International Journal of Cardiology Congenital Heart Disease 15 (2024) 100492

Contents lists available at ScienceDirect

International Journal of Cardiology Congenital Heart Disease

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-congenital-heart-disease

Comparison in the adult congenital heart disease severity classification of ACC/AHA and ESC guidelines in a 3,459 Mexican population

Edgar García-Cruz [a], Montserrat Villalobos-Pedroza [a,*], Neftali Eduardo Antonio-Villa [b], Daniel Manzur-Sandoval [c], Daniel Alejandro Navarro-Martínez [d], Axel J. Barrera-Real [e], Elisa Mier y Terán-Morales [e], Stephanie Teresa Angulo-Cruzado [a], Naybeth Ediel García-González [a], Jorge Luis Cervantes-Salazar [f], Antonio Benita-Bordes [f], Linda Guieniza Díaz-Gallardo [a], Victor Alejandro Quiroz-Martinez [g], Julio César Sauza-Sosa [h], Isis Guadalupe Montalvo-Ocotoxtle [e], Jeyli Estrella Ferrer-Saldaña [e], Emmanuel A. Lazcano-Díaz [b], Nydia Ávila-Vanzzini [i], Francisco Martín Baranda-Tovar [j]

[a] Adult Congenital Heart Disease Clinic, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[b] Department of Endocrinology, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[c] Cardiovascular Critical Care Unit, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[d] Department of Cardiothoracic and Vascular Surgery, University of Texas, Houston, Texas, USA
[e] Education Department, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[f] Congenital Heart Disease Surgery Department, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[g] Cardiology Department, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[h] Cardiology Department, The American British Cowdray Medical Centre, Mexico City, Mexico
[i] General Cardiology Outpatient Clinic, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico
[j] Surgical and Medical Cardiovascular Specialties Direction, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico

ARTICLE INFO

Keywords:
Adult congenital heart disease
Classification system
Functional status
Repair status
Arrhythmias
Heart failure

ABSTRACT

Background: Latin American registries of clinical and demographic profiles of ACHD are scarce. International guidelines classify disease complexity with different approaches. With these two regards, a registry was carried out to examine factors associated with mortality and to compare severity classifications in our population.

Methods and results: Cross-sectional study conducted on ACHD between 2018 and 2022 to evaluate clinical and demographic characteristics and to assess the agreement between the 2020 ESC Guidelines and 2018 AHA/ACC Guidelines for the Management of Adults with Congenital Heart Disease using the *kappa* method. Binomial logistic regression models were used to examine correlates of mortality. 3459 patients were included [56 % women, median age 34 years (IQR 24–50)]; 83.41 % were alive and 4.11 % died. The subjects had the following characteristics: 74.18 % were in NYHA I FC, 87.30 % had SVEF ≥50 %, 18.42 % developed arrhythmias, 58.92 % were surgically repaired, 7.05 % received palliative management, and 0.03 % were in heart transplant protocol. The agreement between ESC and AHA/ACC complexity classifications was low (43.29 %) in moderate ACHD, and high (83.10 %) in severe disease. Mortality was higher in patients with NYHA III-IV FC, arrhythmias and under palliative care.

Conclusion: This study found that ESC and AHA/ACC complexity classifications have limited concordance in categorizing moderate complexity CHD. Reparative procedures had lower mortality odds than palliative care.

1. Introduction

Congenital heart disease (CHD) is a prevalent congenital defect, impacting approximately 1 % of live births worldwide, making it the most common inborn defect [1]. This condition can often be attributed to genetic syndromes, exposure to teratogens, or gestational diabetes,

* Corresponding author. Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, Belisario Domínguez - Sección XVI, Tlalpan, Mexico City, 14080, Mexico.
E-mail address: movspa@hotmail.com (M. Villalobos-Pedroza).

https://doi.org/10.1016/j.ijcchd.2024.100492
Received 13 September 2023; Received in revised form 11 January 2024; Accepted 17 January 2024
Available online 19 January 2024

accounting for up to 20 % of cases [2]. Notably, there has been a significant increase in the population of adults living with CHD globally. Recent studies have shown a marked increase in the birth prevalence of CHD since 2009, which has crucial implications for these patients' healthcare needs, particularly in low to middle income countries (LMIC) [3]. This rise can be linked to advancements in diagnostic and therapeutic technologies, enabling more children with CHD to survive into adulthood [4,5]. Consequently, most CHD in the adult population now surpass that in the pediatric population [6].

Understanding these trends requires data from various sources, including databases in well-standardized national healthcare systems like the United States, the United Kingdom, Finland, and the Netherlands [7,8]. However, the availability of such data is limited in LMIC, particularly in Latin America. For example, the Colombian Ministry of Health reported a CHD prevalence of 75–95 per 10,000 newborns, while in Argentina, the rate stands at 11.46 per 10,000 births [9,10]. Furthermore, an ongoing debate exists about the classification system used to categorize adult congenital heart disease. The American Heart Association (AHA) and American College of Cardiology (ACC) guidelines differ from the European Society of Cardiology (ESC) guidelines in this regard [11,12].

2. Methods

2.1. Aims

Recognizing the clinical characteristics of adults with CHD in LMIC is vital for developing medical programs to enhance care for this population. Therefore, this study aims to achieve three key objectives:

1. To determine adult CHD patients' clinical and demographic profiles based on data from the institutional registry of Adult Congenital Heart Disease (ACHD), known as ReACHD.
2. To compare the agreement between two ACHD complexity classifications: the 2020 ESC Guidelines for the Management of ACHD and the 2018 AHA/ACC Guideline for the Management of Adults with Congenital Heart Disease.
3. To identify the factors associated with overall mortality in a registry comprising 3459 ACHD patients receiving care at a tertiary referral center in Mexico.

