C O N G E N I T A L
C A R D I O L O G Y T O D A Y

Timely News and Information for BC/BE Congenital/Structural Cardiologists and Surgeons

Volume 7 / Issue 11
November 2009
International Edition

IN THIS ISSUE

CONGENITAL CARDIOLOGY TODAY
Editorial and Subscription Offices
16 Cove Rd, Ste. 200
Westerly, RI 02891 USA
www.CongenitalCardiologyToday.com

ISSN: 1544-7787 (print); 1544-0499 (online). Published monthly.

UPCOMING MEDICAL MEETINGS

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EUROECHO 2009
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Bilateral Versus Unilateral Bidirectional Glenn Shunts: Saudi Experience

By Sameh Ibrahim Sersar, MD and Ahmed A. Jamjoom MD

Key Words: Glenn Cavopulmonary anastomosis.

Abstract

Introduction: Bidirectional Cavopulmonary Anastomoses (BDG a.ka. Glenn shunts) as a first or second palliative stage procedure before embarking on a total cavopulmonary connection (‘‘Fontan type’’ procedure) has been used to normalise volume loading of the single ventricle at an early age. The presence of bilateral Superior Vena Cava (SVC) may represent a technical challenge in the performance of the bilateral Cavopulmonary Anastomoses (b-CPA) connections.[1-2]

Methods: The available chart and files data were reviewed and analyzed in 160 cases of unilateral bidirectional glenn (u-CPA) and 44 children undergoing bilateral cavopulmonary anastomoses (b-CPA). Uivariate analysis of the risk factors of mortality, morbidity and ICU and hospital stay was done.

Results: One hundred sixty patients had U-CPA (Group 1) and 44 Patients had b-CPA (Group 2) in King Faisal Specialist Hospital and Research Centre (KFSH&RC), Jeddah, Kingdom of Saudi Arabia, in more than 8 years. They were 127 males and 77 females. Interrupted IVC was present in 14 patients. Hypo RV was evident in 128 cases. The oxygen saturation increased from 77.4% to 82.9% and from 73.8% to 84.7% in Groups 1 and 2 and the pulmonary artery pressure dropped from 24.6 mmHg to 15.8 mmHg and from 27 mmHg to 16.6 mmHg in both groups. Mechanical ventilation, inotropes, nitric oxide and oscillator high frequency jet ventilation were needed more in Group 2. Hospital stay was longer in Group 2. Six cases died in Group 1, and three died in Group 2.

Conclusions: Bidirectional Glenn shunts can be done with acceptable morbidity and mortality in some cases of pulmonary hypertension. Bilateral CPA had a more tough postoperative course than unilateral CPA. The mortality risk factors in bidirectional Glenn shunts are bilateral SVCs, Status post Damus Kaye Stansel (S/P DKS), S/P Norwood and high Pulmonary Artery Pressure (PAP).

Introduction

The bidirectional cavopulmonary anastomoses (CPAs) as a first or second stage procedure before embarking on a total cavopulmonary connection (‘‘Fontan-type’’ procedure) has been used to normalise volume loading of the single ventricle at an early age. The presence of bilateral SVCs may represent a technical challenge in the performance of the BCPAs connections. In addition, bilateral BCPS have been also found associated with a higher operative mortality, an increased risk of thrombus formation, and a lower conversion rate to the ‘‘Fontan-type’’ circulation, if compared to a standard unilateral CPAs.[1]

Application of the concepts for the Fontan circulation have evolved whereby nearly all patients with single ventricle physiology, including those with abnormalities of the systemic venous return are palliated on what has become known as the "Fontan tract." Although the initial results for the extension of the indications for the Fontan procedure were not always favorable, more recent studies have shown improvement.[1, 3]

