Prevalence of Coronary Artery Disease among Adult Patients with Congenital Heart Disease who Underwent Coronary Angiogram at the University of the Philippines-Philippine General Hospital from September 1998 to November 2011

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ABSTRACT

Objectives. To determine prevalence of coronary artery disease (CAD) among adult patients with congenital heart disease (CHD), who underwent Coronary Angiography (CA) at the UP-PGH. Secondary: to determine severity of CAD lesions among these patients.

Methods. This is a descriptive study of adult patients with Congenital Heart Disease who underwent selective coronary angiography from September 1998 to December 2010 at the Philippine General Hospital.

Results. 52 adult patients with CHD underwent CA, Ten (19%) had angiographic evidence of coronary atherosclerosis visually. Significant CAD was found in 11.5% (n=6), all patients being ≥ 40 years old (mean age 54 ± 7.9 years; range 47 -61); 4 (66%) are female; Five (83%) have documented traditional CVD risk factors, mostly hypertensive (33%). None with significant CAD had cyanosis, 4 patients (66%) have typical chest pain. Majority of CHD's were simple (61%), mostly atrial septal defects (36%). Four (n=4)(70%) patients with Simple CHD, 2 (30%) patients with Intermediate CHD and none of those with Complex CHD had significant CAD.

Conclusion. Prevalence of CAD among ACHD patients using CA in this study is 11.5%. This study supports the notion of routine CA among patients with ACHD ≥ 35 years old with traditional CV risk factors. Need for primary prevention of CAD and modification of traditional CV risk factors among these patients is emphasized, as important with the general population.

Key Words: adult congenital heart disease, coronary artery disease, prevalence

Introduction

The diagnosis and the management of Congenital Heart Disease have changed significantly over the last 50 years.[1] With the present advances in cardiac surgery and perioperative care, and with improved understanding of the pathophysiologic characteristics of congenital heart disease (CHD), more than 85% of infants with inborn cardiac defects are now expected to reach adulthood.[2] As these patients grow older, they become more likely to develop coronary artery disease (CAD). Because significant efforts had been focused to address the congenital and hemodynamic aspects of congenital heart disease, the risk of myocardial ischemia may be overlooked. This is accentuated by the lack of data about the burden of CAD in the growing and aging CHD population.

Birth prevalence for all forms of CHD detected in the first year of life is estimated at 8.1 per thousand live births on the basis of the data from the Centers for Disease Control.[3] It is estimated by the National Center for Health Statistics that by 2020, nearly 760,000 individuals will have CHD, with 20,000 in the more severe group.

Since the 1990's, Myocardial Infarction (MI) has become the leading contributing cause of death among non-cyanotic congenital heart disease consistent with late survival and an increasing impact of acquired heart disease, arrhythmia, followed by heart failure were found among adults with cyanotic lesions.[1] Despite the decreasing trend in mortality among adult CHD, the burden of coronary artery disease warrants attention and early detection.

In the general population, the prevalence of coronary vessel wall alteration is unknown. This is due to the fact that coronary angiography is generally only indicated in patients with a history of coronary artery disease.[4] Previous reports on post mortem analyses of asymptomatic patients who died of causes unrelated to coronary artery disease pointed to an

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estimated prevalence of coronary artery disease of 4.5%. Gensini et al demonstrated the incidence of 4.5% in a group of 278 adults undergoing cardiac catheterization with the clinical diagnosis of valvular or congenital heart disease in the absence of symptoms suspicious for coronary artery disease.[5] International data conducted by Giannakoulas in 2009 showed 9.2% of adult patients with CHD was found with significant CAD using quantitative coronary angiography.[2] There is currently no available local data that had determined the prevalence of CAD among CHD.

The striking increase in the estimated number of patients with CHD would require competent care and evaluation in anticipation of the changing profile of this patient population particularly of advancing age associated with the occurrence of significant co-morbid factors. The development of cardiovascular disease in these patients may often compound pre-existing abnormalities. Early and appropriate recognition of Coronary Artery Disease therefore is important in this group of patients.

Objectives

Primary Objective: To determine the prevalence of coronary artery disease (CAD) among adult patients with congenital heart disease who underwent Coronary Angiography at the UP- Philippine General Hospital.