2.2. Study design

The ReACHD study is a retrospective cross-sectional investigation aimed at characterizing the clinical and demographic profiles of ACHD patients who attended follow-up visits at the Instituto Nacional de Cardiología Ignacio Chávez, a tertiary referral center for cardiovascular care in Mexico City. The primary objectives of this registry were to assess CHD prevalence, complexity, treatment status, New York Heart Association (NYHA) functional class (FC), systemic ventricle ejection fraction and the incidence of pulmonary hypertension. Inclusion criteria encompassed patients aged ≥18 with a documented CHD diagnosis who had at least one outpatient visit between January 2018 and January 2022. Exclusions were made for patients with diagnoses not meeting the ESC or AHA/ACC guidelines, pediatric patients not transitioned to the adult CHD clinic, and individuals with incomplete medical records. Sociodemographic and clinical data were extracted from patients' medical records and electronic files, with all information recorded anonymously due to the study's retrospective nature. This study received approval from the local institutional Ethics Committee as protocol INCAR-DG-DI–CI–233-2021. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee, an adhered to the STROBE guidelines for reporting observational studies. Three independent collaborators (AJBR, DANM, and EMYTM) cross-validated the data in the analyzed dataset to enhance data quality and minimize bias. Definitions of study outcomes can be found in the Supplementary Material.

2.3. Data collection

A. *Sociodemographic Variables:* Data included age, sex, place of origin, and current activity. According to established geographic distributions, the area of origin referred to the Mexican state of residence and was further categorized into four geographic regions (northern, central, western, and southern Mexico). We established the classification of 'unemployed' or 'retired' in accordance with the criteria outlined by Mexico's Secretary of Labor and Social Welfare, defining this status as applicable to individuals who have a work history of a minimum of 6 months but who are currently not employed.

B. *Clinical Assessment:* Clinical variables were extracted from patients' most recent clinical notes. Genetic syndrome associations were determined based on clinical records and assessed by a clinical geneticist. CHD repair status followed the 2020 ESC Guidelines [12], categorizing patients as having undergone palliative surgery, reparative surgery, under surveillance, or receiving palliative care for those ineligibles for surgery. To account for anatomical variations, systemic ventricular ejection fraction (SVEF) was evaluated instead of left ventricular ejection fraction (LVEF). SVEF was measured during baseline assessments, using either transthoracic echocardiography or cardiac magnetic resonance, and reported as a percentage. In order to establish the criteria for assessing the probability of pulmonary hypertension via echocardiography, we adhered to the 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, which employs peak tricuspid regurgitation velocity, the presence of other echo PH signs and the presence of risk factors as a parameter for classifying the likelihood of pulmonary hypertension, as described [13]. Arrhythmia diagnoses were made by cardiologists and documented in patient records. The pregnancy history of female patients was determined from clinical records, irrespective of pregnancy outcomes or terminations. The ejection fraction was classified according to the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: preserved (≥50 %), mildly reduced (41–49 %), and reduced (≤40 %) SVEF. Functional status was classified based on current activity and NYHA functional class.

C. *Management:* Study variables encompassed procedures (surgical or interventional), the presence of cardiovascular devices (prosthetic heart valve, pacemaker, implantable cardioverter-defibrillator (ICD), prosthetic tube graft, endovascular devices, valvular ring) and the status of the most recent procedure.

2.4. Statistical analysis

To summarize continuous variables, we conducted the Shapiro-Wilk test to assess normality. Normally distributed data were presented as mean and standard deviation, while non-normally distributed data were expressed as median and interquartile range. Categorical variables were reported as frequencies and percentages. To visualize geographic distribution, we employed the ggplot2 R package [14]. Per ESC guidelines, comparisons between mild, moderate, and severe CHD categories were made using one-way ANOVA or Kruskal-Wallis tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. A significance level of $p < 0.05$ was used. All analyses were performed using R version 3.1.1.

2.4.1. Evaluation of agreement with ESC and AHA/ACC classifications

Using the exact method, we estimated CHD risk category prevalence with a 95 % confidence interval. Agreement between ESC and AHA/ACC classifications was assessed using the *kappa* statistic, calculated via the Fleiss Method. Kappa values were interpreted as follows: <0.2 slight agreement, 0.2–0.4 fair agreement, 0.4–0.6 moderate agreement,

0.6–0.8 substantial agreement, and >0.8 almost perfect agreement. Estimations and assessments were conducted using the epiR R package [15].

2.4.2. Factors associated with mortality

We constructed binomial logistic regression models adjusted for age and sex to assess overall mortality-related factors, with overall mortality status as the dependent variable and sociodemographic, clinical, and management variables as independent variables. McFadden R2 was calculated to evaluate each model's contribution to the explained variance, and model diagnostics relied on Bayesian Information Criteria (BIC). Additional data about mortality can be found in the supplementary material.

3. Results

3.1. ReACHD sociodemographic profile

We gathered clinical data from 3459 adult CHD patients who attended follow-up appointments during the study period. Table 1 provides a comprehensive overview of the patient population. The median age was 34 years (IQR 24–50), with a majority of females (56.03 %). Among females, 44.42 % had reported at least one pregnancy in their clinical records. Of the included patients, 83.41 % were reported as alive, 12.49 % were lost to follow-up, and 4.11 % had passed away. Most patients were active workers, students, or homemakers, with smaller proportions being unemployed, retired, or unable to work due to physical disabilities. Geographic distribution analysis revealed concentration in the central metropolitan area of Mexico (Mexico City and State

Table 1
Characterization of the study population. *NYHA*, New York Heart Association. *SVEF*, Systemic Ventricular Ejection Fraction. *PH*, Pulmonary Hypertension. *AHA*, American Heart Association. *ACC*, American College of Cardiology. *CHD*, Congenital Heart Disease.

