TNFa required for cardio protection with IPostC in the isolated heart model is produced mainly by the cardiomyocytes and is independent of the resident inflammatory cells, such as macrophages and neutrophils.

What triggers ischaemic or pharmacological preconditioning? Evidence for a role for ERKp44/p42 and PKB/Akt

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Ischaemic preconditioning (IPC) refers to the phenomenon whereby exposure of the heart to 1 or more short episodes of ischaemia/reperfusion (IR) elicits protection against a subsequent long period of sustained ischaemia. Similar cardio protection can be induced by transient exposure of the heart to certain pharmacological agents (e.g. isoproterenol, diazoxide), the so-called pharmacological preconditioning (PPC). Although activation of the reperfusion injury salvage kinases (RISK) during early reperfusion has been causally linked to cardio protection, the exact mechanisms involved are still uncertain. It has been hypothesised that events during an IPC or PPC protocol are equally important and should play a pivotal role in triggering protection. Characterisation of events during an IPC or PPC protocol is therefore essential to help unravel the exact mechanisms involved in cardio protection.

Methods: Isolated perfused rat hearts were subjected to IPC (4x5 min I/R) or PPC (1x5 min b1-and/or b2 -adrenergic receptor stimulation), followed by 35 min coronary artery ligation and 30 min reperfusion. Infarct size (determined by tetrazolium staining) and functional recovery

during reperfusion were used as endpoints. Hearts were also freeze-clamped at different times during the preconditioning protocols. Expression and activation of ERKp44/p42, PKB/Akt, and GSK3b were determined using Western blot and appropriate antibodies. Significance of ERKp44/p42 and PKB/Akt activation was determined using the blockers PD98,085, and Wortmannin administered during the preconditioning protocols or during reperfusion.

Results: Significant activation of both ERKp44/p42 and PKB/Akt occurred during both preconditioning protocols, lasting until the onset of sustained ischaemia. For example, PPC with isoproterenol (10-6 M, 1x5 min) caused 2.5 and 3.5 fold increases in ERKp44/p42 and PKB/Akt activation respectively within 5 minutes of administration of the drug. This activation was maintained throughout the 5 minutes washout period until the onset of sustained ischaemia. These kinases were also activated during early reperfusion, associated with a reduction in infarct size and improved functional recovery. Administration of the blockers abolished cardio protection.

Conclusion: Activation of ERKp44/p42 or PKB/Akt during an IPC or PPC protocol before the onset of sustained ischaemia is essential for development of protection during sustained ischaemia.

Initial experience with the Biosense Webster Thermocool SF catheter in 3D mapping-guided robotically assisted RF ablation of atrial fibrillation

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Introduction: Radio Frequency (RF) ablation of Atrial Fibrillation (AF) is challenging. The procedure is time consuming and despite 3D mapping still involves significant radiation exposure to patient and operator. Open irrigated catheters are almost universally employed for AF ablation and patients are often at increased risk of fluid overload. Advances in ablation catheter design have the potential to ameliorate these risks. We compared Biosense Webster's Navistar Thermocool RF Ablation catheter with their new Thermocool SF catheter.

Methods: Data was collected prospectively from successive AF ablation procedures performed with the Navistar Thermocool (N=19) or Thermocool SF catheter (N=19) Patients had comparable clinical backgrounds. The majority had Persistent AF. All patients had Pulmonary Vein Isolation (PVI) with wide encirclement ablation. Additional ablation was performed in some patients as determined by clinical need Fluoroscopy was used during the initial setup and occasionally thereafter to reposition catheters. All procedures were performed with 3D Mapping (Carto 3 or Ensite Velocity) and robotic assistance (Hansen Medical). Four criteria were compared: procedure time, fluoroscopy time, RF ablation time and fluid volume infused for catheter cooling.

Results: PVI was achieved in all cases. The Thermocool SF was superior in all 4 criteria. Procedure times were reduced from 261.47 ± 111.31 min to 165.79 ± 72.06 min (p=0.003). X-ray time was reduced from 33.51 ± 19.83 min to 25.73 ± 14.55 (p=0.17). RF time decreased from 81.35 ± 40.38 min to 42.61 ± 24.06 min (p=0.0097). Total fluid infusion via the Coolflow pump decreased considerably from 1 594.51 ± 791.40 ml to 655.66 ± 367.84 ml (p=0.00004). P-values were calculated using Fishers Test and Levene's Test for Homogeneity of Variances.

Conclusion: Our findings suggest that the design changes in the new Thermocool SF catheter have resulted in significantly increased efficiency of ablation. Patients ablated with the Thermocool SF catheter benefited from a 37% reduction in procedure time, a 24% reduction in x-ray exposure, a 48% reduction in RF time and a 59% reduction in fluid infused. This catheter may be particularly useful in patients with impaired left ventricular function or predisposition to fluid overload.

Pericardial Constriction: Haemodynamics in a nutshell

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We present images of a 41-year-old male with constrictive pericarditis who underwent cardiac catheterisation prior to presentation to cardiothoracic surgery.

The 2 central pathophysiological features that differentiate CP from other causes of restrictive ventricular filling are dissociation of intrathoracic and intracardiac pressures and enhanced ventricular interaction. In the heart with a normal pericardium, inspiration causes a decrease in intrathoracic pressure, which is matched by a similar pressure drop in the left ventricular (LV) cavity, thereby maintaining flow into this cavity during the respiratory cycle. In the case of CP where a thickened, non-distendable peel encases the heart, there is a lack of transmission of respiratory intrathoracic pressure change to the cardiac chambers. This means that during inspiration, the drop in intrathoracic pressure is not transmitted to the LV cavity thereby degrading the flow gradient into this chamber. This dissociation of intrathoracic and intracardiac pressures seen during respiration affects the rate of filling of the LV relative to the right ventricle (RV). The total cardiac volume remains unchanged within the rigid pericardium and because of the varying LV filling rate during the respiratory cycle the interventricular septum shifts into the LV in inspiration and into the RV during expiration, thereby determining the difference in end diastolic volumes in the 2 ventricles. Demonstration of this enhanced ventricular interaction within the fixed volume of the rigid pericardium is the most useful information obtainable by cardiac catheterisation in the diagnosis of CP with a reported sensitivity of 97% and a predictive accuracy of 100%.
We present data in the form of haemodynamic tracings demonstrating dissociation of intrathoracic and intracardiac pressures by analysing the left ventricular and pulmonary artery wedge pressures obtained during respiration. Enhanced ventricular interaction is demonstrated by simultaneous LV and RV pressure acquisition reflecting discordance of the left and right ventricular pressures.

Angiographic prevalence of epicardial coronary artery disease in black hypertensive patients with systolic left ventricular dysfunction

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Introduction: Left ventricular hypertrophy (LVH) is an independent risk factor for heart failure in hypertension. Epidemiological evidence has shown that hypertensive patients with LVH are at increased risk for coronary heart disease. These data have been derived mainly from the Caucasian population. To date, no angiographic data on the prevalence of epicardial coronary artery disease (CAD) in black hypertensive patients with left ventricular (LV) dysfunction have been published.
Methods: 44 consecutive hypertensive patients (office dinamap blood pressure >140/90mmHg) with a (left ventricular ejection fraction) LVEF <45% on treatment had coronary angiography between March 2010 and March 2011. The inclusion criteria were African descent, sinus rhythm, age >30, no diabetes, normal renal function, no comorbid illnesses, and no history of ischaemic heart disease. Transthoracic echocardiography was performed according to American Society of Echocardiography guidelines to determine left ventricular structure and function. Clinical and echocardiographic data were compared between patients with and without coronary artery disease.
Results: Mean LVEF was 34.2% and all patients had left ventricular hypertrophy. Mean age was 58 years with equal M:F ratio(1:1). Mean duration of heart failure was 4.1 years. Six of the forty four patients (13.6%) had significant epicardial coronary artery disease on angiography (5 with single vessel and 1 with double vessel disease). There were no significant differences found between any clinical, biochemical (cholesterol and Pro-BNP) or echocardiographic characteristics in patients with coronary artery disease and normal coronary arteries.
Conclusion: Coronary artery disease in black hypertensive patients with systolic left ventricular dysfunction is not infrequent with a prevalence of 13.6%. The prevalence of coronary artery disease is significantly lower compared to Caucasians. There were no differences in the clinical characteristics and cardiovascular risk profile in those patients with or without coronary artery disease.

Left ventricular twist mechanics in normal black subjects

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Introduction: Speckle tracking has emerged as a sensitive quantitative technique in assessing left ventricular (LV) function. However, no normative data for speckle tracking echocardiography (STE) are available in the black population. LV twist describes the instantaneous

circumferential motion of the apex with respect to the base of the heart and has an important role in LV function. This study evaluates LV twist dynamics by determining LV rotation parameters in different age groups, using speckle-tracking echocardiography.