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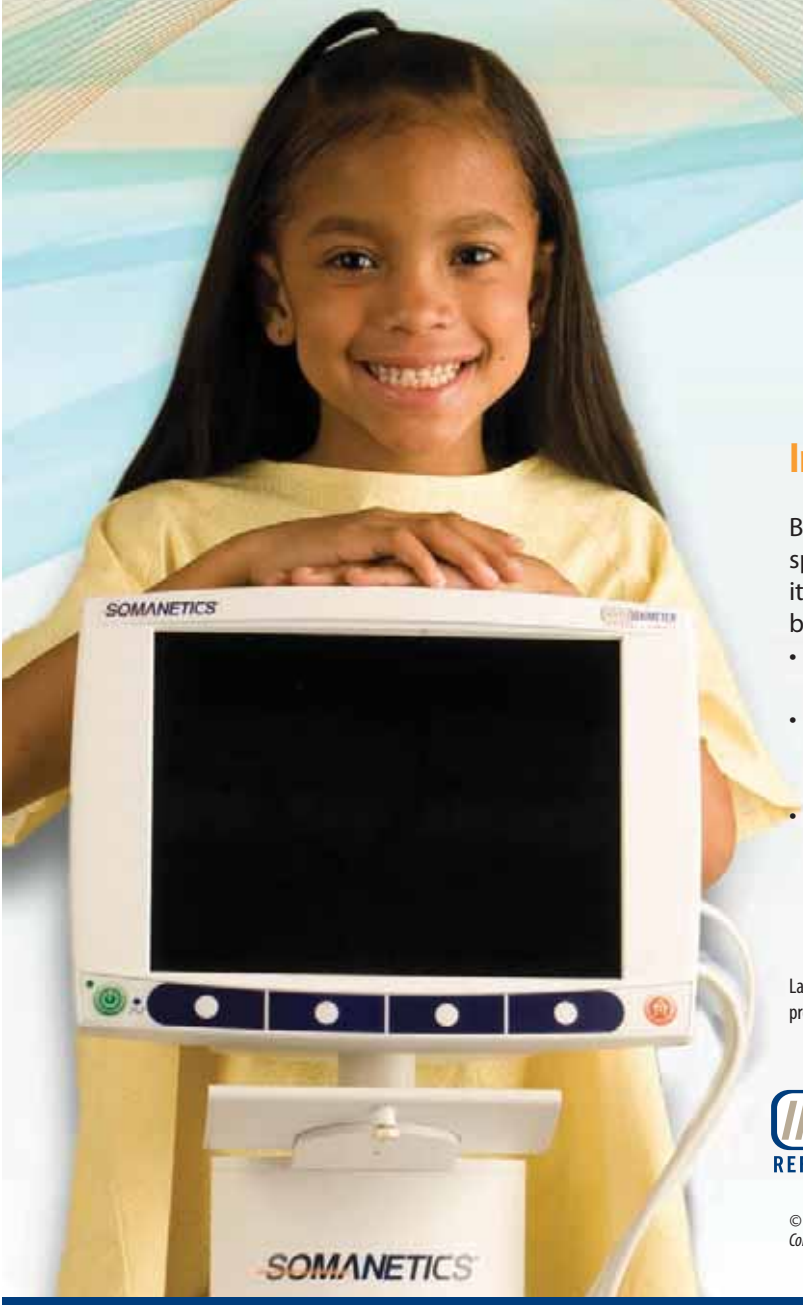

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Patients and Methods

This is a retrospective study including 204 cases of Glenn shunts operated upon in KFSH&RC; Jeddah, KSA, between 2000 and 2009. Preoperative evaluation included history taking, patient examination, routine laboratory and chest x-ray, ECHO diagnosis for all cases and cardiac catheterization for catheterization for higher risk cases, especially those with suspected especially those with suspected or proved pulmonary hypertension. Detailed Consent from the family is taken. All our BDG were done through median sternotomy and with standard cardiopulmonary Bypass (CPB). No cardioplegia was given. Previous systemic to pulmonary artery shunts were disrupted by division, ligation or clipping. The azygos vein was clipped or ligated unless interrupted IVC or Glenn pressure markedly increased. The previous pulmonary artery band was tightened or main pulmonary artery was amputated from the confluence. Pulmonary Artery Banding was done as an associated procedure in forty cases. Pulmonary artery augmentation was done in twenty-four cases. The left SVC was occluded while the pressure in the cephalad side was monitored. If the pressure is more than 20 mmhg, this SVC was cannulated for CPB and a BBDG shunt was performed. Pressure monitoring was needed in the first few cases of our practice; however, we currently perform routinely BBDG in single ventricle with bilateral SVCs. ICU care included: monitoring, inotropes, mechanical ventilation, Nitric oxide and oscillator when needed, Head of the bed up to 45 degrees with furosemide, catopril, aspirin, dipyridamol, sildenafil with or without anticoagulation. Follow-up in the pediatric cardiology clinic was done. The median follow-up was 24 months with a range between 2-96 months.

