Editorial

A welcome to the new journal, International Journal of Cardiology — Heart and Vessels (IJC-H + V)

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ABSTRACT

A new journal has been launched: IJC — Heart and Vessels [1]. It builds upon the success of the main journal International Journal of Cardiology. As an introduction to the new journal we will be publishing a series of summaries of the topics to be covered, highlighting the most important papers in the field that have been published recently in the main journal, International Journal of Cardiology. This article describes a topic review of congenital heart disease. IJC has become one of the most important sources of quality papers in this field and many excellent publications have been published in the main journal. The expansion of space occasioned by the launch of IJC — Heart and Vessels will allow us to publish more high quality papers in the expanding field of congenital heart disease.

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Cardiovascular manifestations of mucopolysaccharidosis type VI (Maroteaux–Lamy syndrome)

The aim of the article is to gather and summarize the published data about the incidence, course of illness, treatment possibilities and complications of cardiovascular disorders in patients with mucopolysaccharidosis type VI (MPS VI) also known as Maroteaux–Lamy syndrome. MPS VI is a lysosomal storage disorder caused by deficient activity of N-acetylogalactosamine-4-sulfatase leading to progressive intracellular accumulation of glycosaminoglycans. The relatively low birth prevalence ranging from 1 in 43,000 to 1 in 1.5 million births mirrors the limited descriptions of the cardiovascular disorders in the medical literature. Patients with MPS VI can be specifically treated with enzyme replacement therapy. Extra-cardiac features include growth retardation, coarse facial features, stiff joints, skeletal malformations (dysostosis multiplex), respiratory problems, corneal clouding, and hepatosplenomegaly. The clinical presentation varies considerably, however the development of heart disease and cardiac dysfunction is a serious problem in the majority of patients. The most characteristic cardiac presentation is valvular disease, while other MPS VI patients also develop cardiomyopathy, fibroelastosis, pulmonary hypertension, cardiac conduction system disorders and other complications. There are also reports on acute heart failure. Early cardiovascular manifestation may escape detection since joint stiffness or skeletal malformations limit maximal exercise levels and respiratory system involvement may mask the underlying cardiac insufficiency. A correct and timely diagnosis offers the possibility of disease-specific treatment leading to sustained clinical benefits for cardiac and non-cardiac MPS VI manifestations [2].

Clinical outcomes of adult survivors of pulmonary atresia with intact ventricular septum

Background

There are no studies on the long term clinical outcomes and complications in the adult patient with pulmonary atresia with intact ventricular septum (PA/IVS). This study reviews our experience with a limited group of adult survivors of PA/IVS seen in our adult congenital clinics.

Methods

Twenty adult patients with PA/IVS (1998 to 2009) were identified from Mayo Clinic adult congenital heart disease databases. Surgical history and clinical outcomes were reviewed.

Results

Mean age at last evaluation was 29 years (19–39 years). There were five deaths within the study period (1998–2009). Median age at death
was 32 years (30–37 years). Seven patients underwent the Fontan operation, eight patients had a biventricular repair, and five patients remained with palliative shunts. All patients required re-interventions in adulthood. Tricuspid valve (TV) (n = 5), pulmonary valve (PV)/ conduit (n = 6), and mitral valve (n = 2) replacements were the most frequent re-intervention in the biventricular repair subset. Atrial arrhythmias were present in 80% of the total cohort, the highest rate among Fontan repairs (n = 7) and biventricular repairs (n = 7). Ventricular arrhythmias occurred in 15% of the cohort.

Conclusions

Although limited in number, the adult PA/IVS patients in this series continue to have high rates of morbidity and mortality, with arrhythmias and need for re-operations as the major causes. Patients with biventricular repairs had the highest re-intervention rate in adulthood. While this subset of patients might not be representative of all adult PA/IVS survivors, continued follow-up at centers with expertise in adult congenital cardiology is recommended for all patients [3].

Aortic and left ventricular remodeling in patients with bicuspid aortic valve without significant valvular dysfunction: a prospective study

Background

Bicuspid aortic valve (BAV) represents the most common cardiac congenital malformation in the adult age. It is frequently associated with dilatation, aneurysm and dissection of the ascending aorta. The purpose of the following study was to evaluate in patients with BAV: 1) the elastic properties of the ascending aorta, 2) the mechanical function of the left ventricle and 3) stiffness, elasticity and strain of the epi-aortic vessels wall.

Methods

Forty BAV patients (28 M/12 F; age 20.9 ± 4.7 years; range 17–26) with no or mild valvular impairment were recruited with 40 control subjects (25 M/15 F; age 23.4 ± 3.4 years; range 15–31) matched for age, gender and body surface area (BSA). Aortic strain, aortic distensibility (AoDIS) and aortic stiffness index (AoSI) were derived. Left ventricular strain was acquired. Elastic properties of epi-aortic vessels were evaluated.

Results

BAVs vs. controls had increased systolic and diastolic aortic diameters (p < 0.001). Aortic strain (%) was lower in BAVs than in controls (8.3 ± 3.6 vs. 11.2 ± 2.6; p < 0.001) as well as AoDIS (10(−6)cm(2) dyn(−1)) (6.5 ± 2.8 vs. 8.8 ± 2.9; p = 0.002), while AoSI was greater in BAVs (6.4 ± 3.5 vs. 3.9 ± 1.2; p < 0.001). Both AoDIS and aortic strain were related to aortic size in BAVs and controls. Left ventricular longitudinal (p = 0.01), circumferential (p = 0.01) and radial (p < 0.001) strains (%) were lower in BAVs. No significant differences were found in elastic properties of epi-aortic vessels.