Methods: Subjects were recruited from our hospital and were staff or patients. The study population consisted of 76 healthy volunteers without hypertension, diabetes, or cardiovascular disease, with a normal 12-lead electrocardiogram, left atrial, LV dimensions and LV function by transthoracic echocardiography. To optimise speckle tracking, two-dimensional gray-scale harmonic images were obtained at a frame rate of 60-80 frames/s. Parasternal short-axis images at LV basal and apical level were obtained with 3 consecutive end-expiratory cardiac cycles. Data was transferred to a QLAB workstation (QLAB Advanced Quantification Software version 8.0, Philips) for off-line analysis. Clockwise rotation was presented as a negative value and counter clockwise rotation as a positive value when viewed from the apex. Apical (APICAL ROT) and basal (BASAL ROT) LV peak systolic rotation during ejection and instantaneous LV peak systolic twist (defined as the maximal value of instantaneous apical LV systolic rotation-basal LV systolic rotation) were measured.

Results: Of the 76 subjects, 12 (15.8%) were excluded because image quality was insufficient for STE analysis. Subjects were divided into 3 age groups: 18-30 yrs (n, 28); 31-40 yrs (n, 23); >40 yrs (n, 13). The mean age was 32.7 ± 9 with 36 females and 28 males in the 64 subjects. The mean ejection fraction (n, 64) was 59.4 % ± 5.6 and mean left ventricular mass index (LVMI) was 70.8g/m^2 ± 22.5. There were no statistically significant differences in the apical and basal rotation parameters and in the net twist parameter amongst the 3 age groups. Mean apical rotation was 4.58 ± 2.56 (mean ± SD), basal rotation was -3.23 ± 1.6 giving a net twist of 7.82 ± 3 degrees.

Conclusion: These data establish the normal values for twist in a normal black population and are similar to previously published studies in Caucasians.

Patterns of left ventricular remodelling and ejection performance in black South African hypertensive patients with heart failure

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Introduction: Hypertension is the commonest cardiovascular disease in black South Africans. The response of the left ventricle to pressure overload is unique in black patients, with a high prevalence of concentric hypertrophy as compared to Caucasians. We sought to evaluate the geometric patterns of remodelling in black hypertensive patients with heart failure.

Methods: Hypertensive patients with an EF<45% on treatment were selected from cardiac clinic from March 2010 to March 2011. Inclusion criteria: African descent, sinus rhythm, age >30, no other comorbid illnesses, and normal epicardial coronary arteries on angiography. Concentric LVH defined as RWT> 0.42 and eccentric LVH as RWT <0.42 with LVMI >95 in females and >115 in males.

Results: Concentric hypertrophy was seen more frequently than eccentric (62% vs. 38%). Mean EF was simliar in the 2 groups (33% CH vs. 36% EH). However, 78.9% of the patients in the concentric hypertrophy group had EF <40% vs. 58.3% in the eccentric group. There were no statistically significant differences in blood pressure, body mass index (BMI), age, and Pro-BNP levels between the concentric and eccentric groups.

Conclusion: We have shown a high proportion of concentric hypertrophy in hypertensive patients with low EF. This differs significantly from the response reported in other studies and may provide insights into the mechanisms linking altered geometric patterns and progression to heart failure in black patients.

Tetralogy of Fallot and major arterial thrombosis – an unusual presentation of a common complication

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Background: Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease (CCHD). The prevalence of TOF ranges from 0.26 to 0.48 per 1 000 live births. Polycythaemia is a common secondary finding in TOF, often resulting in a hypercoagulable state. This

may cause venous systemic circulation thrombosis or rarely arterial thrombosis. An unusual presentation of this complication will be presented.
Case presentation: A 13-year-old boy presented with Tetralogy of Fallot, profound cyanosis, marked polycythaemia, left ventricular dysfunction and poor lower limb pulses. As a young child, he had right and then left modified Blalock-Tausig shunts (MBTS) done but was subsequently lost to follow-up. He presented recently because he was exercise intolerance. A repeat echocardiogram indeed confirmed Tetralogy of Fallot but both shunts were not visualised. A diagnostic cardiac catheterisation was performed which showed a completely blocked right MBTS, a patent left MBTS and an unusual presentation of extensive thrombosis involving the descending abdominal aorta and both left and right iliac arteries. The right iliac artery was partially occluded, whereas the left was completely blocked. Computerised tomography (CT) angiogram showed an occluded infrarenal aorta, plus the iliac arteries up to the origins of the common femoral arteries bilaterally. The right renal artery and superior mesenteric artery were involved as well. The thrombi and possible emboli were treated medically with Streptokinase and Heparin infusions. Three partial exchange transfusions were performed pre-operatively. The patient underwent full repair of TOF. Arterial thrombosis was managed conservatively.
Conclusion: CCHDs increase the risk for development of childhood thrombosis. Risk factors may be due to protracted cyanosis itself; inherited coagulation defects; prolonged surgery; angiography; indwelling central venous catheters; or systemic infections. Our patient had both congenital and acquired risk factors. To our knowledge, this is the first case reported extensively involving a major central systemic arterial system.

Left ventricular function impairment in young adults with mitral valve prolapse

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Introduction: In some inherited connective tissue diseases with involving of the cardiovascular system, e.g. Marfan syndrome, has been reported early impairment of LV function, which have been described as Marfan-related cardiomyopathy. Our aim was to evaluate the LV function in young adults with mitral valve prolapse (MVP) without significant mitral regurgitation (MR) using two-dimensional strain imaging.
Methods: We studied 78 asymptomatic young subjects (mean age 19.7 ± 1.6, 72% male) with MVP in comparison with 80 sex- and age-matched healthy subjects. Longitudinal strain and strain rate (SR) were determined from 3 standard apical views, using spackle tracking (Vivid 7 Dimension, EchoPAC'08) with grey-scale frame rate 50-55/sec.
Results: During the k-means clustering we have identified 2 clusters of subjects with MVP: first (17 subjects, 28% of the MVP group) and second cluster (61 subjects, 72%). In 1 cluster observed a significant reduction in global longitudinal systolic strain compared with the control group (-15.5 ± 2.9% vs. -19.6 ± 3.4%; p=0.00001) and the second cluster (15.5 ± 2.9% vs. -20.6 ± 3.8%; p=0.00001). Diastolic global SR was also decreased compared with the control group (1.3 ± 0.25/s vs. 1.62 ± 0.25/s; p=0.0001) and the second cluster (1.3 ± 0.25/s vs. 1.62 ± 0.25/s; p=0.00001). Global strain in the second cluster did not differ significantly from the control group (p=0.1), but there are significant decreases of local longitudinal systolic strain (-17.1 ± 3.2% vs. -20.7 ± 3.1%; p=0.001) and diastolic SR (1.38 ± 0.25/s vs. 1.55 ± 0.22/s; p=0.00001) in interventricular septum.
Conclusion: These changes of deformation may be the first signs of deterioration of the LV function and existing of cardiomyopathy in young adults with MVP.

The Transoesophageal Echocardiography Registry of Chris Hani Baragwanath Academic Hospital (TORCH)

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Background: The TORCH registry was initiated in February 2010 and has until June 2011 included 388 two-dimensional and three-dimensional TEE's performed in its database.

Aim: To present the safety and efficacy of TEE at a single centre in a large number of patients examined in an inpatient and outpatient setting.
Methods: TEE's were performed consecutively as clinically indicated by 2 consultant cardiologists with the assistance of cardiology fellows and senior technologists as well as an anaesthesiologist when necessary. All TEE's were initiated under conscious sedation with standard monitoring using the X7-2 Philips TEE matrix array probe coupled to a Philips iE-33 system and analysed offline with Q-Lab software (Phillips Technologies). All patients were kept starved for a minimum of 4 hours prior to the procedure.
Findings: 377 patients tolerated the procedure with only topical anaesthesia, Midazolam, Propofol ±Fentanyl as sedation without any complications. Four patients had an oesophageal diverticulum and the probe could not be passed initially, requiring awake intubation. Two patients had respiratory depression requiring short-term ventilation. Five patients had failed attempts at conscious sedation requiring full general anaesthesia. No incidences of perforation, aspiration, bleeding or oro-pharyngeal and oesophageal trauma occurred.
3D TEE was superior to 2D TEE for the evaluation of atrial septal defects, complex congenital heart disease, submitral aneurysms, sinus of valsalva aneurysms, prosthetic valve complications as well as assessment of mechanism of mitral regurgitation and suitability for repair.
3D TEE did not add additional value in evaluating patients for suspected infective endocarditis or in detecting intracardiac shunts where a bubble test confirmed the presence of the shunt on 2D examination but was more useful in evaluating the location and extent of the defect.
Conclusion: The TORCH Registry is the first database of its kind in South Africa and provides unique information to highlight the safety and utility of the technique when performed in a busy cardiology environment.

