Role of B-Type Natriuretic Peptide for the Monitoring of Anthracycline-Induced Cardiotoxicity

Sanjeev Sanjeev, Michael Pettersen, Joelyn Guruzynski, Kanta Bhamani, Thomas J. L'Ecuyer, Children's Hospital of Michigan, Detroit, MI

Background: The major limitation of the anthracyclines (AC) class of cancer chemotherapeutic drugs is progressive cardiotoxicity. Currently, patients receiving AC are monitored by echocardiographic measurement of shortening fraction (SF). Other indices of myocardial contractility are technically difficult to obtain. There is a need for a sensitive and rapid biomarker to detect cardiac injury in these patients. B-type natriuretic peptide (BNP) is a hormone secreted from the ventricles in response to hemodynamic stress. BNP is an objective bedside test that accurately detects asymptomatic cardiac dysfunction and correlates with the severity of congestive heart failure in adults. The purpose of the study is to determine the correlation between plasma BNP and cardiac function on echocardiogram in patients treated with AC.

Material and methods: Sixty-three patients (pts) treated with AC chemotherapy at least 1 year prior to enrollment were included. All patients underwent a detailed echocardiogram [including SF, rate corrected velocity of circumferential fiber shortening (VCFc), end systolic wall stress (ESWS), the relationship between the two (VCFc/ESWS) and diastolic parameters such as mitral inflow velocities (E/A ratio) and isovolumic relaxation time] and simultaneous plasma BNP level.

Results: The cohort included 37 males with the mean age of 13.7 yrs (range, 1-34 yrs). Cancer was diagnosed at a mean age of 7.7 yrs (range, 1-20.5 yrs) and the mean duration of follow up was 5.2 yrs (range, 1-18.5 yrs). Cardiac dysfunction defined as any one of the following: SF<28%, VCFc<60%, an abnormal VCFc/ESWS or abnormal diastolic indices compared to established age specific norms was found in 24 (38%) pts. Nine of the 63 (14%) pts had abnormal SF alone. Plasma BNP in pts with abnormal cardiac function (n=24) was significantly higher than the normal pts (n=39) (24.3 ± 5 vs. 14.1 ± 1.4, p<0.05). Plasma BNP is inversely proportional to SF (p=0.008).

Conclusions: A third of patients who have received AC have an abnormality in cardiac function on detailed echocardiogram. Plasma BNP is a useful bedside screening test that is significantly increased in patients with abnormal cardiac function.

B-Type Natriuretic Peptide: A Bedside Biomarker of Hemodynamically Significant Patent Ductus Arteriosus

Sanjeev Sanjeev, Michael Pettersen, Jorge Lue, Seetha Shankaran, Thomas J. L'Ecuyer, Children's Hospital of Michigan, Detroit, MI

BACKGROUND: A hemodynamically significant patent ductus arteriosus (hsPDA) has important clinical consequences in preterm neonates. Although accurately diagnosed by an echo, cardiac dysfunction may manifest in the form of congestive heart failure (CHF). In this study, we sought to determine if an increased level of BNP indicates impending CHF in preterm neonates.

MATERIAL AND METHODS: This was a prospective study involving preterm neonates with birth weights ≤1500 grams and gestational age ≥34 weeks in whom an echo was performed for clinical suspicion of PDA. Newborns with congenital cardiac defects and congenital heart disease were excluded. Twelve between 71/2 to 1029/2 weeks of age were included. Plasma BNP was measured at echo 48 - 72 hours after treatment. hsPDA was defined by Doppler velocimetry as a left to right shunt of ≥0.7 cc/kg/hr in a patent ductus arteriosus, or a drop in systolic arterial pressure of ≥15 mm Hg.

RESULTS: Twenty-nine neonates with a median weight of 870 grams (560-1325 g) and a median gestation 26 weeks (24-31 weeks) were enrolled. At a median age of 7 days (2-28 days), BNP levels were significantly higher in neonates with hsPDA (n=19) compared to those without (n=46) (450.6 ± 123.9 pg/ml vs. 37 ± 4.6 pg/ml, p<0.001). At a cut off value of 70 pg/ml, BNP had a sensitivity of 94.7%, specificity of 89%, positive predictive value of 98.9% and negative predictive value of 97.6% for detection of hsPDA. BNP levels dropped significantly after medical or surgical closure of hsPDA (n=12) (404.9 ± 159.2 pg/ml to 25.1 ± 4.1 pg/ml, p = 0.03).

CONCLUSIONS: Elevation of plasma BNP accurately detects the presence of hsPDA in premature infants. Changes in BNP with treatment reflect whether therapy has been successful. A BNP cutoff of 70 pg/ml is a useful screening tool for diagnosis and treatment of hsPDA that may improve clinical care and decrease the cost of health care in preterm babies.
**CONCLUSION:** These findings suggest that only adult hearts may profit from the administration of the Na+-channel modulator BDF 9148. It may be speculated that in mature myocardium a well developed sarcoplasmatic reticulum is essential for positive BDF effects. Further studies are necessary to clarify the risk of arrhythmia during application of the Na+-modulator BDF 9148.

**Evaluation of Right Ventricular Function in Patients With Repaired Tetralogy of Fallot With the Use of Tissue Doppler Imaging and Brain Natriuretic Peptide**

Stella Brili, Nikolaos Alexopoulos, Georgios Latsios, Constandina Aggeli, John Barbatesis, Christos Pitasios, Gregory Vysousis, Christodoulos Stefanadis, Athens Medical School, Hippokration Hospital, Athens, Greece

**Background:** Accurate estimation of right ventricular function in patients with repaired tetralogy of Fallot (RTDOF) is often difficult. The aim of the present study is the evaluation of right ventricular function of adult asymptomatic patients with RTDOF by means of Tissue Doppler Imaging (TDI) of the tricuspid annulus and Brain Natriuretic Peptide (BNP) values.

**Methods:** 22 adult patients with RTDOF and 22 age and sex matched healthy controls were studied by means of 2D, Doppler and TDI echo. The following measurements were obtained: Right-ventricular diameter / Left-ventricular diameter (RVD/LVD) at the 4-chamber view as well as systolic (Sa) and diastolic (Ea) velocities at the right ventricular free wall tricuspid annulus site. Serum BNP levels were measured in both groups.

**Results:** Patients with RTDOF showed statistically significant (p<0.001 for all) reduced TDI velocities compared to controls (left figure): Sa (19.1±1.20 vs. 26.16±1.10, Ia (10.66±1.80 vs. 19.04±1.04), Aa (5.24±1.66 vs. 13.76±5.3). The BNP levels were increased in patients compared to controls (47.6 vs. 5.41 pg/ml, p<0.001). The increased BNP concentration of RTDOF correlated to the reduced TDI velocities (r=0.77, p<0.001, right figure).

**Conclusions:** Our results indicate that although our cohort of patients was asymptomatic, the use of TDI and BNP easily discriminated them from the healthy controls. Moreover, right ventricular dilatation is correlated to BNP levels.

**Regional Systolic and Diastolic Dysfunction of the Venous Left Ventricle in Patients With Corrected Transposition of the Great Arteries by Atrial Switch**

Tudor C. Poerner, Bjorn Goebel, Herbert E. Ulmer, Martin Borggrefe, Raoul Arnold, University Hospital Mannheim, Germany

**Objectives:** To investigate regional myocardial function at rest and under exertion in patients with transposition of the great arteries corrected by atrial switch operation (cTGA).

**Methods:** Twenty-four patients with cTGA aged 12-33 years and 17 healthy young subjects underwent tissue Doppler echocardiography with strain rate imaging (TDE) at baseline and during bycicle exercise at 1 Watt / kg body weight. Free wall of the systemic right ventricle (RV), ventricular septum and lateral wall of the venous left ventricle (LV) were scanned from apical 4-chamber-views. Longitudinal systolic (Vs) and diastolic (Ve) velocities, systolic strain rate (SR) and strain were determined as peak values in the basal, mid-wall and respectively apical segments using a dedicated software.

**Results:** Femoral or Internal Jugular venous route.

**Conclusions:** Between Jan 2000 and Aug 2004, 23 patients under 2 years of age (median 17 months) were operated with the following indications: device closure of atrial septal defects in 2, coil occlusion of arterial duct in 1, embolization(2), complete A-V block (2), transient left bundle branch block and transient haemoglobinosis. With the device occlusion through the ductus membrane occluder). Satisfactory device implantation was achieved in 95 pts: a tiny “smoke-like” residual flow though the device was rather common immediately after the procedure, but it disappeared during follow-up, after the second week. The device was removed between 3-4 weeks.

**POSTER SESSION**

**1056 Congenital Heart Disease: Catheter-Based Interventions**

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

**1056-235 Nonsurgical Closure of Congenital Ventricular Septal Defects: Results and Complications**

Massimo Chessa, Mario Carminati, Gianfranco Butera, Edoardo Bossone, Diana Gabriela Negura, Luciane Piazza, Alessandro Giamberti, Giuseppe Pome, Marco Antonio, Dea Torre, Luca Ross, Angelo Gial, Alessandro Frigola, Istituto Policlinico San Donato, san Donato Milanese, Italy, Italy

**Objective:** To report our experience on transcatheter closure of congenital ventricular septal defects (VSD) with Amplatzer septal occluders.

**Patients:** 97 patients (pts) (26 muscular VSDs and 71 perimembranous VSDs; 85 native, 12 residual post surgery), age:16 years (range: 6 months- 64 years), weight: 34 Kgs (range: 0.5-90 Kgs). The VSD size was 8 mm (range: 4.5-16 mm), mean Qp/Qs=2.0±0.5.

**Methods:** All procedures were performed under general anaesthesia, with fluoroscopic and transesophageal echocardiographic control. The device was implanted through the Femoral or Internal Jugular venous route.

**Results:** The procedure was not performed in 2 pts (both when attempting to use the Membranous occluder). Satisfactory device implantation was achieved in 95 pts: a tiny "smoke-like" residual flow though the device was rather common immediately after the procedure (54%), but a residual shunt was detectable in 19 pts after 24 hours and only in 8% at 1 month, and 5% at 6 months follow-up. Additional catheter interventions performed simultaneously: device closure of atrial septal defects in 2, coil occlusion of arterial duct in 1, stenting coarctation in 1, pulmonary valvuloplasty in 2, PA stent in 1.