Parameter	Overall Population (n = 3459)	Mild Complexity (n = 1826)	Moderate Complexity (n = 1111)	Severe Complexity (n = 522)	P-Value
Sociodemographic Variables					
Men (%)	1521 (43.97)	825 (45.18)	463 (41.67)	233 (44.64)	<0.001
Female (%)	1938 (56.03)	1001 (54.82)	648 (58.33)	289 (55.36)	
Age (Years)	34 (24–50)	38 (25–54)	32 (24–46)	29.5 (22.25–39)	<0.001
Outside Metropolitan Area (%)	1337 (38.65)	634 (34.72)	477 (42.93)	226 (43.3)	<0.001
Metropolitan Area (%)	2122 (61.35)	1192 (65.28)	634 (57.07)	296 (56.7)	<0.001
Unemployed or Retired (%)	1690 (48.86)	852 (46.66)	555 (49.95)	283 (54.21)	<0.001
Employed (%)	1114 (32.21)	645 (35.32)	349 (31.41)	120 (22.99)	<0.001
Student (%)	655 (18.94)	329 (18.02)	207 (18.63)	119 (22.8)	<0.001
Pregnancy (%)	861 (44.42)	446 (44.56)	316 (48.77)	99 (34.26)	<0.0001
Clinical Assessment					
NYHA-I (%)	2566 (74.18)	1495 (81.87)	808 (72.73)	263 (50.38)	<0.001
NYHA-II (%)	609 (17.61)	223 (12.21)	225 (20.25)	161 (30.84)	<0.001
NYHA-III (%)	194 (5.61)	71 (3.89)	52 (4.68)	71 (13.6)	<0.001
NYHA-IV (%)	83 (2.4)	36 (1.97)	22 (1.98)	25 (4.78)	<0.001
SVEF ≥50 (%)	3020 (87.3)	1649 (90.3)	1000 (90.01)	371 (71.07)	<0.001
SVEF 41–49 (%)	186 (5.37)	68 (3.72)	56 (5.04)	62 (11.87)	<0.001
SVEF ≤40 (%)	195 (5.63)	88 (4.82)	41 (3.69)	66 (12.64)	<0.001
Arrhythmias (%)	637 (18.42)	298 (16.32)	234 (21.06)	105 (20.69)	0.401
History of Ischemic Cardiomyopathy (%)	26 (0.75)	12 (0.66)	10 (0.9)	4 (0.77)	0.136
History of Acute Coronary Syndrome (%)	3 (0.09)	2 (0.11)	1 (0.09)	0 (0)	0.758
Genetic Syndrome Association (%)	157 (4.54)	83 (4.55)	44 (3.96)	30 (5.75)	0.182
Functional Assessment					
High Probability of PH (%)	517 (14.95)	210 (11.5)	200 (18)	107 (20.5)	<0.001
Pulmonary Hypertension (%)	172 (4.97)	70 (3.83)	62 (5.58)	40 (7.66)	<0.001
Eisenmenger Syndrome (%)	87 (2.52)	7 (0.38)	5 (0.45)	75 (14.37)	<0.001
AHA/ACC Anatomical Classification					
Mild (%)	1551 (44.84)	1027 (56.24)	431 (38.79)	93 (17.82)	<0.001
Moderate (%)	1476 (42.67)	767 (42)	639 (57.52)	70 (13.41)	<0.001
Severe (%)	432 (12.49)	32 (1.75)	41 (3.69)	359 (68.77)	<0.001
AHA/ACC Physiological Classification					
A (%)	1593 (46.05)	1019 (55.81)	471 (42.39)	103 (19.73)	<0.001
B (%)	424 (12.26)	208 (11.39)	159 (14.31)	57 (10.92)	<0.001
C (%)	1107 (32)	436 (23.88)	416 (37.44)	255 (48.85)	<0.001
D (%)	335 (9.68)	163 (8.93)	65 (5.85)	107 (20.49)	<0.001
Management of CHD					
Non-Repaired and Under Surveillance (%)	1176 (33.99)	375 (20.54)	586 (52.75)	215 (41.19)	0.0316
Total Surgical Repair (%)	2038 (58.92)	1449 (79.35)	484 (43.56)	105 (20.11)	<0.001
Heart transplantation protocol	1 (0.03)	0 (0)	0 (0)	1 (0.19)	<0.0001
Palliative Management					
Overall Palliative Management (%)	244 (7.05)	2 (0.11)	41 (3.69)	201 (38.50)	
Palliative Surgery (%)	133 (3.84)	0 (0)	22 (1.98)	111 (21.26)	<0.0001
Non-Repaired and Under Medical Management (%)	111 (3.21)	2 (0.11)	19 (1.71)	90 (17.24)	<0.001
Systemic-Pulmonary Fistulae (%)	65 (1.88)	1 (0.05)	6 (0.54)	58 (11.11)	<0.001
Glenn Procedure (%)	18 (0.52)	0 (0)	6 (0.54)	12 (2.3)	<0.001
Fontan Procedure (%)	34 (0.98)	0 (0)	0 (0)	34 (6.51)	<0.001
Kawashima Procedure (%)	4 (0.12)	0 (0)	1 (0.09)	3 (0.57)	<0.001
Current Status					
Alive (%)	2885 (83.41)	1557 (85.27)	946 (85.15)	382 (73.18)	<0.001
Dead (%)	142 (4.11)	71 (3.89)	29 (2.61)	42 (8.05)	<0.001
Unknown Status (%)	432 (12.49)	198 (10.84)	136 (12.24)	98 (18.77)	0.871
Death Related to CHD (%)	102 (71.83)	51 (71.83)	21 (72.41)	30 (71.43)	0.0135

of Mexico) and the southern region (Fig. 1-A). Atrial septal defect (ASD) was the most prevalent CHD, followed by bicuspid aortic valve (BAV), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and coarctation of the aorta (CoA) (Fig. 1-B). Genetic syndromes were identified in 157 patients (4.54 %), with Trisomy 21, Marfan, and Noonan syndromes being the most common.