Coronary artery disease in pregnancy

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Objectives: To show 5 patients we have been managing at our centre. Each of them posed individual challenges not only to the cardiologists but also to the obstetricians.
Introduction: Until recently coronary artery disease in pregnancy has been described as a rare occurrence. However pregnancy because of its hypercoagulable state is associated with increased risk. Older age at conception and enabling many women to conceive seem to be contributing to this prevalence. In South Africa and Africa at large there have been very few reports of AMI/ACS in pregnancy.
Methods: Patients were selected retrospectively from our database. The patients had to fulfil the criteria: based on the standard definition for coronary artery diseases.
Results: The age range was 34-42 years (mean 38 years). Risk factors profiles: Three hypertensive (60%); 2 diabetics(20%); 1 ex-smoker (20%); 1 positive family history (20%); 1 Dyslipidaemia (20%); 4 with high BMI (80%) and 1 Lupus (20%). One patient had NSTEMI (20%); 4 patients STEMI (80%) – [Distributions = 3 (75%) anterior and 1 was inferior (25%)]. None received thrombolytics and 1 had percutaneous coronary intervention (20%).
Three patients had diagnostic coronary angiogram during pregnancy (60%). Four patients (80%) had caesarean section. No perioperative complications. One had a normal vaginal delivery (20%).
Discussion: Prevalence of coronary artery disease (CAD) in female patients is increasing due to changing lifestyle patterns. Acute coronary syndromes are rare during pregnancy; but often have devastating consequences. Although thought to be rare ; recently during pregnancy CAD is estimated to occur 3 to 4 times at this age group (same age group in our data). Associated with increased maternal and neonatal mortality and morbidity.
Conclusion: Myocardial ischaemia during pregnancy can mimic typical symptoms related to pregnancy itself. This contributes to the increased mortality rate among pregnant women with acute coronary syndrome. Each of the 5 patients posed individual challenges to the managing cardiologists and obstetricians. Diagnostic and therapeutic approaches are influenced by maternal and by foetal safety.

Retrospective study in patients presenting with coronary artery disease complicated by conduction defects requiring pacing; to define the benefits of RV pacing and its long-term prognostic implications

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Introduction: Ischaemic heart disease remains a major challenge for the clinician worldwide and is becoming a major problem in poor countries. Although the reported incidence of complications varies between 0.1% - 2.5 % these remain a significant cause of morbidity and mortality in these patients.

In the setting of complicated or multivesel disease coronary bypass graft is traditionally regarded as the standard of care, because of its well-documented and durable survival advantage. However, percutaneous coronary intervention is frequently favoured as an initial treatment strategy by some interventional cardiologists.

The development of conduction defect in the patients presenting with acute myocardial infarction and in chronic coronary artery disease is a complex condition that requires careful evaluation and investigation for optimal management. Since 2003, changes in health service facilities in the Durban area have resulted in the great majority of patients with complicated coronary artery disease being referred to our centre. This has provided an opportunity to review the management and outcome of conduction defects in this subset of patients.

Methods: This is a retrospective analysis over a seven-year period at our tertiary hospital. All patients' data including demographic details, data on clinical presentation and management, procedures performed at admission and during the course of the acute illness and data on outcomes were recorded onto a clinical software package in a structured format. Patients with conduction abnormalities in the setting of an ACS/IHD requiring RV pacing were retrospectively evaluated. Patient's notes and ECGs were accessed and evaluated. No age restriction/ gender preferences.

Results: At least 150 patients were identified . At least 25% of these patients had chronic A-V block requiring pacing. At least 30% of patients had acute MI with conduction defects requiring pacing. At least 75% of patients who presented with acute infarctions showed occlusion/ narrowing of the dominant right coronary artery. Less than 10% had occlusion of the dominant left circumflex. Less than 3% had occlusion of the anterior descending artery with a large anteroseptal infarct.

Discussion: Some studies have shown the beneficial effects of revascularisation in relieving frequent symptomatic episodes of A-V block in these patients. However others studies and reports were unable to show any benefit for CABG to reverse pre-operative complete heart block. Thus how frequent revascularisation may be effective in relieving conductive symptoms of patients and even abolish the need for permanent pacemaker implantation; must be addressed in other large studies.

Conclusion: In most cases coronary artery disease is associated with chronic heart block and the prevalence of CAD makes the prognosis of the conduction disorder worse. The prevalence of CAD in the chronic conduction disorders has been reported to be 30 - 70% depending on the patients' characteristics and the way to detect CAD. However some studies suggest that significant coronary artery disease is not present in most cases of chronic heart block and that pathological changes are often confined to the conduction system. Acute heart block is uncommon but a serious complication of myocardial infarction; though survivors usually return to sinus rhythm.

Beta Blocker tolerability in a dedicated heart failure clinic

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Introduction: Resting tachycardia in patients with chronic heart failure (CHF) is a risk factor for adverse outcomes. Beta-blockers (BB) are a cornerstone of CHF therapy. The recently published "SHIFT study" concluded that ivabradine, reduced recurrent hospitalisation in CHF patients. However, the study recruited patients on background BB doses lower than those routinely recommended in CHF therapeutic guidelines. This may have exaggerated the effects of ivabradine in the trial. The authors suggested that the lower BB entry dose was judged to be the maximally tolerated BB dose prior to randomisation into the trial.

Aims: To ascertain the rate and dose of BB in a heart failure population of a tertiary public hospital managed in a dedicated heart failure clinic.

Methods: We performed a retrospective analysis of the rate and dose of BB in the last 100 patients attending our CHF clinic. Target dose was considered to be Carvedilol 25mg bd and Atenolol 50 mg bd.

Results: Four of the 100 patients were excluded from analysis (2 were transplant recipients and 2 had inadequate data). Of the remaining 96 patients, 92 (96%) were on BB (83 on carvedilol and 9 on atenolol). Four could not tolerate any dose of BB. 52% (48 patients) were on target doses of BB compared with only 26% in SHIFT. 82% were on more than 50% of target dose compared with only 56% in SHIFT. Of the 44 patients not at target dose, 25 (57%) were still in the "up-titration'" phase of heart failure therapy with only 2 patients intolerant of higher doses of BB. Of the remaining patients not at target, 4 had normalised LV function, 4 were defaulters, 1 had bronchospasm, 1 had symptomatic bradycardia and in 7 there was no clear reason for not being at target.

Conclusion: These results demonstrate that in the South African public health scenario, in a dedicated CHF outpatient clinic, beta-blockers can be used more often and tolerated at much higher doses than those reported on entry into the SHIFT trial. Our data suggest that patients recruited in SHIFT were on inadequate BB doses, which in turn may have exaggerated the heart rate lowering-effects of ivabradine.

Electrocardiographic findings in patients with isolated left ventricular non-compaction

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Background: Isolated left ventricular non-compaction (ILVNC) is a genetic cardiomyopathy characterised by varying degrees of heart failure, cardio embolism and arrhythmia. In Western subjects, electrocardiographic findings have varied from nonspecific abnormalities to life-threatening atrial and ventricular tachyarrythmias. In Africa, electrocardiographic findings of subjects with ILVNC have not been documented.

Methods: A retrospective analysis of the electrocardiographic findings of 75 subjects all of African ancestry diagnosed with ILVNC by the Jenni criteria on echocardiography was conducted. All subjects were referred to a tertiary academic cardiomyopathy clinic and enrolled after satisfying the inclusion and exclusion criteria.

Results: The mean age was 43 and 53% of subjects were female. Heart failure occurred in 74 subjects (98.6%). Four patients (5.3%) had a normal ECG. Sinus rhythm was noted in 71 subjects (94.7%). Atrial fibrillation, focal atrial tachycardia, paced rhythm (biventricular pacemaker) and sinus arrest with a junctional escape rhythm, were each noted in the remaining 4 patients.

Morphologic abnormalities of the QRS complex included: Early repolarisation abnormality in 18 patients (24%); left ventricular hypertrophy (Cornell voltage criteria) in 26 patients (34%); left bundle branch block in 10.7% (8 patients); and right bundle branch block in 4% (3 patients). Electrocardiographic features of pre-excitation or the Wolff Parkinson syndrome was not detected.

Other abnormalities included a prolonged QTc interval, which was detected in 33 patients (44%). No underlying cause could be attributed to this finding in all but 1 subject who was on amiodarone. Non-specific ST- and T-waves changes occurred in 35 (46%) and 53 (70.6%), respectively.

Conclusions: Patients with ILVNC rarely have a normal ECG. The range of ECG abnormalities is wide. The clinical implications of the detected ECG abnormalities need to be determined.

Total anomalous pulmonary venous connection - case report of an unusual drainage pattern

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Introduction: Anomalies of the pulmonary veins are uncommon and vary widely in their anatomic spectrum, clinical presentation, course, and outcome. In total anomalous pulmonary venous connection (TAPVC) the pulmonary veins connect directly to 1 of the systemic veins or drain into the right atrium. TAPVC is categorised as supracardiac, cardiac, infracardiac or mixed forms.

Case presentation: We present a case of an infant with supracardiac TAPVC with an unusual drainage pattern. A 6-week-old male infant

presented with cyanosis and jaundice. The clinical examination did not reveal cardiomegaly or congestive cardiac failure or any abnormal auscultatory findings. The jaundice was an unconjugated hyperbilirubinaemia. He was assessed to have breast milk jaundice.

Detailed cardiac ultrasound showed: a dilated right atrium and right ventricle ; a small left atrium and left ventricle; mild tricuspid regurgitation with a gradient of 42-58mmHg; dilated pulmonary arteries; a 5mm ASD with right to left shunting and in particular an enlarged superior vena cava measuring 8mm. However, the pulmonary venous anatomy was not clearly delineated; the drainage pattern of all 4 pulmonary veins could not be visualised adequately.

