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Incidence and correlates of mortality in adults with congenital heart disease of different age groups

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ABSTRACT

Background: Aging is associated with acquired comorbidities that potentially influence the natural history and outcomes of adults with congenital heart disease (CHD). The purpose of this study was to compare the clinical characteristics, as well as the incidence and correlates of all-cause mortality between different age groups.
Method: Adults with CHD were categorized into 3 age groups based on age at baseline encounter: Group 1 (age 18–40 years); Group 2 (age 41–65 years), and Group 3 (age >65 years).
Results: Of 5930 patients (age 37 ± 15 years), 3009 (51%), 2422 (41%), and 499 (8%) were in Groups 1, 2 and 3, respectively. Compared to Group 1, patients in Groups 2 and 3 were less likely to have complex CHD, but more likely to have acquired comorbidities, end-organ dysfunction, ventricular systolic dysfunction, and valvular heart disease. Compared to Group 1, Groups 2 and 3 had higher incidence of all-cause mortality (7.2 versus 15.3 versus 47.8 per 1000 patient-years, respectively, $p < 0.001$), and lower proportion of deaths from cardiovascular causes (87% versus 77% versus 71%, respectively, $p < 0.001$). Furthermore, the correlates of all-cause mortality were different between the age groups, with acquired comorbidities such as hypertension, coronary artery disease, and hepatorenal dysfunction being associated with mortality in Group 3, while indices of CHD severity such as number of prior cardiac surgery, and presence of complex CHD being associated with all-cause mortality in Group 1.
Conclusions: These results suggest the need for management strategies tailored to address the correlates of outcomes in each age group.

1. Introduction

More than 95% of babies born with congenital heart disease (CHD) now survive to adulthood, and more than 90% live beyond the age of 40 years because of significant improvements in medical, transcatheter, and surgical therapies for CHD over time [1–3]. As a result, there has been a significant expansion of the adult CHD population in the past 2 decades, and CHD is now the most common cause of cardiovascular death in young adults [2–4]. Similar to the general population, adults with CHD develop comorbidities in the course of ageing, and these comorbidities influence the natural history of the underlying CHD lesion, and overall longevity of the patients [5–9]. In spite of these expected age-related changes in health profile, there is a general tendency to approach adults with CHD as a homogenous population without taking into account the impact of age, and comorbidities that come with ageing. The purpose of this study was to compare the clinical characteristics, as well as, the incidence and correlates of all-cause mortality between different age groups using a well-characterized cohort of adults with CHD.

2. Methods

2.1. Study population

This is a retrospective cohort study of adults (>18 years old) with CHD that received care at Mayo Clinic, Rochester, MN from January 1, 2003, to December 31, 2021. The patients were identified through the MACHD (*M*ayo *A*dult *C*ongenital *H*eart *D*isease) Registry. The first clinical encounter in the adult CHD clinic was considered the baseline

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Abbreviations

ACC/AHA	American College of Cardiology/American Heart Association
CHD	Congenital heart disease
CI	Confidence interval
CIED	Cardiac implantable electronic devices
HR	Hazard ratio
MELD-XI	Model for end-stage liver disease excluding international normalized ratio

encounter, and the patients were then divided into 3 age groups based on their age at baseline encounter: (1) Young adults (Group 1) defined as age 18–40 years at baseline encounter; (1) Middle age (Group 2) defined as age 41–65 years at baseline encounter; (3) Older adults (Group 3) defined as age >65 years at baseline encounter. This study was approved by the Mayo Clinic institutional Review Board.

2.2. Data collection

The following medical records were reviewed: clinic notes, hospital dismissal notes, procedure notes, laboratory data, and echocardiograms. Clinical data obtained within 6 months from the baseline encounter were used to define the baseline characteristics of the cohorts. The patients were classified into 3 anatomic groups (simple, moderate, and complex CHD) based on CHD severity according to the 2018 American College of Cardiology/American Heart Association (ACC/AHA) guidelines [10].