Conclusions

Bicuspid aortic valve is associated with an increased aortic stiffness and with a reduction of the aortic and left ventricular deformation properties. Epi-aortic vessels do not seem to be interested by the disease. The use of an echocardiographic method that can estimate the degree of aortic and left ventricular remodeling can provide great benefits in the selection of patients with BAV to be treated and in determining the time for beginning drug therapy [4].

Post-interventional three-dimensional dark blood MRI in the adult with congenital heart disease

Background

Investigate a novel three-dimensional (3D) turbo spin echo (TSE) magnetic resonance imaging (MRI) sequence to assess stented segments in adults with congenital heart disease (CHD) after transcatheter intervention.

Methods

Adults with CHD referred for computed tomography (CT) after transcatheter intervention underwent MR exam with a 3D respiratory gated TSE sequence. Data obtained at the time of the study included type of CHD, radiation dose, length of time between exams, and luminal diameters of stented segments from each exam. Continuous variables were analyzed using Student’s t and Bland–Altman plots performed to analyze measurements obtained from both examinations.

Results

Eleven patients underwent both examinations. Type of defects included Coarctation of the Aorta (n = 6) and Tetralogy of Fallot. The average radiation dose was 19.6 mSv and the average time between CT and MRI was 99 ± 160 days. Luminal diameters of stented segments correlated closely between TSE MRI and CT (r(2) = .85) with a bias toward overestimation with MRI (mean 22.4 ± 4.3 mm and 20.9 ± 3.7 mm, p < .01).

Conclusion

This novel 3D respiratory gated TSE MR technique provides a feasible method to reduce metallic artifact and improve visualization of stented segments and surrounding anatomic structures without exposure to radiation [5].

Structure and process measures of quality of care in adult congenital heart disease patients: a pan-Canadian study

Background

There are more adults than children with congenital heart disease. Of over 96,000 ACHD patients in Canada, approximately 50% require ongoing expert care. In spite of published recommendations, data on the quality of care for ACHD patients are lacking.

Methods

Survey methodology targeted all Canadian Adult Congenital Heart (ACH) network affiliated ACHD centers. Clinics were asked to prospectively collect outpatient and procedural volumes for 2007. In 2008, centers were surveyed regarding infrastructure, staffing, patient volumes and waiting times.

Results

All 15 CACH network registered centers responded. The total number of patients followed in ACHD clinics was 21,879 (median per clinic = 1132 (IQR: 585, 1816)). Of the total 80 adult and pediatric cardiologists affiliated to an ACHD clinic, only 27% had received formal ACHD training. Waiting times for non-urgent consultations were 4 ± 2 months, and 4 ± 3 months for percutaneous and surgical procedures. These were beyond Canadian recommended targets at 11 sites (73%) for non-urgent consultations, at 8 sites (53%) for percutaneous interventions and 13 sites (87%) for surgery.
Conclusions

Of a minimum number of 96,000 ACHD patients in Canada, only 21,879 were being regularly followed in 2007. At most sites waiting times for ACHD services were beyond Canadian recommended targets. In spite of universal health care access, published guidelines for ACHD patient structure and process measures of health care quality are not being met [6].

Factors associated with surgery for active endocarditis in congenital heart disease

Background

Despite the recent progress of cardiac surgery, the indications for surgical intervention during the active phase of infective endocarditis have not yet been established in patients with congenital heart diseases due to the limited number of such patients. The present study aims to determine the surgical indications for active infective endocarditis in congenital heart diseases.

Methods

A retrospective observational cohort multi-center study on infective endocarditis with congenital heart diseases was conducted from January 1997 to December 2001 in Japan and 239 patients were registered. Sixty-one (26%) of the 239 patients had undergone surgical therapy for active infective endocarditis, which was defined as cardiac surgery during administration of intravenous antibiotics.

Results

There were 7 deaths (11%). A univariate regression analysis revealed that the factors significantly associated with the need for surgical intervention for active IE were the lack of diagnosis of cardiac disorders before the onset of infective endocarditis, aortic valve infective endocarditis, perivalvular abscess, presence of heart failure, and change of antibiotics. A stepwise logistic regression analysis revealed that the presence of a perivalvular abscess, and heart failure and a change in the antibiotics were independent determinant factors for the need for surgical treatment of active infective endocarditis in patients with congenital heart diseases.

Conclusions

Surgery should therefore be considered even during the active phase in patients with congenital heart diseases and infective endocarditis, when they develop associated with heart failure, a perivalvular abscess, or the need for a change in antibiotics [7].

The applications of non-ECG-gated MSCT angiography in children with congenital heart disease

Background

To minimize radiation exposure during a multi-slice computed tomography (MSCT) examination in children with congenital heart disease (CHD), we assessed diagnostic value and the various applications of MSCT without electrocardiography (ECG)-gated image acquisition.

Methods

Three-dimensional (3D) images were reconstructed to include volume rendering and differential color-coding of the arteries and veins. The vessel diameter in MSCT was measured with CT attenuation profiles and compared with that of angiography. Ventricular volumetry was initially validated by phantom experiment and followed by comparison with that of cine-angiography (n = 15). Simulation for surgical operation was performed to evaluate the possibility of an intraventricular conduit in patients diagnosed with a double outlet right ventricle.

Results

Differential color-coding was able to provide accurate and understandable anatomical structure in CHD. The diameter of the descending aorta measured in MSCT correlated well with the values obtained by angiography (r(2) = 0.86). According to the results of the phantom experiment, ventricular volume was studied in patients whose heart rate was faster than 120 beat/min. The left and the right ventricular volumes in MSCT correlated well with values obtained by cine-angiography (r(2) = 0.98 for RV, r(2) = 0.94 for LV). Simulative operation of intraventricular rerouting provided appropriate indication for biventricular repair in patients diagnosed with a double outlet right ventricle.