3.2. Complexity characterization by ESC classification

Using the ESC classification, 52.79 % of patients had mild CHD, 32.12 % had moderate CHD, and 15.09 % had severe CHD. Table 1 provides a detailed breakdown. The age distribution revealed the oldest patients in the mild CHD group, with a female predominance across all three categories (54.82 %, 58.33 %, and 55.36 %, respectively). According to the ESC classification, the most prevalent anomalies in the mild CHD group were BAV (35.20 %), ASD (27.70 %), and VSD (15.40 %). In the moderate CHD group, unrepaired ASD was the most prevalent defect (38 %), followed by CoA (15.10 %). In the severe CHD group, the most prevalent CHDs were double outlet right ventricle (DORV) (11.90 %), congenitally corrected transposition of the great arteries (10.3 %), and pulmonary atresia with VSD (9.60 %). The severe complexity group has the greatest percentage of Unemployed or Retired (54.21 %), and the least percentage of pregnancies (34.26 %); besides, it has the lowest prevalence of totally repaired patients (20.11 %) but it is also the one with the highest percentage of Fontan, Glenn procedure, and Systemic-Pulmonary Fistulae (6.51 %, 2.30 %, and 11.11 %, respectively).

The NYHA functional class was significantly associated with the SVEF, the highest proportion of NYHA class I patients was observed in the mild complexity group, followed by the moderate and severe complexity groups. A higher proportion of NYHA class III and IV patients was found in the severe complexity group, as shown in Fig. 2. In the mild complexity group, 90.30 % had SVEF $\geq$50 %, while only 4.82 % had SVEF $\leq$40 %. In the moderate complexity group, 3.69 % had SVEF $\leq$40 % and 12.64 % had SVEF $\leq$40 % in the severe complexity group.

3.3. Management and complications in the ReACHD

Concerning management, most patients had undergone complete correction surgery or were currently being evaluated for repair. Only 7.05 % of patients received palliative care, including 3.84 % undergoing palliative procedures and 3.21 % receiving palliative medical treatment. Cardiovascular prosthetic devices were reported in 43 % of the population, including mechanical and biological prosthetic heart valves, endovascular devices, prosthetic tube grafts, vascular rings, systemic-pulmonary fistulae, pacemakers, and ICDs (Supplementary Material). Complications included a high probability of pulmonary arterial hypertension (PAH) in 14.95 % of patients and a diagnosis of Eisenmenger Syndrome (ES) in 2.52 %. Arrhythmias were reported in 18.42 % of the sample, including atrial flutter or fibrillation, supraventricular tachycardia, ventricular tachycardia and ventricular fibrillation (Supplementary Material).

3.4. Concordance of ESC and AHA/ACC classifications

We aimed to assess the agreement between the ESC and AHA/ACC ACHD complexity classifications. According to the AHA/ACC classification, 44.84 % of our patients had mild, 42.67 % had moderate, and 12.49 % had severe CHD. Upon applying both systems, we observed differences in the prevalence of each complexity group. Fig. 3, concordance analysis table, shows that both classification systems consistently categorized mild and severe complexities, concordant in 66.22 % and 83.10 %, respectively. However, a significant discrepancy emerged in classifying moderate heart defects between the ESC and AHA/ACC systems, with only 43.29 % of concordance in these heart defects. We calculated a kappa statistic of 0.32 (95 % CI: 0.29–0.34, $p < 0.001$), indicating fair agreement between the two scales.

3.5. Mortality

The leading causes of death related to ACHD in the 102 patients were as follows: arrhythmias in 40 % of cases, congestive heart failure in 40 %, and 20 % were due to pulmonary hypertension, thromboembolic events, or hypoxic spells.

Adjusted binomial logistic regression results revealed that any arrhythmia increased the odds of mortality (OR 1.75; 95 % CI 1.18–2.59, $p = 0.005$). NYHA FC III was associated with a 13.1-fold increase in the odds of mortality (95 % CI 7.44–23.06, $p < 0.001$), and NYHA FC IV was associated with an 18.68-fold increase in the odds of mortality (95 % CI 8.44–41.32, $p < 0.001$). Additionally, palliative strategy, including surgery and medical treatment, was associated with higher odds of mortality (OR 2.64; 95 % CI 1.53–4.49, $p < 0.001$) compared to those who underwent complete repair (Table 2).

4. Discussion

This study aimed to elucidate the sociodemographic and clinical characteristics of adults with CHD receiving care at a tertiary referral center in Mexico. Additionally, we aimed to explore the discrepancies and moderate agreement between the ACHD classification systems delineated in the 2020 ESC guidelines and the 2018 AHA/ACC guidelines, recognizing the potential challenges these discrepancies pose for accurately classifying ACHD patients given the complexity of their defects, associated anomalies, and the prevalence of unrepaired or palliated cases. Lastly, we examined the influence of arrhythmias and palliative care on mortality.

The global upsurge in the prevalence of adults living with CHD can be attributed to improved prognosis resulting from advances in surgical techniques and enhanced perioperative and intensive care management

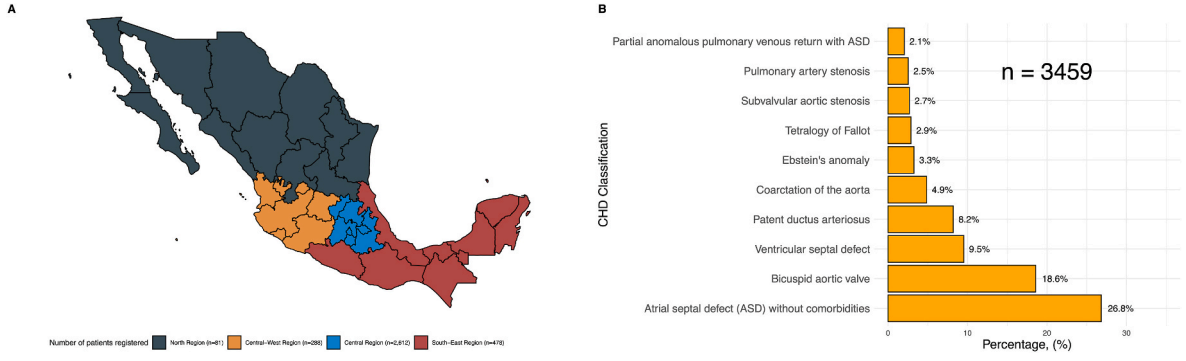

Fig. 1. A) Distribution of adult congenital heart disease in Mexico. B) Prevalence of adult congenital heart disease in our overall study population based on the ESC classification. *Abbreviations*: CHD, Congenital Heart Disease. ASD, Atrial Septal Defect. ESC, European Society of Cardiology.