Comprehensive echocardiogram was performed according to contemporary guidelines [11–13], and offline image analyses and measurements were performed in all patients. Systemic ventricular dysfunction was defined as systemic left ventricular ejection fraction <50% or systemic right ventricular fractional area change <35% [11–13]. Hemodynamically significant atrioventricular valve regurgitation was defined as ≥ moderate regurgitation assessed using qualitative Doppler echocardiography [11–13]. Hepatorenal function was assessed using the model for end-stage liver disease excluding international normalized ratio (MELD-XI), and hepatorenal dysfunction was defined as MELD-XI score >11 [14].

All-cause mortality was ascertained by review of medical records, from the baseline encounter to the last follow-up. The patients that did not meet the study outcome (all-cause mortality) were censored at the time of last follow-up. Cardiovascular death was defined as death due to heart failure, arrhythmia/sudden cardiac death, postprocedural death after cardiac procedure, and cardiovascular hemorrhage/stroke-related death [15].

Table 1
Baseline characteristics.

	All (N = 5930)	Age 18–40 y (N = 3,009, 51%)	Age 41–65 y (N = 2,422, 41%)	Age >65 y (N = 499, 8%)	P
Age, years	37 ± 15	25 ± 6	48 ± 7*	69 ± 3*	<0.001
Male sex	3039 (51%)	1535 (51%)	1249 (52%)	255 (51%)	0.7
Body mass index, kg/m^2	26 (23–30)	24 (22–28)	27 (24–31) *	27 (24–31) *	<0.001
Prosthetic valves	1475 (25%)	723 (24%)	682 (28%) *	70 (14%) *	<0.001
CIED	658 (11%)	286 (10%)	308 (13%) *	64 (13%) *	0.008
CHD anatomic severity					
Simple	832 (14%)	286 (10%)	369 (15%)	177 (36%)	<0.001
Moderate	3801 (64%)	1845 (61%)	1670 (69%)	286 (57%)	
Complex	1297 (22%)	878 (29%)	383 (16%)	36 (7%)	
Comorbidities					
Hypertension	1458 (25%)	397 (13%)	780 (32%) *	281 (56%) *	<0.001
Type 2 Diabetes	406 (7%)	92 (3%)	242 (10%) *	72 (14%) *	<0.001
Coronary artery disease	313 (5%)	29 (1%)	182 (8%) *	102 (20%) *	<0.001
Hyperlipidemia	1280 (22%)	276 (9%)	758 (31%) *	246 (49%) *	<0.001
Obesity	1187 (20%)	481 (16%)	579 (24%) *	127 (26%) *	<0.001
Atrial fibrillation	917 (16%)	256 (9%)	482 (20%) *	179 (36%) *	<0.001
Atrial flutter/tachycardia	749 (13%)	339 (11%)	331 (14%)	79 (16%) *	0.002
Chronic kidney disease ≥ III	221 (4%)	53 (2%)	119 (5%)	49 (10%) *	<0.001
Hepatorenal renal dysfunction	1541 (26%)	499 (17%)	841 (35%) *	201 (40%) *	<0.001
Medications					
Diuretics	1385 (23%)	531 (18%)	683 (28%) *	171 (34%) *	<0.001
Beta blockers	2010 (34%)	822 (27%)	968 (40%) *	220 (44%) *	<0.001
Calcium channel blockers	531 (9%)	152 (5%)	272 (11%) *	107 (21%) *	<0.001
ACEI/ARB	1780 (30%)	783 (26%)	784 (32%)	213 (43%) *	<0.001
MRA	419 (7%)	194 (6%)	187 (8%)	38 (8%)	0.2
Vitamin K antagonist	1786 (30%)	747 (25%)	854 (35%) *	185 (37%) *	<0.001
DOAC	268 (5%)	64 (2%)	126 (5%)	78 (16%)	<0.001
Laboratory data					
MELD-XI score	9.6 (9.4–12.9)	9.5 (9.4–10.9)	10.4 (9.8–11.6)*	10.9 (10.1–12.5)*	<0.001
eGFR, ml/min/1.73 m^2	98 ± 39	118 ± 26	91 ± 21 *	85 ± 23 *	<0.001
Echocardiogram					
S-ventricular systolic dysfn	711 (12%)	307 (10%)	311 (13%)*	93 (19%)*	<0.001
≥Moderate S-AVVR	299 (5%)	121 (4%)	139 (6%)*	39 (8%)*	0.2
NS-ventricular systolic dysfn	1998 (34%)	881 (29%)	903 (37%)*	214 (43%)*	<0.001
≥Moderate NS-AVVR	1183 (20%)	405 (13%)	615 (25%)*	163 (33%)*	<0.001