Cardiac catheterisation and angiography showed that the 2 pulmonary veins from the left lung converged into a common channel, which then ascended and were joined by the right lower pulmonary vein. Venous return from the right upper pulmonary vein could not be visualised clearly. In addition a mass of tortuous veins were seen in the base of the neck.

A computed tomographic angiogram was performed which further delineated the pulmonary venous drainage. The CTA confirmed the above findings with respect to the left pulmonary veins and the right lower pulmonary vein. The right superior pulmonary vein appeared to enter the confluence. The common pulmonary vein ascended further into the neck, where there was an associated network of tortuous venous channels bilaterally. The major common channel finally drained high into the right internal jugular vein. There were probable accessory pulmonary venous connections to the internal jugular vein on the left as well, which could not be readily traced. Unfortunately the child died suddenly before surgery could be performed.

Conclusion: There have been case reports of unusual supracardiac TAPVC but none with a final drainage point into the internal jugular. In TAPVC, delineating the individual pulmonary veins and the exact drainage of the pulmonary venous confluence is important to decrease surgical mortality. Multiple imaging modalities are sometimes required to make an accurate assessment of a complex pulmonary venous drainage system.

The identification of a novel TNNI3 gene mutation in South African patients with hypertrophic cardiomyopathy

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Introduction: Hypertrophic cardiomyopathy (HCM) is an autosomal dominant cardiac muscle disease that affects approximately 0.2% of individuals between the ages of 25 and 35 years. The primary clinical features are left ventricular hypertrophy and increased risk of sudden cardiac death. Over 1 000 HCM-causing mutations have been identified, many of them in genes encoding sarcomeric proteins. One such gene encodes cardiac troponin I (cTNI), a subunit of the troponin complex that serves as a calcium-sensitive switch involved in the regulation of striated muscle contraction.

Methods: The present study reports the mutation screening of the cTNI gene (TNNI3) for HCM-causing mutations using high-resolution melt (HRM) analysis. The study cohort consisted of 113 South African HCM probands, with and without known founder HCM mutations and 100 ethnically matched control individuals.

Results: Fifteen genetic sequence variants were identified, of which 2 were novel (p.Leu144, p.Leu144His). Four previously described HCM-causing mutations were also observed. Three family members with similar clinical symptoms were identified with the novel Leu144His mutation, which were absent in controls individuals. Furthermore, conservation of the Leucine amino acid residue 144 was confirmed by an alignment between cTNI isoforms and across species. A previous study identified the Leu144Gln mutation in a patient presenting with restrictive cardiomyopathy (RCM), with distinct clinical features of HCM. In our study cohort we observed the Leu144His mutation in patients with clinical similar phenotype to the patients identified with the Leu144Gln mutation.

Conclusion: The results of the present investigation demonstrate the usefulness of HRM analysis for identifying disease-causing mutations. Clinically the identification of the novel disease-causing Leu144His mutation allows for screening of families with similar clinical symptoms and asymptomatic family members.

Pulmonary arterial hypertension in patients with idiopathic dilated cardiomyopathy

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Introduction: Idiopathic dilated cardiomyopathy (IDCMO) is a important cause of heart failure in Africa. Pulmonary hypertension (HPT) is a recognised complication that occurs in patients with IDCMO and contributes to an adverse outcome. We sought to identify the prevalence of PHT in subjects with IDCMO, as well as the echocardiographic predictors of PHT.

Methods: A total of 66 subjects with IDCMO were evaluated using echocardiography after satisfying the inclusion and exclusion criteria of this study. All studies were performed by 2 experienced sonographers and interpreted offline by a single cardiologist in accordance with the America Society of Echocardiography chamber quantification and right heart guidelines. PHT was defined as a peak systolic pulmonary artery pressure (PASP) of greater than 35mmHg.

Results: The mean age of all patients was 48.5 ± 12.8, and 59.1% patients were male. Mean left ventricular ejection fraction (LVEF) was 25.3 ± 8.8%, and mean left atrial volume index (LA vol) was 44.5 ± 19.8ml/m^2. Mitral regurgitation (MR) occurred in 56/66 (84.8%) of patients with moderate or severe MR detected in 60.6% of all cases of IDCMO.

PAH was documented in 47 patients (71.2%, 95% CI 59 - 83%). Tricuspid regurgitation was found in 56 patients (84.9%). Right ventricular dilatation was present in 65 patients (98.5%). S' was measured in all patients from the lateral tricuspid annulus using pulse wave TDI, with a mean of 9.5 ± 2.7cm/s. Abnormal right ventricular function was documented in 48/66 (72.7%) of patients.

Age, MR, LA vol and LVEF were included into a multivariate logistic regression model to predict PHT. Only MR presence was independently associated with PHT (adjusted odds ratio =6.02, 95% CI: 1.15- 31.47; p-value= 0.03)

Conclusion: The prevalence of PAH in IDCMO patients was 712%. The major factor predisposing to the development PHT is MR.

Relationship between body mass index and arterial stiffness in HIV positive participants and HIV negative participants

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Pulse wave velocity (PWV) is considered as the "gold-standard" measurement of arterial stiffness. It has been demonstrated that individuals with a high body mass index (BMI) are likely to have increased arterial stiffness. Arterial stiffness is associated with increased risks of cardio-vascular events. The aim of this study was to understand the impact of sex, aging, and obesity on arterial stiffness in participants infected with the Human Immunodeficiency Virus (HIV) and those who are negative.

Thirteen HIV positive participants were studied and 15 HIV negative were used as controls. This was a pilot study. Participants were randomly recruited from Walter Sisulu University, Infections Disease Clinic (IDC), and Gateway Clinics of Mthatha. PWV was measured using the Sphygmcor device. BMI, body fat percentage, muscle percentage, visceral fat, resting metabolism and weight of the participants was measured by the Omron BF500 (HBF-500-E) and these were analysed for any association with arterial stiffness. Using the t-test, a statistical significance between age and HIV infection ($P<0.0001$) was established. There was 92% of HIV positive participants in older people (>30 years) and 7.7% HIV negative participants in younger people (<30 years).

The results showed that BMI in HIV negative participants was at a normal range of 25 - 26 while HIV positive participants had a lower BMI. HIV positive participants had a higher PWV value of 6.3 compared with HIV negative participants with a PWV value of 5.7. It was therefore concluded that arterial stiffness increases in HIV positive people as indicated by the increased PWV.

Review of South African data for obese and non-obese patients

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Introduction and Methods: The South African WellScreen Programme; a retail pharmacy (clinic) led Health Risk Assessment (HRA) survey was used to capture and analyse sitting blood pressure (BP), finger prick total cholesterol (TC), glucose and Body Mass Index (BMI) measurements in a predominantly medical aid subsidised client population.
A repeat BP was taken if the initial was ≥140/90. The data was analysed in 2 distinct groups classified according to BMI (Obesity defined as BMI ≥30). Pregnant females were excluded from the analysis.
Results: Analysis based on 15 645 consecutive assessments between January and June 2011. 4 011 had a BMI >30 (mean 37 + 6). The mean BMI of the remaining patients was 25 + 3. Total cholesterol levels and smoking did not differ between the 2 groups but the obese group included more diabetics (6% vs. 2.1%) and the blood pressures (131/83 ± 18/12 vs. 121/77 ± 16/11) and glucose levels (5.8 ± 2.0 vs. 5.2 ± 1.3) were significantly higher in this group. 4% of the obese groups had had prior cardiac events compared to 2.4% in the non-obese group.
Conclusion: The obese group were significantly older, had more diabetes, higher blood pressures and glucose levels. Finger prick total cholesterol was not significantly different between the two groups.
Although only representing 26% of the population studied, the obese medical aid supported individual poses a significantly increased overall cardiovascular risk and should be specifically targeted for lifestyle and pharmaceutical intervention.

WellScreen: Review of real world data in South Africa

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Introduction and Methods: The South African WellScreen Programme; a retail pharmacy (clinic) led Health Risk Assessment (HRA) survey was used to capture and analyse sitting blood pressure (BP), finger prick total cholesterol (TC), and glucose measurements in a predominantly medical aid subsidised client population. A repeat BP was taken if the initial was ≥140/90.
Increased cardiovascular (CVS) risk: was defined as BP ≥140/90, TC >5mmol/l. (primary prevention), and BP ≥130/80; TC >4.5 (secondary prevention). Random glucose >11mmol/l and fasting glucose >7mmol/l was considered hyperglycaemic. Individuals on lipid lowering and/or antihypertensive medication were surveyed to determine "awareness of their drug therapy regime". Family history of premature CVS disease and/or diabetes as well as pre-existing diabetes and/or CVS disease was recorded.
Results: Analysis based on 16 236 consecutive assessments between January and June 2011. The average age of the cohort was 43 years, 56% were female, 8% current smokers (8% prior smokers), 26% obese (BMI ≥30), 3% diabetic and 3% had a prior CVS event. The following increased cardiovascular risk was noted: 4 281 subjects were hypertensive (26.7%), 7 453 (47.5%) hyperlipidemic and 354 (2.2%) hyperglycaemic. 1 816 hypertensives were medicated (42%) of which 82% was aware of their drug therapy regime and 1 039 (57%) risk was controlled on medication. 1 898 hyperlipidemic (16%) were medicated of which 83% was aware of their drug therapy regime and 682 (57%) risk was controlled on medication.
Interpretation and Conclusion: 25% of these young adults were hypertensives and 50% hyperlipidemic. A minority of this group were on drug therapy. Of those on therapy, 60% were deemed controlled. This is supported by a high awareness of their therapeutic regime.
The high prevalence of cardiovascular risk is of concern in this relatively young population. Lifestyle advice (smoking cessation and weight reduction) would be crucial as this population ages. Further investigations are required to determine reasons for the under prescription of lipid lowering therapy as opposed to antihypertensive use.