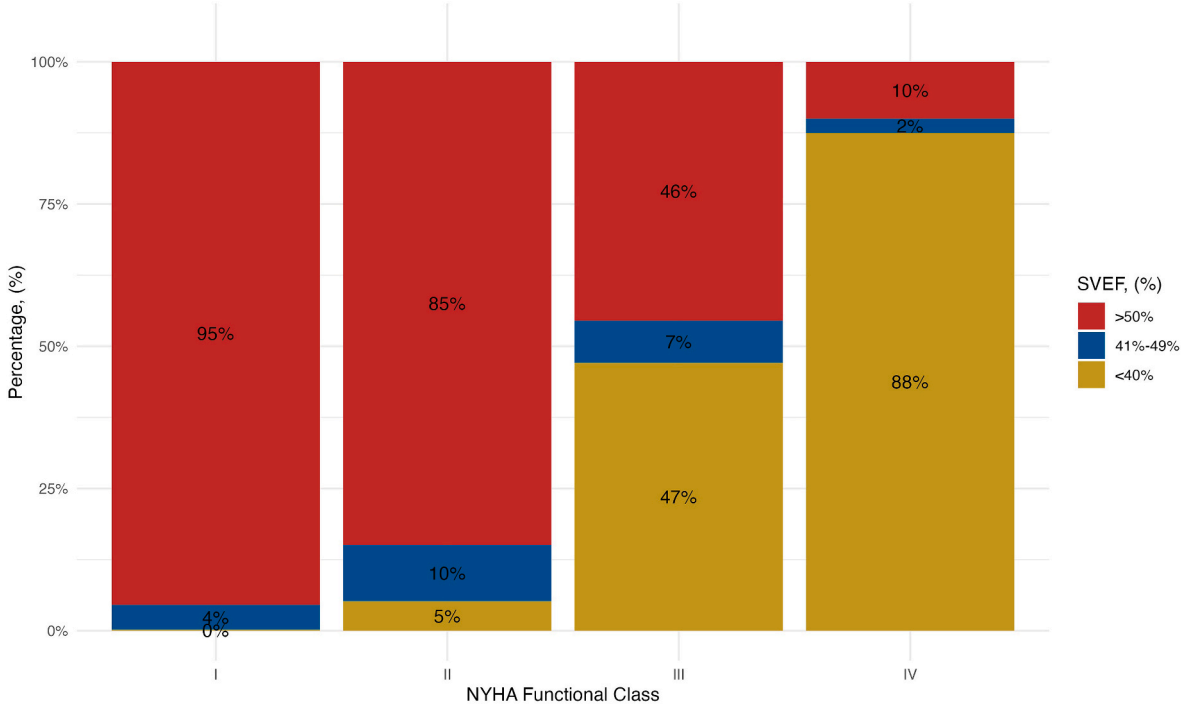

Fig. 2. Distribution of NYHA functional class and systemic ventricle ejection fraction.

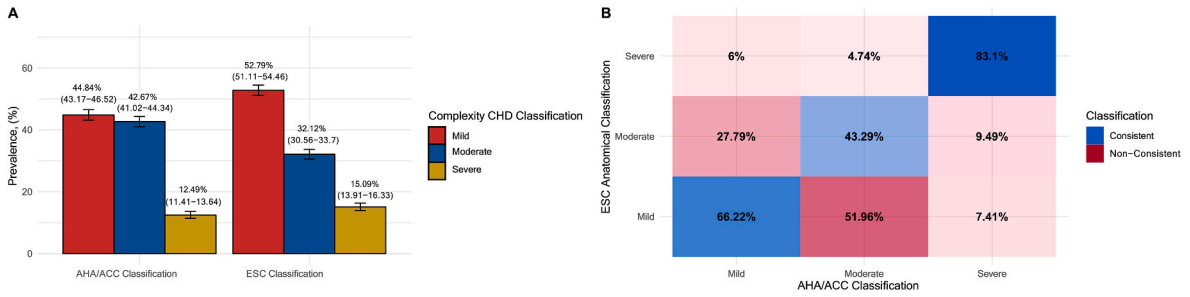

Fig. 3. A) AHA/ACC CHD complexity classification and ESC CHD complexity classification. B) Concordance analysis table between AHA/ACC and ESC CHD complexity classifications. *Abbreviations*: AHA, American Heart Association. ACC, American College of Cardiology. ESC, European Society of Cardiology. CHD, Congenital Heart Disease.

[5,16]. National registries are becoming indispensable for addressing the needs of these patients and guiding policy decisions to establish well-equipped ACHD centers [17]. The ReACHD registry shares similarities and disparities with international registries reported in the literature. Atrial septal defect (ASD) emerged as the most prevalent CHD type, consistent with the Danish Registry findings, followed by ventricular septal defect (VSD), mirroring our results [18]. The low association prevalence with genetic syndromes may partly be due to underdiagnosis, reflecting limited access to genetic testing in our region.