Secondary Objective: To determine the severity of CAD lesions among patients with CHD.

Materials and Methods

Study Design

This is a descriptive study of adult patients with Congenital Heart Disease who underwent selective coronary angiography from September 1998 to December 2010 at the Philippine General Hospital.

Inclusion Criteria

All adult patients (aged above 18 years old) with congenital heart disease of any type who underwent coronary angiography from September 1998 to December 2010 were identified using the PGH Cardiac Catheterization Laboratory Database and were included in the study.

Data Collection

Clinical variables and hemodynamic data were retrieved from the Medical Records Section at the UP-PGH Cardiac Catheterization Laboratory database. Data were reviewed and recorded using a standardized data collection form.

The following data were collected: demographics, which include age and sex; clinical history (presence or absence of cyanosis, chest pain, functional classification and current medications, 2-D Echocardiographic and Angiographic Findings); and risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking history and family history of CAD). Patients were classified according to reasons for referral to angiography, age group, and types of congenital heart disease. Coronary angiogram was independently reviewed by two interventional cardiologists blinded to the patients' clinical data.

Data Analyses

The information gathered from each data collection forms were encoded and tabulated in a personal computer using the Microsoft Excel Software. Data were then analyzed and described.

Institutional Approval

The study was reviewed by the UP- PGH Technical Review Board and was approved by the UP-PGH Ethical Review Board. Information gathered remained confidential and patients were anonymized. There was no extramural funding.

Ethical considerations

There were no ethical issues considered in this particular study because it had only utilized review of existing medical records. Neither was there direct interaction nor intervention with the patient.

Definition of Terms

1. CHD – Congenital Heart Disease; abnormality in cardiovascular structure or function that is present at birth, even if it is discovered much later.[6,7]
   - **a.** Simple CHD – Native Disease: isolated congenital aortic valve, isolated congenital mitral valve (e.g., except parachute valve, cleft leaflet), isolated patent foramen ovale or small atrial septal defect, isolated small ventricular septal defect (no associated lesions), mild pulmonic stenosis. Repaired Conditions: previously ligated or occluded ductus arteriosus, repaired secundum or sinus venosus atrial septal defect without residua, repaired ventricular septal defect without residual;
   - **b.** Intermediate CHD – aorto-left ventricular fistula, anomalous pulmonary venous drainage (partial or total), atrioventricular canal defects (partial or complete), coarctation of the aorta, Ebstein anomaly, infundibular right ventricular outflow obstruction of significance, ostium primun atrial septal defect, patent ductus arteriosus (not closed), pulmonary valve regurgitation moderate to severe, pulmonic valve stenosis moderate to severe, Sinus of Valsalva, sinus venosus ASD, subvalvar or supravalvar aortic stenosis except HOCM, Tetralogy of Fallot, ventricular septal defect (with

absent valves, aortic regurgitation, coarctation of the aorta, mitral disease, right ventricular outflow tract obstruction, straddling tricuspid/mitral valve, subaortic stenosis);

c. Complex CHD – conduits; valved or nonvalved, all forms of cyanotic congenital heart disease, double outlet ventricle, eisenmenger syndrome, fontan procedure, mitral atresia, single ventricle, pulmonary atresia all forms, pulmonary vascular obstructive disease, transposition of great arteries, tricuspid atresia, truncus arteriosus/hemitruncus, other abnormalities of atrioventricular or ventriculoatrial connection not included above (crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion)

2. CAD – Coronary Artery Disease; obstruction of the coronary arteries by atheromatous plaque proven on coronary angiography.
   a. Angiographically-significant CAD – presence of ≥ 1 lesion with diameter stenosis > 50% in any of the three major coronary arteries or > 50% in the left main coronary artery.

Results

A total of 90 adult patients with congenital heart disease (CHD) underwent hemodynamic assessment and interventions at the UP-PGH Catheterization laboratory during the study period. Of these, 52 patients underwent coronary angiography (Table 1), 27 (52%) of whom were 40 years old and above, who underwent coronary angiography as routine diagnostic assessment to rule out presence of coronary artery disease prior to planned interventions. Among those patients below 40 years old, coronary angiography was performed as part of the diagnostic hemodynamic assessment, to rule out congenital coronary vascular anomalies and diagnostic evaluation of patients with left ventricular dysfunction presenting with wall motion abnormalities on echocardiography.