Abbreviations: ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin-II receptor blockers; CHD: congenital heart disease; AVVR: atrioventricular valve regurgitation; CIED: cardiac implantable electronic devices; DOAC: Direct oral anticoagulant; eGFR: estimated glomerular filtration rate; MRA: Mineralocorticoid receptor antagonist; MELD-XI: Model for end-stage liver disease excluding international normalized ratio; NS: non-systemic; S: systemic; TGA: transposition of great arteries.

Footnote: p values were derived from comparisons across all 3 groups using analysis of variance test and chi squared test for continuous and categorical variables respectively. "*" denotes statistically significant difference from pairwise comparisons using the age group 18–40 years as the reference. Ventricular systolic dysfunction was defined as calculated or estimated left ventricular ejection fraction <50% or right ventricular fractional area change <35%. Atrioventricular valve regurgitation was based on qualitative Doppler assessment.

Table 2
Congenital heart lesions.

	All (N = 5930)	Age 18–40 y (N = 3,009, 51%)	Age 41–65 y (N = 2,422, 41%)	Age >65 y (N = 499, 8%)
Fontan palliation	442 (8%)	363 (12%)	79 (3%)	0
Tetralogy of Fallot	893 (15%)	492 (16%)	360 (15%)	41 (8%)
Coarctation of aorta	893 (15%)	485 (16%)	318 (13%)	90 (18%)
Ebstein anomaly	753 (13%)	351 (12%)	319 (13%)	83 (17%)
cc-TGA	234 (4%)	99 (3%)	108 (5%)	27 (5%)
d-TGA s/p atrial switch op	189 (3%)	127 (4%)	62 (3%)	0
Valvular pulmonic stenosis	291 (5%)	131 (4%)	124 (5%)	36 (7%)
Pulmonary atresia with IVS	53 (0.9%)	51 (2%)	2 (0.1%)	0
Truncus arteriosus	46 (0.8%)	37 (1%)	9 (0.4%)	0
d-TGA s/p arterial switch/Rastelli op	164 (3%)	144 (5%)	19 (0.8%)	1 (0.2%)
Aortic stenosis	757 (13%)	273 (9%)	453 (19%)	31 (6%)
Atrioventricular canal defect	335 (6%)	174 (6%)	135 (6%)	26 (5%)
ASD/PAPVR	430 (7%)	116 (4%)	193 (8%)	121 (24%)
Double chambered right ventricle	37 (0.6%)	15 (0.5%)	14 (0.6%)	8 (2%)
Subaortic stenosis	170 (3%)	70 (2%)	85 (4%)	15 (3%)
Ventricular septal defect	74 (1%)	24 (0.8%)	38 (2%)	12 (2%)
Others	169 (3%)	57 (2%)	104 (4%)	8 (2%)

Abbreviation: ASD: Atrial septal defect; cc-TGA: Congenitally corrected transposition of great arteries; IVS: Intact ventricular septum; PAPVR: Partial anomalous pulmonary venous return.