Nevertheless, the Danish registry reported a lower incidence of genetic syndromes (2.5 %) among patients with mild complexity CHD, less than half of our findings (4.55 %) [18]. Our mortality rate aligns with the Dutch national registry's data [19]. Previous research by Engelfriet et al. identified higher mortality rates in males, possibly influenced by smoking, comorbidities (e.g., diabetes, hypertension, ischemic heart disease), and a higher incidence of CHD-related complications [20]. Additionally, García et al. found that along with greater survival in this population comes more prevalence of cardiovascular risk factors, such as prevalence of low HDL cholesterol, insulin resistance, and prediabetes [21]. Furthermore, we observed a significant proportion of the CHD population actively participating in the workforce, with one-third maintaining stable employment and less than 4 % unable to work, echoing the findings of Sarno et al. [22]. Regarding the greater representation of students within the severe complexity group compared to other cohorts, the specific rationale escapes us. Nevertheless, we hypothesize this discrepancy could be attributed to their potentially better functional status. Finally, a substantial proportion of women had experienced pregnancies regardless of the severity of their heart defects, possibly attributed to limited access to contraception education and services in our country. Notably, most patients persist in NYHA functional class I, implying that they hold the potential for employment despite limited job opportunities.

Regarding complications, the prevalence of PAH in our ReACHD series was lower than reported in other international data [23,24]. For instance, the UK registry reported 30.2 % patients with PAH secondary to CHD [24]. The prevalence of Eisenmenger syndrome was 2.52 %, lower than global references [23]. The diagnosis of Eisenmenger syndrome can be clinical and echocardiography-based, but for diagnostic confirmation, we specifically relied on catheterization, understanding the challenges posed by patients with cyanosis who lack PAH or shunts, which is especially relevant in our retrospective study. In the case of PAH, catheterization is indispensable for confirmation, whereas echocardiography, according to guidelines, only offers a probability assessment. It's worth noting that not all patients have access to cardiac

Table 2
Adjusted binomial logistic regression model to assess the probability of death status related to clinical variables.

Model	Characteristics	Odds Ratio	95 % C. I.	p-value
Death Status	**Age, (Years)**	1.01	1.00, 1.03	0.039
$\chi^2(11) = 216.40$ (p<0.001)	**Sex, (%)**			
BIC: 961.46	*Men*	Ref		
R2 = 0.20	*Women*	0.99	0.67, 1.48	0.980
	Arrhythmias, (%)	1.57	1.03, 2.37	0.036
	NYHA, (%)			
	I	Ref		
	II	1.91	1.10, 3.24	0.018
	III	11.4	6.27, 20.6	<0.001
	IV	15.3	6.66, 34.9	<0.001
	Palliative Care, (%)			
	No	Ref		
	Yes	2.64	1.53, 4.49	<0.001
	Pulmonary Hypertension or			
	0	Ref		
	Probable PH	0.83	0.46, 1.42	0.507
	PH or Eisenmenger Syndrome	0.59	0.28, 1.16	0.147
	SVEF, (%)			
	>50 %	Ref		
	41%-49 %	1.72	0.83, 3.30	0.120
	<40 %	1.22	0.63, 2.33	0.551

catheterization for confirming a PAH diagnosis. Consequently, given that 14.95 % of patients exhibit a high likelihood of having PAH, there is a possibility of underestimating these two diagnoses (PAH and Eisenmenger syndrome) in our population.

Regarding arrhythmias, the frequency was similar to worldwide records, up to 50 % of CHD patients are expected to develop some arrhythmia throughout their lifetime, according to the ESC Guidelines [25]. This phenomenon is linked to structural abnormalities and electrophysiological remodeling, aligning with our findings [26].

One of our study's objectives was to show discrepancies among CHD classification systems. When employing the ESC and AHA/ACC systems, we noticed 8 % difference in the mild category, 10 % disparity in the moderate category, and less than 3 % contrast in the severe category, highlighting substantial distinctions between both classification systems. Additionally, we observed a notable prevalence of severe diseases, opposite to global data based on the 2020 ESC guidelines, where severe cases account for less than 15 %. The lowest agreement between both scales was detected in the moderate complexity category. For general cardiologists, classifying the severity of CHD subtypes presents an added challenge. Egidy Assenza et al. compared, identifying differences in critical areas between the ESC and AHA/ACC guidelines, but still need to assess the level of agreement in terms of classification. They concluded that relying solely on anatomical impairments to classify CHD can limit patient management [27]. In our setting, for CHD of moderate and severe complexity, most cardiologists tend to believe that these patients have limited treatment options and that any interventional or surgical procedure carries high risks. However, our mortality analysis of moderate and severe complexity ACHD surgeries demonstrated a low death rate (12.2 %), even considering the presence of comorbidities, CHD progression into adulthood, and surgeries performed in adulthood [28]. Our results substantiate the hypothesis that CHD classification is intricate and inconsistent depending on the system used. In the coming years, guidelines should be established considering cardiovascular factors and congenital heart disease impairments. It's essential to mention that the ESC classification lacks a physiological category, potentially leading to an underestimation of the severity of CHD. Conversely, the AHA/ACC classification allows for complexity categorization based on physiological implications, offering valuable insights for the Heart Team in understanding and managing various CHD types. In our population, where specialized ACHD centers are limited, we believe that classifying patients using the AHA/ACC scale provides greater confidence.

Lastly, we aimed to evaluate factors associated with mortality. We identified associations between arrhythmias, unrepaired CHD, and increased mortality risk, consistent with findings that arrhythmias, worse NYHA functional class, and cardiovascular procedures (surgical or interventional catheter-based procedures) are common reasons for emergency room visits, hospitalizations, and death [29–31]. Heart failure has been the leading cause of death in approximately 26 % of these patients [28,32]. Notably, we observed a low proportion of patients with reduced ejection fraction, the ejection fraction was unknown in 58 patients. One limiting factor that could account for this is the absence of NT-proBNP data, attributed to the retrospective nature of the study. Nonetheless, leveraging insights gained from this registry, patients are currently undergoing NT-proBNP testing to facilitate a more comprehensive diagnostic approach, augmenting the reliance on both imaging and clinical assessments. Our results underscore the need for further exploration of mortality-related risk factors, as these findings can guide cardiologists in prioritizing patient care and influencing management and prognosis in resource-constrained settings. We also consider that the fact that the reparative procedure had a positive OR could be related to the surgical risk, as 43.56 % of the moderate and 20.11 % of the complex ACHD patients have undergone total surgical repair, we attribute this tendency to higher mortality to the intrinsically-related surgical risk [33]. Besides, it is possible that the most severe cases are the ones who could not reach adulthood and died in a younger age, leaving the mild and moderate categories with more patients, hence, more proportion of death risk.