Conclusions

Non-ECG-gated MSCT angiography is applicable for precise anatomical diagnosis, ventricular volumetric study, and simulation surgery in children with CHD [8].

Hypoxia in early life is associated with lasting changes in left ventricular structure and function at maturity in the rat

Background

There is a growing population of adults with repaired cyanotic congenital heart disease. These patients have increased risk of impaired cardiac health and premature death. We hypothesized that hypoxia in early life before surgical intervention causes lasting changes in left ventricular structure and function with physiological implications in later life.

Methods

Sprague-Dawley rats reared initially hypoxic conditions (FiO(2) = 0.12) for days 1–10 of life were compared to rats reared only in ambient air. Cellular morphology and viability were compared among LV cardiomyocytes and histological analyses were performed on LV myocardium and arterioles. Intracellular calcium transients and cell shortening were measured in freshly-isolated cardiomyocytes, and mitochondrial hexokinase 2 (HK2) expression and activity were determined. Transthoracic echocardiography was used to assess LV function in anesthetized animals.

Results

Cardiomyocytes from adult animals following hypoxia in early life had greater cellular volumes but significantly reduced viability. Echocardiographic analyses revealed LV hypertrophy and diastolic dysfunction, and alterations in cardiomyocyte calcium transients and cell shortening suggested impaired diastolic calcium reuptake. Histological analyses revealed significantly greater intima-media thickness and decreased lumen area in LV arterioles from hypoxic animals. Alterations in mitochondrial HK2 protein distribution and activity were also observed which may contribute to cardiomyocyte fragility.
Conclusions

Hypoxia in early life causes lasting changes in left ventricular structure and function that may negatively influence myocardial and vascular responses to physiological stress in later life. These data have implications for the growing population of adults with repaired or palliated cyanotic congenital heart disease [9].

End-of-life in adults with congenital heart disease: a call for early communication

Background

We investigated preferences of adults with congenital heart disease (CHD) and their health care providers regarding end-of-life (EOL) communication.

Methods

Adult CHD outpatients and health care providers completed surveys about preferences for and experiences with EOL communication. Responses were compared between patients and providers.

Results

Two hundred patients (18–79 years) and 48 CHD health care providers (primarily cardiologists) completed surveys. Only 2 patients (1%) indicated that they had discussed EOL planning with their medical team. In contrast, 50% of providers reported that they typically discuss issues including life expectancy, advance planning, and resuscitation preferences with their outpatients. Seventy-eight percent (156/199) of patients wanted their medical team to raise EOL issues; this preference was independent of disease complexity and socio-demographic factors. In contrast, providers reported that their EOL discussions increase in accordance with disease complexity (p < 0.001). Early initiation of EOL discussions, before diagnosis with life-threatening complications, was favored by 62% of patients but only 38% of providers (p < 0.001).

Conclusion

Health professionals caring for adults with CHD should explore preferences of their patients for EOL discussions earlier in the disease course, and not only with patients facing life-threatening complications and/or with complex conditions. When EOL discussions do occur, health care providers should attempt to ensure that patients better understand these conversations. Increased attention to EOL issues is proposed in order to improve the care of patients with CHD across the lifespan [10].

Bosentan–sildenafil association in patients with congenital heart disease-related pulmonary arterial hypertension and Eisenmenger physiology

Objectives

The aim of the present study was to evaluate the safety, tolerability, and clinical and haemodynamic impacts of add-on sildenafil in patients with congenital heart disease (CHD)-related pulmonary arterial hypertension (PAH) and Eisenmenger physiology after failure of oral bosentan therapy.

Methods

Thirty-two patients with CHD-related PAH (14 male, mean age 37.1 ± 13.7 years) treated with oral bosentan underwent right heart catheterization (RHC) for clinical worsening. After RHC, all patients received oral sildenafil 20 mg thrice daily in addition to bosentan. Clinical status, resting transcutaneous oxygen saturation (SpO2), 6-minute walk test (6MWT), serology and RHC were assessed at baseline (before add-on sildenafil) and after 6 months of combination therapy.

Results

Twelve patients had ventricular septal defect, 8 atrio-ventricular canal, 6 single ventricle, and 6 atrial septal defect. 28/32 had Eisenmenger physiology and 4 (all with atrial septal defect) did not. All patients well tolerated combination therapy. After 6 months of therapy, an improvement in clinical status (WHO functional class 2.1 ± 0.4 vs 2.9 ± 0.3; p = 0.042), 6-minute walk distance (306 ± 51 vs 293 ± 68 m; p = 0.005), SpO2(2) at the end of the 6MWT (72 ± 10 vs 63 ± 15%; p = 0.047), Borg score (2.9 ± 1.5 vs 4.4 ± 2.3; p = 0.036), serology (pro-brain natriuretic peptide 303 ± 366 vs 760 ± 943 pg/mL; p = 0.008) and haemodynamics (pulmonary blood flow 3.4 ± 1.0 vs 3.1 ± 1.2 L/min/m2, p = 0.002; pulmonary vascular resistances index 19 ± 9 vs 24 ± 16 WU/m2, p = 0.003) was observed.

Conclusions

Addition of sildenafil in adult patients with CHD-related PAH and Eisenmenger syndrome after oral bosentan therapy failure is safe and well tolerated at 6-month follow-up, resulting in a significant improvement in clinical status, effort SpO2(2), exercise tolerance and haemodynamics [11].

