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INTRODUCTION

The Selected Summary Section is being revived in this issue after a gap of nearly a year. In this issue we have attempted to list all significant publications that would be of potential interest to pediatric cardiac professionals in the past 1 year; June 2013-June 2014 [Table 1]. We have then chosen four publications that are being discussed in some detail.

These publications were identified through an online academic discussion group called Childheart (Figure) that was created by one of the authors (Dr. Anil Kumar Singhi)."Childheart" group had its origin in 2006. The primary purpose was to share and discuss new publications in the field of pediatric and structural heart disease. Publications of potential interest were initially identified by Dr. Anil Kumar Singhi and sent to a Google group of members through a common e-mail ID. Over time members of the group also identified publications of potential interest and shared it through this medium. Initially just the abstracts were made available. Full texts were also shared depending on availability. A brief summary was subsequently added to the e-mail text. The number grew from 50 to nearly 300 While initial membership was from India, the group has become truly global with members from all parts of the world.

The group membership is by invitation to all who are interested in pediatric and structural heart disease. The invitation request can be made to childheart@googlegroups.com. Since 2009 all posts to the group are archived with nearly 600 mail posts. Members can access the group by logging into Google group (email ID of the member is the user ID and an individual password can be created). The members are encouraged to post replies and eventually it is hoped that this would function as an online journal club where users post critiques on shared publications.

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Risk stratification at diagnosis for children with hypertrophic cardiomyopathy: An analysis of data from the Pediatric Cardiomyopathy registry. Lipshultz SE1, Orav EJ, Wilkinson JD, Towbin JA, Messere JE, Lowe AM, Sleeper LA, Cox GF, Hsu DT, Canter CE, Hunter JA, Colan SD Lancet. 2013 Dec 7;382(9908):1889-97.

Critique by Sangeetha Viswanathan

This retrospective analysis of existing pediatric cardiomyopathy registry data was published in the September issue of the Lancet. It sets out to identify risk factors at the time of diagnosis of pediatric patients (age <18 years) with hypertrophic cardiomyopathy that predict adverse outcome, *i.e.* death or transplantation. The pediatric cardiomyopathy registry collected data over a 20-year period (1990-2009) for 1085 children with hypertrophic cardiomyopathy.

The study retrospectively uses the prospectively collected data of the registry. The methodologies for the study, i.e. inclusion/exclusion criteria, phenotypic classification, echocardiographic definitions, data collection methods and clinical endpoints have previously been defined at the time of data collection. The current study performs a data trawl focusing on the time of diagnosis and correlating several variables at the time of diagnosis with adverse outcome.

The study classifies patients according to phenotype into those with isolated hypertrophic cardiomyopathy ($n = 958$) and those with a mixed phenotype {hypertrophic + dilated ($n = 69$) and hypertrophic + restrictive ($n = 58$)}. It further classifies the isolated HCM group according to etiology and age into HCM with malformation syndromes MS ($n = 60$), HCM with inborn errors of metabolism IEM ($n = 69$), idiopathic HCM diagnosed at age <1 year ($n = 252$) and idiopathic HCM diagnosed at >/= 1 year (407). It excludes 170 patients from the isolated HCM group (familial HCM and HCM associated with neuromuscular problems), as there are too few clinical outcomes. The study finds that patients with isolated hypertrophic cardiomyopathy have a significantly lower incidence of death or transplantation (16% *versus* 41%) as opposed to the mixed phenotypes. The exclusion of the 170 patients with pure HCM at this stage seems unnecessary.

The group with IEM has a very poor outcome with a 64% incidence of death/transplantation. On the other hand

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Table 1: A summary of key publications in pediatric cardiac specialties from June 2013 to June 2014; articles selected for in depth commentary is shown in a bold typeface