Results

One hundred sixty patients had U-CPA (Group 1) and forty-four patients had b-CPA (Group 2) in King Faisal Specialist Hospital and Research Centre (KFSH&RC), Jeddah, in more than 8 years. They were 127 (94 in Group 1 plus 33 in Group 2) males and 77 (66 in Group 1 plus 11 in Group 1) females. BTS was previously done for 104 cases (80+24) and Pulmonary Artery Banding was done for 36 (29 and 7). Interrupted IVC was present in 14 (4 in Group 1 plus 10 in Group 2) patients. Hypo RV was evident in 128 (102+26) cases. The preoperative oxygen saturation increased from 77.4% to 82.9% postoperatively, and from 73.8% to 84.7% in Groups 1 and 2 postoperatively. Indexed pulmonary vascular resistance was <3.5 Units in 125 (95+30), > 3.5 units in 21 cases (15+6), and not assessed in 58 cases (50+8). The pulmonary artery pressure dropped from 24.6 mmHg to 15.8mmHg, and from 27 to 16.6 mmHg in both groups. CPB time was longer in Group 2 (69 min vs. 48min). Pulmonary artery banding was done concomitantly in 31 cases (25+6) and pulmonary artery augmentation in 22 cases (15+7). Mechanical ventilation, inotropes, nitric oxide and oscillator were needed more in Group 2 (0.8 days -5 hours -3 h.-1h. vs. 1 day -6h -5h -3h -1h) respectively in (Group 1 and 2). The hospital stay was longer in Group 2. Six cases died in Group 1, and three died in Group 2. ICU and hospital stay were longer in Group 2 (2.1 and 7 days vs. 2.6 and 10 days). Chylothorax was detected in 21 and 8 cases in both groups. Significant arrhythmias were detected and investigated in 30 and 6 cases. Re-intervention was needed in 13 cases (10+3) in the form of thrombosis of the Glenn shunt in 4 cases (3+1), bleeding in 6 cases (4+2) and thoracic duct ligation in

three cases all in Group 1. Incorporation of the hepatic veins was needed in three cases (one in Group 1, and two in Group 2), and Fontan was performed in 42 cases (38+4). The data was statistically analysed using the Mann–Whitney test for continuous variables and chi-square test for categoric variables. Regression model was used for the potential risk factors. The continuous variables were: Age, Weight and CPB time, while the non-continuous variables included: Ventricular morphology dominance, bilaterality of SVCs with or without interrupted IVC, previous surgeries, use of CPB or not, and associated procedures (Table 1).

Table 1. Showing the Demographic, Radiological, Operative, Clinical, Therapeutic and Prognostic Data of Both Groups.

	Unilateral Glenn	Bilateral Glenn	
Morphology			
No.	160	44	
Hypo RV	102	26	
Hypo LV	58	18	
Sex			
Male	94	33	
Female	66	11	
Age (months)	17.9	19.3	
Weight (Kgm)	10.5	10.9	
S/P			
PAB	29	7	
BTS	80	24	
DKS	2	2	
Norwood	1	1	
LV diverticum excision	1	0	
IIVC	4	10	P<0.05
Preop. Saturation	77.4	73.8	
Postop. Saturation	82.9	84.7	
Preop. PAP	24.6	27	
Postop. PAP	15.8	16.6	
PVRI			
< 3.5	95 (53.1%)	30 (68%)	
>3.5	15 (9.3%)	P<0.05	
NA	50 (37.6%)	6 (13.6%)	
		P<0.05	
		8 (18.4%)	
		P<0.05	
Bypass Time	48	69	P<0.05
Associated			
PAB	25	6	
Pulm. A. Augment.	15	7	
ICU Stay	2.1 d	2.6 d	P<0.05
Mechanical ventilation	0.8 d	1 d	
Inotropes	5 h.	6 h.	
Nitric Oxide	3 h	5 h	
Oscillator	1 h	3 h	
Hospital Stay	7 d	10 d	P<0.05
Chylothorax	21 (13.1%)	8 (18.1%)	P<0.05
Arrhythmias	30	6	
Reoperation			
Thrombosis	3	1	
Bleeding	4	2	P<0.05
Thoracic duct ligation	3	0	P<0.05
Mortality	6	3	P<0.05
Next Surgery	39	6	
Fontan	38	4	
Incorporation	1	2	