Mean age was 45 ± 12.2 years old (range 18 – 66 years) (Table 2) and 43 % (n=23) were male (Table 1). Patients with all types of CHD were included and classified as simple, intermediate or complex CHD (Figure 1). Majority (61%) of congenital heart diseases in our study were simple CHD (Table 2), comprised mostly of atrial septal defects (36%) and ventricular septal defects (16%). One (1.9%) patient had a history of myocardial infarction.

Overall, 10 patients (19%) had angiographic evidence of coronary atherosclerosis on visual assessment, of which 6 patients (11.5 %) was significant. Mean age of patients with significant CAD was 54 ± 7.9 years (range 47 -61) (Table 2).

Table 1. Demographic and Clinical Characteristics of Adult patients with Congenital Heart Disease according to Gender who underwent Coronary Angiography at the UP-PGH.

VARIABLES	Male n= 23 (44 %)	n= 29 (56 %)	Total n= 52 (100 %)
Average Age (yrs)	35 ±12.2 yo (18 – 59 yo)	27± 13.8yo (20 – 66 yo)	45±12.2yo (18 – 66 yo)
CHD			
Simple	13(57%)	19 (66%)	32 (62%)
Intermediate	9 (39%)	9 (31%)	18 (35%)
Complex	1 (4%)	1 (03%)	2 (4%)
Functional Capacity			
I	4 (17%)	12 (41%)	16 (31%)
II	17 (74%)	12 (41%)	29 (56%)
III/IV	2 (09 %)	5 (17%)	7(13%)
CVD Risk Factors	7 (30%)	8 (28%)	15 (29%)
HPN	2 (09%)	3 (10%)	5 (10%)
DM	1 (04%)	1 (03%)	2 (04%)
Dyslipidemia	1 (04%)	1 (03%0	2 (04%)
Smoker	2 (09%)	3 (10%)	5 (10%)
Family Hx of CAD	1 (04%)	0(0%)	1 (02%)
Heart Failure Symptoms*	20(53%)	21 (72%)	41 (79%)
Medications	11 (48%)	10 (34%)	21 (40%)
Bblockers	2 (09%)	5(17%)	7 (13%)
ACEI	9 (39%)	8(28%)	17 (33%)
CCB	1(04%)	1(03%)	2 (04%)
Digoxin	6(26%)	3(10%)	9 (17%)
ASA	4(23%)	2 (07%)	6 (11%)
Diuretics	5(22%)	6(21%)	11 (21%)
Warfarin	0(0%)	0(0%)	0(0%)

*Note: **Simple CHD** – Native Disease : Isolated congenital aortic valve, Isolated congenital mitral valve (e.g. except parachute valve, cleft leaflet), Isolated patent foramen ovale or small atrial septal defect, Isolated small VSD (no associated lesions), Mild pulmonic stenosis. Repaired Conditions: Previously ligated or occluded ductus arteriosus, Repaired secundum or sinus venosus atrial septal defect without residua, Repaired ventricular septal defect without residua.**Intermediate CHD** – Aorto-left ventricular fistula, anomalous pulmonary venous drainage (partial or total), Atrioventricular canal defects (partial or complete), Coarctation of the aorta, Ebstein anomaly,Infundibular right ventricular outflow obstruction of significance, Ostium primun atrial septal defect, Patent ductus arteriosus (not closed), Pulmonary valve regurgitation moderate to severe, Pulmonic valve stenosis moderate to severe, Sinus of valsalva, Sinus Venosus ASD, Subvalvar or supravalvar aortic stenosis except HOCM, Tetralogy of Fallot, Ventricular septal defect (with absent valves, aortic regurgitation, coarctation of the aorta, mitral disease, right ventricular outflow tract obstruction, straddling tricuspid/mitral valve, subaortic stenosis)**Complex CHD** – Conduits; valved or nonvalved, all forms of cyanotic congenital heart disease, double outlet ventricle, eisenmenger syndrome, fontan procedure, Mitral atresia, Single ventricle, Pulmonary atresia all forms, Pulmonary vascular obstructive disease, Transposition of great arteries, Tricuspid atresia, Truncus arteriosus/hemitruncus, Other abnormalities of atrioventricular or ventriculoatrial connection not included above (crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion) . * Heart failure symptoms included, difficulty of breathing, shortness of breathing, easy fatigue.*

Table 2. Risk Factors, Clinical Presentation and CAD among Adult CHD Patients.