Category	Reference (Pubmed citation)	Study design	Specific study question	Main conclusions
General pediatric cardiology	Rushani D, Kaufman JS, Ionescu-Ittu R, Mackie AS, Pilote L, Therrien J,Marelli AJ. Infective endocarditis in children with congenital heart disease: Cumulative incidence and predictors. Circulation 2013;128:1412-9	Analysis of a population based congenital heart disease database from the state of Quebec, Canada	What is the risk of infective endocarditis in children with congenital heart disease?	Cumulative incidence of IE was estimated in the subset of 34 279 children with CHD followed since birth, in whom the risk of IE up to 18 years of age was 6.1/1000 children (95% confidence interval, 5.0-7.5). Specific high risk groups identified included, endocardial cushion defects, left sided lesions, cardiasurgery within 6 months and age < 3 years
General pediatric cardiology; pediatric cardiac surgery	Wessel DL, Berger F, Li JS, Dähnert I, Rakhit A, Fontecave S, Newburger JW; CLARINET Investigators. Clopidogrel in infants with systemic-to-pulmonary-artery shunts. N Engl J Med 2013;368:2377-84	Multi-center, double blind, randomised controlled trial	Does addition of clopidogrel (0.2 mg/kg)to conventional therapy in young infants (<92 days) undergoing systemic-pulmonary arteryshunts reduce mortality from any cause and morbidity related to the shunt?	Clopidogrel therapy in infants with cyanotic congenital heart disease palliated with a systemic-to-pulmonary-artery shunt, most of whom received concomitant aspirin therapy, did not reduce either mortality from any cause or shunt-related morbidity
Imaging; magnetic resonance imaging (MRI)	Fiechter M, Stehli J, Fuchs TA, Dougoud S, Gaemperli O, Kaufmann PA. Impact of cardiac magnetic resonance imaging on human lymphocyte DNA integrity. Eur Heart J 2013;34:2340-5	Prospective study; Single centre (mean age 53±13 years)	Are DNA double-strand breaks identifiable in human blood lymphocytes before and after CMR examination?	Immunofluorescence microscopic and flow cytometric analysis revealed a significant increase in median numbers of DNA DSBs in lymphocytes induced by routine 1.5 T contrast enhancd CMR examination. The present findings indicate that CMR should be used with caution and that similar restrictions may apply as for X-ray-based and nuclear imaging techniques
General cardiology	Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, Beqaraj F, Demarie D, Forno D, Ferro S, Maestroni S, Belli R, Trinchero R, Spodick DH, Adler Y; ICAP Investigators. Arandomized trial of colchicine for acute pericarditis. N Engl J Med 2013;369:1522-8	Multi-center double blind randomized controlled trial	How effective is colchicine in terminatinga first attack of acute pericarditis and in the prevention of recurrent symptoms?	In patients with acute pericarditis, colchicine, when added to conventional antiinflammatory therapy, significantly reduced the rate of incessant or recurrent pericarditis
General pediatric cardiology	Cantinotti M, Assanta N, Murzi B, Lopez L. Controversies in the definition and management of insignificant left-to-right shunts. Heart 2014;100:200-5	Systematic Review; literature search performed within the National Library of Medicine	How should hemodynamically insignificant left to right cardiac shunts be defined, classified and followed up?	Standards and guidelines using consensus opinion for the management of insignificant left-to-right shunts are needed to address the heterogeneity in diagnosis and management as well as use of resources, ethical and psychosocial issues
General pediatric cardiology	Lipshultz SE, Orav EJ, Wilkinson JD, Towbin JA, Messere JE, Lowe AM, Sleeper LA, Cox GF, Hsu DT, Canter CE, Hunter JA, Colan SD. Risk stratification at diagnosis for children with hypertrophic cardiomyopathy: An analysis of data from the pediatric cardiomyopathy registry. Lancet 2013;382:1889-97	Retrospective cohort; analysis of data from the Pediatric Cardiomyopathy Registry	What are the risk factors (at presentation) for death and transplantation in children with hypertrophic cardiomyopathy?	In children with hypertrophic cardiomyopathy, the risk of death or heart transplantation was greatest for those who presented as infants or with inborn errors of metabolism or with mixed hypertrophic and dilated or restrictive cardiomyopathy. Risk stratification by subgroup of cardiomyopathy, by characteristics such as low weight, congestive heart failure, or abnormal echocardiographic findings, and by the presence of multiple risk factors allows for more informed clinical decision making and prognosis at the time of diagnosis

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Table 1: (Continued)