2.3. Statistical analysis

Data were presented as mean ± standard deviation, median (interquartile range), and count (%). Normality was assessed using Shapiro-Wilk test. Between-group comparison was performed using chi-squared test and analysis of variance test as appropriate. The incidence of all-cause mortality was calculated as the quotient of the total number of events and the total duration of at-risk period and expressed as events (95% confidence interval [CI]) per 1000 patient years. The correlates of all-cause mortality were assessed in each age group using multivariable Cox regression analysis. The models were adjusted for the following covariates: (1) Demographic indices (age, sex); (2) Indices of CHD severity as defined by the ACC/AHA CHD severity class, number of prior cardiac surgeries, New York Heart Association functional class, prosthetic heart valves, and cardiac implantable electronic devices (CIED); (3) Echocardiographic indices of ventricular and valvular dysfunction; (4) Comorbidities (hypertension, coronary artery disease, type 2 diabetes, atrial fibrillation, chronic kidney disease, and hepatorenal dysfunction). The final covariate selection for the multivariable Cox regression models were determined using stepwise backwards selection with $p < 0.05$ required for a covariate to remain in the model. All statistical analyses were performed with BlueSky Statistics software (version. 7.10; BlueSky Statistics LLC, Chicago, IL, USA). A p value < 0.05 was considered statistically significant for all analyses.

Table 3
Cox regression model showing correlates of all-cause mortality in group 1 (age 18–40 years at baseline encounter).

	Univariable analysis		Multivariable analysis	
	HR (95%CI)	P	HR (95%CI)	P
Age, years	1.04 (1.02–1.06)	0.01		
Male sex	1.22 (0.86–1.65)	0.3		
Number cardiac surgeries	1.09 (1.04–1.14)	<0.001	1.07 (1.03–1.11)	0.02
NYHA III/IV (vs I/II)	2.18 (1.46–2.75)	<0.001		
Complex CHD (vs simple/moderate)	3.17 (1.94–4.43)	<0.001	2.63 (1.84–3.42)	<0.001
Prosthetic valve	1.67 (1.33–2.08)	0.004		
CIED	1.82 (1.39–2.46)	0.002	1.53 (1.27–1.81)	0.008
Comorbidities				
Hypertension	1.08 (0.97–1.17)	0.4		
Coronary artery disease	1.44 (1.12–1.78)	0.01		
Type 2 diabetes	1.04 (0.67–1.48)	0.6		
Atrial fibrillation	2.16 (1.44–2.86)	<0.001	1.89 (1.52–2.31)	<0.001
Chronic kidney disease ≥ III	0.98 (0.83–1.14)	0.3		
Hepatorenal dysfunction (MELD-XI >11)	1.08 (1.02–1.14)	0.03		
Echocardiographic indices				
Systemic ventricular systolic dysfunction	1.14 (1.05–1.26)	0.02	1.12 (1.06–1.18)	0.02
Non-systemic ventricular systolic dysfunction	1.10 (1.03–1.17)	0.01		
≥Moderate systemic AVVR	0.94 (0.74–1.16)	0.4		
≥Moderate non-systemic AVVR	1.27 (1.08–1.49)	0.03		

Abbreviation: AVVR: Atrioventricular valve regurgitation; CIED: cardiac implantable electronic device; CI: confidence interval; CHD: congenital heart disease; HR: hazard ratio; MELD-XI: Model for end-stage liver disease excluding international normalized ratio; NYHA: New York Heart Association.
Footnote: The multivariable model was created using stepwise backwards variable selection, and only the variables with $p < 0.05$ remained in the model.

3. Results

3.1. Baseline characteristics

There were 5930 patients that met study inclusion criteria (mean age 37 ± 15, and 3039 [51%] were males). Of the 5930 patients, 3009 (51%) were in Group 1 (age 18–40 years), 2422 (41%) were in Group 2 (age 41–65 years), and 499 (8%) were in Group 3 (age >65 years). Table 1 shows a comparison of the baseline characteristics of the cohort. Compared to Group 1, patients in Groups 2 and 3 were less likely to have complex CHD, but more likely to have comorbidities, end-organ dysfunction, ventricular systolic dysfunction, and valvular heart disease. Table 2 shows the prevalence of each CHD diagnosis in the different age groups.

3.2. Outcomes

3.2.1. All-cause mortality

Of the 5930 patients, 774 (13%) died during 10.9 ± 3.6 years of follow-up, and the average age at the time of death of 53 ± 8 years. Of the 611 patients with documented cause of death, 483 (79%) died from a cardiovascular cause. The unadjusted incidence of all-cause mortality in the overall cohort was 12.1 (95% CI 11.7–12.5) per 1000 patient-years.