**Conclusions:** Acute complications: aortic regurgitation (2), tricuspid regurgitation (2), device embolization(2), complete A-V block (2), transient left bundle branch block and transient haemoglobinosis (2). No complications were observed during a median follow-up of 8 months (range:2-36 months).

**1056-236 Symptomatic Atrial Septal Defects In Children Under 2 Years Of Age: To Close Or Not To Close?**

Iman Kajwahi, David Teitel, Paul Stanger, Phillip Moore, University of California San Francisco, San Francisco, CA

**Objectives:** To assess the efficacy of transcatheter device closure of atrial septal defects (ASD) in symptomatic children under 2 years of age.

**Background:** Symptoms associated with ASD in children under 2 years of age include respiratory distress, pulmonary hypertension, and failure to thrive, particularly in children with associated abnormalities. The efficacy of device closure in these children is unknown.

**Methods:** Between Jan 2000 and Aug 2004, 23 patients under 2 years of age (median age 1 year, 9 to 22 m, median weight 8 Kg, 3 to 12 Kg) had device closure of ASD using...
moderate sedation and transesophageal echocardiography (TTE). Of 23 patients 13 had associated abnormalities including Ebstein’s, tricuspid valve disease, endocarditis, and idiopathic valve disease. The Amplatzer device was used in 21 of 23 patients. The CardioSEAL device in 2. Clinical follow-up, echocardiographic, and catheterization details were reviewed.

Results: Symptoms were present in 21 (91%) including respiratory in 10 (recurrent infections), pulmonary hypertension (PHTN) in 7, failure to thrive (FTT) in 2, and cyanosis in 2. Baseline Qp/Qs was median of 2 (1.5 to 2.6). Device closure was successful in all with a follow-up time of 38 +/- 24 minutes. Procedural complications included transient supraventricular tachycardia in one and trivial paricalvial effusion not requiring treatment in 3. A median follow-up of 14 months (1 to 54 months), 810 patients with respiratory symptoms had resolution, 6/7 patients with PHTN had normalization of right ventricular pressure by TTE, both patients with FTT gained above the 50th percentile for weight, and both patients with cyanosis had normal saturations. Twenty of 23 had complete closure by TTE and 3 had trivial residual leaks. Late events included deaths in 4 patients in 1.67, 16 and 17 months (Ebstein’s 1, immunodeficiency 1, respiratory failure 2), and progression of a preexisting 2nd degree AV block to asymptomatic 3rd degree AV block at one month.

Conclusions: Transcatheter device closure of ASD in symptomatic children under 2 years of age is feasible and safe. The majority of patients showed marked improvement in symptoms, although effect on late outcome is unclear.

1058-239
Experimental Atrial Septal Defect Occlusion Using the Transcatheter Patch and Surgical Adhesive
Eleftherios B. Sidiris, Benjamin Macaluf, Vasilli E. Sidiris, Spyridon D. Mouloupoulos, Athenian Institute of Pediatric Cardiology, Athens, Greece

Background: The Transcatheter Patch (TP) has several theoretical advantages over on- disk devices in heart defect occlusion, including wider spectrum of application (minimal rim requirement) and absence of wire related complications; however the method is relatively inconvenient requiring 48 hours of hospitalization. Accelerated TP release using subcutaneously administered thrombin could correct this disadvantage.

Method: Atrial septal defect (ASD) occlusion was performed in 9 piglets, using the TP with SA. There were 6 ASDs 10-12 mm in diameter and 3 cases of patient foramen ovale (PFO); in one animal the left atrial appendage (LAA) and the PFO were sequentially occluded. A TP (25mm x 25mm x 1mm) made of polyethylene glycol, applied in an inactive form to the wall of the patch, with later activation inside the heart. The patch was released in 15-30 mm. Heparin was used in 5 cases. The TP was supported by a single balloon without retention disk or proximal balloon. Fluoroscopy and angiography were used on implantation; all animals were followed for a period up to 3 weeks and had autopsies.

Results: All patches were released in 15-45 minutes. There were no instances of patch embolization or thromboembolism. Endothelialization was complete in 3 weeks. In one case the TP + SA was explanted because the patch was retracted to the inferior vena cava. It was retrieved and replaced by another one. In the case of sequential LAA and PFO occlusion, the LAA was first occluded with the patch released in 15 minutes, followed by PFO occlusion and patch released in 15 more minutes.

Conclusion: Accelerated TP occlusion of experimental ASDs is feasible and safe using a polyethylene glycol surgical adhesive. The TP construction is simplified (no need for double balloon or retention disk). Heparin use is not contraindicated. Careful echocardiographic and fluoroscopic guidance is required for the initial precise placement of the patch, since subsequent manipulations are not possible.

1058-240
Balloon Sizing is Not Necessary for Closure of Secundum Atrial Septal Defects
Zahid Amin, David A. Danford, University of Nebraska/Creighton University/Children’s Hospital of Omaha, Omaha, NE

Background: Balloon sizing (BS) is considered an integral part of atrial septal defect (ASD) closure. In large defects with inadequate atrial septal rims, BS may increase the A-S distance and the risk of residual shunt. BS is not easy to appreciate, and symptomatic complications may occur if the balloon inflation time is long. These factors may make device selection inaccurate, if the balloon inflation time is long. These factors may make device selection inaccurate, perhaps "jailing" vessels & increasing vascular trauma. Interoperative angiography (IA) can be obtained w/ a portable C-arm fluoroscopy unit in the operating room (OR). IA offers dynamic data useful to both surgeon & cardiologist in planning interventions or evaluating work during the procedure. IA may reveal historic problems such as vessel stenosis or occlusion that can then be dealt with immediately in the OR. IA can be obtained during the procedure to facilitate diagnosis & management of acute complications during intervention.

Objectives: To review our institution’s experience w/ BS & IA.

Methods: The records of pts who had IA or BS were noted as well as any intervention. Hemodynamic & angiographic data were analyzed.

Results: 32 pts were included. Median age was 4.6 yrs (range: 2 to 34.4 yrs). 16 pts had interventions while only 8 pts had IA. The remaining 8 pts had interventions only. Most pts had a preexisting 2nd degree AV block to asymptomatic 3rd degree AV block at one month. Few patients showed transient ischemic attack (TIA) who underwent PFO closure. IA is available on the frequency of hypercoagulable states in these patients. We reviewed coagulation parameters in patients with cryptogenic stroke, peripheral embolism or any other complication. There were 25 pts in group A and 10 in group B.

Conclusion: IA is a viable & useful tool to aid surgery or ISI for congenital heart disease. Dynamic data obtained by IA can be acted upon surgically or by catheter intervention during a single anesthesia session. S can be more accurately placed w/ IA. Rare complications can easily be addressed w/ the chest open. Further studies are necessary to determine which pts are best suited for this procedure.
V-Leiden. Homocysteine was elevated in 11% of patients while other abnormalities including lupus anticoagulant, prothrombin mutation 20210, protein S, C or antithrombin-III deficiency were rare (<3%).

Conclusion: Elevated levels of lipoprotein(a) and anti-phospholipid antibodies may be a risk factor for paradoxical embolism in individuals with PFO, therefore patients may benefit from a more aggressive treatment strategy.

Inherent risk factors for thrombosis in patients with presumed paradoxical embolism and PFO

<table>
<thead>
<tr>
<th>Lipoprotein(a)</th>
<th>N Tested</th>
<th>N Abnormal</th>
<th>Percent abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>17 (30 mg/dL)</td>
<td>25.4</td>
<td></td>
</tr>
<tr>
<td>Anti-phospholipid Antibodies</td>
<td>94</td>
<td>23</td>
<td>24.5</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>89</td>
<td>10 (11.4 mcmm/L)</td>
<td>11.2</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>63</td>
<td>72 (heterozygous)</td>
<td>18.9</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>72</td>
<td>2 (heterozygous)</td>
<td>2.8</td>
</tr>
<tr>
<td>Prothrombin mutation 20210</td>
<td>66</td>
<td>1 (heterozygous)</td>
<td>1.5</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>72</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>84</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Antithrombin III deficiency</td>
<td>81</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: These unique findings provide insight into spatiotemporal pattern of MMP-9 transcriptional activation following discrete myocardial injury and provide a temporal window to interdict in MMP-9 activation as a means to attenuate post-RF scar expansion.

Poster Session

1085 Pediatric and Congenital Heart Disease: Electrophysiology

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1085-238 Spatial and Temporal Regulation of Matrix Metalloproteinase-9 Transcriptional Activation Following Discrete Myocardial Injury

J. Philip Saul, Rupak Mukherjee, James A. Bruce, David M. McClister, Jr., Claire M. Allen, Jeffrey S. Austin, M. Elizabeth Fini, Medical University of South Carolina, Charleston, SC, University of Miami School of Medicine, Miami, FL

Background: Radiofrequency (RF) ablation of the myocardium causes discrete sites of injury. RF scars can expand, altering the extracellular matrix (ECM). Matrix metalloproteinases (MMPs) contribute to ECM remodeling and one MMP type, MMP-9, contributes to adverse myocardial remodeling. However, transcriptional induction of MMP-9 following myocardial injury remains unexplored. This study examined MMP-9 gene promoter (M9PROM) activation post-myocardial RF injury using mice in which the M9PROM was fused to a β-galactosidase (β-gal) reporter.

Methods and Results: RF lesions (0.5 mm probe, 80°C, 30s) were created on the LV epicardium of M9PROM mice (n=62) and terminally studied at 1hr, 1d, 3d, 7d, 14d, and 28d post-RF. M9PROM activation was localized through β-gal staining. RF scar area and the area of β-gal staining were measured and normalized to LV area (Figure). RF scar size increased from 1hr post-RF values by 7d and continued to increase through 28d, indicative of RF scar expansion. M9PROM activation became evident at 3d, peaked at 7d, and was non-detectable by 28d post-RF. At 3d and 7d post-RF, M9PROM activation radiated from the scar towards the remote myocardium, recruiting previously viable myocardium in the RF scar expansion process.