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General pediatric cardiology	Pees C, Laccone F, Hagl M, Debrauwer V, Moser E, Michel-Behnke I. Usefulness of losartan on the size of the ascending aorta in an unselected cohort of children, adolescents, and young adults with Marfan syndrome. Am J Cardiol 2013;112:1477-83	Prospective uncontrolled, single center, study involving a small cohort of 20 patients (1.7-21.6 years) with genetically proven Marfan Syndrome	Does Losartan therapy reduce the risk of progression of aortic dilation in patients with Marfan Syndrome?	Over a mean follow-up period of 33 ± 11 months, a significant reduction in the normalized aortic dimensions with losartan was observed in the valve, root, sinotubular junction, and ascending aortic segment
Electrophysiology	Huang C, Kaza AK, Hitchcock RW, Sachse FB. Identification of nodal tissue in the living heart using rapid scanning fiber-optics confocal microscopy and extracellular fluorophores. Circ Cardiovasc Imaging 2013;6:739-46	Experimental animal model	Whether nodal tissue can be visualized during surgery?	The study demonstrates feasibility of identifying nodal tissue in living heart using extracellular fluorophores and fiber-optics confocal microscopy. Application of the approach in pediatric reconstructive heart surgery may reduce risks of injuring nodal tissues
Pediatric cardiac surgery	Newburger JW, Sleeper LA, Frommelt PC2, Pearson GD, Mahle WT, Chen S, Dunbar-Masterson C, Mital S, Williams IA, Ghanayem NS, Goldberg CS, Jacobs JP, Krawczeski CD, Lewis AB, Pasquali SK, Pizarro C, Gruber PJ, Atz AM, Khaikin S, Gaynor JW, Ohye RG. Transplantation-free survival and interventions at 3 years in the single ventricle reconstruction trial. Circulation 2014;129:2013-20	Randomised controlled trial	What is the difference in transplantation-free survival, echocardiographic right ventricular ejection fraction, and unplanned interventions between Blalock Taussig shunts (MBT) and right ventricle to pulmonary artery conduits (RVPAS) in newborns undergoing the Norwood operation?	At 3 years, the Norwood procedure with RVPAS was not associated with superior transplantation-free survival When compared with MBT. Moreover, RVPAS subjects had slightly worse right ventricular ejection fraction and underwent more catheter interventions with increasing hazard ratio over time
Fetal cardiolgy	Kawazu Y, Inamura N, Shiono N, Kanagawa N, Narita J, Hamamichi Y, Kayatani F. "Post-LA space index" as a potential novel marker for the prenatal diagnosis of isolated total anomalous pulmonary venous connection. Ultrasound Obstet Gynecol 2014	Retrospective review	Whether TAPVC without any intracardiac defect can be diagnosed with surrogate marker Post LA space index	The post-LA space index can be used as a potential novel index for foetal TAPVC diagnosis. A diagnosis of TAPVC is very likely in cases with a post-LA space index > 1.27
General pediatric cardiology, catheter interventions, pediatric cardiac surgery	Yang J, Yang L, Yu S, Liu J, Zuo J, Chen W, Duan W, Zheng Q, Xu X, Li J, Zhang J, Xu J, Sun L, Yang X, Xiong L, Yi D, Wang L, Liu Q, Ge S, Ren J. Transcatheter versus surgical closure of perimembranous ventricular septal defects in children: A randomized controlled trial. J Am Coll Cardiol 2014;63:1159-68	Randomised controlled trial	Safety and efficacy study of catheter closure of membranous VSD versus. Transcather and surgical closure	Transcatheter device closure and surgical repair are effective interventions with excellent midterm results for treating pmVSD in children. Transcatheter device closure has a lower incidence of myocardial injury, less blood transfused, faster recovery, shorter hospital stay, and lower medical expenses
Catheter intervention	Huggins N, Nugent A, Modem V, Rodriguez JS, Forbess J, Scott W, Dimas VV. Incidence of acute kidney injury following cardiac catheterization prior to cardiopulmonary bypass in children. Catheter Cardiovasc Interv 2014	Retrospective study	Whether contrast injection in the immediate preoperative period (<48 hrs) is a risk factor for post oprenal injury	Contrast administration within 48 hr prior to CPB was not an additional risk factor for the development of acute kidney Injury

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Table 1: (Continued)