Utility of cardiac MRI (CMR) at a large referral hospital in South Africa – the Chris Hani Baragwanath Academic Hospital experience

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Introduction: CMR has established itself as the gold standard technique for assessment of cardiovascular structural and functional abnormalities, particularly in Western countries. However, its clinical utility in developing countries has not been evaluated.

Objective: To investigate the usefulness of CMR for management of cardiovascular conditions in a large tertiary hospital that serves the community of Soweto and surrounding areas.

Methods: We undertook a systematic review of records of CMR scans performed at our institution over an 18 months period in order to look at the demographic profile of patients referred and compare the initial reasons for referral and final diagnosis from CMR.

Results: A total of 134 patients (75 males and 59 females) were referred for CMR imaging. The majority 69 (51.5%) were Black Africans (43.8% females); 39 (29.1%) were Caucasians (37.5% females); and 26 (19.4%) were Asians (57.1% females). Median age was 43.9 years (minimum, 7 and maximum, 79).

The main reasons for referral were possible cardiomyopathy (CMO) 41 (30.6%); ventricular tachycardia or ectopics 29 (21.6%); adult congenital heart disease 24 (17.9%; myocardial viability 15 (11.2%); and others (atrial or ventricular mass, cute myocarditis, aortic aneurysm, constrictive pericarditis, iron overload, left ventricular non-compaction and subaortic aneurysm), 25 (18.7%).

Among cardiomyopathy referrals, the majority (34.1%) of cases were for possible HOCM; 29.3% were for possible ARVC; and 36.6% were for unspecified CMO.

Excluding case referred for viability (15), the initial diagnosis was confirmed in 44 (37.0%) cases. In 37 (31.1%) patients a different diagnosis was made or suggested, and in 38 (31.9%) CMR demonstrated a normal heart and the initial diagnoses were discarded. Furthermore, CMR provided additional useful diagnostic information in 19 (16%) subjects.

Conclusion: From this initial 18 months experience with CMR at a large referral hospital in Soweto, South Africa, the majority of patients undergoing imaging with this technique were Black African males. The majority of referrals were for cardiomyopathy, mainly HOCM. In most cases the initial diagnosis was either changed or discarded after CMR and this technique provided additional diagnostic information in a significant number of patients.

Management of coronary cameral fistulae in a paediatric population

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Coronary cameral fistulae are communications between 1 of the coronary arteries and either a chamber of the heart or a segment of the systemic or pulmonary circulation that bypasses the myocardial bed. The most common sites of origin are the right coronary artery in 40 - 60% and the LAD in 30 - 60%, with termination into the right side of the heart in 90% of cases. The most common termination sites are the right ventricle, right atrium, coronary sinus and pulmonary vasculature in that order. They are uncommon lesions, accounting for 0.2 to 0.4 of congenital abnormalities and 50% of paediatric coronary abnormalities.

We describe the management and course of 3 paediatric patients with coronary cameral fistulae managed at our unit between January 2005 and December 2010. The first is a 2-week-old infant referred with cardiac failure and respiratory distress. A continuous murmur was audible at left sternal border. ECG showed right axis deviation and RVH and cardiomegaly with venous congestion were present on chest radiology. Echocardiogram suggested a coronary cameral fistula from left coronary artery. CT angiography confirmed a large coronary fistula from the left coronary artery to the right ventricle for which the child underwent successful surgical ligation.

Two further cases were those of 21-month and 4-year-old females who had incidental findings of systolic murmurs on routine follow-ups. Both their chest x-rays and ECGs were unremarkable. Echocardiogram diagnosed a coronary cameral fistula from left coronary artery to right

atrium on the former and right coronary artery fistula to right ventricle on the latter patient, both confirmed angiographically. The former underwent a successful percutaneous closure of the fistula with a vascular plug. She was commenced on anticoagulation and remains stable with no complications. In the 4-year-old female percutaneous closure was attempted, however there was concern that the occlusion device was impinging on part of the coronary supply. Closure was therefore deferred until the child was older.

Small fistulas are clinically silent and spontaneous closure occurs in 23% of them. However large fistulae progressively dilate over time and complications such as congestive cardiac failure, arrhythmias, infective endocarditis, aneurysm formation and rupture have been described. Transcatheter closure has become the treatment modality of choice for these with surgical closure reserved for those lesions not amenable to transcatheter closure.

Chronic rheumatic heart disease in Abeokuta, Nigeria: Data from the Abeokuta Heart Disease Registry

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Introduction: Rheumatic heart disease (RHD) is a major public health problem in resource poor countries. According to the World Health Organisation (WHO), rheumatic fever(RF)/ RHD affects about 15.6 million people worldwide, with 282 000 new cases and 233 000 deaths each year. There are 2.4 million affected children between 5 and 14 years of age in low-income countries, out of which 1 million live in sub-Saharan Africa, making the continent the major RF/RHD hotspot. About 1% of schoolchildren in Africa, Asia, the eastern Mediterranean region and Latin America show signs of RHD. There are about 2 million people with RHD requiring repeated hospitalisation and 1 million likely to require surgery globally.

The pattern of RHD has never been explored in the city of Abeokuta before. Employing the data from the Abeokuta Heart disease registry, we report on the prevalence and patterns of RHD in this city.

Methods: This retrospective analysis of a prospectively collected data over a period of 4 years (January 2006 to December 2009). We collected information on the bio data, clinical features and echocardiographic diagnoses.

Results: During this period, a total of 107 cases of RHD were seen, 66 females (61.7%) and 41 males (38.3%) aged 43.9 ± 19.3 years (range 7 to 92 years). Mitral regurgitation was the commonest lesion (63.6%). Other common lesions include pure mitral stenosis (14.0%) mixed mitral valve disease (6.5%) and mixed mitral and aortic regurgitation (5.6%). Complications of RHD observed included secondary pulmonary hypertension, valvular cardiomyopathy, atrial fibrillation, stroke and infective endocarditis.

Conclusion: Our data shows that RHD is an important cause of heart disease in this city although the prevalence is lower than studies done in southern Nigeria in the 60s and 70s. Most present with complications and many do not have access to surgical therapy. There is therefore an urgent need to implement the ASAP programme of the Drakensberg declaration in order to stem the scourge of this disease.

Markers of left and right ventricular remodelling in a Nigerian hypertensive cohort

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Background: Although hypertension affects every ethnic group, the consequences are said to be more devastating among blacks. One of the main manifestations of hypertension's end-organ effects especially in blacks is hypertensive heart disease, which includes left ventricular

hypertrophy (LVH), increasing vascular and ventricular stiffness and diastolic dysfunction, which ultimately lead to heart failure (HF) if not adequately treated. Although brain natriuretic peptide is recognised as an indicator of the presence and severity of heart failure including hypertensive (HF) in native Africans, the diagnostic value in differentiating hypertensive LVH without HF from hypertensive HF due to systolic and/or diastolic dysfunction is unclear. We initiated a cohort study in 200 Nigerian patients to study the role of novel biomarkers as well as natriuretic peptides in this cohort.

Methods: It is a prospective cohort study. Echocardiography was performed on all subjects. Measurements taken include left ventricular dimensions and transmitral pulse wave Doppler flow. Right ventricular (RV) systolic function was assessed on echocardiography using tricuspid annular systolic excursion (TAPSE) method. Plasma NT-pro BNP was measured using electrochemiluminescence type immunoassay.

Results: Preliminary data on a subgroup of patients studied will be presented. 55.6% were male, 44.4% female and mean age was 51.1(11.2) years. There was no significant difference in the NT pro BNP levels between hypertensive subjects with LVH and those without (422.3fmol/ml vs. 406.6fmol/ml, p-value=0.72).There is however a trend towards significance when the NT pro BNP levels of hypertensive subjects with LVH but without HF was compared with those with hypertensive HF (394.8fmol/ml vs .515.6fmol/ml, p-value=0.056). In addition, subjects with hypertensive HF have significantly worse RV systolic function compared to hypertensive subjects with LVH but without HF, with TAPSE values of 15.5mm vs. 23.4mm respectively, and p-value=0.000)

Conclusion: NT pro BNP may be a useful biochemical marker in differentiating between hypertensive heart failure and hypertensive left ventricular wall hypertrophy without heart failure in native African population. The contribution of RV function to progression of disease needs to be further investigated.

Spectrum of hypertension and hypertension-related diseases in Abuja, Nigeria

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Introduction: In spite of the high prevalence of hypertension and its complications in sub-Saharan Africa, there is still a paucity of data describing the pattern of presentation of hypertension and its complications.