Right ventricular–left ventricular interaction in adults with Tetralogy of Fallot: a combined cardiac magnetic resonance and echocardiographic speckle tracking study

Objectives

To assess ventricular dysfunction and ventricular interaction after repair of Tetralogy of Fallot (ToF) employing echocardiography speckle-tracking and cardiac magnetic resonance imaging (CMR).

Background

Severe pulmonary regurgitation and right ventricular (RV) dysfunction are common after repair of ToF and may also affect the shape and function of the left ventricle (LV). Recent studies suggest that LV dysfunction may be of particular prognostic value.

Methods and results

Twenty-one consecutive adults with repaired ToF (15 male, mean age 38 ± 11 years, 7 with severe PR) underwent a comprehensive echocardiographic exam including speckle-tracking analysis, CMR and cardiopulmonary exercise testing. Twenty-one subjects without relevant heart disease served as controls. Echocardiographically measured RV diameters correlated with RV volumes obtained from CMR (r = 0.63; p = 0.006). In addition, a close correlation was found between RV and LV functions on CMR (r = 0.74, p = 0.002), speckle-tracking LV and RV peak longitudinal 2D strain (r = 0.66, p = 0.003) and mitral and tricuspid annular plain systolic excursion (r = 0.71, p = 0.0003). While LV ejection fraction was normal in the majority of patients and not different from controls, LV longitudinal strain was significantly reduced in ToF patients (−16.5 ± 3.3 vs. −20.5 ± 2.7%, p = 0.0001).
Conclusion

Left and right ventricular function both by CMR and speckle-tracking is interrelated in adults with repaired ToF. Despite normal LV ejection fraction, 2D longitudinal strain is significantly reduced in ToF patients, suggesting subclinical LV myocardial damage. Considering the potential prognostic value of LV dysfunction in ToF, this measurement may gain importance and should be included in future outcome studies [12].

Outcome of direct current cardioversion for atrial arrhythmias in adults with congenital heart disease

Objectives

We sought to evaluate safety, efficacy, and outcome of direct current cardioversion (DCCV) for atrial arrhythmias in adults with congenital heart disease (CHD).

Background

Atrial arrhythmias are increasingly noted in adults with CHD. The outcome of DCCV for atrial arrhythmias in this population is unknown.

Methods

Our study was a retrospective review of patients 18 years or older with CHD who underwent DCCV between June 2000 and July 2003. This constituted the CHD group. Patient characteristics reviewed included the specific cardiac diagnosis and arrhythmia history. A subset of patients had transesophageal echocardiography (TEE) before DCCV; this subset was reviewed to evaluate spontaneous echocardiographic contrast. The outcome data evaluated included success of DCCV, complications, recurrence of arrhythmia, antiarrhythmic medication use, electrophysiology or pacemaker procedure in follow-up, and all-cause mortality. The recurrence rate of the arrhythmia was compared to a control group consisting of an age, gender, and rhythm matched group of patients who have no CHD and who underwent DCCV for atrial arrhythmias.

Results

Sixty-three patients in the CHD group underwent 80 DCCVs, 59 of which were TEE-guided. Atrial flutter was more common in the CHD group (37 of 80 DCCV, 46%) than in the control group (13 of 56, 23%) (p < 0.001). DCCV was successful in 75 (94%). Mean follow-up was 387 days. No thromboembolic events were noted. All-cause mortality on follow-up was 11%. There was no death related to DCCV. Twenty-five patients in the CHD group (40%) remained in sinus rhythm throughout follow-up. This was similar to that observed in the control group (30/56, 54%, p = 0.13). Recurrent arrhythmia in the CHD group was predicted by the presence of atrial fibrillation (p = 0.009) and less spontaneous echo contrast in the left atrium (p = 0.05).

Conclusions

DCCV with appropriate anticoagulation is safe and effective for patients with CHD, even in the presence of an intracardiac shunt and spontaneous contrast on TEE. However, the recurrence rate is substantial. Spontaneous echo contrast in the left atrium along with atrial fibrillation predicts arrhythmia recurrence following DCCV in patients with CHD [13].

Circumstances of death in adult congenital heart disease

Background

Circumstances of death have been described for various cardiovascular diseases, but this study is the first for adults with congenital heart disease (CHD).

Methods

Review of medical records and additional information from treating cardiologists and general practitioners, for circumstances of all deaths in a national registry of over 8000 adults with CHD.

Results

Of 8995 patients, 231 (2.7%) patients died over 26,500 patient years. Main causes of death were progressive heart failure (26%) and sudden cardiac death (22%). Mortality was highest in the northern, most rural region of the country (p ≤ 0.05). Overall, death occurred out-of-hospital in approximately 35%, but more frequently in rural than in urban areas (35% versus 32%, p ≤ 0.05). Mortality was almost equally distributed throughout the seasons, although fall showed a slightly higher mortality rate. Cardiovascular death occurred suddenly in nearly 40%. Sudden cardiovascular death occurred in 8% during exercise, and most often out-of-hospital (62%). Of non-sudden cardiovascular deaths 18% had occurred out-of-hospital.

Conclusion

In adult patients with congenital heart disease, mortality shows substantial regional and subtle seasonal variation. Death usually occurs at rest; approximately 1 of 10 sudden cardiovascular deaths occurs during exercise [14].

Minor symptoms of depression in patients with congenital heart disease have a larger impact on quality of life than limited exercise capacity

Objective

In patients with congenital heart disease quality of life is only marginally associated with exercise capacity. The aim of this study was to determine the prevalence of depression and its impact on quality of life and exercise capacity.