Category	Reference (Pubmed citation)	Study design	Specific study question	Main conclusions
Generalcardiology, pulmonary hypertension	Robbins IM, Hemnes AR, Pugh ME, Brittain EL, Zhao DX, Piana RN, Fong PP, Newman JH. High prevalence of occult pulmonary venous hypertension revealed by fluid challenge in pulmonary hypertension.Circ Heart Fail 2014;7:116-22	Prospective observationalstudy	Does fluid challenge during right heart catheterization in patients with pulmonary arterial hypertension identify occult pulmonary venous hypertension?	Fluid challenge at the time of right heart catheterization is easily performed, safe, and identifies a large group of patients diagnosed initially with PAH, but for whom OPVH contributes to pulmonary hypertension
Catheter intervention	Mah DY, Porras D, Bergersen L, Marshall AC, Walsh EP, Triedman JK. Incidence of and risk factors for catheterization-induced complete heart block in the pediatric cardiac catheterization laboratory. Circ Arrhythm Electrophysiol 2014;7:127-33	Retrospective study	What is the incidence for development of complete heart block following pediatric cardiac catheterization?What are the risk factors? What is the eventual outcome?	The incidence of CIHB in the pediatric cardiac catheterization laboratory is low at 2.2%. Risk factors include young age and long case duration. The recovery of atrioventricular nodal function after CIHB is high and follows a similar time course to that of postsurgical heart block
Imaging, MRI, cardiac catheterization	Downing TE, Whitehead KK, Dori Y, Gillespie MJ, Harris MA, Fogel MA, Rome JJ, Glatz AC. Accuracy of conventional oximetry for flow estimation in patients with superior cavopulmonary connection: A comparison with phase-contrast cardiac MRI.Circ Cardiovasc Imaging 2013;6:943-9	Retrospectivestudy	What is the error in oximetry-derived flow parameters using phase-contrast cardiac MRI (CMR) as a reference?	Fick-derived estimates of flow are inherently unreliable in patients with superior cavopulmonary connections. Integrating flows measured by CMR and pressures measured by catheter will provide the best characterization of superior cavopulmonary connection physiology
General pediatric cardiology, neonatology	Dang D, Wang D, Zhang C, Zhou W, Zhou Q, Wu H. Comparison of oral paracetamol versus ibuprofen in premature infants with patent ductus arteriosus: A randomized controlled trial. PLoS One20134;8:e77888	Randomized, non-blinded, parallel-controlled and non-inferiority trial	What is the efficacy and safety profile of oral paracetamol when compared with standard ibuprofen for PDA closure in premature infants?	Oral paracetamol was comparable to ibuprofen in terms of the rate of ductal closure with a decreased risk of hyperbilirubinemia or gastrointestinal bleeding?
General cardiology, imaging	Kang JW, Song HG, Yang DH, Baek S, Kim DH, Song JM, Kang DH, Lim TH, Song JK. Association between bicuspid aortic valve phenotype and patterns of valvular dysfunction and bicuspid aortopathy: Comprehensive evaluation using MDCT and echocardiography. JACC Cardiovasc Imaging 2013;6:150-61	Retrospectivestudy	What is the clinical importance of an integrated classification of bicuspid aortic valve (BAV) phenotypes and aortopathy using multidetector computed tomography?	The patterns of valvular dysfunction and bicuspid aortopathy differed significantly between the two BAV phenotypes. moderate-to-severe aortic stenosis predominating in patients with BAV-Right lefta nd moderate-to-severe aortic regurgitation in BAV-Anteroposterior
Imaging, catheter interventions, rheumatic heart disease	Nunes MC, Tan TC, Elmariah S, do Lago R, Margey R, Cruz-Gonzalez I, Zheng H, Handschumacher MD, Inglessis I, Palacios IF, Weyman AE, Hung J. The echo score revisited: Impact of incorporating commissural morphology and leaflet displacement to the prediction of outcome for patients undergoing percutaneous mitral valvuloplasty. Circulation 2014;129:886-95	Prospective observational study	What is the incremental value of new, more quantitative methods for predicting the immediate and long-term outcome after percutaneous mitral valvotomy for rheumatic mitral valve stenosis?	A scoring system incorporating new quantitative echocardiographic parameters more accurately predicts outcome following PMV than existing models. Long-term post-PMV event-free survival was predicted by age, degree of mitral regurgitation, and postprocedural hemodynamic data