Methods: We prospectively collected the data of all hypertensive patients presenting at the Cardiology Unit of University of Abuja Teaching Hospital over a four-year period. 1 149 (76.9%) had echocardiography. Right ventricular (RV) systolic function was assessed on echocardiography using tricuspid annular systolic excursion (TAPSE) method.

Results: 1 494 subjects were studied. 753 (50.4 %) were female while 741 (49.6%) were male. The mean age of all the subjects was 51 ± 13.8 years, with male having a mean age of 51.1 ± 11.3 years and female having a mean age of 50.3 ± 12.7 years. 338 (22.6%) presented with dyspnoea on mild to moderate exertion, 113 (7.6%) presented with palpitations and 36 (2.4%) presented with easy fatigability. 332 (22.2%) presented in heart failure, 69 (4.6%) had 1 form of arrhythmia or the other, 65 (4.3%) had cerebrovascular accident, 126 (8.4%) had concomitant diabetes mellitus, 16 (1.1%) had chronic kidney disease, 9 (0.6%) had concomitant retroviral disease and 6 (0.4%) had hypertensive encephalopathy.

Out of the 1 149 subjects who had echocardiography, 260 subjects representing 22.6% had left ventricular wall hypertrophy as assessed by left ventricular mass index greater 46gm/m 2.7. In addition, of the 1 149 subjects that had echocardiography, 266 (23.2%) had estimated left ventricular ejection fraction less than 50%. In addition, subjects with hypertensive heart failure have significantly worse RV systolic function compared to hypertensive subjects with LVH but without heart failure, with TAPSE values of 15.6mm vs. 22.2 respectively, and p-value=0000.

Conclusion: The burden of hypertension and its complications in our environment is enormous with more than half of our subjects having 1 form of complication or the other on initial presentation. The need therefore for an effective primary and secondary preventive measures to be mapped out to tackle this problem cannot be over emphasised.

Pacemaker implantation in South Africa: Implant practices and differences in indications, modes and demographics from the Panorama Registry

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Introduction: World surveys of cardiac pacing show enormous differences amongst countries with implant rates as high as 900 per million in Europe, to <5 per million in most of Africa. In South Africa, the implant rate has increased from 47 to 60 per million from 2005 to 2009. Despite this, provision of pacing is not homogenous in South Africa and variations in implantation rates as great as those noted internationally have previously been reported between sections of the population. Indications and implant practices are likely to differ too.
Methods: Implantation data of South Africans enrolled between 2005 and 2011 in the multi-centre prospective, longitudinal, observational Panorama registry of patients with Medtronic pacemakers were analysed.
Results: Baseline characteristics of 904 patients in 13 hospitals: age 68 ± 16 yrs, 57% male, 85% white, 23% in atrial fibrillation, 23% with heart failure. Primary indication at enrolment varied by hospital type (1 public and 12 private): AV block: 69.1% vs. 19.3%; Sinus node disease: 19.8% vs. 66.9%; other 11.1% vs. 13.7%, respectively ($p<0.001$). Devices (number of chambers paced) implanted also differed by hospital type: 1 chamber: public 86.4% vs. private 22% ($p<0.0001$); 2 chamber: 12.3% vs. 76.6%; and 3: 1.2% vs. 1.3%. Of patients with sinus node disease, 75% in public received a 1-chamber pacemaker and 20% in private, pacing the atrium in 62.5% vs. 3.6% respectively. Of patients with AV block, a 2- or 3-chamber pacemaker was implanted in 12.5% in public and 76.1% in private.
Conclusions: Despite limitations of this registry, it is evident that significant differences in indications and especially implantation practice exist in South Africa particularly between public and private centres. Types of patients and referral patterns clearly differ between these centres. Choices of pacemaker in the public hospital included in this registry are not constrained by financial issues and follow international evidence-based guidelines yet differ markedly from the pacemaker implantation practiced in private. These differences need to be recognised in analysis of any pacemaker related data included in surveys from South Africa.

Differentiating between transanastomotic and transmural endothelialisation: An isolation-loop-graft model in the Wistar rat

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Introduction: Synthetic graft endothelialisation in humans is limited to 20mm from the adjacent arterial anastomosis. Although previous animal studies have attempted to demonstrate transmural endothelialisation, none have been able to show that it occurs independently of trans-anstomotic endothelial outgrowth. Differentiating between transmural and transanastomotic endothelialisation requires the isolation of highly porous graft material from the anastomosis by an impervious material.
Methods: Segments of high porosity (150µm pore) polyurethane (PU) were interposed between impervious expanded polytetrafluoroethylene (ePTFE) in order to isolate the experimental mid-graft from transanastomotic endothelialisation. Grafts were anastomosed end-to-end in the abdominal aorta of male Wistar rats (443g ± 47). Looping the graft increased the isolation segment to 35mm transanastomotic endothelial growth rate: Three equal groups of rats (n=18) with an ePTFE graft (ID 1.7mm, IND 15-25µm), were measured at 2, 4 and 6 weeks. Endothelial coverage of interposition segment: (n=34) Straight group: Three equal sets (n=18) of straight interposition grafts (ePTFE-PU-ePTFE) at 2, 4 and 6 weeks. Looped group: 2 equal sets (n=16) of similar looped interposition grafts at 12 and 24 weeks. The presence of transmural endothelialisation in isolation grafts was determined using light, immune-fluorescence (CD31) and scanning electron microscopy.
Results: There was a statistically significant difference in endothelial growth rate between the proximal and distal anastomoses (0.9 ± 0.1 vs. 0.5 ± 0.3 $p=0.0001$). No difference was noted when comparing transanastomotic proximal and distal growth rates in the 12 and 24 week loop models (0.5 ± 0.2 vs. 0.5 ± 0.3, $p=0.5$). Thirty-one (91%) grafts in the isolation model were patent allowing for transmural in-growth analysis. Eighteen (100%) of the straight grafts showed evidence of partial to full transmural endothelial coverage of the PU, 6 (33%) of these

independent of transanastomotic growth. Thirteen (100%) patent loop grafts had a confluent endothelial on the PU segment, all of which were independent of transanastomotic endothelialisation.

Conclusion: Proximal transanastomotic growth rate is significantly faster than distal growth in the 4- and 6-week group. Transmural endothelialisation through high porosity material can be achieved independently of transanastomotic outgrowth in the Wistar rat. A looped interposition-graft model provides sufficient isolation-length to separate the 2 events.

Ductal closure using Amplatzer Duct Occluder Type II, early experience in Port Elizabeth Hospital Complex, South Africa

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Introduction: Percutaneous closure of Patent Ductus Arteriosus (PDA) was first reported by Porstmann in 1967, and has become the mainstay management of this defect. Devices for PDA closure have evolved over time. Amplatzer Duct Occluder Type II was introduced in 2008. We report our early experience with the use of this device.

Methods: Records of patients admitted to Port Elizabeth Hospital Complex for percutaneous closure of PDA were reviewed. Demographics, haemodynamic and angiographic characteristics, device for closure of PDA and closure approach, screening time, complications and outcomes were recorded.

Results: From May 2009 to June 2011, 41 patients were selected for ductal closure. 25 patients were assigned to closure using Amplatzer Ductal Occluder Type II. Of these patients, there were 15 females and 10 males; with an age mean of 34 months (range, 3 months - 233 months), and a weight mean of 12kg (range 3.94kg - 22.5kg). The QP: Qs ratio mean was 2.11 (range 1.1 - 8.72) with a pulmonary vascular resistance mean of 1.82 Wood Units (range 0.27 - 5.53 Wood Units). The ductal size mean was 2.72mm (range 0.6mm- 5.5mm).

Ten patients had Krichenko Type A duct; 3, type B; 4, type C; 2, type D and 6, type E. The screening duration mean was 24.31 minutes (range 7.1 - 88.7 minutes). Seven patients were occluded with a 3mm device; 7 with 4mm; 2 with 5mm and 9 with 6mm device. In 21 patients, the device was deployed via the pulmonary side; in 4, via the aorta. Complete ductal occlusion was achieved in 87.5% (n=20) of patients before discharge (day 1), whilst 91.7 % (n=22) achieved complete closure by 1 month. In 1 patient, the device dislodged to the pulmonary arteries immediately following deployment, with successful retrieval. Two patients with residual duct were lost to follow up.

Conclusion: The Amplatzer Duct Occluder Type II is capable of closing a wide range of ducts in carefully selected patients. Our findings are comparable to other studies regarding ductal closure rates. However, efficacy, safety and long-term results in large studies are needed; and the search for a device that closes large complex ducts continues.

Chronic diseases of lifestyle risk profiling in an urban African community: An essential role for healthy living intervention strategies

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Background: The Heart of Soweto study (HOS) previously described the impact of epidemiological transition in broadening the spectrum of heart disease. In order to assess chronic diseases of lifestyle, such as heart disease, diabetes, high blood pressure and obesity, risk factors and plan to plan appropriate intervention strategies, we extended our research into the Soweto community and primary health care setting.

Methods: A clinical registry captured data on 1311 consecutive primary care patients (99% African) from 2 primary care clinics in Soweto, South Africa.