In Latin America, a significant epidemiological shift is impacting the ACHD population. Despite timely diagnosis and treatment challenges, most patients maintain good functional status, enabling economic productivity, contrary to common prognostic beliefs. However, care programs for adults living with CHD in Latin America must be improved, lagging behind reference centers worldwide by at least 20 years. Nevertheless, despite these limitations, the prognosis and survival of these patients in Latin America are similar to global reports. We advocate for establishing a decentralized care system, creating CHD specialty centers nationwide, and developing effective transitional care programs. These efforts could serve as a model for other Latin American low to middle-income countries.

5. Strengths and limitations

Our study boasts both strengths and limitations. Including comprehensive clinical and functional evaluations within one of Mexico's largest registries helped thorough characterization of adults living with CHD in our country. However, there are noteworthy limitations to acknowledge. First, this study adopted a cross-sectional design, lacking follow-up data, potentially impacting the mortality rate. Moreover, many patients were unable to contact, making it impossible to confirm their status. Second, the COVID-19 pandemic reduced ACHD outpatient clinic visits, leading to data gaps and incomplete information due to restrictions on multimodal imaging studies. Furthermore, many patients were referred from pediatric hospitals, and due to inadequate transitional care, crucial medical history and diagnostic information were lost.

6. Conclusion

The ReACHD initiative is one of the largest efforts to

comprehensively assess the sociodemographic and clinical characteristics of the adult CHD population in Mexico. Our findings reveal a noteworthy proportion of individuals who have undergone surgical management and repair, coupled with a relatively low prevalence of complications. Furthermore, this population demonstrates a high level of economic activity, allowing them to actively participate in the workforce despite the challenges they encounter in Mexico's healthcare landscape. This study also sheds light on significant discrepancies between our cohort's ESC and AHA/ACC complexity classifications, particularly in the classification of moderate complexity cases; these disparities can create challenges in accurately categorizing patients, potentially impacting their clinical management. And our analysis identified that NYHA functional class, arrhythmias and palliative care were associated with higher mortality in this population.

Grant support

No funding or financial support was received for this project. There are no conflicts of interest from any of the authors.

Statement

During the preparation of this work the authors used ChatGPT August 3 Version in order to assess the clarity, structure, grammar, and cohesion of the narrative in the text. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Disclosure

One or more of the co-authors serve as members of the Editorial Board for IJC Congenital Heart Disease. They had no role in the editorial review of or decision to publish this article.

CRediT authorship contribution statement

Edgar García-Cruz: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Montserrat Villalobos-Pedroza:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **Neftali Eduardo Antonio-Villa:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Daniel Manzur-Sandoval:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Daniel Alejandro Navarro-Martínez:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Axel J. Barrera-Real:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Elisa Mier y Terán-Morales:** Writing – original draft, Methodology, Investigation, Data curation. **Stephanie Teresa Angulo-Cruzado:** Project administration, Methodology, Conceptualization. **Naybeth Ediel García-González:** Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation. **Jorge Luis Cervantes-Salazar:** Project administration, Methodology, Formal analysis. **Antonio Benita-Bordes:** Resources, Methodology, Investigation. **Linda Guieniza Díaz-Gallardo:** Project administration, Methodology. **Victor Alejandro Quiroz-Martinez:** Investigation, Funding acquisition. **Julio César Sauza-Sosa:** Investigation, Conceptualization. **Isis Guadalupe Montalvo-Ocotoxtle:** Methodology, Investigation. **Jeyli Estrella Ferrer-Saldaña:** Methodology. **Emmanuel A. Lazcano-Díaz:** Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Nydia Ávila-Vanzzini:** Resources, Data curation. **Francisco Martín Baranda-Tovar:** Resources, Project administration, Methodology, Investigation.

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.

Acknowledgments

To the team of the *Oficina de Apoyo Sistemático para la Investigación Superior (OASIS)* team from the Instituto Nacional de Cardiología Ignacio Chávez. We also gratefully thank our colleagues who collaborated on the database and development of the study in all ways for their valuable help.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcchd.2024.100492.