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General pediatric cardiology	Molina KM, Shrader P, Colan SD, Mital S, Margossian R, Sleeper LA, Shirali G, Barker P, Canter CE, Altmann K, Radojewski E, Tierney ES, Rychik J, Tani LY; Pediatric Heart Network Investigators. Predictors of disease progression in pediatric dilated cardiomyopathy. Circ Heart Fail 2013;6:1214-22	Preospective, multi center, observational study of a cohort of children with dilated cardiomyopathy	What are the predictors of disease progression in pediatric dilated cardiomyopathy?	Multivariable analysis identified older age at diagnosis, larger left ventricular (LV) end-diastolic M-mode dimension z-score and lower septal peak systolic tissue Doppler velocity z-score as independent predictors of disease progression
General pediatric cardiology, pulmonary hypertension	Myers PO, Tissot C, Beghetti M. Assessment of operability of patients with pulmonary arterial hypertension associated with congenital heart disease. Circ J 2013;78:4-11	Review	What are the current methods for assessing operability in PAH associated with congenital heart disease in the era of pulmonary vasodilators?	Review focussingon current methods for assessing operability in PAH associated with congenital heart disease, and the possibility of “treat-and-repair” vs. “repair-and-treat” strategies for patients with inoperable or borderline PAH
Imaging, echocardiograhy	Groh GK, Levy PT, Holland MR, Murphy JJ, Sekarski TJ, Myers CL, Hartman DP, Roiger RD, Singh GK. Doppler echocardiography inaccurately estimates right ventricular pressure in children with elevated right heart pressure. J Am Soc Echocardiogr 2014;27:163-71	Prospective observational study	What is the accuracy of Doppler echocardiographyin predicting simultaneously measured right ventricular pressure by right heart catheterization (RHC) in pediatric patients?	Despite a reasonable correlation between Doppler and RHC in all groups, there was poor agreement between techniques as the ratio of right ventricular systolic pressure to systolic blood pressure increased
Adult congenital Heart disease; electrophysiology	Valente AM, Gauvreau K, Assenza GE, Babu-Narayan SV, Schreier J, Gatzoulis MA, Groenink M, Inuzuka R, Kilner PJ, Koyak Z, Landzberg MJ, Mulder B, Powell AJ, Wald R, Geva T. Contemporary predictors of death and sustained ventricular tachycardia in patients with repaired tetralogy of fallot enrolled in the indicator cohort. Heart 2014;100:247-53	Prospective observational study, multicenter	What are the risk factors for death and ventricular tachycardia (VT) in a large contemporary cohort of patients with repaired Tetralogy of Fallot (TOF)?	Right Ventricular hypertrophy, ventricular dysfunction and atrial tachyarrhythmias are predictive of death and sustained VT in adults with repaired TOF
General pediatric cardiology	Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010. Circulation 2014. [Epub ahead of print]	Analysis of longitudinally collected population based data on CHD from the state of Quebec, Canada	What is point and interval prevalence estimates (95% CI) of CHD in the first year of life, in children (<18 years of age) and in adults?	Prevalence of CHD in the first year of life was 8.21/1000 live-births.With an increase of more than 50% in CHD prevalence since 2000, by 2010 adults accounted for two-thirds of patients with severe and other forms of CHD in the general population

idiopathic HCM age >/= 1 year has only a 7% incidence of adverse outcome. The mixed phenotype group also has a poor outlook with a 41% incidence of death/transplantation. The cause of death has been classified into cardiac, non-cardiac, unknown, *etc.* This classification is somewhat ill defined and makes it difficult to interpret the results in any constructive fashion.

The study identifies univariate risk factors for adverse outcome in the different groups and then applies multiple regression analysis to identify multivariate risk factors for death/transplantation. Female sex and decreased LV fractional shortening have statistical significance in the idiopathic HCM >/= 1 year group. Decreased weight and presence of congestive heart failure (CHF) appear significant in the idiopathic HCM <1-year group. The presence of CHF and earlier presentation appear to be important risk factors in most of the sub groups. In addition various echo parameters like LV posterior wall thickness and fractional shortening also feature importantly. The study then develops a model to determine the risk of death or transplantation at 2 years after diagnosis according to the number of risk factors and finds that patients with 2

or more risk factors have a significantly poorer outcome. For example in the group with isolated HCM age < 1 y, the presence of 2 risk factors increases the probability of adverse outcome from 4% to 38%. There are defined threshold values for scoring points in this model which could prove useful in individual patient management and risk stratification at the time of diagnosis.

This study is an elegantly executed retrospective analysis of a large volume of data collected on a rare condition. It not only identifies risk factors for adverse outcome but also illustrates the additive effect of multiple risk factors. One of the deficiencies to be pointed out is that there appears to be a significant attrition in the number of patients at risk during the study period and there is no clear data or explanation of what happened to these patients and whether these patients were similar in their baseline characteristics to the patients who remained under follow up. The authors express hope that their model will help identify patients who would benefit from early transplantation. This will need to be validated further before it can be put to widespread clinical use to determine the timing of transplantation in pediatric patients with HCM.

Transcatheter versus surgical closure of perimembranous ventricular septal defects in children: A randomized controlled trial. Yang J, Yang L, Yu S, Liu J, Zuo J, Chen W, Duan W, Zheng Q, Xu X, Li J, Zhang J, Xu J, Sun L, Yang X, Xiong L, Yi D, Wang L, Liu Q, Ge S, Ren J.J Am Coll Cardiol. 2014 Apr 1;63(12):1159-68.