Baseline Variable	NORMAL CORONARIES n= 42 (81 %)	NONSIGNIFICANT CAD n= 4 (7.6%)	SIGNFICANT CAD n= 6 (11.5 %)	TOTAL n= 52(100%)
Age (years)	37.67 (18 -66yo)	51 yo (35 – 66 yo)	54 yo (47 – 61 yo)	45±12.2yo (18 - 66 yo)
≥ 40 y.o	17 (40%)	4 (100%)	6 (100%)	26 (50%)
Gender (Male)	25 (60%)	4 (100%)	2 (33%)	30 (58%)
No Documented Risk Factors	39 (93%)	3 (75%)	1 (17%)	42 (81%)
HPN	2 (05%)	1 (25%)	2 (33%)	5 (10%)
Dyslipidemia	1 (02%)	0 (0%)	1 (17%)	2 (04%)
DM	1 (02%)	0(0%)	1 (17%)	2 (04%)
Smoker	3 (07%)	1 (25%)	1 (17%)	5 (10%)
Family Hx of CAD	0(0%)	0(0%)	0 (0%)	0(0%)
SYMPTOMS				
Cyanosis	3 (07%)	0(0%)	0(0%)	3 (06%)
Typical Chest Pain	2 (05%)	1(25%)	4 (66%)	7 (30%)
Atypical Chest Pain	4 (10%)	4(100%)	1 (17%)	9 (17%)
SYSTOLIC FUNCTION				
Depressed	6 (11.5%)	0(0%)	1 (17%)	7 (13%)
Wall Motion Abnormality	6 (11.5%)	0(0%)	2 (33%)	8 (15%)
ANGIOGRAPHICALY DETERMINED CORONARY ARTERY DISEASE				
Simple	25(59%)	4(100%)	3 (50%)	32 (61%)
Intermediate	15(36%)	1(25%)	2 (33%)	18 (35%)
Complex	2 (05%)	0(0%)	0 (0%)	2 (04%)

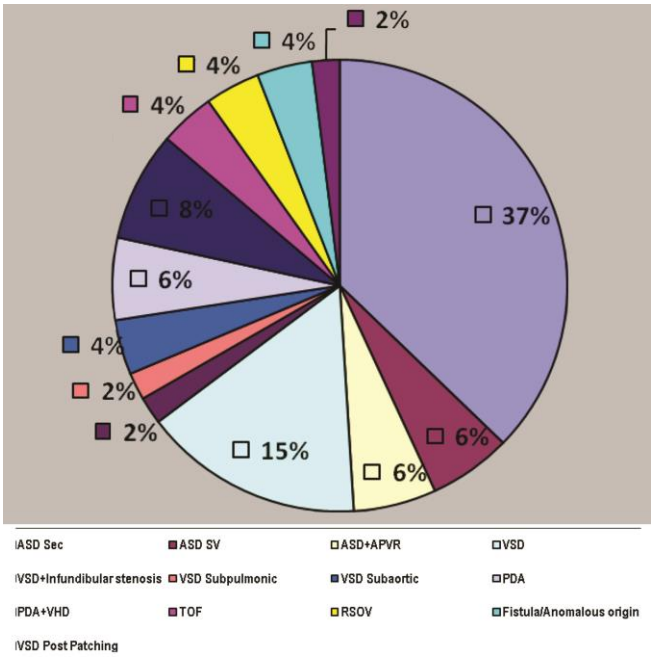

Figure 1. Frequency of Adult CHD who underwent Coronary Angiogram at UP-PGH (n=52)
ASD Sec = Atrial septal defect secundum type, ASD SV = atrial septal defect sinus venosus type, ASD+APVR = ASD with anomalous pulmonary venous return to the right atrium, PDA + VHD = Patent ductus arterious with valvular heart disease, VSD = ventricular septal defect, TOF = Tetralogy of Fallot, RSOV = ruptured sinus of valsalva/aneurysmal