Discussion

We are presenting a reasonably large series in a tertiary care centre in Jeddah over a span of more than 8 years. It includes 204 cases of Glenn anstomoses. More than 25% of them are b-CPAs. This ratio is higher than those of Iyer et. al., 2000, Chowdhury et. al., 2001 and Kim et. et. al., 2006, but less than those of Tanoue Y. et. al., 2007, who reported a ratio of 14.2%, 16%, 3.2% and 27.9%. This may be due to the random nature of the study with different socioeconomic and ethnic status.[1, 4, 5, 6] Male/Female was 1.64/1. The mean age was 17.9 months and 19.3 months, which is relatively high as we are a tertiary centre managing cases from all over our region with some delay and sub-optimal general and cardiac conditions. As per Mitchell ME et. al., 2006, and Tanoue Y. et. al., 2007, BDG should be performed between three to six months to achieve maximum benefits.[7]

However, BDG can be done up to two years old.[6] Our youngest case was 1 month, and the oldest was 13 years. BTS was previously done in 104 (51%), and previous PAB was done in 17.6% of cases, so about 68.6% received a first step palliation in the form of BTS and/or PAB. We followed a staged strategy in most cases, as the quality of life in patients after Blalock-Taussig shunt operation may be better than that in patients after BDG, as BDG is not used as the final operation for patients who cannot be completed by the Fontan circulation.[6] The median follow-up in our series was 24 months with a range between 2-96 months. Fontan was done for 38 and 4 cases in both groups (23.7% and 9%) respectively. Incorporation of the hepatic veins was done in three Kawashima cases. The aetiology of desaturation after Glenn is usually due to development of venous collaterals from the SVC to the IVC and intra-pulmonary arteriovenous shunting and reduction of the SVC/IVC flow ratio with age.[8]

We did believe in the staged palliation of single ventricle, especially early in our centre experience, However, we started to be a little more aggressive towards primary Glenn, so 31.4% received primary Glenn without previous palliation. The indication of BDG should be decided according to the surgical strategy aiming at the Fontan operation.[6] Concerns about the performance of BCPS in young infants may have to do with the history of unfavorable results after performing a classic Glenn shunt in infants along with uncertainty regarding the reactivity of the pulmonary vasculature in this group of patients. Between 1990 and 1995, over one-third (36%) of all BCPS procedures performed at the University of California at San Francisco were in infants <6 months of age. Early results in this cohort of young infants have been similar to those in all patients undergoing BCPS during the same period, with mortality rates of 4.8% and 5.1% and BCPS failure rates of 11.9% and 8.5%, respectively. The only independent risk factor for early death and BCPS failure was age, <1 month; and the strongest risk factor for early or late BCPS failure (death or take-down) was age < 2 months.[9]

BDG procedure offers several potential advantages over the use of systemic to pulmonary shunts. In particular, it avoids pulmonary arterial distortion and also the additional volume load on the systemic ventricle created by the use of systemic to pulmonary shunts. Both these complications are important risk factors for subsequent Fontan repair. In addition, bidirectional cavopulmonary anastomosis is a more logical strategy as it represents an evolution of the patients' anatomy towards the final Fontan circulation.[10]

In all cases, we abolished the retrograde accessory pulmonary flow coming through the BT shunt as the goal is to try to achieve an effective/total pulmonary blood flow ratio of about 1. The more the effective and the total pulmonary blood flows coincide, the better the palliation. All efforts were made to obtain the maximum oxygen saturation with the minimum ventricular overload. The advantage of the BCPA over the Blalock-Taussig shunt is to allow an increase of effective pulmonary blood flow without an increase in total pulmonary blood flow and cardiac work. BCPA with Antegrade Pulmonary Blood Flow a better step towards Fontan than BCPA with an additional pulmonary blood flow through a Blalock-Taussig shunt.[11]

"Bidirectional Glenn whether unilateral or bilateral can be done with acceptable morbidity and mortality. The mortality risk factors in bidirectional Glenn Shunts are bilateral SVCs, S/P DKS, S/P Norwood and high PAP. Using the univariate risk analysis, only the bilaterality of SVCS, interruption of IVC and PVRI >3.5 are the significant risk factor for the longer ICU and hospital stay and chylothorax."

There was a significantly higher percentage of patients with Pulmonary Vascular Resistance Index (PVRI) >3.5 in Group 2 (13.6% vs. 9.3%), which may be a well-known high risk factor although there was no significant difference in the preoperative or postoperative PAP. This, in addition to longer CPB and heterogenous anatomical diagnosis, may explain the finding of longer Mechanical ventilation, inotropes, Nitric Oxide and Oscillator in Group 2 (0.8 days -5 hours -3 h. -1h. vs. 1 day -6h -5h -3h.) respectively in (Group 1 and 2), and the hospital stay was longer in Group 2, and that six cases died in Group 1, and three died in Group 2.