Patients and methods

From November 2007 to October 2009 a total of 767 patients (352 female, 14–67 years) with various congenital heart diseases (37 palliated/native cyanotic, 57 Fontan, 74 Transposition of the Great Arteries (TGA) after atrial switch, 50 other TGA, 136 Fallot, 38 Ebstein, 47 Pulmonic stenosis/regurgitation, 68 aortic coarctation, 103 aortic stenosis, 90 isolated shunts, 67 other) completed the health-related quality of life questionnaire SF-36 and the German translation of the “Center for Epidemiologic Studies Depression Scale” (CES-D) to assess depressive symptoms. Afterwards a cardiopulmonary exercise test was performed.

Results

Only 66 patients (8.6%) showed depressive symptoms fulfilling the CES-D definition for depression. The total prevalence of depression was lower than in the general population (Wilcoxon test, p < 0.001) and did not differ substantially in between the diagnostic subgroups (Kruskal–Wallis test, p = 0.195). CES-D score was correlated to all of...
the nine dimensions of quality of life \((r = -0.170\) to \(r = -0.740, p < 0.001)\) and less pronounced to exercise capacity \((r = -0.164, p < 0.001)\). Correlation of peak oxygen uptake to quality of life was weaker than the CES-D scores in all subscales of life quality.

Conclusions

Patients with congenital heart disease are rarely depressive. However, even minor depressive symptoms have a stronger impact on quality of life than limited exercise capacity as seen in many patients [15].

Validation of an animal model of right ventricular dysfunction and right bundle branch block to create close physiology to postoperative tetralogy of Fallot

Background

In the past 5 years a few number of studies and case reports have come out focusing on biventricular (BiV) stimulation for treatment of congenital heart disease related ventricular dysfunction. The few available studies include a diverse group of pathophysiological entities ranging from a previously repaired tetralogy of Fallot (ToF) to a functional single ventricle anatomy. Patient's status is too heterogeneous to build important prospective study. To well understand the implication of prolonged electromechanical dyssynchrony we performed a chronic animal model that mimics essential parameters of postoperative ToF.

Methods

Significant pulmonary regurgitation, mild stenosis, as well as right ventricular outflow tract (RVOT) scars were induced in 15 piglets to mimic repaired ToF. 4 months after hemodynamics and dyssynchrony parameters were compared with a control group and with a population of symptomatic adult with repaired ToF.

Results

Comparing the animal model with the animal control group on echocardiography, RV dilatation, RV and LV dysfunction, broad QRS complex and dyssynchrony was observed on the animal model piglets. Moreover, epicardial electrical mapping showed activation consistent with a right bundle branch block. The animal models displayed the same pathophysiological parameters as the post ToF repair patients in terms of QRS duration, pulmonary regurgitation biventricular dysfunction and dyssynchrony.

Conclusion

This chronic swine model mimics electromechanical ventricular activation delay, RV and LV dysfunction, as in adult population of repair ToF. It does appear to be a very useful and interesting model to study the implication of dyssynchrony and the interest of resynchronization therapy in ToF failing ventricle [16].

Measures of exercise capacity in adults with congenital heart disease

Background

Exercise capacity in grown-ups with congenital heart disease (GUCH) is mostly reported by peak oxygen consumption (peak VO(2)). Our aim was to evaluate the maximal character of exercise tests, and to investigate submaximal measures of exercise capacity.

Methods

Adults with Coarctation of the Aorta (CoA, \(n = 155\)), Tetralogy of Fallot (ToF, \(n = 98\)), dextro-Transposition of the Great Arteries (dTGA, \(n = 68\)) and Univentricular Heart (UVH, \(n = 10\)), and 122 healthy adults performed cardiopulmonary exercise testing until exhaustion. Gas exchange was measured breath by breath. The maximal performance of the test was evaluated by respiratory exchange ratio (RER), ventilatory equivalent for oxygen and Borg scale. Oxygen uptake efficiency slope (OUES), VE/VCO(2) slope and VO(2)/WR slope were calculated and ventilatory anaerobic threshold (VAT) was defined. Correlations of these measures with peak VO(2) were calculated.

Results

GUCH showed significantly lower peak VO(2) than controls \((p < 0.001)\), declining from 80% in COA, 74% in ToF, 64% in dTGA, to 55% in UVH. Compared to the suggested criteria, mean peak RER and median Borg scale indicated a maximal effort in GUCH, however these results were significantly lower than controls \((p < 0.05)\). OUES, VO(2)/WR slope and VAT were significantly lower in patients compared to controls. OUES \((r = 0.853)\) and VAT \((r = 0.840)\) correlated best with peak VO(2); VO(2)/WR slope \((r = 0.551)\) and VE/VCO(2) slope \((r = -0.421)\) correlated to a lesser degree \((p < 0.001)\).

Conclusion

The investigated GUCH show reduced exercise tolerance compared to controls, related to the underlying heart defect. Different expressions of exercise tolerance clearly reveal the same differences in exercise capacity across groups of GUCH [17].

The prevalence and risk factors for cholelithiasis and asymptomatic gallstones in adults with congenital heart disease [18]

Purpose

Cyanosis is considered to be a risk factor for cholelithiasis which is an important complication of cyanotic congenital heart disease (CCHD) in adults. In this study, the prevalence of cholelithiasis and asymptomatic calcium bilirubinate gallstones was evaluated in adults with congenital heart disease (CHD). Furthermore, risk factors for this potentially high risk complication were assessed.