Among patients with evidence of coronary atherosclerosis (Table 3), 6 (60%) had single vessel disease, 2 (20 %) had 2-vessel disease and 2 (20 %) had 3-vessel disease. The left main coronary artery was involved in 2 patients, left anterior descending artery in 6, left circumflex artery in 5, and right coronary artery in 5. Four (70 %) patients with Simple CHD, 2 (30%) patients with Intermediate CHD, and none of those with Complex CHD, were found to have significant CAD. The prevalence of significant CAD in patients aged > 40 years was 100%, 4 (66%) of whom were female. Five (83%) of them have documented traditional CVD risk factors mostly hypertension. None of the patients with significant CAD had cyanosis. 4 patients (66%) have typical chest pain (Table 2).

Table 3. Type of Congenital Heart Disease and Coronary Artery Lesions among Adult CHD Patients

CHD	ANY ANGIOGRAPHICALY DETERMINED CORONARY ARTERY DISEASE (n= 10)			
	1-VD n= 6 (60%)	2- VD n= 2 (20%)	3- VD n= 2 (20%)	Total n= 10 (100 %)
Simple	4 (40%)	1 (10%)	2 (20%)	7(70%)
Intermediate	2 (20%)	1 (10%)	0(0%)	3 (30%)
Complex	0 (0%)	0 (0%)	0(0%)	0 (0%)

VD = Vessel Disease

Discussion

The last 50 years have witnessed the dramatic change in the diagnosis, management and prognosis of congenital heart diseases. Advances in diagnostic modalities and surgical techniques have provided excellent immediate and long term survival among ACHD patients.

It was estimated that more than 95% of patients with congenital heart disease who survived the first year of life could survive until adulthood.[8] Thus, the striking increase in survival among patients with ACHD will require competent

care within 20 years which mandates careful observation, follow up and advance recognition of further complications. Because the onset of some medical problems in this growing population can be subtle, early recognition of adverse changes may enable rapid intervention to slow progressive myocardial deterioration.

In a study conducted by Pillutla et al,[1] myocardial infarction has become the leading contributing cause of mortality among adult non-cyanotic congenital patients after 1990. This observation emphasizes the need for preventive measures and detection for acquired disease such as coronary artery disease in this population.

This cohort showed that the prevalence of significant CAD in our adult CHD was 11.5%. All of those with significant coronary artery disease were 40 years old and above and 67% were females, 83% were with traditional cardiovascular risk factors and 67% with typical chest pain. Because coronary angiography is an invasive procedure, it can not be used as a screening tool for coronary artery disease. But it is usually performed when strong suspicion of CAD exists and also, as recommended by AHA/ACC 2008 Guidelines for Management of Adult Congenital Heart Diseases. In this cohort, coronary angiography was mostly done among patients above 40 years old presenting with wall motion abnormalities on 2-D echocardiography, with CV risk factors and with typical chest pain. Other than preoperative evaluation of coronary artery disease, diagnostic catheterization was done as part of pulmonary vascular disease assessment and its response to vasoactive agents prior to planned intervention and as an adjunct to non-invasive assessment of the morphologic and functional characteristics of many complex congenital lesions.

There is difficulty comparing the prevalence of CAD reported in other studies due to heterogeneity of the population being studied. In this cohort, 60% of those with significant CAD were simple lesions and 40% were lesions with intermediate complexities. There were no complex lesions evaluated for CAD due to their expected short course survival after delivery. The prevalence of CAD in general population without suspicion of CAD, with mean age of 53 ± 7 (40 – 70 years old) was 7.3%.[4] In a study conducted by Giannakoulas on adult congenital heart patients and the burden of coronary artery disease relating to the traditional risk factors, the prevalence of significant CAD was 9.2% among patients 40 years old and above[2] and no cyanotic patients had significant CAD. Our estimate of 11.5% appeared similar to the prevalence of CAD among adult patients with CHD and higher than the prevalence of CAD on the general population without suspicion of CAD of similar age.