ICU and hospital stays were longer in Group 2 (2.1 and 7 days vs. 2.6- and 10 days). Using the univariate risk analysis, only the bilaterality of SVCS, interruption of IVC and PVRI >3.5 were significant risk factor for the longer ICU and hospital stay and chylothorax. As per Reddy VM et. al., 1997, elevated pulmonary vascular resistance did not appear to be a problem among any of the neonates and very young infants who fared badly after the operation, because they had normal pulmonary artery pressures and transpulmonary gradients throughout their postoperative courses. However, it has been pointed out that pulmonary artery pressures and gradients are not necessarily reliable indicators of resistance when pulmonary blood flow is low or when no good estimate of flow is available. Therefore, BCPS does not appear to be a viable option in neonates and should preferably be postponed beyond 2 months of age.[9]

In 2000, KFSH&RC; Jeddah, instituted a policy of offering BDG shunts to patients with pulmonary hypertension if their PVRI decreased to 3.5 WU/m2 on 100% oxygen irrespective of mean PAP and PVR in room air and mean PAP on 100% oxygen. Current suggested criteria to not offer BDG shunting to those with PVRI >3 WU and/or mean PAP >18 to 20 mm Hg by some and >25 to 30 mm Hg by others work well with respect to good outcomes and low mortality. However, there are three reservations to these guidelines. First, in the absence of pulmonary stenosis, elevated mean PAP does not necessarily indicate the presence of obstructive pulmonary vascular disease and may reflect only the transmission of systemic pressure to pulmonary circulation and high pulmonary flow. Second, because PAP and PVR are flow dependent, it seems inappropriate to use a uniform level of PAP or PVR as a criterion for patients with "under circulated" or "over circulated" pulmonary circulation. The former reduces and the latter increases pulmonary flow, which affects PAP and PVR, and the current approach ignores this important variable. Third, it has not been well-studied, in the presence of unrestricted and increased pulmonary flow and elevated PAP, what degree of elevated PVR would lead to the failure of a BDG shunt.[12]

Chylothorax was detected in 29 cases (21+8). It was suspected when the amount of drainage has a milky nature and diagnosis is confirmed by the presence of chylomicrons in the drained fluid with lymphocytes more than 80% with fluid triglycerides/cholesterol ratio more than 1 or pleural fluid triglyceride level is >1.1 mmol/L. We think that it is due to high venous pressure (systemic and/or pulmonary), disruption of the minor lymphatic channels rather than thoracic duct injury. Our first line of treatment is a fat-free diet; monogen for at least 3-6 weeks with or without NPO, diuretics, captopril. For resistant cases, we may use a week course of steroids and or octreotides. We needed thoracic duct ligation in three cases; all were of the u CPAs group. So, although chylothorax incidence was significantly higher in Group 2 (18.1% vs. 13.1%), refractory chylothorax requiring thoracic duct ligation was only in Group 1. The higher incidence in Group 2 may be related to higher PAP and/or PVRI. However, we could not explain the refractory nature of three cases in Group 1. Chylothorax may be an indicator of additional pulmonary blood flow. Monogen is designed for infants and children with lipid and lymphatic disorders. The osmolality of Monogen is substantially lower than Portagen and most other elemental or fat-free formulas, a difference that improves gastrointestinal tolerance of the feed. Monogen also has a substantially higher energy level than alternative feeds. This point is important because patients with chylothorax have high energy requirements due to increased metabolic demand from the combination of chyle loss and hyper metabolism associated with surgery.[13, 14] Nine cases (4.4%) died during the follow-up - six cases from the Group 1 (3.75%) and three cases (6.8%) from Group 2. So, we can say that bidirectional glenn, whether unilateral or bilateral, can be done with acceptable morbidity and mortality. The median survival of those nine mortalities after the Glenn was 6 months. The accused causes of death were myocardial dysfunction, arrhythmias, tension pneumothorax and cerebrovascular strokes. The mortality risk factors in our study were bilateral SVCs, S/P DKS, S/P Norwood and high PAP. Kogon BE et. al., 2007 found longer CPB time and High CVP as the only significant mortality risk factor. They also found those two factors plus high transpulmonary gradient and right ventricular morphology and low body weight at the surgery time as the significant risk factors for the longer ICU and hospital stay.[15]

Conclusion

Bidirectional glenn whether unilateral or bilateral can be done with acceptable morbidity and mortality. The mortality risk factors in bidirectional Glenn Shunts are bilateral SVCs, S/P DKS, S/P Norwood and high PAP. Using the univariate risk analysis, only the bilaterality of SVCS, interruption of IVC and PVRI >3.5 are the significant risk factor for the longer ICU and hospital stay and chylothorax.