81 0 0
84 0 0
Lupus anticoagulant
83 5 (heterozygous) 6.0
Homocysteine
89 10 (>11.4 mcmm/L) 11.2
Protein C deficiency
72 0 0
Factor V Leiden
63 72 (heterozygous) 18.9
Anti-phospholipid Antibodies
94 23 24.5
Prothrombin mutation 20210
66 1 (heterozygous) 1.5
Lipoprotein(a)
67 17 (30 mg/dL) 25.4
Anti-phospholipid Antibodies
94 23 24.5
Homocysteine
89 10 (11.4 mcmm/L) 11.2
Factor V Leiden
63 72 (heterozygous) 18.9
Prothrombin mutation 20210
66 1 (heterozygous) 1.5
Protein S deficiency
72 2 (heterozygous) 2.8
Protein C deficiency
72 2 0
Lupus anticoagulant
84 0 0
Antithrombin III deficiency
81 0 0

Poster Session

1085 Pediatric and Congenital Heart Disease: Electrophysiology

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1085-237 Predictors Of Junctional Ectopic Tachycardia Following Surgery For Congenital Heart Disease

Arian S. Bhatt, Davis S. Chun, Tiffanie R. Johnson, Elaine M. Maldonado, Brandy A. Kashyap, Jackie Maiers, Chris L. Lindblade, John Brown, Mark Rodolfick, Joyce E. Hubbard, Indiana University School of Medicine, Indianapolis, IN

Background: Junctional ectopic tachycardia (JET) often follows surgery for congenital heart disease and is associated with increased morbidity. Previous reports investigating predictors of JET have found a correlation between JET and surgeries involving direct injury to the conduction system, hypomagnesemia, and use of inotropes. The exact cause of JET however remains unclear. This study is designed to evaluate the predictors of JET in this population.

Methods: We prospectively followed 336 consecutive patients with a mean age of 4.02 ± 7.04 years undergoing surgery for congenital heart disease at our institution over a 1-year period. Continuous electrocardiography was reviewed every 24 hours from surgery until discharge.

Results: The incidence of JET was 8% (n=27). Repairs with the highest incidence of JET included arterial switch operation (31/3%, 23%), AV canal repair (4/19, 21%), and Norwood palliation (2/10, 20%). When compared to patients with no arrhythmias, patients with JET were more likely to be younger (1.52 ± 2.34 vs. 3.87 ± 6.65 years, p<0.001), have had longer cardiopulmonary bypass times (131 ± 44 vs. 110 ± 55, p<0.01) and have a higher isotropic score in the postoperative period (6.26 ± 7.55 vs. 5.76 ± 4.69, p<0.01).

Conclusion: JET is related to surgery involving direct injury to the conduction system, hypomagnesemia, and use of inotropes. Predictors of JET are not readily apparent and may require more comprehensive studies to elucidate the underlying cause.
Efficacy of Biphasic Waveform Compared with Monophasic Waveform for Cardioversion of Atrial Tachycardia in Patients with Congenital Heart Disease

Arian S. Bhat, Babar S. Hasan, Helen Fippin, Roger A. Hurwitz, Indiana University School of Medicine, Indianapolis, IN

Background: Transhoracic electrical cardioversion using a biphasic waveform has been the most common method converting persistent atrial flutter into sinus rhythm. Recently, cardioversion with a biphasic waveform has shown promising results for treatment of atrial flutter. However, this efficacy has not been demonstrated in patients with congenital heart disease. This study compares cardioversion outcomes in 2 sequential groups of patients with atrial flutter and congenital heart disease undergoing transhoracic cardioversion.

Methods: Records of 102 consecutive cardioversions undertaken in the electrophysiology laboratory at Jatene from January 1998 to February 2004 were reviewed. Mean age 16.7 ± 3.2 yrs (range 2 to 100% (48/48) in the biphasic group (p=0.028). The mean number of attempts before achieving procedural success was 1.7 ± 1.1 in the monophasic group compared to 1.08 ± 0.9 in the biphasic group (p=0.002). The mean number of attempts before achieving procedural success was 1.7 ± 1.1 for the monophasic cardioversion group and 1.3 ± 0.9 for the biphasic cardioversion group (p=0.007). No major acute complications were observed in either group. Conclusion: Biphasic waveform shock transhoracic cardioversion for atrial flutter in patients with congenital heart disease is associated with higher cardioversion success rates and fewer requirements for procedural monophasic waveform shocks. These findings provide the impetus for more widespread use of devices utilizing biphasic waveforms in patients with congenital heart disease.

The Pure Potassium Channel Blocker (Nikelalant Hydrochloride) for Postoperative Functional Ectopic Tachycardia and Ectopic Atrial Tachycardia in Infants with Congenital Heart Disease and Impaired Ventricular Contraction

Satoshi Yasukochi, Nagano Children’s Hospital, Toyoshina, Japan

Background: Nikelalant Hydrochloride (Ni), pure potassium channel (K+), blocker, is a new anti-arrhythmic drug for ventricular tachycardia (VT) without deteriorating ventricular function. However, no evidence has been reported in use for infants with congenital heart disease (CHD) who had functional ectopic tachycardia (JET) or ectopic atrial tachycardia (EAT).

Aim: The purpose of this study is to clarify the feasibility and efficacy of Ni in infants, presenting atrial and ventricular arrhythmia. JET and EAT after surgery for CHD with impaired ventricular contraction (PSC). Subjects and methods: Five infants with various CHD (Age: 12 days to 13 months: 3 mo. as a median) and Body Weight: 2.3 to 7.45 kg (4.8) (2) were operated JET/EAT from 0 to 12 days after surgery (Jatene(1), Bi-directional Glenn(1), Norwood(1), VSD closure(1), and Body Weight: 2.3 to 7.45 kg (4.8)) developed JET/EAT from 0 to 100% (48/48) in the biphasic group (p=0.028). The mean number of attempts before achieving procedural success was 1.7 ± 1.1 in the monophasic group compared to 1.08 ± 0.9 in the biphasic group (p=0.002). The mean number of attempts before achieving procedural success was 1.7 ± 1.1 for the monophasic cardioversion group and 1.3 ± 0.9 for the biphasic cardioversion group (p=0.007). No major acute complications were observed in either group. Conclusion: Biphasic waveform shock transhoracic cardioversion for atrial flutter in patients with congenital heart disease is associated with higher cardioversion success rates and fewer requirements for procedural monophasic waveform shocks. These findings provide the impetus for more widespread use of devices utilizing biphasic waveforms in patients with congenital heart disease.

Tissue Doppler Echocardiography Combined With a New 2D Strain Method for Analysis of Left Ventricular Function in Resynchronization Therapy in Children With Congenital Heart Disease

Phat Pham, Seshadri Balaj, Irving Shen, David Stuessie, Richard Reed, Ross M. Ungerleider, David J. Sahn, Oregon Health & Science University, Portland, OR

Background: We correlated tissue Doppler imaging (TDI) and a new 2D strain method as efficacy indices for resynchronization therapy in acutely post-operative congenital heart disease (CHD) pts.

Methods: We studied 10 children (3mo - 5.4yrs, median 5.5mo), with CHD (TOF=3, atrioventricular septal defect=2, VSD=2, sinus venosus ASD=2, TGA=1), immediately post-operative for definitive repair, with epicardial (2 RA) and ventricular wires (2 right ventricular [RV], 1 left ventricular [LV]). Packing strategies include atrial pacing (A00), conventional dual-chamber pacing (CCDO) using RV leads, and biventricular pacing (BDOO) using RV and LV leads. Packing sequences lasted 10 minutes, then echo, standard ECG, TDI, and tissue Doppler imaging. RV and LV strain was evaluated using TDI encoded data from 4-chamber views (120-160 fps), analyzed with EchoPac®. Results: TDI derived strain rate defined isovolumic systolic strain (I'VT) and systolic contraction (PSC). Compared to A00, CCDO showed no change in the timing of RV' and PSC, however, the LV'VT and PSC time was significantly delayed (p=0.0002) from the initial QRS. Timing between RV and LV events was not significantly changed in BDOO when compared to A00. LV global strain as a function of synchronization was significantly decreased in CCDO (p=0.001), and improved with BDOO (p=0.002).

Conclusions: The new 2D strain method is effective in the assessment of ventricular resynchronization in children.
markers of neurohormonal activation like BNP may further improve the prognostic value. The combined use of HRT, HRV and cortisol (p=0.0003), TS (p=0.0135), SDNN (p=0.004), SDANN (p=0.005), HRVTI (p=0.009), arterial oxygen saturation (SaO2) and age were found to be the strongest independent risk stratifier (hazard ratio 61.5, p=0.0002).

Results: TWA was positive in 5 patients (29%), negative in 10 patients (58%) and indeterminate in 2 (11%). There was a trend towards decreased RVEF and increased RV mass in the 5 patients with TWA (44 ± 23 vs 62 ± 5%, NS; 119 ± 53 vs 81 ± 18, NS). All positive TWA tests were in the RV fibrosis group (5/9 vs 0/10, p=0.005). Patients with RV myocardial fibrosis were older than those without (32 vs 23, p<0.01).

Conclusion: TWA was relatively common and related to RV myocardial fibrosis seen in adult patients late after the Mustard operation. This may suggest that myocardial fibrosis plays a role in the etiology of sudden cardiac death in this group of patients and warrants further investigation.

1113-241
Atrial Flutter in Adults With Congenital Heart Disease: Mapping and Long Term Outcome
Steven K. Furer, David B. Bharchuja, J. Anthony Gomes, Davendra Mehta, Mount Sinai School of Medicine, New York, NY

Background: Atrial flutter (AFL) is the most frequently encountered cardiac arrhythmia in adults with congenital heart disease (ACHD). Radiofrequency ablation (RFA) is often attempted in these patients, but the anatomical circuit and consequently, ablative therapy, may differ from AFL in patients with no underlying heart disease. This study sought to assess the AFL circuits and outcome of RFA in ACHD.

Methods: Conventional activation mapping, electro-anatomical mapping, and entrainment mapping were performed for 20 AFLs in 13 (9 female) patients with ACHD (mean age 38, range 24-67 years). All patients had previous surgical repair, for atrial septal defects, 4 for atrial septal defect, and 2 for tetralogy of Fallot. Two for transposition of the great arteries and one for ventricular septal defect. All patients presented with electrocardiographic features suggestive of AFL. Following mapping, RFA was attempted in all patients. Patients have been followed for a mean of 23 months (range 5-43 months).

Results: Based on all three mapping techniques, typical isthmus-dependent counter clockwise AFL was seen in 10 (50%) of 20 cases. RFA was attempted in these patients, but the anatomic circuit and consequently, ablative therapy, may differ from AFL in patients with no underlying heart disease. This study sought to assess the AFL circuits and outcome of RFA in ACHD.

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Background: Serum tri-iodothyronine (T3) levels are reduced following cardiopulmonary bypass (CPB), reaching a nadir 48-72 hours postoperatively. This may be physiologically important, because T3 has inotropic properties. Several studies have suggested that T3 supplementation after pediatric cardiac surgery improves clinical outcomes.