Results: Overall, 862 women (41 ± 16 years) and 449 men (38 ± 14 years) were studied. Of these, 613 women (71%) and 131 men (29%) were unemployed. Women were more likely than men to be obese, with an average BMI of 29.9 vs. 24.8 for men. We found that total sleep time decreased as BMI increased for both women and men and that the women slept 30 minutes less than the men. Our data showed a gradient in total cholesterol levels according to educational experience; 3.6 ± 1.4, 3.7 ± 1.3, and 4.2 ± 1.5 mmol/L in those with <6, 6-10 years and >10 years education, respectively. More men than women smoked (47 % vs. 14%) and 787 of women (91%) and 385 of men (86%) reported no regular exercise.

Conclusion: These data demonstrate that like many other urban communities in sub-Saharan Africa, Soweto is sitting on a potential time bomb of modifiable lifestyle risk factors, such as obesity, declining sleep time, smoking and lack of exercise. Creating awareness around these possible risk factors and implementing appropriate intervention strategies at community and primary care level for the prevention there of, has become essential in this urban African population.

Anomalous left coronary artery to pulmonary artery (ALCAPA) patients in Red Cross War Memorial Children's Hospital

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Introduction: Dilated cardiomyopathy (DCM) has a poor prognosis in the developing world where ICU beds, mechanical assist devices and cardiac transplants are limited. ALCAPA present like DCM but is surgical treatable. It is therefore important to have a high index of suspicion for ALCAPA when investigating DCM children.

Aim: To audit patients admitted to RCWMCH with a new diagnosis of ALCAPA.

Method: Retrospective descriptive folder review of ALCAPA patients admitted between July 2004 and July 2011.

Results: 24 patients newly diagnosed with ALCAPA.

Demographics included:

- Median age at presentation 5.4 (range 0.5 - 30) months.
- Male: female ratio 16:12.
- 21 patients were from the Western Cape Province where 10% of the children in South Africa live. Three patients came from the Eastern Cape that house 15% of the childhood population.

The common presenting symptoms were recession and tachypnea in 95%, cardiomegaly 91%, coughing 87%, failure to thrive 56%, feeding difficulty 50%, desaturation 43%, and gallop in 41%. Median length of symptoms before presenting to RCWMCH was 24 days (range 1 - 300). The median time from RCWMCH admission to diagnosis and surgery was 1.5 (range 0 - 16) and 5.2 (range 1 - 20) days respectively. The diagnosis was made on echocardiography in 66% and remainder via catheterisation. All the patients underwent re-inplantation, 4 needed PDA ligation and 2 needed mitral valve annuloplasty in addition. Median cross clamp and bypass time was 71 and 140 minutes. 21% had delayed sternal closure. Median length of hospital stay, ICU stay, ventilation and inotropic support was 21, 10.7, 7 and 8.9 days respectively. Median Wernovsky inotrope score was 32 during ICU stay. Perioperative complications included sepsis 76%, pleural effusion 20%, arrhythmias needing pacing 16%, infarction, cardiac arrest, bleeding, renal replacement therapy 12.5% respectively and pericardial effusion needing drainage 8%. 91% (22/24) survived to hospital discharge, 1 patient died pre-surgery and 1 during surgery.

Conclusion: RCWMCH can expect 3 new ALCAPA cases per year presenting in congestive cardiac failure. Treatment is successful. ALCAPA may be under diagnosed in the Eastern Cape Province.

Does the treatment of HIV infection have significant impact on body composition, lipid profile, adiponectin level and resting energy expenditure?

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Aim and objective: The aim of this study was to determine the impact of the Human Immunodeficiency Virus and its treatment on lipid profile, body composition indices, adiponectin levels and resting energy expenditure

Design: This was a descriptive and comparative study. The study population consisted of 81 participants recruited from the public clinics in Mthatha, South Africa. They were categorised into the following groups: 27 HAART treated HIV participants (group A), 27 HAART naïve HIV participants (group B) and 27 healthy non HIV patients (group C).

Methods: Omron BF 500, formulas were used for body composition, human adiponectin Radio Immuno Assay (RIA) kit for adiponectin, and quantitative colorimetric determination kits for lipid profile.

Results: The participants with normal nutritional status (BMI=18.5-24.9kg/m^2) in the 3 groups had no significant variation in the following parameters: serum triglyceride level, BMI, visceral fat, skeletal muscle fat, body fat, resting metabolism, lean mass, body nitrogen and body fat mass (ANOVA P>0.05). Participants with normal nutritional status and who are HIV positive (these include those who are treatment naïve and experienced) had lower resting energy expenditure (REE), lower High Density Lipoprotein Cholesterol (HDL-C) and total body water than HIV negative participants. In the underweight subgroup, the adiponectin level of the only participants on HAART (group A) was lower than that of the only participant in group B. The HIV positive participants on HAART (group A) were older than the participants in groups B and C. For those who are overweight and obese not all the variables were significant across the groups except for total cholesterol and ideal weight.

Conclusion: These findings suggest that the treatment of HIV infection has an impact on the adiponectin levels, body composition, resting energy expenditure and lipid profiles of HIV infected participants who are underweight and with normal nutritional status.

Anthracycline-induced-cardiotoxicity: Role of proteolytic pathways

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Introduction: Cardiotoxicity is a major hurdle limiting the use of Doxorubicin (DXR), the most effective and extensively used anti-cancer agent of the Anthracycline family. Although the precise mechanism by which DXR damages the heart remains to be fully elucidated, free radical-induced oxidative stress from DXR metabolites play a fundamental role. Antioxidant therapy however has not been able to entirely eliminate cardiotoxicity, thus indicating that DXR-induced cardiotoxicity is multifaceted and complex. Autophagy, an intralysosomal degradation of the cells' own constituents, is used as an important survival mechanism in the presence of external stressors, intracellular stimuli and provides protection against diverse pathologies including heart disease. This study thus aimed to determine whether elevated autophagy would prove beneficial during chemotherapeutic treatment.

Materials & methods: Elevated autophagy was induced using rapamycin (50 nM) for 24 hours in H9c2 myoblasts where after DXR (3 µM) was added for an additional 24 hours. Mitochondrial viability and cell death were assessed using various assays. Furthermore, mitochondrial morphology, DXR localisation and ROS production was assessed using fluorescence microscopy and flow cytometry.

Results: Significant reductions in mitochondrial viability were observed in the DXR treatment group whereas the combination of rapamycin and DXR produced significant improvement. Cell death through apoptosis demonstrated increased death during DXR treatment, however cell death decreased when autophagy was unregulated in the presence of DXR. ROS analysis proved that mitochondria are the source of ROS production during DXR treatment. In addition, elevated autophagy was able to significantly reduce mitochondrial ROS.

Conclusion: We have demonstrated that increased autophagy is a vital survival mechanism in H9c2 myoblasts during acute DXR treatment. This evidence can provide novel treatment strategies for patients who developed Anthracycline-induced cardiotoxicity.

Retrospective audit of percutaneous balloon mitral valvuloplasty: Experience over the last 14 years at Tygerberg Hospital

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Mitral stenosis (MS) as a result of rheumatic heart disease is still frequently encountered in South Africa. Percutaneous balloon mitral valvuloplasty (PBMV) has become the accepted approach in the management of severe mitral stenosis without significant regurgitation. The study objective is to review local experience with this procedure and evaluate our success rates and safety of PBMV.

Methods: A retrospective audit was conducted on patients undergoing PBMV for MS at the Tygerberg Hospital Cardiology Unit between 1997 and 2010. Clinical, echocardiographic and procedural data was collected and analysed regarding immediate and long-term outcomes as well as complications related to the procedure.

Results: Two hundred and fourteen cases of PBMV were assessed comprising of 198 (93%) female and 16 (7%) male patients. The mean age of patients assessed was 34.7 years. Procedural success defined as a doubling of initial mitral valve area (MVA), MVA = 1.5cm^2 or a 50% reduction in the mean transmitral gradient was achieved in 89.4% of patients. Forty eight patients (22.4%) reported on were pregnant. Emergency procedures were carried out on 5 ventilated patients with 4/5 being discharged from hospital in good health. Complications occurred in 28.5% of procedures with worsening mitral regurgitation (21.5%) being the most commonly encountered complication. The most serious complication of thromboembolism occurred in 1.4% of cases. Mortality for PBMV was 0%.

Conclusion: This retrospective audit confirms that PBMV is a safe and effective means of treating mitral valve stenosis in suitably selected patients. Our data would suggest that the Massachusetts General Hospital (MGH) score is a good tool to select patients suitable for PBMV (high likelihood of success and low complication rate) but that it is not useful in differentiating within this group those who are likely to have a poorer outcome or complication. The low complication rate of PBMV is clearly demonstrated but the importance of thromboembolic risk in patients with pre-existing thrombi underscores the need for routine trans-oesophageal echo prior to PBMV. The high procedural success rate and sustained long-term benefit in this South African population with a high burden of RHD mirrors results reported from other populations.