References

[1] van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol 2011;58(21):2241–7.
[2] Blue GM, Kirk EP, Sholler GF, Harvey RP, Winlaw DS. Congenital heart disease: current knowledge about causes and inheritance. Med J Aust 2012;197(3):155–9.
[3] Liu Y, Chen S, Zuhlke L, Black GC, Choy MK, Li N, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. Int J Epidemiol 2019;48(2):455–63.
[4] Mandalenakis Z, Giang KW, Eriksson P, Liden H, Synnergren M, Wahlander H, et al. Survival in children with congenital heart disease: have we reached a peak at 97. J Am Heart Assoc 2020;9(22):e017704.
[5] Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JIE, et al. Task Force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol 2001;37(5):1170–5.
[6] 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;130(9):749–56.
[7] Engelfriet P, Boersma E, Oechslin E, Tijssen J, Gatzoulis MA, Thilen U, et al. The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period. The Euro Heart Survey on adult congenital heart disease. Eur Heart J 2005;26(21):2325–33.
[8] Nieminen H, Sairanen H, Tikanoja T, Leskinen M, Ekblad H, Galambosi P, et al. Long-term results of pediatric cardiac surgery in Finland: education, employment, marital status, and parenthood. Pediatrics 2003;112(6 Pt 1):1345–50.
[9] Baltaxe E, Zarante I. Prevalence of congenital heart disease in 44,985 newborns in Colombia. Arch Cardiol Mex 2006;76(3):263–8.
[10] Groisman B, Barbero P, Liascovich R, Brun P, Bidondo MP. Detection of critical congenital heart disease among newborns in Argentina through the national surveillance system of congenital heart disease (RENAC). Arch Argent Pediatr 2022;120(1):6–13.
[11] Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, et al. AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American heart association task force on clinical practice guidelines. Circulation 2018;139(14). 2019.
[12] Baumgartner H, De Backer J, Babu-Narayan SV, Budts W, Chessa M, Diller GP, et al. ESC Guidelines for the management of adult congenital heart disease. Eur Heart J 2020;42(6):563–645. 2021.
[13] Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, et al. ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J 2023 Jan 6;61(1):2200879.
[14] R package GGPLOT2. version 3.4.0 [Internet]. The Comprehensive R Archive Network. Comprehensive R Archive Network (CRAN); 2022 [cited 2022Aug20]. Available from: https://cran.r-project.org/web/packages/ggplot2/index.html.
[15] Package epir. CRAN. Comprehensive R Archive Network (CRAN); [cited 2022Aug20]. Available from: https://cran.r-project.org/web/packages/epiR/index.html.
[16] Lui GK, Rogers IS, Ding VY, Hedlin HK, MacMillen K, Maron DJ, et al. Risk estimates for Atherosclerotic cardiovascular disease in adults with congenital heart disease. Am J Cardiol 2017;119(1):112–8.
[17] Ashkanani H, Mohiyaldeen I, ElShenawy H, Alanbaei M. Epidemiology of adult congenital heart disease among the general population in Kuwait. Clin Cardiol 2021;44(4):526–30.
[18] El-Chouli M, Meddis A, Christensen DM, Gerds TA, Sehested T, Malmborg M, et al. Lifetime risk of comorbidity in patients with simple congenital heart disease: a Danish nationwide study. Eur Heart J 2022.
[19] Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, van Dijk AP, et al. Mortality in adult congenital heart disease. Eur Heart J 2010;31(10):1220–9.

[20] Engelfriet P, Mulder BJ. Gender differences in adult congenital heart disease. Neth Heart J 2009;17(11):414–7.
[21] García-Cruz E, Manzur-Sandoval D, Gopar-Nieto R, et al. Cardiometabolic risk factors in Mexican adults with congenital heart disease. JACC Adv 2023 Oct;2(8).
[22] Sarno LA, Cortright L, Stanley T, Tumin D, Li JS, Sang CJ. Clinical and socio-economic predictors of work participation in adult CHD patients. Cardiol Young 2020;30(8):1081–5.
[23] Diller GP, Kempny A, Alonso-Gonzalez R, Swan L, Uebing A, Li W, et al. Survival prospects and circumstances of death in contemporary adult congenital heart disease patients under follow-up at a large tertiary centre. Circulation 2015;132 (22):2118–25.
[24] Constantine A, Dimopoulos K, Opotowsky AR. Congenital heart disease and pulmonary hypertension. Cardiol Clin 2020;38(3):445–56.
[25] Hernandez-Madrid A, Paul T, Abrams D, Aziz PF, Blom NA, Chen J, et al. Arrhythmias in congenital heart disease: a position paper of the European heart rhythm association (EHRA), association for European paediatric and congenital Cardiology (AEPC), and the European society of Cardiology (ESC) working group on grown-up congenital heart disease, endorsed by HRS, PACES, APHRS, and SOLAECE. Europace 2018;20(11):1719–53.
[26] Wu MH, Lu CW, Chen HC, Kao FY, Huang SK. Adult congenital heart disease in a nationwide population 2000-2014: epidemiological trends, arrhythmia, and standardized mortality ratio. J Am Heart Assoc 2018;7(4).
[27] Egidy Assenza G, Krieger EV, Baumgartner H, Cupido B, Dimopoulos K, Louis C, et al. AHA/ACC vs ESC Guidelines for management of adults with congenital heart disease. J Am Coll Cardiol 2021;78(19):1904–18.
[28] Hsu D. Chronic heart failure in congenital heart disease. In: Shaddy R, Wernovsky G, editors. Pediatric heart failure. Bosa Roca, USA: CRC Press; 2005. p. 567–88.
[29] Van Bulck L, Goossens E, Morin L, Luyckx K, Ombelet F, Willems R, et al. Last year of life of adults with congenital heart diseases: causes of death and patterns of care. Eur Heart J 2022;43(42):4483–92.
[30] Oliver JM, Gallego P, Gonzalez AE, Garcia-Hamilton D, Avila P, Yotti R, et al. Risk factors for excess mortality in adults with congenital heart diseases. Eur Heart J 2017;38(16):1233–41.
[31] Chessa M, Brida M, Gatzoulis MA, Diller G-P, Roos-Hesselink JW, Dimopoulos K, et al. Emergency department management of patients with adult congenital heart disease: a consensus paper from the ESC Working Group on adult congenital heart disease, the European Society for Emergency Medicine (EUSEM), the European Association for Cardio-Thoracic Surgery (EACTS), and the Association for Acute Cardiovascular Care (ACVC). Eur Heart J 2021;42(26):2527–35.
[32] Arnaert S, De Meester P, Troost E, Droogne W, Van Aelst L, Van Cleemput J, et al. Heart failure related to adult congenital heart disease: prevalence, outcome and risk factors. ESC Heart Fail 2021;8(4):2940–50.
[33] García-Cruz E, et al. Clinical characteristics and outcomes in adults with moderate-to-severe complexity congenital heart disease undergoing palliation or surgical repair. CJC Pediatric and Congenital Heart Disease 2023;2(2):63–73.