Table 4
Multivariable cox regression model showing correlates of all-cause mortality in group 2 (age 41–65 years at baseline encounter).

	Univariable analysis		Multivariable analysis	
	HR (95%CI)	P	HR (95%CI)	P
Age, years	1.06 (1.03–1.09)	0.006	1.04 (1.01–1.07)	0.01
Male sex	1.18 (0.92–1.55)	0.2		
Number cardiac surgeries	1.06 (1.02–1.10)	0.007		
NYHA III/IV (vs I/II)	1.74 (1.33–2.06)	<0.001		
Complex CHD (vs simple/ moderate)	2.43 (1.84–3.57)	<0.001	1.95 (1.42–2.47)	0.008
Prosthetic valve	1.27 (1.03–1.53)	0.006		
CIED	1.53 (1.22–1.92)	0.004	1.37 (1.09–1.71)	0.002
Comorbidities				
Hypertension	1.04 (0.91–1.13)	0.5		
Coronary artery disease	1.29 (1.14–1.63)	0.008		
Type 2 diabetes	1.08 (0.84–1.57)	0.4		
Atrial fibrillation	1.97 (1.42–2.46)	<0.001	1.64 (1.34–1.96)	0.007
Chronic kidney disease ≥ III	1.03 (0.81–1.19)	0.2		
Hepatorenal dysfunction (MELD-XI >11)	1.15 (1.04–1.26)	0.03	1.12 (1.06–1.18)	0.02
Echocardiographic indices				
Systemic ventricular systolic dysfunction	1.19 (1.08–1.31)	0.01	1.15 (1.07–1.22)	0.01
Non-systemic ventricular systolic dysfunction	1.06 (1.01–1.12)	0.03		
≥Moderate systemic AVVR	1.26 (0.81–1.64)	0.5		
≥Moderate non-systemic AVVR	1.22 (1.08–1.49)	0.03	1.19 (1.12–1.26)	0.01

Abbreviation: AVVR: Atrioventricular valve regurgitation; CIED: cardiac implantable electronic device; CI: confidence interval; CHD: congenital heart disease; HR: hazard ratio; MELD-XI: Model for end-stage liver disease excluding international normalized ratio; NYHA: New York Heart Association.
Footnote: The multivariable model was created using stepwise backwards variable selection, and only the variables with $p < 0.05$ remained in the model.

Table 5
Multivariable cox regression models showing correlates of all-cause mortality in group 3 (age >65 years at baseline encounter).

	Univariable analysis		Multivariable analysis	
	HR (95%CI)	P	HR (95%CI)	P
Age, years	1.08 (1.05–1.11)	<0.001	1.26 (1.14–1.38)	<0.001
Male sex	1.12 (0.96–1.44)	0.3		
Number cardiac surgeries	1.02 (0.94–1.06)	0.4		
NYHA III/IV (vs I/II)	1.61 (1.39–1.84)	0.008		
Complex CHD (vs simple/ moderate)	1.22 (1.07–1.41)	0.04		
Prosthetic valve	1.16 (1.07–1.26)	0.03		
CIED	1.43 (1.17–1.75)	0.04		
Comorbidities				
Hypertension	1.37 (1.14–1.63)	0.004	1.21 (1.04–1.42)	0.01
Coronary artery disease	2.01 (1.42–2.72)	0.003	1.68 (1.30–1.97)	0.009
Type 2 diabetes	1.09 (0.87–1.35)	0.2		
Atrial fibrillation	1.51 (1.26–2.03)	0.005	1.46 (1.21–1.72)	0.02
Chronic kidney disease ≥ III	1.06 (0.84–1.22)	0.4		
Hepatorenal dysfunction (MELD-XI >11)	1.12 (1.02–1.23)	0.01	1.10 (1.03–1.17)	0.03
Echocardiographic indices				
Systemic ventricular systolic dysfunction	1.38 (1.14–1.74)	0.009	1.17 (1.04–1.28)	0.02
Non-systemic ventricular systolic dysfunction	1.09 (1.03–1.15)	0.01	1.14 (1.09–1.20)	0.009
≥Moderate systemic AVVR	1.18 (0.86–1.45)	0.4		
≥Moderate non-systemic AVVR	1.26 (1.12–1.51)	0.02		