Methods: We performed a single-center, randomized, double-blinded, placebo-controlled trial of T3 supplementation in neonates undergoing either a Norwood procedure or two-ventricle repair of interrupted aortic arch. Randomization was stratified by surgeon and cardiac diagnosis. Patients were assigned to either a continuous infusion of T3 (0.05 mcg/kg/hr) or placebo for 72 hours after CPB. Primary endpoints were cardiac index (CI) 48 hours after surgery and a composite clinical outcome score consisting of death, use of inotropic support, need for postoperative ventilation, and length of hospital stay.

Results: We enrolled 42 patients (T3: 22, placebo: 20). Baseline characteristics were similar in the treatment groups. Study drug was discontinued prematurely for 2 patients in the T3 group, due to hypertension (n=1) and ectopic atrial tachycardia (n=1). Free and total T3 levels were significantly higher in the T3 as compared to the placebo group at 24, 48, and 72 hours postoperatively (p<0.001). CI was 2.11 ± 0.64 L/min/m2 (T3) versus 2.05 ± 0.72 L/min/m2 (placebo) (p<0.001). Time to achieve a negative fluid balance was shorter in the T3 as compared to the placebo group (2.05 ± 0.79 versus 2.50 ± 0.51 days, respectively) (p=0.027). No serious adverse events were attributed to T3 supplementation or placebo.

Conclusions: Neurodevelopmental outcome at one year of age was within the normal limits for most patients who underwent repair of a VSD or VSD with coarctation during infancy. Low birth weight and genetic syndromes were most predictive of lower scores. ND outcome at one year was independent of anatomic and intraoperative factors.

A Randomized, Double-Blinded, Placebo-Controlled Trial of Tri-iodothyronine in Neonatal Heart Surgery

Andrew Mackie, Karen Booth, Jane Newburger, Kimberlie Gauvreau, Peter Laussen, James Dean Nardo, Pedro del Nido, Stephen Huang, Jodi Bartlett, Ellen McGrath, Stephen Roth, Children's Hospital Boston, Boston, MA

Neurodevelopmental Outcome Following VSD Repair in Infancy


Background: Cross-sectional studies of intermediate term survivors of infant cardiac surgery have revealed a high frequency of neurodevelopmental (ND) disabilities. Little data exists regarding ND outcome of infants having surgery for ventricular septal defect (VSD).

Methods: All children < 6 months with VSD (with or without coexisting coarctation of the aorta) participating in a prospective trial assessing the effects of genetic polymorphisms on ND disabilities were eligible. Assessment at 1 year of age included the Bayley Scales of Infant Development, which yields the Mental Development Index (MDI) and Psychomotor Development Index (PDI), both with expected mean of 100 ± 15.

Results: At age 1 year, 50 (VSD alone = 36; VSD/coarctation = 14) returned for evaluation. At birth, microcephaly (head circumference <5th percentile) was present in 18%; median birth weight was 3.2 kg (range 1.6 - 5.1). Median age at surgery was 2.3 months (range 0 - 5.9). The median cumulative total support time was 66.5 minutes (range 24 - 250). 23 pts underwent at least one period of deep hypothermic circulatory arrest. Two patients required one additional operation. At 1 year, microcephaly was present in 18%. There was a confirmed or suspected genetic syndrome in 18 pts, including 4 with 22q11 deletion. The median MDI was 93 (56 - 117); 6% had scores < 70. The median PDI was 89 (50 - 117); 20% had scores < 70. Mean MDI and PDI scores were significantly lower in pts with genetic syndromes than those without (MDI: 86.4 ± 14.9 vs. 96.3 ± 8.5, p = 0.017; PDI: 77.4 ± 19.2 vs. 90.0 ± 12.2, p = 0.001). Arch obstruction had no effect on MDI or PDI. By multivariate analysis, lower birth weight predicted worse PDI score (p = 0.006) and the presence of a confirmed/suspected genetic syndrome predicted worse MDI score (p = 0.005). Age at surgery, coexisting arch obstruction and intraoperative support times were not predictive of outcome.

Conclusions: Neurodevelopmental outcome at one year of age was within the normal limits for most patients who underwent repair of a VSD or VSD with coarctation during infancy. Low birth weight and genetic syndromes were most predictive of lower scores. ND outcome at one year was independent of anatomic and intraoperative factors.

Low Preoperative Cerebral Oxygen Saturation Predicts Perioperative Mortality In Children With Congenital Heart Disease

Kathleen N. Fenton, Kimberly Glogowski, Sherrie Fogg, Katherine Freeman, Kim F. Duncan, Children's Hospital, Omaha, NE

Background: Recent studies in adults undergoing cardiac surgery indicate that monitoring the cerebral oxygen saturation (CSAT) predicts adverse neurologic events, and that making appropriate changes to correct low CSAT can improve outcome. Expected values for children with congenital heart disease have not been reported nor correlated with clinical outcome.

Methods: CSAT was continuously recorded in 98 infants and children undergoing repair of congenital heart defects on cardiopulmonary bypass. Baseline CSAT was obtained prior to induction of anesthesia. Preoperative and postoperative saturations were correlated with the patients' physiology and outcome.

Results: Patient age ranged from 2 days to 17 years. Mean CSAT was 63% at baseline and 65% hours after CPB. CSAT improved postoperatively in patients without residual left-to-right shunts (even if they were still cyanotic, Figure), but was lower postoperatively in patients undergoing Stage I palliation for single ventricle anatomy. Baseline CSAT was 41.8% in 4 patients with perioperative death compared to 63.5% in survivors (p=0.004).

Conclusions: Low baseline CSAT predicts perioperative mortality in children with congenital heart disease. Patients undergoing Stage I palliation have lower postoperative CSAT. Measurement of CSAT preoperatively will provide additional information for parental counseling, and preoperative optimization of cerebral oxygen saturation may improve outcome.

Aortic Arch Obstruction is Associated With Low Preoperative CBF in Neonates with Severe Congenital Heart Defects


BACKGROUND: Poor neurocognitive outcome in survivors of early heart surgery has become a major focus for study as the survival rate from these surgeries increases. The hypothesis of this study is that preoperative cerebral blood flow (CBF) is significantly different in neonates with aortic arch syndrome (MAS) and that this difference is associated with the severity of the cardiac anatomy.

Methods: We measured CBF in infants with CHD utilizing a novel non-invasive MRI technique termed pulsed arterial spin label perfusion MRI (PASL-pMRI) which also allows non-invasive MRA. We measured CBF in 16 infants with MAS using a non-invasive MRI technique termed pulsed arterial spin label perfusion MRI (PASL-pMRI) which also allows non-invasive MRA.

RESULTS: 60 term infants were studied, 32 were male, average weight 3.19 ± 0.53 kg (range 2.16 - 4.99), average gestational age 38.7 ± 1.2 weeks, and average head circumference (HC) 33.7 ± 1.6 cm (normal = 35cm). All patients were ventilated and sedated. Variations of 16 different CHD diagnoses were studied, including single ventricle physiology (n=33), with (n=30) or without (n=3) aortic arch obstruction. Hypoplastic left heart syndrome (HLHS, n=21) was the most common diagnosis. Baseline CBF for the entire cohort was 18.0 ± 4.7 ml/100g/min, well below the expected 50 ± 4.6 ml/min/kg. Expected values in normal term newborns and the value (20ml/100g/min) reported as a concerning increased risk for poor neurocognitive outcome. Fourteen infants (23%) had CBF below 10ml/100g/min, a level associated with moderate ischemic injury in a piglet model. Stepwise selection procedures identified the presence of aortic arch obstruction as predictive of lower baseline CBF (p=0.008).
CONCLUSION: Pre-operative CBF in infants with complex CHD is low and may be an unrecognized risk factor for poor neurocognitive development. The presence of aortic arch obstruction was identified as being associated with low resting CBF.

ORAL CONTRIBUTIONS

837 Congenital Heart Disease: Multicenter Outcomes
Tuesday, March 08, 2005, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 230D

8:30 a.m.

Quality of Life Assessment After Fontan Differences Between Children and Their Parents

Background: Quality of life (QOL) assessments are often completed by parents rather than patients. As long-term Fontan survival improves, it is important to understand how child/parent perceptions differ.

Methods: To compare child/parent QOL perceptions after Fontan and to determine if the child's age or gender affects this comparison.

Results: Of the 544 children enrolled, 352 were 10 - 19 years and 322 (91%) included child/parent dyads who completed the forms. Age was 13.9 ± 2.6 yrs, 60% were male, 153 (48%) were child scores higher than parent scores. In 4/9 domains, the size and direction of child/parent differences depended on age. No gender interactions were found.

Conclusion: Based on these differences between child/parent perceptions of QOL after Fontan, healthcare planning must include both child and parent to balance risk-taking behavior with avoidance of unnecessary restrictions.

8:45 a.m.

The Effect of Age, Diagnosis and Previous Surgery in 488 Children and Adults Who Undergo Heart Transplantation for Congenital Heart Disease

Congenital heart disease (CHD) is considered a risk factor for mortality after heart transplantation (HT) yet this unique group represents a spectrum of complexity. We sought to identify risk factors for early and late mortality after HT for CHD in infants, children and adults.

Methods: There were 488 patients transplanted for CHD from the combined Pediatric Heart Transplant Study (1993-2002, n=367) and the Cardiac Transplant Registry Database (1980-2002, n=121). The age distribution at HT was 152 patients from 6mth to 6yr (31%), 83 patients from 6yr to 12yr (17%), 139 patients from 12yr to 20yr (28%), and 113 patients >20yr (23%). The median age at HT was 12.4 yrs; range 6mth to 62 yrs.

Results: Primary HT diagnosis included: single ventricle (SV) (36%), d-transposition of the great arteries (TGA) (12%), right ventricular/atrial outflow tract obstruction (RVOTO) (10%), L-TGA (8%), ventricular/atrial septal defects (8%), LVOTO (8%), other (18%). The final major operation prior to HT included palliative surgeries in SV pts including Bidirectional Glenn shunt (26%) and Fontan (48%). Overall survival post-HT was 80% at 1 year and 70% at 5 years. By multi-variable analysis, risk factors for earlier mortality were older recipient age (p<.02), older donors with longer ischemic times (p<.0007), pre-HT Fontans (p<.003) and higher right atrial pressure (RAP) in patients without pre-HT Fontan (p<.0001). Predicted survival in Fontan patients was lower (77% and 70% at 1yr and 5yrs) vs. the non-Fontan patients (88% and 81% at 1yr and 5yrs). The effect of ischemic time was most prominent in donors above the age of 30 years. CONCLUSIONS: Patients transplanted for CHD have a good late survival especially if they survive the early post-operative period. The major surgery prior to transplant is more predictive of survival than the actual congenital diagnosis with Fontan patients having a higher early mortality. When utilizing older donors (>30 years) for recipients with CHD, care should be taken to keep the ischemic time low in order to minimize early mortality.