Limitations of the Study

This is a retrospective study with all the defects of retrospective studies with lack of randomization and unequal group sample sizes.

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GE Healthcare Introduces New Intracardiac Echo Functionality for the Vividi and Vividq Ultrasound Systems

Wauwatosa, WI, September 24, 2009 – GE Healthcare and Biosense Webster, Inc. (BWI) announced new versions of the Vivid i and Vivid q Cardiovascular Ultrasound systems, with support for two new intracardiac echo (ICE) catheters. The Vividi systems with version BT10 software now support the Biosense Webster Acunav® 8F ICE catheter. The 8F catheter has a 33% smaller cross-sectional area than the AcuNav 10F catheter, making it well suited for patients that cannot tolerate a larger catheter.

The companies also announced new support of the Vividi and Vividq systems with the SoundStar™ 3D ICE catheters, as well as compatibility for the Vividi and Vividq systems with the Biosense Webster CartoXP system with the CartoSound version 9.7 software module. The CARTOSOUND Module and SOUNDSTAR 3D Catheter integrate real-time intracardiac echocardiography (ICE) imaging into the CARTO System environment, enhancing visualization and navigational confidence during complex EP procedures.

Biosense Webster is a pioneer in EP diagnostic catheters and is an innovative provider of advanced diagnostic, therapeutic, and mapping tools. GE and Biosense first announced the intent to create a combined AcuNav catheter/Vivid i system at HRS in 2009 and offered the first unit for sale, with support for the Biosense Webster 10F ICE catheter, in October 2008.

The small and compact Vivid i systems deliver imaging performance comparable to that of today's high-end console ultrasound systems without crowding the lab. Combined with the exceptional ICE catheter technology performance and navigational versatility of the ACUSON AcuNavTM 10F and 8F ultrasound catheter, the system helps cardiologists confidently navigate complex interventional procedures for a wide range of patients.

According to Hooman Hakami, General Manager, Interventional at GE Healthcare, "Customers value the ICE images they are getting from the Vividi system using the AcuNav 10F catheter. Support for these new ICE catheters from our partner, Biosense Webster, l allows our customers to utilize the Vividi system for a wider population of patients and procedures."

For more information about GE Healthcare, visit our Web site at www.gehealthcare.com.

Children with Fatter Midsections at Increased Risk for Cardiovascular Disease

Children with more fat around their midsections could be at a higher risk of developing cardiovascular disease later in life, researchers say.

"While general obesity certainly has its own set of risks for the heart, we now know that all fat is not created equally," says Dr. Reda Bassali, an Associate Professor of Pediatrics in the Medical College of Georgia School of Medicine and co-author of a study published online in the *International Journal of Pediatric Obesity.*

Increased waist circumference has long been linked to cardiovascular risk in adults because visceral fat — found in and around organs in the abdominal cavity — is more metabolically active, which can dramatically increase the risk of cardiovascular disease and type 2 diabetes.

The study suggests routine waist measurements in obese children could predict which ones had developed risk factors for cardiovascular disease, such as higher fasting insulin levels, a precursor for diabetes; lower levels of high density lipo-protiens, also known as the good cholesterol; and higher levels of triglycerides, the fatty particles found in the blood.

"What we are asking is whether the children with larger waists already showed signs that put them at higher risk," Dr. Bassali, also a pediatrician at the MCG Health Children's Medical Center, says. "To find out whether children eventually developed cardiovascular disease, we'd have to follow them long term."

In a sample of 188 obese children, ages 7-11, those with the largest waist circumferences – above the 90th percentile for their age – were three times more likely to have high triglycerides and nearly four times more likely to have lower levels of HDL. They were also 3.7 times more likely to have high fasting insulin levels.

"What that means is that children with a waist circumference at or above the 90th percentile are at a greater risk of developing the warning signs of cardiovascular disease," Dr. Bassali says. "Our results indicate that routine clinical measurement of the waist may help clinicians identify which obese children are at a greater risk."

"There is a lot of discussion about the apple versus the pear body shape, with the pear being more desirable," Dr. Bassali says. "Unfortunately, we don't have a real explanation why some people gain weight in the center of their body and others gain it, for instance, in their thighs. It could be environmental. It could be genetic. It could be a combination of the two."

These results, however, could provide researchers and clinicians with another way to measure possible risk and possibly prevent future health complications.