Abbreviation: AVVR: Atrioventricular valve regurgitation; CIED: cardiac implantable electronic device; CI: confidence interval; CHD: congenital heart disease; HR: hazard ratio; MELD-XI: Model for end-stage liver disease excluding international normalized ratio; NYHA: New York Heart Association.
Footnote: The multivariable model was created using stepwise backwards variable selection, and only the variables with $p < 0.05$ remained in the model.

Of the 3009 patients in Group 1, 250 (8%) died during a mean follow-up of 11.6 ± 3.2 years, and the average age at the time of death was 34 ± 5 years. Of the 204 patients with documented cause of death, 178 (87%) died from a cardiovascular cause. The unadjusted incidence of all-cause mortality of 7.2 (95% CI 6.8–7.6) per 1000 patient-years. The correlates of all-cause mortality in Group 1 were number of prior cardiac surgeries (hazard ratio [HR] 1.07, 95% CI 1.03–1.11, $p = 0.02$) for every additional prior cardiac surgery, having complex CHD versus simple/moderately complex CHD (HR 2.63, 95% CI 1.84–3.43, $p < 0.001$), history of atrial fibrillation (HR 1.89, 95% CI 1.52–2.31, $p < 0.001$), prior CIED implantation (HR 1.53, 95% CI 1.27–1.81, $p = 0.008$), and having ≥moderate systemic ventricular systolic dysfunction (HR 1.12, 95% CI 1.06–1.18, $p = 0.02$), Table 3.

Of the 2422 patients in Group 2, 374 (15%) died during a mean follow-up of 10.1 ± 3.9 years, and the average age at the time of death was 56 ± 8 years. Of the 286 patients with documented cause of death, 218 (77%) died from a cardiovascular cause. The unadjusted incidence of all-cause mortality of 15.3 (95%CI 14.6–16.1) per 1000 patient-years. The correlates of all-cause mortality in Group 2 were older age (HR 1.04, 95% CI 1.01–1.07, $p = 0.01$) per 1 year increase in age at baseline encounter, having complex CHD versus simple/moderately complex CHD (HR 1.95, 95% CI 1.42–2.47, $p = 0.008$), prior CIED implantation (HR 1.37, 95% CI 1.09–1.71, $p = 0.002$), hepatorenal dysfunction (HR 1.12, 95% CI 1.06–1.18, $p = 0.02$), history of atrial fibrillation (HR 1.64, 95% CI 1.34–1.96, $p = 0.07$), presence of ≥moderate systemic ventricular systolic dysfunction (HR 1.15, 95% CI 1.07–1.22, $p = 0.01$), and presence of ≥moderate non-systemic atrioventricular valve regurgitation (HR 1.19, 95% CI 1.07–1.26, $p = 0.01$), Table 4.

Of the 499 patients in Group 3, 150 (30%) died during a mean follow-up of 6.3 ± 2.94 years, and the average age at the time of death was 74 ± 5 years. Of the 121 patients with documented cause of death, 88 (71%) died from a cardiovascular cause. The unadjusted incidence of all-cause mortality of 47.8 (95%CI 43.6–51.2) per 1000 patient-years. The correlates of all-cause mortality in Group 3 were older age (HR 1.26, 95% CI 1.14–1.38, $p < 0.001$) per 1 year increase in age at baseline encounter, hypertension (HR 1.21, 95% CI 1.04–1.42, $p = 0.008$), coronary artery disease (HR 1.68, 95% CI 1.30–1.97, $p = 0.009$), history of atrial fibrillation (HR 1.46, 1.21–1.72, $p = 0.02$), hepatorenal dysfunction (HR 1.10, 95% CI 1.03–1.17, $p = 0.03$), presence of ≥moderate systemic ventricular systolic dysfunction (HR 1.17, 95% CI 1.04–1.28, $p = 0.02$), and presence of ≥moderate non-systemic ventricular systolic dysfunction (HR 1.14, 95% CI 1.09–1.20, $p = 0.009$), Table 5.