Materials and methods

Subjects were derived from 114 consecutive congenital patients who visited our center from May 2008 to January 2009. For analyses of risk factors, we divided them into 4 groups: group A, 15 CCHD patients without reparative surgery \(7\) men, 31.8 ± 7.0 years old); group B, 41 CCHD patients rendered acyanotic by reparative surgery \(21\) men, 32.5 ± 11.8 years old); group C, 23 unoperated acyanotic CHD patients \(11\) men, 42.4 ± 16.4 years old); and group D, 35 patients who were acyanotic before and after operation \(18\) men, 36.3 ± 14.8 years old). Gallstones were identified by abdominal ultrasound and risk factors were analyzed by a multivariate logistic regression model.

Results

Cholecystectomy was performed in 5/114 (4.3%), asymptomatic gallstones were seen in 16/114 (14%), and symptomatic gallstones except for patients after cholecystectomy were seen in 7/114 (6.1%). In group A, 4 patients (27%) with gallstones underwent cholecystectomy \((p < 0.01)\). Non-cholesterol gallstones were observed in 5 patients (33%) in group A, 12 patients (29%) in group B, nobody in group C, and 3 patients (8.6%) in group D. By a multivariate logistic regression model,
CCHD by nature regardless of repair, prolonged cyanosis periods, higher frequency of cardiopulmonary bypass (CPB), and lower platelet counts were significant factors predicting gallstones (odds ratio 4.48, 10.8, 3.96, and 0.87, 95% CI, 1.14–17.5, 1.00–1.18, 1.65–9.54, and 0.75–0.99, respectively).

**Conclusion**

The prevalence of cholelithiasis and asymptomatic gallstones is significantly high in CCHD patients regardless of cardiac repairs. CCHD by nature, prolonged cyanosis durations, high frequency of CPB and low platelet counts have influences on gallstone formation in adults with CHD.

**Mortality in adult congenital heart disease: are national registries reliable for cause of death?**

**Background**

Statistics on cause-specific mortality are important for prognostic research. The aim of this study was to assess the utility of the national mortality registry in research on causes of death in adult patients with congenital heart disease (CHD).

**Methods**

The CONCOR registry of over 10,000 adults with CHD was used to verify the causes of death provided by the WHO guidelines based national mortality registry, by linkage.

**Results**

Of 7277 patients linked to the national mortality registry, 196 (2.4%) were recorded deceased, versus 228 deceased patients (3.1%) recorded in the CONCOR registry, during a follow-up of 25,900 patient years. Median age at death was 48.9 years. Of all deaths in the CONCOR registry, 77% had a cardiovascular origin; nearly 50% were due to progressive heart failure and arrhythmias. The national mortality registry recorded death due to progressive heart failure and arrhythmias in only 8.5%. Moreover, this registry recorded death with an ‘unspecified’ cause in approximately 30%, primarily containing patients who died due to progressive heart failure and arrhythmias according to their medical records.

**Conclusion**

WHO guidelines based national mortality registries lack the specificity and completeness needed for accurate research on causes of death in adult patients with CHD [19].

**Prediction of complications in pregnant women with cardiac diseases referred to a tertiary center**

**Background**

Prediction of adverse maternal and neonatal events in women with heart disease is not well established. We aimed to assess cardiac, obstetrical and neonatal complications in pregnant women with congenital heart disease referred to our tertiary care center and validate a previously proposed risk index.

**Methods**

We included 227 women with cardiac disease followed for 312 pregnancies at our tertiary center from 1992 to 2007. Cardiac risk was assessed using the previously proposed Cardiac Disease in Pregnancy (CARPREG) score and its association with maternal and neonatal outcomes was determined.

**Results**

Maternal cardiac lesions were predominantly congenital (81.4%). CARPREG risk was low (score = 0) in 66.3% and intermediate (score = 1) in 33.7% pregnancies. Maternal cardiac events complicated 7.4% pregnancies, with pulmonary edema occurring most frequently (3.8%). An intermediate score was associated with a higher rate of cardiac events (19.0% vs. 1.4%, odds ratio [OR] 15.6, 95% confidence interval (95%CI) 4.5–54.4, p < 0.0001). Adverse events occurred in 27.5% neonates. Preterm deliveries occurred in 16.7% pregnancies, more commonly in patients with intermediate scores (OR 2.4, 95%CI 1.2–4.6, p = 0.01). The sensitivity and negative predictive values of a low score were respectively 87% and 99% for total cardiac events and both 100% for primary cardiac events including pulmonary edema and sustained arrhythmia.

**Conclusion**

The CARPREG risk index has a high sensitivity and negative predictive value with regards to cardiac complications in pregnant women with heart disease. It may, therefore, be routinely used to improve the assessment of cardiac risk before and during pregnancy [20].

**Pulmonary valve replacement in chronic pulmonary regurgitation in adults with congenital heart disease: impact of preoperative QRS-duration and NT-proBNP levels on postoperative right ventricular function**

**Background**

Chronic severe pulmonary regurgitation (PR) causes progressive right ventricular (RV) dysfunction and heart failure. Parameters defining the optimal time point for surgery of chronic PR are lacking. The present study prospectively evaluated the impact of preoperative clinical parameters, cardiorespiratory function, QRS duration and NT-proBNP levels on post operative RV function and volumes assessed by cardiac magnetic resonance imaging (CMR) in patients with chronic severe PR undergoing pulmonary valve replacement.