"The gold standard, when it comes to intervention strategies, has always been whether a child fell into a certain range with their body mass index (calculated using height and weight)," he says. "These results suggest that waist circumference could provide an additional measurement of risk. The intervention strategies would be the same."

Other authors on the paper included Jennifer Waller, Associate Professor of Biostatistics; Jerry Allison, professor of radiology; and Catherine Davis, Clinical Health Psychologist in the Georgia Prevention Institute.

Pioneering Research Forms Basis for First-Ever Paediatric Hypertension Guidelines

Newswise - Comprehensive guidelines for the treatment and management of hypertension in children and adolescents are being published for the first time in the latest issue of the *Journal of Hypertension*.

Prepared by a Task Force established by the European Society of Hypertension, the guidelines should prove to be an invaluable source of information for physicians, nurses and families dealing with hypertension in young people.

The necessity for the guidelines has become increasingly clear to physicians in light of growing evidence that cases of mild hypertension in children and adolescents are much more common than previously thought. In addition, progress made in pathophysiological and clinical research has made clear links between paediatric hypertension and cardiovascular disease later in life, highlighting the need for improved cardiovascular prevention strategies for pre-adult individuals.

The Task Force, set up by the European Society of Hypertension and headed by Dr Empar Lurbe of the University of Valencia, has combined considerable amounts of scientific data with clinical experience in order to represent a consensus among specialists involved in the detection and control of high blood pressure (BP) in children and adolescents. It is hoped that the publication of these guidelines will call attention to the burden of hypertension in children and adolescents, and encourage public policy makers to develop a global effort to improve identification and treatment of high BP among young people. Primarily, however, these guidelines provide practical strategies for diagnosing and treating hypertension in children and adolescents. They include:

- Definition and classification of hypertension
- Diagnostic evaluation
- Preventative measures
- Evidence for therapeutic management
- Therapeutic strategies and approaches under special conditions
- Treatment of associated risk factors
- Screening for secondary forms of hypertension

The Task Force also suggests strategies for long term follow up, and make recommendations for future research in the field.

The guidelines will certainly prove vital in combating the growing epidemic of cardiovascular disease in adults, by emphasising the need for preventative strategies to be implemented from an early age. As Dr Lurbe comments, "Action is required to address this problem in one of the most vulnerable and precious sectors of our society: children and adolescents."

New Genetic Link Between Cardiac Arrhythmias and Thyroid Dysfunction Identified

Newswise — Genes previously known to be essential to the coordinated, rhythmic electrical activity of cardiac muscle -- a healthy heartbeat -- have now also been found to play a key role in thyroid hormone (TH) biosynthesis, according to Weill Cornell Medical College researchers.

The authors' findings, published online this week by the peer-reviewed journal Nature Medicine, suggest that mutations of either of two gene products -- proteins called KCNE2 and KCNQ1 -- already known to be involved in human cardiac arrhythmias, could also cause thyroid dysfunction.

"It has long been known that the thyroid influences cardiac function and cardiac arrhythmias," says study senior author Dr. Geoffrey W. Abbott, associate professor of pharmacology in medicine at Weill Cornell Medical College, "but our findings demonstrate a novel genetic link between inherited cardiac arrhythmia and thyroid dysfunction."

Additionally, it is the authors' suggestion that assessment of the thyroid status of patients with KCNE2- and KCNQ1-linked cardiac arrhythmias could in some cases reveal a potential endocrine component to their cardiac arrhythmias that may not have been previously determined. This, in turn, could indicate treatment of the thyroid condition, with potentially beneficial effects on cardiac function.

KCNQ1 and KCNE2 were each recognized more than a decade ago as forming potassium channels in cardiac muscle that help end each heartbeat in a timely fashion. Inherited mutations in KCNQ1 and KCNE2 cause ventricular and atrial cardiac arrhythmias, previously presumed to be due entirely to the role of these proteins in cardiac muscle. The researchers have now discovered that KCNQ1 and KCNE2 also form a potassium channel in the thyroid gland.

"When the thyroid does not produce enough TH, a person may experience symptoms such as fatigue and a lowered heart rate, but there is also a more complex interplay between thyroid function, cardiac structure and cardiac arrhythmias. Our new findings may begin to explain some of these interrelationships," explains Dr. Abbott.

While studying mice that had the KCNE2 gene removed from their genome, the researchers observed that the animals developed symptoms of hypothyroidism, especially during pregnancy, and gave birth to pups with dwarfism, alopecia (baldness) and cardiomegaly (enlarged heart).