8:45 a.m.

837-5 Gender-Related Disparity in Surgical Mortality Among Pediatric Patients Undergoing Cardiac Surgery
Ruey-Kang Chang, Sandra Rodriguez, Maggie Lee, Thomas Kitzner, David Geffen School of Medicine at UCLA, Los Angeles, CA, CA

Background: Little is known whether sex differences in cardiovascular outcomes found in adults also exist in children who undergo surgical repair for congenital heart disease.

Methods: Statewide hospital discharge data from California in 1989-1999 were used. Children <18 years who had a procedure code (by ICD9-CM) indicating cardiac surgery were selected. The outcome variable was in-hospital death. Cardiac surgical procedures were grouped into 23 categories to adjust for risk involved with the procedures. Hospitals were divided into low (<100 cases/year) and high volume hospitals (>100 cases/year). We used logistic regression to evaluate the effect of gender on in-hospital mortality controlling for age, race and ethnicity, type of insurance, income, date and month of surgery, type of admission, hospitals case volume and various types of procedures.

Results: There were 25,420 cardiac surgery cases with 1505 in-hospital deaths, and 49 out-of-hospital deaths within 30 days, yielding a mortality rate of 6.12%. Crude mortality rates for males (6.18%) and females (6.04%) were not significantly different. However the females group had fewer neonatal operations and had more low risk procedures than males. Logistic regression showed that females, compared to males, had a significantly higher odds ratio (OR) for in-hospital mortality (OR=1.18, p<0.01) and overall (up to 30 days post-discharge) mortality (OR=1.19, p<0.01). The odds ratio for mortality was 2.28 for neonates and 1.82 for infants when compared with children >1 year. Low volume hospitals had higher mortality than high volume hospitals (OR=1.26). The risk adjusted length of hospital stay was similar between females and males.

Conclusions: Females sex is associated with 18% higher in-hospital and 30-day mortality than male sex. There was no difference in length of hospital stay between males and females. The mechanism by which female sex acts as a risk factor requires further investigation.

9:15 a.m.

837-6 U.S. Multicenter Pivotal Study of the HELEX Septal Occluder
Thomas K. Jones, Thomas E. Fagan, Evan M. Zahn, Joel L. Jacobson, Larry A. Latson, for the HELEX Septal Occluder U.S. Pivotal Study Investigators, Children’s Hosp. & Regional Medical Center, Seattle, WA

Background: The HELEX® Septal Occluder (HSO) is a low profile, double disk occluder device for percutaneous closure of secundum atrial septal defect (ASD). This study compares the safety and efficacy of the HSO to surgical repair of ASD.

Methods: Patients were enrolled (HSO arm prospectively; surgery arm prospectively/retrospectively) from 14 US sites and followed for 12 months post procedure. Investigator-reported outcomes were evaluated including clinical success (no or clinically insignificant residual shunt) and the incidence of adverse events (AE). The first 3 HSO pts at each site were considered training cases and excluded from analysis.

Results: Between 3/01 and 4/03, 132 non-training cases received a HSO and 124 had surgical repair with reduced anesthesia time and hospital stay.

Conclusions: Although stenting for branch pulmonary artery (PA) stenosis is widely accepted, little is known about the risks involved in this procedure. A retrospective multicenter study in 7 centers in The Netherlands and Belgium was performed to uncover short term complications.

9:30 a.m.

837-7 Short Term Complications of Branch Pulmonary Artery Stenting: a Multicenter Study
Maarten Witsenburg, Marc Geewitz, Menno Van Gemen, Mathias Freund, Regina Boekkamp, Daniel De Wolf, Anton Van Oort, Mele Talisma, Hanneke Takkenberg, ErasmusMC-Sophia Children’s Hospital, Rotterdam, The Netherlands, University Hospital Gasthuisberg, Leuven, Belgium

Background: Although stenting for branch pulmonary artery (PA) stenosis is widely accepted, little is known about the risks involved in this procedure. A retrospective multicenter study in 7 centers in The Netherlands and Belgium was performed to uncover short term complications.
METHODS: Tbx1 function in pharyngeal development. cre mutants allow us to delete Tbx1 expression in a tissue specific way in order to dissect cardiovascular development. For this we are using a Cre/loxP recombination system. The mice Tbx1 haploinsufficiency causes hypoplasia of the 4th pharyngeal arch arteries (PAA), an anomaly. Genetic manipulation in the mouse and mutational analysis in patients have been recorded: arrhythmia (n=9); heart failure (n=1); endocarditis (n=1, postpartum); nonsyndromic, were enrolled. Sixty-two pregnancies were observed including 12 miscarriages and 2 elective abortion. In the 48 completed pregnancies (>20 weeks of gestation, 26 women; 48 children) the following maternal clinically significant cardiac complications were recorded: arrhythmia (n=9); heart failure (n=1); endocarditis (n=1, postpartum); NYHA class deterioration (n=29, which persisted postpartum after 11 gestations) and deterioration of LV valve regurgitation (n=8: 4/6: respectively). Anhydremia during pregnancy was related to a history of anhydremia, and NYHA class deterioration was associated with a residual ASD. Deterioration left right AV valve regurgitation was only seen in the patients with pre-existing regurgitation. Non-cardiac events included gestational hypertension (n=7) and preclampsia (n=1). Assisted delivery (forceps n=5, vacuum n=4, cesarean section n=7) were necessary in 33% of pregnancies, which is high compared to the general Dutch population. Congenital defects recurred in 6 patients: AVSD associated with left sided hypoplasia (n=3), AVSD (n=1), persistent ductus arteriosus (n=1) and ostium primum or secundum ASD (n=1).

Conclusion: In this largest report, so far, we found a high incidence of clinical significant maternal and foetal complications during pregnancy in AVSD patients.

POSTER SESSION

1142 Congenital Heart Disease: Genetic and Vascular Mechanisms of Disease

Tuesday, March 08, 2005, 9:00 a.m.-11:20 p.m.
Orange County Convention Center, Hall E
Presentation Hour: 10:00 a.m.-11:00 a.m.

1142-237 Conditional Deletion Of Tbx1 Provides Insights Into The Pathogenesis Of Aortic Arch Abnormalities

Fabiana Ceratto, Huansheng Xu, Masae Morishima, Antonio Baldini, Elizabeth Lindsay, Baylor College of Medicine, Houston, TX

BACKGROUND: Di George syndrome (DGS) is a relatively frequent genetic disorder caused by an intracellular heterozygous deletion of 22q11.2. DGS is characterized by aortic arch and conotruncal defects, thymus and parathyroid aplasia/hypoplasia and craniofacial anomalies. Genetic manipulation in the mouse and mutational analysis in patients have shown that Tbx1, a T-box transcription factor has a key role in the pathogenesis of DGS. In mice, loss of Tbx1 haploinsufficiency causes hypoplasia of the aortic arch and arch arteries; while Tbx1 loss of function prevents the formation of cardiac aortic arches and arch arteries (III-9). The embryonic PKAs are later remodelled to form specific segments of the great vessels. Our goal is to understand in which tissue Tbx1 function is important for cardiovascular development. For this we are using a Cre/oop recombinase system. The cre mutants allow us to delete Tbx1 expression in a tissue specific way in order to dissect Tbx1 function in pharyngeal development.

METHODS: Here we have tested two Cre mutants: Nkx2.5cre and FoxIcre, both of which have the capability of partial mutation that partial overlap with Tbx1 expression. The latter drives more extensive recombination in pharyngeal arch epithelia than Nkx2.5cre.

RESULTS: Nkx2.5cre-driven deletion of Tbx1 results in severe outflow tract (QFT) defects like Tbx1 null mice, but a milder pharyngeal phenotype, in that the caudal arches develop apparently normally. In contrast, FoxIcre-driven deletion of Tbx1 results in severe OEF and aortic arch defects that are incompletely penetrant from those of the Nkx2.5cre mutants. Comparison of Tbx1 expression with that of the cre drivers shows the difference between FoxIcre- and Nkx2.5cre-induced deletion to be largely confined to the pharyngeal epithelia, (pharyngeal endoderm and ectoderm) while both drivers are expected to ablate Tbx1 expression in the core mesoderm of the pharyngeal arches and in the second heart field.

CONCLUSION: These results strongly suggest that expression of Tbx1 in pharyngeal epithelia is required for PAA formation.

1142-243 Intramyocardial Expression Of Cardiotrophin-1 In Infants With Congenital Cardiac Defects

Qing Mo, Kathrin Schumacher, Edith Wehage, Magda Sokalska, Felix Haase, Marie Christine Seyhaye, Aachen University of Technology, Aachen, Germany, German Heart Center Munich, Munich, Germany

Background and aim: Expression of cardiotrophin-1 (CT-1) induced by hypoxia and/or hemodynamic overload results in myocardial hypertrophy. The hypertrophic response to CT-1 involves the Jak/STAT pathway while hypoxia and CT-1 are known to act through HIF and upregulate HSPs. Therefore we aimed to examine whether CT-1 is differentially expressed in infants with congenital cardiac defects.

Methods: Fifteen infants with tetralogy of Fallot (TOF) (n=7) or with ventricular septum defect (VSD) (n=8) were enrolled. The gene- and protein expression of CT-1, HSP70, and HSP90 were detected by real-time PCR and Western blotting.

Results: Expression of CT-1, HSP70, and HSP90 was detected in all patients at mRNA and protein level. Concentrations of CT-1 were higher in infants with TOF than in those with VSD (p<0.05). Considering CT-1 mRNA concentrations with arterial oxygen saturation (Spearmann: r=-0.57, p=0.03). Levels of CT-1 and HSP70 were not significantly higher in infants with TOF than in those with VSD (p>0.05). Cleavage of caspase-3 was increased in the myocardium of patients with TOF.