Micro vascular endothelial cell responses to inflammatory stimulation

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Vascular endothelial cells are primary targets of various harmful stimuli such as TNF-a, ADMA and hypoxia. These stimuli are known to elicit distinct responses in endothelial cells that can affect NOS-NO signalling and oxidative/nitro-oxidative stress, which often culminate in atherogenesis if exposure is sustained. The exact cellular mechanisms of these responses are still unclear, particularly in micro vascular endothelial cells. In this study, we examined NO and ROS-production, NOS and NOS-associated signalling, oxidative/nitro-oxidative stress responses, and apoptosis and necrosis in TNF-a stimulated cardiac micro vascular endothelial cells. Our results show that TNF-a exerted a modest time- and dose-dependent increase in NO-production, which was associated with generally decreased eNOS activation/phosphorylation, but increased iNOS expression. The eNOS-signalling proteins PKB/Akt (upstream eNOS activator), Hsp-90 (mediator of eNOS phosphorylation), and caveolin-1 (eNOS inhibitory protein) were either down, regulated or demonstrated decreased activation. Both superoxide and peroxynitrite levels were reduced in TNF-a treated cells at 24h, as was nitrotyrosine; however, expression of p22-phox (NADPH-oxidase subunit) was significantly increased.

Interestingly, TNF-a stimulation exerted anti-apoptotic and anti-necrotic effects at most concentrations and time-points tested. In summary, the results of this study reveal that micro vascular endothelial cells respond to stimulation by the pro-inflammatory cytokine, TNF-a, by down regulating and/or decreasing the activation of the PKB/Akt-eNOS signalling pathway. It appears as if the modest increase in NO-production was iNOS-derived. Superoxide and peroxynitrite measurements showed reduced oxidative and nitro-oxidative stress, despite the significant up regulation of p22-phox. From our data, it appears that the cells were adapting to TNF-a stimulation by up regulating anti-apoptosis and anti-necrosis mechanisms.

Conclusion: Cardiac micro vascular endothelial cells in this study responded to stimulation by TNF-a by adopting a protective and anti-oxidative stress phenotype, despite reduced expression and activation of the normally protective PKB/Akt-eNOS pathway and significant up regulation of a major superoxide-generating protein. We could find no convincing evidence of endothelial dysfunction at 24-hour incubation.

Familial aggregation of dilated cardiomyopathy in patients with peripartum cardiomyopathy

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Introduction: Peripartum cardiomyopathy (PPCM) is a form of unexplained pregnancy-associated heart failure that is associated with considerable morbidity and mortality. Most patients present with acute postpartal heart failure that otherwise resembles the clinical presentation of dilated cardiomyopathy (DCM). Insufficient data exists to formally evaluate any genetic contribution; most being case reports of PPCM cases whose mothers or sisters had the same diagnosis. Two recent Western studies and 1 local study favour theories that some cases of PPCM may be part of the spectrum of familial DCM (FDCM). We hereby report a study of familial aggregation of DCM in patients with PPCM.

Methods: Of prevalent and incident PPCM patients seen at 2 tertiary hospitals across South Africa, 51 were approached for consent to screen their first-degree relatives. Consenting relatives underwent screening for DCM that included interview, clinical examination, ECG, 2D-transthoracic echocardiography, and, only in relatives thought to bear signs of DCM, the necessary additional investigations to exclude other causes of heart failure. For the sake of comparison, a subset of 9 patients manifesting hypertensive heart failure of pregnancy (HHFP; i.e. pregnancy-associated heart failure with current or prior history of hypertension) also underwent family screening.

Results: A total of 18 index patients with PPCM had at least 1 first-degree relative who was screened for DCM. Of these, 4 index cases (22%) had confirmed familial disease (i.e., DCM on echocardiography), whilst an additional 3 (17%) had possible familial disease, (i.e., early echocardiographic signs of DCM). Of these, autosomal dominant patterns of inheritance were observed in 4 families, while 3 families displayed autosomal recessive inheritance. None of the HHFP cases had confirmed familial DCM, but 1 (11%) had possible familial disease; and displayed autosomal dominance.

Conclusion: Our findings support the notion that over a third of PPCM cases bear familial DCM, thus confirming the notion that PPCM is part of the spectrum of familial DCM. Our study also suggests that while HHFP are at far lower risk of familial disease, larger studies will still be needed to better quantify this risk. Detailed family history and routine family screening may be as much merited in PPCM as it is in DCM.

Identification of novel titin-interacting sarcomeric proteins and their possible roles as modifiers of hypertrophy in hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is an inherited cardiac disorder characterised by left ventricular hypertrophy (LVH) and increased risk of sudden cardiac death. LVH is an important predictor of morbidity and mortality and is a feature of complex disorders such as hypertension and diabetes. Since LVH is a primary feature of HCM, this disorder has been considered a model disease to study the complex mechanisms leading to LVH.

Over 1 000 HCM causing mutations in 14 genes have been identified to date. Interestingly, a large degree of phenotypic variability exists across families as well as within families harbouring the same primary HCM-causing mutation. This observation has directed the focus of several research endeavours to the identification of possible genetic modifiers of the hypertrophic phenotype.

Here, we aim to identify putative HCM-modifying genes by searching for novel interactors of titin, a protein known to be involved in HCM. We hypothesise that proteins that interact with proteins known to be mutated in HCM, can be considered potential HCM-modifiers.

Yeast two-hybrid analysis was performed using the 11 domain super repeat of titin as "bait". The putative interactions are subsequently being confirmed by three-dimensional co-localisation. Thus far, 27 possible putative titin interactors have been identified and are currently being verified. The genes encoding these interactors will be used in family-based association studies to determine whether they are potential HCM-modifying genes.

The identification of HCM-modifying genes may help researchers better understand the molecular mechanisms involved in the development of LVH in HCM as well as in hypertension and diabetes.

Screening for cardiac disease using computer-assisted auscultation

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Background: Cardiac auscultation is inherently qualitative, highly subjective and requires considerable skill and experience. The decline in teaching of auscultation and poor accuracy at diagnosing heart sounds and murmurs has resulted in a reduced ability to discern an innocent murmur from 1 suspicious of pathology. Computer-assisted auscultation (CAA) is a referral-decision support tool that could increase sensitivity and specificity of echocardiography referral decisions, thereby minimising inappropriate referrals. This study evaluated the sensitivity and specificity of 2 computer-assisted systems in detecting echo confirmed structural abnormalities.
Methods: 79 patients referred for assessment to 1 of 2 tertiary cardiac clinics were recruited for the study. Participants underwent an examination using computer-assisted auscultation (CAA) methods as well as the standard clinical examination and echocardiogram.
Results: Echocardiography-confirmed prevalence of structural heart disease was 53% (n=42). The CAA systems were able to complete the examinations in over 94% of the cases. The quality of the recordings was deemed excellent in the majority (92% with Cardioscan® and 86% with Sensi®). The overall sensitivity of Cardioscan® to identify cardiac abnormalities in children was 92% (71 - 99%) and 60% (41 - 77%) in adults. The specificity was 47% (21 - 73%) and 67% (30 - 93%) in children and adults respectively. The sensitivity of the Sensi® system in identifying cardiac abnormalities in children was 79% (45 - 93%) and 84% (61 - 97%) in adults. The specificity was 57% (29 - 82%) and 67% (30 - 93%) in children and adults respectively. In subgroup analyses, the sensitivity for detecting acyanotic heart disease was 100% using both Cardioscan® and Sensi® while Sensi® also demonstrated a sensitivity of 100% in detecting cyanotic heart lesions.
Conclusion: Computer-assisted auscultation demonstrates suboptimal sensitivity and specificity in detecting cardiac abnormalities in children and adults. As both systems demonstrate 100% sensitivity in detecting acyanotic heart disease, and theoretically carries significant potential in resource-limited settings, further development of algorithms to improve sensitivity and specificity and define clinical applications is still warranted.

The unmet needs of children with rheumatic heart disease: First insights from REMEDY

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Background: Although Rheumatic Heart Disease (RHD) has waned significantly in the developed world, it continues to reign rampant in the developing world, particularly afflicting children, adolescents and young adults. Conservative estimates report 470 000 new cases of rheumatic fever and 233 000 deaths each year. These numbers demand a new approach to this disease.
Confirmed cases of RHD in children aged 5 - 15 years represent 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 recently launched Rheumatic Heart Disease Global Registry (REMEDY) provides a unique opportunity to both assess the burden of disease while simultaneously managing patients with established disease.
Method: This is a prospective, international, multicenter, hospital-based registry. This paper will focus on observations relating to the patients under the age of 18 years enrolled in this vanguard phase.
Results: There were 90 children enrolled in the Registry database from 12 different sites. Almost 60% of the children had been diagnosed with congestive heart failure with 22% being classified as being in NYHA III or IV. No patient was enrolled with quadrivalvar disease although all other valve lesions of every severity were represented. A total of 44% of the cohort had had surgery while a past history of infective endocarditis, major bleeding or episode of stroke was present in almost 10% of the participants. A quarter of the children on anti-coagulants had no INR measurement in the 6 months prior to enrolment and. 65% were unaware of their target INR. Only 86% of the patients who had had surgery were on secondary prophylaxis.
Conclusion: RHD remains an unrestrained killer of children, adolescents and young adults in the developing world. The in-hospital burden of disease is irrefutable while surgery remains a luxury in most centres in sub-Saharan Africa. We maintain that good quality global disease burden data around RHD, such as is being generated from the REMEDY database, will advocate for increased political will and assign the appropriate priority to urgent action around RHD.