Critique by Sangeetha Viswanathan

This randomized controlled trial is from northwest China and compares the safety and efficacy of trans-catheter *versus* surgical closure of perimembranous VSDs. Stringent inclusion and exclusion criteria were applied and 229 out of 465 children between 3 and 12 years of age with a perimembranous VSD were found suitable for randomization. Out of the 229 patients enrolled, 114 were enrolled in the transcatheter group and 115 in the surgical group. Of these, 200 patients completed the study and this data were analyzed.

All patients underwent echocardiography and cardiac catheterization prior to VSD closure. A set protocol was followed and data recorded in a systematic fashion. Following VSD closure (surgical and device) biochemical tests were performed to assess the liver (AST/ALT), kidney (BUN/Creatinine) and heart (Troponin and CK-MB). Patients were followed up for 2 years at regular intervals as follows at 3 days, 3 months, 6 months, 1 year, and 2 years.

The baseline characteristics were compared and found to be similar. Mean defect size was comparable (5.9 mm *vs.* 5.2 mm) as was the weight (20.5 kg *vs.* 22.1 kg). The mean Qp/Qs was 2.3 in the surgical group and 2.5 in the transcatheter group. Various echocardiographic and hemodynamic parameters were also found to be similar between the two groups. The mean LVEDD z score was elevated in both groups (+1.8 *vs.* + 1.7). There were altogether 53 patients who had a Qp/Qs value of less than 1.5:1 and of these 38 patients did not have significant left ventricular dilation. These patients were enrolled into the study due to refractory symptoms or parental insistence. Although this is a significant number of patients who do not strictly fulfill the inclusion criteria for VSD closure this situation mirrors reality in many ways.

The outcome variables that were compared included average procedural time, major and minor adverse events including death, complete AV block, AV valve leak requiring surgery, bleeding requiring re-exploration, need for blood transfusion, rhythm disturbance, and residual shunts. The periprocedural data revealed that transcatheter closure required a shorter procedure time (38.2 min *vs.* 180.5 min); shorter ICU and hospital stay (3.3 days *vs.* 7.2 days) and incurred a lower cost. There was also less blood loss and lower incidence of blood transfusion with this method. It was found that there was a significant difference in the incidence of minor adverse events mainly related to the increased need for blood transfusion in the surgical group (23 *vs.* 0) and an overall low incidence of major adverse events in both groups of patients with no mortality and no incidence of complete heart block. The transcatheter closure group showed no change in the biochemical parameters while the surgical group showed a clear increase in values with a return to normal levels at 72 h post surgery.

At 2 year follow up patients in both the groups remained well and the LVEDD had reduced significantly in both groups with no significant difference between the groups. Minor rhythm disturbances, AV valve leak and small residual shunts either resolved or remained unchanged. The authors therefore conclude that the mid-term results of the two procedures are comparable with a lower need for transfusions, shorter hospitalization duration and lower cost in the transcatheter group. They recommend transcatheter closure in the group of patients between 3 and 12 years of age with a hemodynamically significant perimembranous VSD (Qp/Qs 1.5:1 to 2.5:1) and anatomy that is suitable for transcatheter closure.

The authors take pains to point out their strict inclusion and exclusion criteria based on age and hemodynamic significance of the VSD and caution against extrapolating their results to all patients with perimembranous VSDs. Overall a very well conducted clinical trial; which compares two treatment modalities. Due to the nature of the treatment modality the study cannot be blinded and cross over is not possible. However the data obtained does in its own right add value to the existing literature. Although the authors clearly point out the limited applicability of their results at the conclusion of the

paper perhaps the inclusion and exclusion criteria could be stated more clearly at the outset.

Accuracy of conventional oximetry for flow estimation in patients with superior cavopulmonary connection: A comparison with phase-contrast cardiac MRI. Downing TE, Whitehead KK, Dori Y, Gillespie MJ, Harris MA, Fogel MA, Rome JJ, Glatz AC. Circ Cardiovasc Imaging 2013 Nov;6(6):943-9.

Critique by Mahesh Kappanayil

Superior cavopulmonary connection (SCPC) is interim palliation for a wide spectrum of single-ventricle lesions. Accurate hemodynamic assessment is critical to planning management. Cardiac catheterization is the conventional modality for assessment of flows, pressures and vascular resistances. However, it is subject to potential errors resulting from inherent fallacies of applying Fick principle, as well as the uniqueness of SCPC physiology, *e.g.*, presence of multiple sources of pulmonary blood flow, presence of aorto-pulmonary collaterals, inaccuracies in measured SO_2 and assumption of oxygen consumption, which in-turn impact calculation of flows and resistances. Cardiac MRI (CMRI) is a powerful, non-invasive tool for hemodynamic assessment and its accuracy in simple flow assessment has been adequately validated previously.