Conclusions: Our results show for the first time that CT-1 is differentially expressed in the myocardium of infants with congenital cardiac defects. Over-expression of CT-1 may contribute to myocyte hypertrophy via the Jak/STAT pathway. Additionally, over-expression of CT-1 before CPB as detected in RA may play a protective role by upregulating HSPs and by preventing the activation of caspase-3 and hereby reducing apoptosis via ERK1/2 MAPK pathway.

1142-245 Rapid Screening of Complex Genetic Disorders Associated With Heart Disease Using Direct Whole Blood RT-PCR

Todd E. Miller, Lijing You, Paul J. Benke, Nanette Bishopric, University of Miami School of Medicine, Miami, FL

Background: Significant problems limit the feasibility of genetic screening for many inherited cardiovascular diseases. Affected patients are often adults, necessitating large families for linkage analysis. Disorders such as hypertrophic cardiomyopathy (HCM) and Long QT Syndrome (LQTS) are associated with multiple genes, and many of these genes are very large, with more than 15 exons. Furthermore, these disorders are characterized by multiple missense and nonsense mutations that are scattered throughout the coding sequences rather than localizing to “hot spots”. Traditional exon-based approaches are costly in terms of consuming, and genomic DNA amplification has been successfully applied in some cases, it has not been used for genotyping or screening because of the difficulty in amplifying cardiac-specific coding sequences from non-cardiac tissue and/or the need to perform cell culture to obtain sufficient mRNA.

Methods: To provide a comprehensive solution to this problem and enable wider genetic screening, we have employed a new sample collection method that optimizes the preservation of whole blood RNA templates for RT-PCR. Using this method we have been able to directly sequence mRNA transcripts of KCNQ1, KCNH2, KCNE1, KCNE2 and KCNE4 (LQT5, MYBPC3 (HCM), LAMA and TAZ (isolated cardiomyopathy) and FBN1 (Marfan Syndrome) from peripheral blood. For example, a complete coding sequence screening for mutations in FBN1, a 300 kb gene with 65 exons and a coding sequence of 8.5 kb, can be completed in 2 days using 14 PCR primer pairs. Results: To date we have sequenced 32 samples from 20 patients and 4 controls. We have detected a total of 29 heterozygous SNPs in the primary RNA sequences. All were confirmed in subsequent genomic sequencing. We have also identified 3 mutations in KCNQ1 (T1444A, F3395S, R904P), 2 in FBN1 (4904+5dsC, 6354C-T which leads to deletion of exon 51), a splicing mutation in TAZ (238G>A), and a previously identified mutation in MYBPC3 (R502Q).

Conclusions: These results demonstrate the feasibility of high-throughput screening for inherited cardiovascular genetic disorders in patients of all ages. We anticipate that this method may be extended to other genes of interest.

1142-246 Localization of Dendritic Cells and Monocytes to the Graft Matrix of Polytetrafluoroethylene Grafts Used in the Palliation of Cyanotic Heart Defects

John L. Jeffries, Debra L. Kearney, Charles D. Fraser, E. Dean McKenzie, Antonio R. Mott, Baylor College of Medicine, Houston, TX

Background: Polytetrafluoroethylene (PTFE) grafts, commonly used in the creation of aortopulmonary shunts (APS), may have compromised blood flow due to neointimal proliferation. The use of such grafts in patients with hypoplastic left heart syndrome (HLHS) who are the most common recipients of PTFE conduit are limited by the necessity of native coronary arteries and bypass grafts however recent studies challenge the traditional dogma of origin of the SMC from the native vessel wall. Other postulated sources
include transdifferentiation of circulating monocytes, bone marrow stem cells, and tissue macrophage/dendritic cells. Study populations have included adults and experimental animal models. We describe the cellular histologic profile of APS placed in infants.

**Methods:** The surgically excised distal end of the APS was formalin fixed/processed by routine histologic techniques for light microscopy. Routine H & E sections were examined as well as immunohistochemical stains for lymphocytes (Pan T and Pan B), macrophages (KP-1), dendritic cells (HLADR, S-100), and smooth muscle actin.

**Results:** Ten patients (22%) developed ARF 24-72h after CPB. Patients without ARF had a small rise in NGAL which normalized within 1d. In contrast, ARF patients had a marked increase in urine and serum NGAL, evident in the very first urine after CPB and persisting throughout the study. In ARF patients, there was a significant correlation between CPB time and peak urinary NGAL (p<0.05, r=0.65).

**Conclusion:** As a sensitive urine and serum biomarker, NGAL allows very early diagnosis of ARF after CPB. Early treatment of ARF after CPB could significantly improve outcome in high-risk patients.

**Methods:** All patients (n=72) with classic HLHS born between 8/96 and 5/02 who underwent stage I palliation at the Children’s Hospital of Wisconsin had presenting echocardiographic data reviewed for an identifiable LV cavity and patency of the MV and AoV. The patients were divided into 3 groups; AoV atresia/MV atresia (AA/MA), AoV patent/MV patent (AS/MS), and AoV atresia/MV patent (AA/MS). Chi-square test, t-test and Wilcoxon Score test were used for analysis. Actual survival analysis was done using Kaplan-Meier method with Log Rank test.

**Results:** Of the 72 patients, 75% had an AoV atresia and 44% had a patent MV. AoV atresia alone was not associated with increased mortality, however when AoV atresia was combined with a patent MV, mortality was increased (p<0.05). The groups, AA/MA (n=39), AS/MS (n=17), and AA/MS (n=16), did not differ in age or weight at the time of stage I palliation. The 30 day survival of all patients was 97% and the overall mortality to date is 21%. Thirty day survival was 100% in AA/MA, 100% in AS/MS, and 88% in AA/MS (AA/MA < AS/MS, p<0.05). Survival to stage II palliation was 95% in AA/MA, 94% in AS/MS, and 56% in AA/MS (p<0.05 for AA/MA vs AS/MS). Mortality to date is 13% in AA/MA, 18% in AS/MS, and 44% in AA/MS (p<0.05 for AS/MS).

**Conclusion:** AoV atresia was associated with increased mortality only in the presence of a patent MV. A LV with AoV atresia and a patent MV negatively impacted the survival of patients with HLHS as seen in 30 day survival, survival to stage II palliation, and mortality to date.

**Central Pulmonary Artery Growth After Central Shunt Placement in Patients With Pulmonary Atresia and Ventricular Septal Defect With Severe Pulmonary Artery Hypoplasia**

Brandy A. Kashyap, Mark W. Turpertine, Robert K. Darragh, Marcus S. Schamberger, Indiana University School of Medicine, Indianapolis, IN

**Background:** Various surgical approaches have been designed to promote pulmonary artery (PA) growth in pulmonary atresia. However, patients with severely hypoplastic pulmonary arteries (<3mm) may not be candidates for traditional palliation. Our approach is to place a central shunt from the aorta to the hypoplastic main pulmonary segment. This promotes uniform proximal and central PA growth while maintaining RV-PA continuity for future transannular repair.

**Methods:** Nine pts. with pulmonary atresia and ventricular septal defect (VSD) with severely hypoplastic PA (HPA) underwent placement of an aorto-pulmonary central shunt by the same surgeon from 1996 to 2003. Pulmonary artery growth measurements were performed on angiograms at different stages of repair and standardized using the McGoon and Nakata indices. The McGoon ratio is calculated from the diameter of the aortic valve (AoV) atresia negatively impacts survival of infants with HLHS after staged palliation.
Adults With Congenital Heart Disease: Functional Capacity and Outcomes

Tuesday, March 08, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 230D

Excerpt:

**Is Exercise Training Beneficial In Adults With Congenital Heart Disease?**

Jaspal Singh Dua, Alan Graham Stuart, Kenneth Richard Fox, Bristol Heart Institute, Bristol, United Kingdom, University of Bristol, Bristol, United Kingdom

**Background:** A wide range of health benefits are associated with regular exercise training but its influence on exercise capacity & quality of life in adults with congenital heart disease (CHD) has not been fully investigated.

**Methods:** 56 patients were recruited & divided into 3 subgroups depending upon their NYHA class. Exercise capacity was determined by treadmill walking.

**Results:** Mean age 33.1±12.7 y, NYHA I 16.2±2.2% patients reached 80% of their age predicted maximal heart rate. NYHA II 42.9±7.3% patients were defined as the inability to reach 80% of the age predicted maximal heart rate (220-age).

**Conclusions:** Is exercise training beneficial in adults with congenital heart disease (ACHD), but little is known about its comparative severity, its determining factors and prognostic implications across the spectrum of contemporary patients with ACHD.

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**Conclusions:** Is exercise training beneficial in adults with congenital heart disease (ACHD), but little is known about its comparative severity, its determining factors and prognostic implications across the spectrum of contemporary patients with ACHD.

**Is Exercise Training Beneficial In Adults With Congenital Heart Disease?**

Jaspal Singh Dua, Alan Graham Stuart, Kenneth Richard Fox, Bristol Heart Institute, Bristol, United Kingdom, University of Bristol, Bristol, United Kingdom

**Background:** A wide range of health benefits are associated with regular exercise training but its influence on exercise capacity & quality of life in adults with congenital heart disease (CHD) has not been fully investigated.

**Methods:** 56 patients were recruited & divided into 3 subgroups depending upon their NYHA class. Exercise capacity was determined by treadmill walking.

**Results:** Mean age 33.1±12.7 y, NYHA I 16.2±2.2% patients reached 80% of their age predicted maximal heart rate. NYHA II 42.9±7.3% patients were defined as the inability to reach 80% of the age predicted maximal heart rate (220-age).

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High Complication Rate During Pregnancy In Women With Atrial Corrected Complete Transposition Of The Great Arteries.

Willem Donthn, Eis Pieper, Martine Ploeg, Adriaan Voors, Jolien Roos-Hesselink, Barbara Mulder, Dirk A. van Veldhuisen, University Hospital Groningen, Groningen, The Netherlands

Background: Due to advances in surgical care, patients with D-transposition of great arteries (D-TGA), nowadays, reach childbearing age. Limited information is available regarding the potential complications during pregnancy in these women.

Methods: From the nationwide Congenital Corvilia (CONCOR) registry, 80 women with D-TGA were enrolled. Detailed records of each pregnancy were obtained after receiving written informed consent. Results were compared with results in the general population and available literature.