Compared to Group 1, Group 2 had a higher unadjusted incidence of all-cause mortality (15.3 [95%CI 14.6–16.1] versus 7.2 [95% CI 6.8–7.6] per 1000 patient-years, $p < 0.001$), and lower proportion of deaths from cardiovascular causes (77% versus 87%, $p = 0.003$) (Fig. 1).

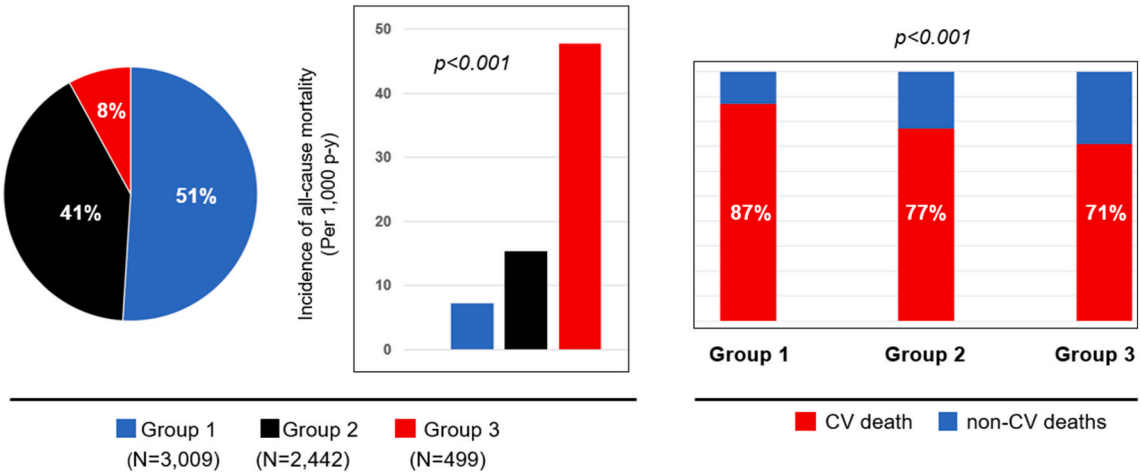

Fig. 1. (Left) Pie chart showing the proportion of patients in each age group. Group 1 (age 18–40 y), Group (age 41–65 y), Group (age >65 y). **(Middle)** Bar graphs comparing the incidence of all-cause mortality between Groups 1, 2 and 3. P value represents comparison across the 3 groups. **(Right)** Bar graphs comparing the proportion of deaths due to cardiovascular (CV) deaths between Groups 1, 2 and 3. P value represents comparison across the 3 groups.

Similarly, Group 3 had a higher unadjusted incidence of all-cause mortality (47.8 [95% CI 43.6–51.2] versus 7.2 [95% CI 6.8–7.6] per 1000 patient-years, $p < 0.001$), and lower proportion of deaths from cardiovascular causes (71% versus 87%, $p < 0.001$), compared to Group 1 (Fig. 1). Furthermore, the correlates of all-cause mortality were different between the age groups, with acquired comorbidities such as hypertension, coronary artery disease, and hepatorenal dysfunction having significant association with mortality in Group 3, while indices of CHD severity such as number of prior cardiac surgeries, presence of complex CHD, and prior CIED implantation having significant association with mortality in Group 1 (Tables 3–5).