**Methods and results**

CMR was performed pre- and 6 months postoperatively in 27 patients (23.6 ± 2.9 years, 15 women) with severe PR. Postoperatively, RV endsystolic (RVESV) and enddiastolic volume indices (RVEDV) decreased significantly (RVESV pre 78.2 ± 20.4 mL/m² BSA vs. RVESV post 52.2 ± 16.8 mL/m²BSA, p < 0.001; RVEDV pre 150.7 ± 27.7 mL/m²BSA vs. RVEDV post 105.7 ± 26.7 mL/m²BSA; p < 0.001). With increasing preoperative QRS-duration, postoperative RVEF decreased significantly (r = −0.57; p < 0.005). Preoperative QRS-duration smaller than the median (156 ms) predicted an improved RVEF compared to QRS-duration ≥156 ms (54.9% vs 46.8%, p < 0.05). Multivariate analysis identified preoperative QRS duration as an independent predictor of postoperative RVEF (p < 0.005). NT-proBNP levels correlated with changes in RVEDI (r = 0.58 p < 0.005) and RVEDV (r = 0.63; p < 0.0001). Multivariate analysis identified NT-proBNP levels prior to PVR as an independent predictor of volume changes (p < 0.05).

**Conclusion**

Valve replacement in severe pulmonary regurgitation causes significant reduction of RV volumes. Both, preoperative NT-proBNP level elevation and QRS prolongation indicate patients with poorer outcome regarding RV function and volumes [21].
Replacement therapy for iron deficiency improves exercise capacity and quality of life in patients with cyanotic congenital heart disease and/or the Eisenmenger syndrome

Introduction

Iron deficiency is common in cyanotic congenital heart disease (CHD) and results in reduced exercise tolerance. Currently, iron replacement is advocated with limited evidence in cyanotic CHD. We investigated the safety and efficacy of iron replacement therapy in this population.

Methods

Twenty-five iron-deficient cyanotic CHD patients were prospectively studied between August 2008 and January 2009. Oral ferrous fumarate was titrated to a maximum dose of 200 mg thrice-daily. The CAMPHOR QoL questionnaire, 6 minute walk test (6MWT) and cardiopulmonary exercise testing were conducted at baseline and after 3 months of treatment.

Results

Mean age was 39.9 ± 10.9 years, 80% females. Fourteen had Eisenmenger syndrome, 6 complex cyanotic disease and 5 Fontan circulation. There were no adverse effects necessitating termination of treatment. After 3 months of treatment, hemoglobin (19.0 ± 2.9 g/dL to 20.4 ± 2.7 g/dL, p < 0.001), ferritin (13.3 ± 4.7 μg/L to 54.1 ± 24.2 μg/L, p < 0.001) and transferrin saturation (17.8 ± 9.6% to 34.8 ± 23.4%, p < 0.001) significantly increased. Significant improvements were also detected in the total CAMPHOR score (20.7 ± 10.9 to 16.2 ± 10.4, p = 0.001) and 6MWT distance (371.7 ± 84.7 m to 402.8.0 ± 74.9 m, p = 0.001). Peak VO(2) remained unchanged (40.7 ± 9.2% to 43.8 ± 12.4% of predicted, p = 0.15).

Conclusion

Three months of iron replacement therapy in iron-deficient cyanotic CHD patients was safe and resulted in significant improvement in exercise tolerance and quality of life. Identification of iron deficiency and appropriate replacement should be advocated in these patients [22].

Long-term prognostic value of cardiac autonomic nervous activity in postoperative patients with congenital heart disease

Background

Abnormal cardiac autonomic nervous activity (CANA) is not uncommon in postoperative patients with congenital heart disease (CHD).

Methods and results

We attempted to clarify the prognostic value of the CANA variables in postoperative CHD patients and prospectively evaluated the CANA variables in 292 consecutive biventricular and 91 Fontan repair patients. The CANA variables included the heart rate variability, arterial baroreflex sensitivity (BRS), washout ratio of the myocardial metaiodobenzylguanidine scintigraphy, and plasma norepinephrine level. With a follow-up of 10 ± 2 years, 98 total events that required hospitalization, including 13 deaths and 48 unscheduled cardiac events (UCEs), occurred. In all the CHD patients, all the CANA indices predicted the total events and UCEs. Of those, the NE level (p = 0.0004) and BRS (p = 0.0373) predicted the mortality. In a multivariate analysis, the BRS was an independent CANA-predictor for the total events (p = 0.007). In the biventricular patients, the plasma NE level, heart rate variability, and BRS predicted the total events and UCEs and the BRS was the only independent CANA-predictor for the total events (p = 0.0329). In the Fontan patients, the plasma NE level was the only predictor for the UCEs (p = 0.0242) and no other CANA variables were independent predictors of the total events or UCEs.

Conclusions

All CANA variables, especially the BRS, were useful predictors for future clinical events in biventricular CHD patients, whereas no CANA variables, except for the plasma NE level, predicted future clinical events in the Fontan patients [23].

Pathophysiology of coronary blood flow in congenital heart disease

Objectives

The aim was to investigate the effects of volume and pressure overload and increased coronary perfusion pressure on coronary flow (CF) in congenital heart disease (CHD) patients.

Background

The effects of CHD on CF are poorly mapped.

Methods

A total of 65 patients with acyanotic CHD and 49 age-matched healthy controls were examined by transthoracic Doppler echocardiography. Posterior descending artery flow was measured in patients with pulmonary valve stenosis (PS) and atrial septal defects (ASDs) i.e. in lesions with right ventricular pressure or volume overload, and left anterior descending artery flow in patients with Coarctation of the Aorta (CoA) and ventricular septal defect (VSD), in lesions with left ventricular pressure or volume overload. The CF data in each patient group were expressed as the percent of the median for healthy controls from the same age group.