After allowing the mouse pups to drink milk only from mothers without the genetic alteration, the pups' symptoms were alleviated. The healthy mothers' milk contains normal levels of TH -- essentially acting as a TH replacement therapy. The symptoms were also treated by direct TH supplementation of pups or mothers.

"We then wanted to test what the mechanism was in the mice that caused deletion of the KCNE2 gene to have negative consequences for the thyroid," says Dr. Abbott.

Using micro positron emission tomography (microPET), Dr. Abbott and his team visualized the accumulation in the mouse thyroid of an iodine radioisotope in real-time. They found that absorption of the radioisotope in the thyroid was greatly impaired in mice lacking the

KCNE2 gene. They believe that, normally, the KCNQ1-KCNE2 potassium channel helps another protein (the sodium/iodide symporter) to transport iodide into the thyroid.

Without the KCNQ1-KCNE2 potassium channel, the efficiency of iodide absorption by the thyroid is greatly reduced. Because iodide is an essential component of TH, this means that KCNE2 deletion also impairs TH production.

Future studies will now center on determining how applicable the research team's findings in the mouse are to the human population.

"While we have identified KCNQ1 and KCNE2 in both mouse and human thyroid, much additional work is required before we can fully understand how inherited mutations in the genes coding these proteins affect human thyroid function, how this in turn influences the health of human heart and other tissues, and how useful our discoveries will be in developing therapies to treat thyroid and thyroid-related human disease," explains Dr. Abbott.

Cardiac arrhythmias affect up to three million people in the United States. The majority of these suffer from atrial fibrillation, a chronic arrhythmia most often observed in the aging population. Ventricular arrhythmias account for the large majority of the 300,000 cases of sudden cardiac death annually in the United States. Thyroid dysfunction is estimated to affect one to four percent of the world's population.

Additional co-authors include Torsten K. Roepke, Elizabeth C. King and Kerry Purtell from Weill Cornell; Daniel J. Lerner from CV Ingenuity, San Francisco, CA USA; and Andrea Reyna-Neyra, Monika Paroder,Wade Koba, Eugene Fine and Nancy Carrasco from the Albert Einstein College of Medicine, The Bronx, NY USA.

The study received support from the National Institutes of Health and the American Heart Association.

For more information, visit www.med.cornell.edu.

JANUARY 2010 MEDICAL MEETING FOCUS

Evolving Concepts in the Management of Complex Congenital Heart Disease II
January 14 -16, 2010
San Diego, CA USA
www.chsd.org/body.cfm?id=1753

Selected Meeting Objectives:
- Determine optimal management strategies for common diagnostic and treatment problems encountered in an outpatient office practice.
- Understand and manage the diagnosis and treatment of cardiomyopathy and pulmonary hypertension in infants, children, young adults
- Optimize imaging modality selection to obtain an efficient & cost effective diagnosis.
- Diagnose and treat common and complex arrhythmias in patients of all ages.
- Utilize modern catheterization techniques as part of an integrated invasive treatment program for congenital heart disease.
- Integrate the Hybrid approach with modern variations of the Norwood and Fontan procedure to optimize care of infants with HLHS.
- Utilize modern medical and surgical strategies to treat complex CHD.
- and more….

Program Coordinators (serve as moderators):
- John J. Lamberti, MD
- John W. Moore, MD, MPH

Faculty:
- Zahid Amin, MD
- Anjan S. Batra, MD
- Daniel Bernstein, MD
- Jane C. Burns, MD
- John P. Cheatham, MD, FAAP, FACC, FSCAI
- John S. Child, MD
- Joseph A. Dearani, MD
- Howaida G. EL-Said, MD
- Frank L. Hanley, MD
- D. Dunbar Ivy, MD
- Jeffrey P. Jacobs, MD, FACS, FACC, FCCP
- Joel Kirsh, MD
- Steven E. Lipshultz, MD, FAHA, FAAP
- James Lock, MD
- Audrey C. Marshall, MD
- Gerald Ross Marx, MD
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- Lloyd Y. Tani, MD
- James S. Tweddell, MD
- George F. Van Hare, MD
- Victoria L. Vetter, MD
- Gary Webb, MD
- Gil Wernovsky, MD, FACC, FAAP

Do you or your colleagues have interesting research results, observations, human interest stories, reports of meetings, etc. that you would like to share with the congenital cardiology community?

Submit a summary of your proposed article to Congenital Cardiology Today at: RichardK@CCT.bz

CONGENITAL CARDIOLOGY TODAY

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