Results: 69 pregnancies were observed in 28 (73%) Mustard D-TGA patients: 49 completed pregnancies, 17 spontaneous miscarriages for 3 elective miscarriages. Analysis of the 49 completed pregnancies showed mostly non-cardiac complications: all cause hospitalisation (n=20, 41%), premature delivery (n=16, two twins, 31.4%), premature labour (n=12, one twin pregnancy, 24.4%), hypertensive disorders (18.4%; preeclampsia n=5, gestational hypertension n=4; premature rupture of membranes (n=7, 14.3%) and thrombo-embolic complications (n=2). Cardiac complications were also documented: clinically significant arrhythmia (n=12, 24%), NYHA class deterioration (n=17, 34.7%), persisted postpartum n=4 and heart failure (n=2). Forty-seven children (29 boys) were born alive. Four children died in utero (7.8%) and 2 died shortly after birth (3.9%). Eleven children (21.6%) were small for gestational age. No recurrence of congenital heart disease was documented.

Conclusion: In this largest report so far, pregnancy in women with atrial corrected D-TGA is not always well tolerated in contrast to current general consensus. Clinically significant, especially non-cardiac, maternal and fetal complications did occur, and significantly more often than in the general Dutch population. In counselling patients prior to a pregnancy, these results need to be discussed.

POSTER SESSION

1169 Pediatric and Congenital Heart Disease: Imaging Insights

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1169-237 Myocardial Scarring and Fibrosis in the Failing Single Ventricle After Fontan Operation: A New Insight by MRI Studies

Gautam K. Singh, Madelyn Stazzone, Pam Woodard, Brian Cupps, Sherry Lassota-Cliaxton, Michael Pasque, Glenn Foster, Joseph Billadello, Philip Ludbrook, Michael Beardslee, Achui Ludomirsky, Charles Canter, Washington University School of Medicine, St. Louis, MO

Significant numbers of patients have long term progressive ventricular failure following Fontan procedure (cavo-pulmonary and pulmonary arteries connection) in heart with single ventricle. The exact mechanism for this phenomenon is unclear. The purpose of this study was to assess if myocardial fibrosis/scarring occurred and contributed to the abnormal regional and global contractile mechanics in the single ventricle.

Methods: Ten pts with single left (ventricle) median age 20 yrs, 5 M) >10 yrs post-Fontan, who were in NYHA class I(3)/II(7) functional status, underwent dual contrast-enhanced magnetic resonances imaging for quantitative assessment of myocardial scarring. Inversion time was selected to null normal myocardium. Ventricular function was assessed by cine steady-state gradient-echo imaging and myocardial strain by myocardial tagging in pts and in 27 normal subjects (median age 29 yrs, 14 M). Eight slices of images were obtained in short axis from ventricular base to apex. Each slice was divided into 6-segments to assess regions of signal abnormality, abnormal wall motion and strain.

Results: Three patterns: diffuse, punctuate and segmental transmuaral types of scarring were seen in 62/480 segments of 9/10 pts, mostly confined to septal and adjacent segments representing 4 to 11% of LV mass. Compared to normal subjects myocardial shortening strains at midventricular level in pts (20±3%) vs.-15±5%) were significantly (p < 0.05) decreased, more in segments with (<11±2%) than without (>16±3%) scar. Scar affected segments also showed decreased thickening and abnormal wall motion. Single ventricle EF (median 42%, range 29% to 59%) was decreased as compared to normal population (65±5%).

Conclusions: Segmental and diffuse myocardial fibrosis/scarring occur at long term in Fontan-palliated single ventricles. It may contribute to abnormal contractile mechanics resulting in impaired ventricular function and progressive ventricular failure.

1169-238 Sedation for Pediatric Echocardiography: Physiologic Responses, Adverse Events, and Risk Factors

Lisa C. Heisten, Claudio Ramaciotti, William A. Scott, Melanie Coursey, Matthew S. Lemler, The University of Texas Southwestern Medical Center & Children's Medical Center, Dallas, TX

Background: The pediatric response to sedation has not been well documented, nor has the population at risk been adequately identified. Current guidelines for sedation are based on insufficient data. We reviewed our experience in a Pediatric Echocardiography Laboratory to describe the physiologic responses to sedation, incidence of adverse events, and risk factors.

Methods: We analyzed 1,095 consecutive patients sedated for echocardiography from 12/01 to 12/03. Fasting times were based on hospital policy with adjustment as clinically indicated. Risk scores were assigned using the American Society of Anesthesiologists (ASA) Classification. Oral chlorhydrate was the primary agent used. Vital signs and oxygen saturations were recorded every 5 minutes, and adverse events were recorded.

Results: The physiologic responses to sedation included decreases in heart rate (median 14%, range 0-68%) and blood pressure (median 23%, range 0-58%), with decreases <20% of baseline being 24% and 58% respectively, which was well tolerated. There were no deaths or morbidity. Adverse events included vomiting (n= 4, 0.4%), apnea (n= 3, 0.3%), airway obstruction (n= 16, 1.5%), hypoxia (n= 66, 6%), hypotension with poor perfusion (n= 4, 0.4%), and prolonged sedation (n= 36, 3%). Age < 6 months (p< 0.01), cyanotic heart disease (p< 0.01), and hospitalization at the time of study (p= 0.02) were predictive of patients with adverse events, whereas ASA score (p= 0.11), fasting time (p= 0.36), baseline oxygen requirement (p= 0.11), and use of additional sedation (p= 0.44) were not predictive. Multiple regression analysis identified only age < 6 months as a predictor for adverse events.

Conclusion: The observed reactions to pediatric sedation include decrease in heart rate and blood pressure without major deleterious effects. Our data indicate that significant adverse events are uncommon, and that current sedation practices are safe for children with either suspected heart disease. Adverse scores and fasting times do not predict risk for adverse events. Age < 6 months should be considered during risk assessment for sedated echocardiography.
Results: Use of fast field echo (FFE) produced artifact-free, high-resolution cine images to evaluate anatomy and function and T1-weighted single-shot survey imaging. SNR ratio for single-shot T1-weighted imaging of contrast enhancement at 3T was high enough for use of parallel acquisition techniques (SENSE) with acceleration factors of 2; echo times of approx. 1 ms. High quality angi or perfusion images were obtained without appearance of susceptibility artifacts during peak contrast enhancement. 2D and 3D gadolinium angiographic sequences were also shortened with parallel acquisitions. In small infants, MRI tagging with 6 mm tag-line spacing and 2 mm in-plane resolution allowed coverage of the entire cardiac cycle with less tag-line fading than at 1.5 T. FFE with steady state free precession (SSFP) was more prone to flow and chemical shift (fat/water or air/issue) artifacts than FFE without SSFP. Image susceptibility artifacts with SSFP could only be partially avoided by shimming over the heart, and only standard FFE could be useful in infants.

Conclusions: Early experience suggests significant advantages for 3T MRI in CHD.

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**1169-241 Three-Dimensional Echo Quantification of Conotruncal Areas in Human Fetal Hearts**

Aarti Weintraub-Bog, Christine S. Sahm, Rima S. Bader, Jeanne M. Baker, Laura S. Bedewit, Roja Sohary, David J. Sahm, Oregon Health & Science University, Portland, OR

**Background:** Discrete anechoic and pulmonary arterial roots develop and differentiate from a common conotruncus. 3D fetal echocardiography should be able to quantify the volumetric commitment of the outflow tract to pulmonary artery (PA) and aorta (Ao) during gestation.

**Method:** Prenatal echocardiographic images on normal fetuses referred to the perinatal unit of OHSU were done with the GE Voluson 730E 3D system using a 4-8MHz broadband curved array with mechanical rotational sweep, acquiring an optimized volume data set. Though nrogated, image acquisition is rapid enough to virtually freeze the heart in an indeterminate cardiac phase. Moving 4D loops were available during the latter part of the study. 3D/4D Sonoview® was used for tracing and measurements after navigating in the volume to recreate clean short and long axis equivalents of the outflow tracts.

**Results:** Satisfactory studies were possible in 47/61 normal fetuses (15.5-37, mean 24.5 wks gestation). Conotruncal area including Ao and PA areas in "short axis" was 0.19-2.02 cm² (mean 0.63), Ao annulus 0.13-0.91 cm (0.4 ± 0.2), PA annulus 0.14-0.92 cm (0.5 ± 0.2). There was good correlation between the "short" and "long" axis estimates of Ao and PA annulus (0.82 and 0.85). PA area exceeded Ao area throughout gestation, but the PA/Ao area ratio decreased toward term.

**Conclusions:** Differential volume commitment to each major arterial trunk persists throughout gestation, with greater PA dominance in early gestation and a tendency toward equalization towards term.

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**1169-242 Dynamic Insights Into Myocardial Function and Fluid Dynamics in Stage 14-18 Chick Embryos From High Resolution 60 MHz Real-Time Ultrasound Scanning**

David J. Sahm, Morteza Gharib, Kent L. Thornburg, Jeffrey Pentecost, Oregon Health & Science University, Portland, OR, California Institute of Technology, Pasadena, CA

**Background:** The earliest heart movements in the valveless curved embryonic heart tube were believed to be poorly synchronized and almost peristaltic.

**Methods:** We recently performed high resolution 60 MHz, 30 fps ultrasound imaging on 14-24 days chick embryos, using a VisualSonics VEO 680 system with 40 micron axial/70 micron lateral resolution. Eggs were uncooked and kept in an infrared warmer. A mound of gel was built over the embryo location and a curved transducer with a motor drive was lowered gently onto the embryo. Rotational motions of the probe allowed selective scanning of inflow and outflow areas.

**Results:** Dynamic atrioventricular coordination was seen even within 6-10 hours of the first Doppler detectable blood flow motions. In addition, sphincter-like areas defined the aortoventricular sulcus and the junction of the muscular corus with a primitive truncus arteriosus. The high speckle from nucleated red cells allowed velocity vector tracking of flow, and vorticity observations corresponded with steerable spectral pulsed Doppler to define a regurgitant flow vector across the sphincter-like constrictions where valve structures would later develop.

**Conclusions:** These dynamic observations obtainable at this early looping stage of embryonic development should provide new insights into heart formation in normal and abnormal embryos.

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**1169-245 Magnetic Resonance Angiography And Gadolinium-Enhanced Magnetic Resonance Imaging Offer A Noninvasive “One Stop” Assessment In Patients With Kawasaki Disease**

Sophie Mavrogeni, Giorgos Papadopoulos, Marouso Doukou, Savas Kaklis, Alexios Giakos, George Varlantis, John Steimn, Polixeni Nikolaidou, Chryssia Bakoula, Evangelos Karanassos, Dimosthenis Cokinos, Dennis V. Kokkinos, Onassis Cardiac Surgery Center, Athens, Greece

Coronary artery abnormalities in Kawasaki disease (KD) develop in about 15-25% of young patients, mostly in the form of aneurysms. Although the incidence of pediatric disease is low (2-3%), the mortality rate due to myocardial infarction is 22%. Magnetic resonance angiography (MRA) and coronary MRA can reliably identify coronary aneurysms in affected patients. Gadolinium-enhanced MRI (Gd-enMRI) is the gold standard for scar detection due to myocardial infarction.