This paper from Children's Hospital of Philadelphia attempts to elucidate the validity and inherent errors of conventional oximetry-based approach to determining flows (Qp, Qs) and PVR in a subset of single-ventricle patients palliated with SCPC, by comparing oximetry-derived data against flow-data obtained on phase contrast MRI (PC-MRI).

This retrospective analysis looks at data from 30 patients (median age 2.6 years) with SCPC who underwent combined CMRI and catheterization (XMR) for hemodynamic assessment, between June 2008 and July 2011. All patients were mechanically ventilated on room air for both modalities, under the same general anesthetic, and underwent CMRI immediately before catheterization .*Qp* on PC-MRI was defined as sum-total of pulmonary venous returns, and *Qs* was defined as the sum-total of caval flows (SVC + IVC). Systemic-to-pulmonary arterial collateral flows were calculated as difference between pulmonary arterial and venous flows, or aortic minus caval flows. All MRI analyses were done by a single physician blinded to the catheterization data, and withstood internal validation.

Flows were calculated on catheterization using conventional oximetry techniques and assumed oxygen consumption (aVO2). While PVR was calculated by conventional method using Fick-derived Qp, "MRI-corrected PVR" was calculated by substituting Fick-Qp by MRI-derived Qp.Qp, Qs and PVR derived by catheterization were compared to the MRI-derived Qp, Qs, and MRI-corrected PVR.

Authors found significant discrepancy between the two modalities. Fick-derived Qp *underestimate*d MRI-based Qp measurements by an average of 1.1 L/min/m^2, or 32% of CMR value ($P < 0.0001$) with a range of discrepancy as wide as 0.1-2.5 L/min, and overall poor agreement ($\rho_c = 0.33$). This discrepancy showed modest correlation with presence of systemic-to-arterial collaterals ($r = 0.39$). This is explainable by the fact that while CMR calculates Qp by measuring total pulmonary venous return, oximetry is unable to account for the collateral flows in Qp derivation and thereby gives a lower value. Qp underestimation may also partly result from using a lower assumed VO2 value than the actual VO2. On the other hand, Oximetry-derived Qs exceeded CMR-derived Qs by an average of 0.5 L/min/m^2, or 15% of CMR value ($P = 0.009$), with weak linear correlation and poor overall agreement ($\rho_c = 0.24$). Authors explain it by the possibility that the upper body (SVC) receives a disproportionately higher blood flow than the actual metabolic demand, resulting in higher SVC SO2, overestimating mixed venous saturation and thereby Qs.

These significant and opposite errors in Fick-derived Qp and Qs calculations translated into erroneous Qp:Qs ratios, with no correlation to the "actual" CMR-derived Qp:Qs. Fick-based PVR was higher than CMR-corrected PVR in all but one patient, with a mean difference of 0.6 Wood units ($P < 0.0001$), discrepancy most notable in patients with higher PVR. These discrepancies in Qp:Qs and PVR may have considerable impact on determining suitability for Fontan operation.

Authors also investigated the possibility of erroneous VO2 assumptions impacting flow calculations by Fick principle. They calculated VO2 combining CMR-derived flow-measurements in the SVC, IVC, Aorta and pulmonary veins, with SO2-measurements obtained on catheterization, in Fick principle equations. Median *calculated* VO2 was found to be 173 ml/min/m^2 compared to median *assumed* VO2 of 160 ml/min/m^2. While this contributed to the underestimation of Qp by oximetry, it does not explain the "overestimation" of Fick-derived Qs.

The authors concluded that Fick-derived estimates of flow are inherently flawed in superior cavopulmonary connections and wherever possible, an integrated approach combining CMR-derived flow-measurements and catheterization-derived pressures and SO_2 will give the best characterization of physiology. In the absence of access to CMR, catheterization data must be interpreted with caution, understanding its limitations.

Specific limitations of this study include its retrospective nature and inherent selection bias. Primary indications

for subjecting these 30 patients to a combined catheterization-and-CMR protocol are not specified, nor are the impact of XMR on their eventual clinical management or outcomes. Further studies are warranted to validate such an approach combining cardiac catheterization and CMR in comprehensive evaluation of single ventricle physiology.

Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010. Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Circulation 2014 Jun 18. pii: CIRCULATIONAHA.113.008396. [Epub ahead of print]

Critique by S Mani Ram Krishna

The incidence of congenital heart disease (CHD) in any birth cohort is widely quoted to be 1%. Data published by the Center for Disease Control (CDC) for a period of 17 years from Atlanta puts the number at 8.14/live births. The incidence of congenital heart diseases are believed to be similar in most parts of the world and no significant ethnic or racial differences in the incidence have been reported in congenital heart diseases unlike some other birth defects. Birth defects represent the fourth largest sub-group requiring use of medical services in the western world and may account for almost two-thirds of the healthcare cost for birth defects. Results of interventions for congenital heart disease are probably more gratifying than most other birth defects. In this scenario, identifying the prevalence of congenital heart diseases in a given population is of value to policy makers. However, estimation of prevalence of CHD in the general population is a monumental task. This is further complicated by the widely variable natural histories of many of the lesions as well as the multitude of permutations and combinations possible within each subset of disease making the coding of such diseases very challenging.

This study from Marelli and colleagues from Montreal attempts to identify the prevalence of congenital heart diseases in children and adults in Quebec province of Canada and analyze longitudinal trends in the prevalence over a quarter of a century based on the Quebec Congenital Heart Disease database. This study is unique, as the challenges involved in collecting such data have previously been mentioned. The study was possible because Quebec province has a stable population with low emigration rates, there is universal health coverage for the entire population and a comprehensive database records all contacts of individual patients with the healthcare network. Indeed such data are likely to be available in very few regions of the world.

The study is an extension of a previous report from the same group in 2007 analyzing trends from 1985 to 2000. The Quebec CHD database was established during research for the previous report. A unique Medicare ID number is allotted to each infant in Quebec province and is used for record maintenance in all centers in the province. The authors used data from physician services, hospital discharge summaries and death registries to identify patients with congenital heart disease. One-third of all entries were manually audited by the authors to further lend credibility to the data. The patients with CHD were further classified into complex lesions, which included Tetralogy of Fallot, Truncus arteriosus, Transposition, Endocardial Cushion defects, univentricular hearts, and the hypoplastic left heart spectrum. The rest were marked as other lesions. This is probably a somewhat simplistic outlook.

The lifetime prevalence of congenital heart disease among children was 13.11/1000 and among adults, 6.12/1000. However, the prevalence of complex congenital lesions among children and adults were 1.76/1000 and 0.62/1000, respectively. Simple lesions clearly outnumber the complex lesions by a factor of 10. The outcomes of interventions for such lesions are also vastly superior to complex lesions and this data validates the need for an aggressive approach to identify children with simple defects and intervene early in the natural history.

Table 2 illustrates that there has not been a major change in the number of children with congenital heart diseases. This implies that the incidence of CHD has remained fairly constant over the decade with no major epidemiological shift. However there is a rapid increase in the number of adults with congenital heart disease. The increase in prevalence rate is only 11% for children, while for adults the increase is 57%. While a number of these adults may have simple defects that have been completely corrected with no major difference in long-term outcome, the analysis for complex lesions also throws up similar numbers. This shows that advancements in management of complex lesions have resulted in increased survival to adulthood. These patients will be exposed to adult healthcare workers with limited experience in managing these lesions. There is hence a need to substantially improve facilities for care of adult congenital heart disease care on a war footing. This data has important implications for our country. Organized healthcare for infants and young children with CHD is still in a budding stage in our country and is localized to a few pockets of the country. Services for adults with CHD are practically non-existent. However, given the large population of our country and the

Table 2: Total numbers identified with congenital heart disease in the years 2000-2010

Year	2000%	2005%	2010%
Children	18,913	20,111	22,291
Adults	22,291	24,851	39,051
Percentage of adults	54	57	66

potential for large number of adults with unidentified CHD, focused improvement in pediatric CHD care will result in a large number of adults with complex health care needs and virtually no available services. Great vision is hence needed in concomitantly developing resources for management of adult CHD while expanding services for identifying and treating children with heart disease. Age group analysis showed doubling of the prevalence of CHD in adults above 26 years of age from the year 2000 to the year 2010. This reiterates the urgent need for specialized adult CHD services especially to cater to adults with complex lesions.

The authors need to be lauded for the effort and time dedicated to the development of the database and this paper should serve as an encouragement for pediatric cardiologists in other parts of the world to develop similar databases. Though complex statistical methods were used to validate the data, the conclusions make clinical sense and clearly identify areas of healthcare that need urgent strengthening. In spite of that fact that the results of the paper has Global appeal, the entire discussion has been dedicated toward establishing the similarity of this population to that of the United States, perhaps suggesting a somewhat narrow perspective.

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