Similar to other studies, in our population there were no cyanotic patients who had CAD. Angiographic and necropsy data in cyanotic adult CHD patients found that dilatation and tortuosity are the prevalent findings in these patients. It was suggested that cyanosis may exert a protective effects against coronary atherosclerosis. A lower prevalence of coronary atherosclerosis was observed in hypoxic patients living at high altitudes with erythrocytosis. Factors contributing to the low incidence of CAD in cyanotic adult patients with CHD were low cholesterol, increased bioavailability of nitric oxide, hyperbilirubinemia, low platelet count and preservation of coronary flow reserve through remodeling of the coronary microcirculation.[2]

Systemic arterial hypertension was noted to be the most frequent traditional risk factor occurring in our study population. Other risk factors noted were dyslipidemia and diabetes. This finding was similar to other studies which found systemic arterial hypertension and hyperlipidemia to be strongly associated with CAD in adult CHD population.[2] In our study 100% with significant CAD had ≥ 1 cardiovascular risk factors similar to the study of Giannakoulas[2] emphasizing the importance of primary prevention of CAD in ACHD population. In the same study, smoking was not associated with CAD in ACHD patients. In our study population, 1 in 5 (20%) of those with significant CAD had smoking history. Though in our cohort, correlation of these CV risk factors with CAD was not done due to limited sample population.

Typical chest pain was common in our study population with significant CAD affecting 4 of 5 patients (80%). Mechanisms that may explain the presence of chest pain in these population other than CAD including ventricular volume and pressure overload and hypertrophy causing mismatch between coronary demand and supply, dilation of the great vessels, coronary anomalies or external compressions.[2]

Recent American Heart Association / American College of Cardiology 2008 Guidelines for the management of adults CHD[9] suggested that men aged ≥ 35 years and premenopausal women ≥ 35 years with risk factors for atherosclerosis should be evaluated using coronary angiography to rule out associated CAD before they underwent cardiac surgery. Our data, similar to other studies, have also supported the notion of routine coronary angiography for patients ≥ 40 years old who were to undergo cardiac surgery because 12% were shown to have CAD.

Our cohort supports the need for primary prevention of CAD and screening for traditional risk factors in adult patients with CHD and the presence of CHD should not deviate the routine evaluation in minimizing the risk of coronary atherosclerosis in this population as is usually done in the non-CHD population.

Limitations of the Study and Recommendations

Our analysis has several limitations. First, our population sample size was limited achieving only 40% (n=52) of the target sample size (n= 129) hence we were

unable to correlate and analyze the association of cardiovascular risk factors to the presence of CAD. This has drawn us to purely descriptive analysis. Second, this was a retrospective population-based study in which data gathered were dependent only on those indicated in the clinical record and some of the specific indications of doing coronary angiography was not indicated. Finally, we only looked at the population including all adult congenital patients who underwent coronary angiogram and were not able to look at those who did not undergo coronary angiogram that may give us a the exact prevalence of CAD in this population.

Our cohort, despite the limited number of population, has reflected the findings of previous cohort studies about CAD in ACHD patients. This emphasizes that ACHD patients requires lifelong care not only for the original defect but also for the diseases affecting the general population such as coronary artery disease. This study has supported the recommendation of routine coronary angiography among patients with ACHD ≥ 35 years old with traditional CV risk factors and emphasizes the need of primary prevention of CAD and modification of traditional CV risk factors which are as importantly applied to the general population.

We recommend future research efforts by formulating local ACHD registry in this institution and national registry in our country, for a larger cohort that may provide us a more detailed prospective data that will further guide us in our management. Outcomes of those congenital heart disease patients with Coronary Heart disease may be compared with their CAD-less counterparts as well.

Due to the complexity of the clinical presentation of CHD, we suggest this study to be continued with large population size to determine the association of different cardiovascular risk factors and symptomatology of this population with the presence of coronary artery disease to make us clinically vigilant with the use of diagnostic modalities such as coronary angiography in ACHD patients that would further increase detection of coronary artery disease.

Conclusion

The prevalence of coronary artery disease among ACHD patients using coronary angiography in this study is 11.5%. Among adult congenital heart disease patients with angiographically determined coronary artery disease, 60% (6/10) had one-vessel disease, while two-vessel and three-vessel disease were each seen in 20% (2/10).

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