Results

The CF values were in VSD 172%, ASD 185%, PS 233%, and CoA 773% patients. In CoA patients body surface area (r = 0.90, p < 0.0001), systolic blood pressure (r = 0.72, p < 0.0001), diastolic blood pressure (r = 0.77, p < 0.0001), systolic wall tension (r = −0.77, p = 0.004), and signs of inflammation (log CRP, r = −0.75, p = 0.007) correlated with CF.

Conclusions

The increase in CF and velocity was most significant in patients with CoA. In newborns, increased coronary perfusion pressure seems to be the most important factor for increased CF, even if the pressure is not assumed to cause a significant increase in flow over the auto-regulatory range of 70–130 mm Hg. We also showed that inflammation decreases CF [24].

Emergency admissions in Asians with adult congenital heart disease

Background and aim

In the area of acute emergency care, the needs of adult congenital heart disease patients (AChD) are unique and burden on hospital resources are likely substantial. We aim to understand the reasons for emergency admissions and associations of increased hospital length of stay (LOS).
Methods

We evaluated 600 ACHD patients in our adult congenital database. Patients who required emergency admissions between January 2007 and December 2007 were studied from hospital records.

Results

Sixty-eight ACHD patients (11%) required emergency admissions, culminating in a total of 108 admissions. Mean age was 37.6 years (SD 18.0), with a female preponderance (56%). Most were either schooling or working (62%) and were single (62%). Atrial septal defect (24%), ventricular septal defect (19%) and Tetralogy of Fallot (13%) formed the majority of diagnoses, mirroring proportions in our cohort. A third of the admissions were for cardiac reasons including arrhythmia, heart failure, endocarditis, and thromboembolism; the remaining two-thirds were for non-cardiac reasons. Median hospital LOS was 5.0 days. Those who were older (p = 0.02) and neither employed nor schooling (p = 0.021) had longer LOS. Thromboembolism accounted for longer LOS (p = 0.047). One-third of the admissions that required interdisci- plinary referrals had increased LOS (p < 0.001), with utilization of non-cardiac investigations (p = 0.002). Increased LOS was not associated with adverse clinical outcome (p = 0.68).

Conclusions

ACHD patients require emergency admissions for both cardiac and non-cardiac reasons. Older age groups, unemployment and thromboembolic complications were associated with increased LOS. Non-cardiac conditions required interdisciplinary resources and were associated with increased LOS. Understanding their diverse acute needs may potentially improve care and outcome for these patients [25].

Acute hemodynamic responses to adenosine and iloprost in patients with congenital heart defects and severe pulmonary arterial hypertension

Background

Detection of pulmonary vasoreactivity is important for the evaluation of patient with pulmonary arterial hypertension (PAH). The present study aimed to investigate the acute hemodynamic responses to adenosine and iloprost in patients with congenital heart defects (CHDs) and severe PAH.

Patients and methods

From Mar 2007 to Nov 2009, 75 patients with severe PAH secondary to left-to-right shunt CHDs underwent acute vasodilator test using aerosolized iloprost (n = 50) or intravenous adenosine (n = 25). The hemodynamics were detected and analyzed.

Results

Decreased mean pulmonary arterial pressure (PAP) and pulmonary vascular resistance (PVR) were observed in 39 and 43 patients in the iloprost group, and in 16 and 19 patients in the adenosine group, respectively. However, the mean PAP was higher than 40 mm Hg in both groups. No significant difference was observed in the age and baseline hemodynamics between the patients with the decrease of PVR and mean pulmonary-to-aortic pressure (Pp/Ps) ratio greater than 10% and the remaining patients. Adenosine decreased both PAP and systemic arterial pressure significantly, while iloprost inhalation selectively reduced the PAP and increased the oxygen saturation of femoral arterial blood and the pulmonary-to-systemic flow (Qp/Qs) ratio. Compared with adenosine, iloprost caused a more profound decline in the Pp/Ps ratio, PVR and pulmonary-to-systemic vascular resistance ratio, and increase in the Qp/Qs ratio.

Conclusions

The acute hemodynamic responses to adenosine and iloprost varied among the patients with CHDs and severe PAH. Different to adenosine, inhaled iloprost exerted selective pulmonary vasodilative effects and was beneficial for pulmonary gas exchange [26].

Recommendations for adult and pediatric cardiologists on obtaining additional qualification in “Adults with Congenital Heart Disease“ (ACHD)

Background

The number of adult congenital heart disease (ACHD) patients will be larger in the medium to long term than that of children and adolescents with congenital heart disease. The present structures for the medical care of ACHD patients are not sufficient and need to be improved. Therefore the Task Force aimed at developing recommendations for adult and pediatric cardiologists to acquire the additional qualification “Adults with Congenital Heart Disease“ (ACHD).

Methods

The members of the interdisciplinary Task Force were selected on the basis of their special clinical, scientific and organizational expertise. The leading author submitted a draft version, which was revised by a sub-group of the interdisciplinary Task Force. It was subsequently agreed upon and re-circulated by all the members of the Task Force. The recommendations were then presented to the relevant committees of all participating associations and groups and approved following detailed discussion.

Results

A training program for acquiring an additional qualification in the treatment of adults with congenital heart disease was created successfully.

Conclusions

The medical care of adults with congenital heart disease is a subspecialty in the border area between adult cardiology and pediatric cardiology. ACHD cardiologists are to be specially trained experts with appropriate knowledge and special skills and experience in the diagnosis and therapy of congenital heart disease in adults. ACHD cardiologists should be able to recognize and treat problems that occur in adulthood in connection with congenital heart disease [27].

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Editorial

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