4. Discussion

In this study, we assessed the clinical characteristics, as well as the incidence and correlates of all-cause mortality across different age groups of adults with CHD. The main findings were: (1) About half of adults with CHD were less than 40 years of age, and only 8% were over the age of 65 years at the time of baseline encounter in a tertiary adult CHD center. (2) Patients in the older age group were less likely to have complex CHD, but more likely to have acquired comorbidities, end-organ dysfunction, ventricular systolic dysfunction, and valvular heart disease as compared to the younger age groups. (3) The older age groups had significantly higher incidence of all-cause mortality (as expected), but lower proportion of death due to cardiovascular causes as compared to the younger age groups. (4) The correlates of all-cause mortality in the older age group were more likely be acquired comorbidities in contrast to the younger age groups where the indices of CHD severity were the more significant correlates of mortality. (5) Systemic ventricular dysfunction was associated with all-cause mortality in the overall cohort, and across all age groups.

Prior to the 2000s, CHD was predominantly a pediatric disease because a greater proportion of CHD patients were less than 18 years of age [2,3,16,17]. In the current era, on the other hand, CHD is now a predominantly an adult disease because a great proportion of CHD patients are now older than 18 years of age [2,3,16–18]. This demographic change is due to improved long-term survival of CHD patients. While longevity is a desired outcome, aging is associated with acquired comorbidities and end-organ dysfunction. These changes are expected to modify the natural history ofthe underlying CHD. The current study showS that young adults (Group 1) had a higher prevalence of complex CHD but lower prevalence of acquired comorbidities, and the indices of CHD severity were important correlates of all-cause mortality as compared to the other age groups. In contrast to the younger adults (Group 1), the middle-aged (Group 2) and older patients (Group 3), had a relatively higher prevalence of acquired comorbidities and end-organ dysfunction as compared to the young adult group, and these comorbidities (instead of CHD severity) were associated with all-cause mortality.

Several studies have reported the incidence, etiology, and risk factors for mortality in adults with CHD [2,3,16,17]. In a retrospective cohort study based on the Dutch CONCOR (Congenital Corvita) registry, Verheugt et al. reported that, among 6933 patients, the median age at the time of death was 49 years, and that 77% of deaths were due to cardiovascular causes [19]. The correlates of mortality in that cohort were older age and CHD severity [19]. Similar findings were reported in another retrospective cohort study based on the German National Registry for Congenital Heart Defects containing data of 2596 adults with CHD [20]. In that study, the annual incidence of all-cause mortality was 1.7% per year, the median age at the time of death was 40 years, and more than 80% of the patients died from cardiovascular causes [20]. While the estimate from the previous studies were comparable to the results of the current study, a novel finding from the current study was that the correlates of all-cause mortality differed across the age groups, which in turn, suggests that different sets of interventions would be required to address the risk factors in each age group. These findings would enable the providers to prioritize care around factors associated with mortality for the different age groups. For instance, the primary focus should be on the underlying congenital heart lesion in the younger age group, while there should be a greater emphasis on screening and treatment of hypertension and coronary artery disease, as well as prevention of end-organ dysfunction in the middle age and older age groups.

Another important observation from the current study was the consistent association between systemic ventricular dysfunction and all-cause mortality in the overall cohort, and across all 3 age groups. This provides an important target for intervention since standard guideline directed medical therapy for heart failure has been shown to be effective in reversing systemic ventricular systolic dysfunction, and reducing the risk of cardiovascular events in CHD patients with systemic left ventricle [21,22]. This underscores the need for early initiation and titration of heart failure therapy in order to reduce the incidence of mortality in this population.

4.1. Limitations

This is a retrospective single center study and is therefore prone to selection and ascertainment bias. The proportion of patients with

moderate and complex CHD in this study is significantly higher than reported in other studies, and this may limit the generalizability of the results. We relied on mortality data from the medical records, and hence we could have underestimated the risk of mortality in this cohort.

5. Conclusions

About half of adults with CHD were young adults at the time of baseline encounter in our adult CHD clinic, and these patients had different clinical characteristics and risk profile as compared to the middle-aged and older patients. These results suggest a need for management strategies tailored to address the correlates of outcomes in each age group, and to modify these management strategies as the patients progress from one age group to the next. Furthermore, the association between systemic ventricular dysfunction and mortality was consistent across all age groups, thereby providing a viable target for intervention considering the known benefits of medical therapy for this lesion.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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