The purpose of this study was: a) to measure the dimensions of coronary artery aneurysms using magnetic resonance coronary angiography (MRA) and b) to correlate the dimensions of coronary artery aneurysms measured by MRA with the presence of myocardial infarction measured by Gd-enMRI in a pediatric population.

Ten patients, aged 1-12 yrs., were studied. The maximal diameter and length of the aneurysm was recorded. Coronary MRA was performed using a 1.5 T Philips Intera CV MR scanner with two ECG-triggered pulse sequences. The first was a three-dimensional segmented k-space gradient-echo sequence (TE=2.1 ms, TR=7.5 ms, flip angle=30°, eff. slice thickness=1.5 mm) employing T2-weighted preparatory prepulse and a frequency selective fat-suppression prepulse, with free breathing. Gd-enMRI images were acquired 15 minutes after the IV injection of 0.2 mmol/kg Gd-DTPA using an inversion recovery gradient echo pulse sequence.

In 6 patients discrete aneurysms (AN) of the coronary arteries were identified, while diffuse coronary ectasia (EC) alone was present in the remaining 4 patients. Aneurysm diameter ranged from 2 to 9 mm (5.7±2.8), aneurysm length ranged from 4.4 to 16 mm (10.1±5.0), and ectasia diameter ranged from 2.5 to 4.6 mm (3.8±0.6). Transmural apical scar, due to myocardial infarction, was detected by Gd-enMRI only in one case, while small patchy necrosis was identified in another case. No correlation between aneurysm diameter or ectasia length and myocardial infarction was found.

In conclusion, MRA and Gd-enMRI is a reliable diagnostic tool in Kawasaki disease able to perform noninvasive coronary artery evaluation and infarct size detection in a single study. MRA and Gd-enMRI may prove of great value for the serial follow-up of these patients.

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**1169-246 Determinants of Aortic Root Growth in Pediatric Marfan Subjects**

Marieke Bos, Hee Park, Suzanna Vidmar, Jonathan Sterne, Martin Delatycki, Ravi Savantrayan, Robert G. Weintraub, Royal Children’s Hospital, Melbourne, Australia

**Background:** The severity of cardiovascular involvement in Marfan syndrome (MFS) determines survival but varies considerably between affected individuals. This study examines determinants of aortic root growth in pediatric Marfan subjects.

**Methods:** The study population comprised all children with Marfan syndrome seen by a single clinical genetics service between 1973 and 1991, who had at least one cardiac evaluation and echocardiogram prior to 20 years of age. Subjects were divided into groups according to whether they had a family history of severe disease (aortic dissection, early non-ischemic cardiac death or requirement for aortic surgery) in an affected
relative), a family history of mild disease or no family history (sporadic group). Serial echocardiographic aortic root measurements were standardized as Z scores, based on body surface area. Multilevel models were used to estimate the relationship between standardized aortic diameter and age, according to family history grouping, adjusting for the use of beta-blocker therapy.

**Results:** There were 131 Marfan subjects seen during this time with a mean (SD) age of 9.46 (5.22) years at first evaluation, and a mean duration of follow-up of 8.11 (6.46) years. 72 subjects had a positive family history, which was severe in 39 cases. The median number of echocardiographic examinations per patient was 5 (range 1-15). 93% of all study subjects were treated at some time with a beta-blocker. The mean rate of increase in standardized aortic diameter (Z score) was significantly higher in the sporadic and severe family history groups (0.15±year, 95% CI 0.04± to 0.27±year, and 0.11±year, 95% CI 0.04± to 0.19±, respectively), compared to the mild family history group (0.01±year, 95% CI -0.09± to 0.09±).

**Conclusions:** Among children with Marfan syndrome receiving appropriate therapy, those with sporadic disease or a severe family history manifest faster progression of aortic root dilatation, compared to those with a family history of mild disease.

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**871-5**

**Plasma B-Type Natriuretic Peptide In Children With Heart Failure**

Dana Conway, Kelley Roots, Sharada McGuire, Michael Artman, New York University School of Medicine, New York, NY

**BACKGROUND:** Plasma B-type natriuretic peptide (BNP) is an accepted marker of heart failure in adults and has recently been shown to be useful in the pediatric population. BNP has been noted to be of value not only in the diagnosis of heart failure but also to help stratify severity of illness and predict clinical outcomes. Evidence in the adult literature demonstrates that BNP values of greater than 100 pg/ml are both highly sensitive and specific for the diagnosis of congestive heart failure and cardiac dysfunction. Additionally, BNP values of greater than 400 pg/ml are predictive of severe congestive heart failure and poor clinical outcomes. The purpose of this study was to explore the clinical outcomes of children with BNP levels greater than 100 pg/ml.

**METHODS:** Plasma BNP levels were drawn in a series of 50 children, ages 0-17 years (5.5 ± 5.86 years) with varying degrees of heart failure as measured by the New York University Pediatric Heart Failure Index. Clinical outcomes were assessed 16 weeks after BNP levels were drawn.

**RESULTS:** All of the children with normal BNP levels were alive at 16 weeks follow-up. The mortality rate for children with a BNP of <100 pg/ml (n=21) was 3.2% vs 28.3% with a BNP of >100 pg/ml (n=19; p< 0.05). The mortality rate for children with a BNP of <400 pg/ml (n=39) was 5.1% vs 36.4% with a BNP of >400 pg/ml (n=11; p< 0.02) Combining both mortality and severe morbidity of heart transplant (M&M), children with a BNP of >100 pg/ml had a M&M of 3.2% vs 36.8% with a BNP of >100 pg/ml (p< 0.003).

**CONCLUSIONS:** Plasma BNP was shown to have definite diagnostic value in children with heart failure. A BNP level of 100 pg/ml is semingingly, as in adults, suggestive of severe heart failure and poor clinical outcomes. The purpose of this study was to explore the clinical outcomes of children with BNP levels greater than 100 pg/ml. Plasma BNP levels were drawn. 93% of all study subjects were treated at some time with a beta-blocker. The mean rate of increase in standardized aortic diameter (Z score) was significantly higher in the sporadic and severe family history groups (0.15±year, 95% CI 0.04± to 0.27±year, and 0.11±year, 95% CI 0.04± to 0.19±, respectively), compared to the mild family history group (0.01±year, 95% CI -0.09± to 0.09±).

**Conclusions:** Among children with Marfan syndrome receiving appropriate therapy, those with sporadic disease or a severe family history manifest faster progression of aortic root dilatation, compared to those with a family history of mild disease.

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**871-6**

**Interactive Real-Time Magnetic Resonance-Guided Atrial Septal Puncture and Atrial Balloon Septostomy are Feasible in Swine**

Amar N. Raval, Parag V. Kamarkar, Michael A. Gutman, Cengizhan Ozturk, Ranil DeSilva, Ronnie J. Aviles, Elliot R. McViegh, Ergin Atalar, Robert J. Lederman, National Heart Lung and Blood Institute/National Institutes of Health, Bethesda, MD, Johns Hopkins University, Baltimore, MD

Atrial septal puncture (ASP) guided by xray fluoroscopy (XRF) is an initial step in many procedures, including atrial balloon septostomy (ABS). Compared to XRF, interactive real-time magnetic resonance imaging (IR-MRI) using modified interventional devices offers superior tissue imaging without ionizing radiation exposure, which is harmful in children. We studied whether ASP and ABS are feasible using an IR-MRI platform. Method: 10 swine underwent IR-MRI guided ASP/ABS. Active ASP needles were inserted into 61±10F idiatri and introducer sheaths with passive tip markers. Incrementally sized 8-18mm balloon catheters inflated with 5ml Gd-DTPA were passed over an active wire for ABS after successful ASP. Interactive, simultaneous multi-slice, rapid SSFP image acquisition/reconstruction was performed. Results: ASP was successful in 10/10 animals. ABS was successfully achieved in 4/5 animals. In one case, inadvertent contrast staining of the septum caused image distortion and procedure termination. Following ABS, a left to right shunt of 1:5.1 was measured invasively Figures 1a and 1b demonstrate active needle and balloon/active wire across the inter-aural septum. Conclusion: ASP and ABS are feasible using an IR-MRI interventional platform. Further imaging and device development toward future clinical application are warranted.
871-7 Technical Aspects Of Fetal Aortic Valve Dilation
Audrey C. Marshall, Wayne Tworetzky, Lisa Bergersen, Russell W. Jennings, Louise Wilkins-Haug, Carol E. Lock, Children’s Hospital, Boston, MA, Brigham and Women’s Hospital, Boston, MA

**Background:** Aortic valve dilation in the second trimester fetus with aortic stenosis and left ventricular dysfunction is feasible, and may prevent progression to hypoplastic left heart syndrome. Technical characteristics of successful valvuloplasty have not been described in detail.

**Methods:** We reviewed procedures performed on 26 fetuses between 21 and 31 weeks gestation. Dilations were carried out with commercially available equipment through a 19G introducer cannula. A limited laparotomy was performed for uterine exposure in 12/26 (46%) of cases.

**Results:** Technical success was achieved in 20 cases (77%). The diameter of the fetal aortic annulus ranged from 2.0 to 4.5mm (median 2.9mm). Neither gestational age nor aortic annulus size was associated with technical success. Dilating the valve with balloons averaging 110% of the aortic annulus diameter, improved antegrade flow was seen in all technically successful cases. Moderate to severe aortic regurgitation (AR) occurred in 5 cases. In each of these cases, AR improved prior to delivery. Use of a novel catheter-marking system resulted in an average intracardiac procedure time of 7 min 9 seconds.

**Conclusions:** Fetal aortic valvuloplasty has been performed with technical success in 20 of 26 fetuses between 21 and 31 weeks gestational age. A balloon:annulus ratio of 1.1:1 resulted in improvement in antegrade flow, with at least moderate AR occurring in 25% of cases. This AR appears to be well tolerated and can improve over time. These findings suggest that the stenotic fetal aortic valve responds uniquely to balloon valvuloplasty.