HHS Public Access

Author manuscript

Pediatr Res. Author manuscript; available in PMC 2026 January 05.

Cardiovascular disease risk factors in congenital heart disease survivors are associated with heart failure

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Abstract

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AUTHOR CONTRIBUTIONS

Andrew P. Landstrom: Conceived of study and design; Data analysis; Site data generation; Drafted the manuscript; Revised and approved final manuscript. Tracy Spears: Data analysis; Statistical analysis; Revised and approved final manuscript. Alfred D'Ottavio Data management; Data analysis; Revised and approved final manuscript. Karen Chiswell: Data analysis; Statistical analysis; Revised and approved final manuscript. Kristin Sommerhalter: Site data generation; Revised and approved final manuscript. Aida Soim: Site data generation; Revised and approved final manuscript. Sherry L. Farr: Conceived of study and design; Revised and approved final manuscript; Study oversight and funding support. Tessa Crume: Site data generation; Revised and approved final manuscript. Wendy M. Book: Site data generation; Revised and approved final manuscript. Kevin Whitehead: Site data generation; Revised and approved final manuscript. Lorenzo D. Botto: Site data generation; Revised and approved final manuscript. Jennifer S. Li: Conceived of study and design; Data analysis; Site data generation; Revised and approved final manuscript; Study oversight and funding support. Daphne T. Hsu: Conceived of study and design; Data analysis; Site data generation; Revised and approved final manuscript; Study oversight and funding support.

COMPETING INTERESTS

The authors have no disclosures or conflicts of interest. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41390-024-03352-8.

BACKGROUND: Despite advances in treatment and survival, individuals with congenital heart defects (CHD) have a higher risk of heart failure (HF) compared to the general population.

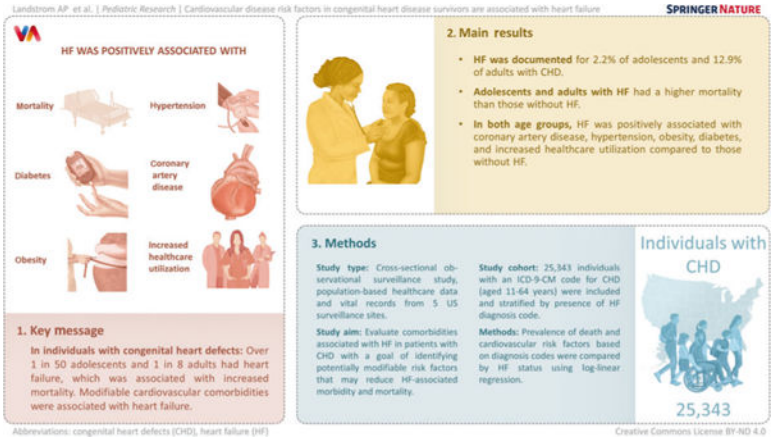
OBJECTIVE: To evaluate comorbidities associated with HF in patients with CHD with a goal of identifying potentially modifiable risk factors that may reduce HF-associated morbidity and mortality.

METHODS: Five surveillance sites in the United States linked population-based healthcare data and vital records. Individuals with an ICD-9-CM code for CHD aged 11–64 years were included and were stratified by presence of HF diagnosis code. Prevalence of death and cardiovascular risk factors based on diagnosis codes were compared by HF status using log-linear regression.

RESULTS: A total of 25,343 individuals met inclusion/exclusion criteria. HF was documented for 2.2% of adolescents and 12.9% of adults with CHD. Adolescents and adults with HF had a higher mortality than those without HF. In both age groups, HF was positively associated with coronary artery disease, hypertension, obesity, diabetes, and increased healthcare utilization compared to those without HF.

CONCLUSIONS: Within this population-based cohort, over 1 in 50 adolescents and 1 in 8 adults with CHD had HF, which was associated with increased mortality. Modifiable cardiovascular comorbidities were associated with HF.

Graphical Abstract



INTRODUCTION

Congenital heart disease (CHD), defined as structural anomalies of the heart present at birth, occurs in ~1% of all live births.[1] Rapid advancement in prenatal and neonatal diagnosis, medical management, surgical and percutaneous intervention of CHD have led to tremendous gains in survival of individuals with CHD, including those with the most "severe" lesions.[2] A major cause of CHD mortality.[3] in individuals with CHD as they age is heart failure (HF), defined as the inability of the heart to meet the metabolic demands of the body. Specifically, recent large registry studies have determined that HF is the leading cause of death in adults with CHD, resulting in the deaths of 1 in 4 individuals.[4] HF also contributes to significant morbidity and healthcare resource utilization in people with CHD, resulting in 2- to 3-fold higher hospitalization rates than the overall population.[5] As survival

in individuals with CHD continues to improve, the population burden of HF is likely to increase.

While the mechanisms of HF in people with CHD are complex and potentially multifactorial, a variety of causes related to the physiology of the CHD lesion have been hypothesized, including volume overload, pressure overload, dysfunction of the myocardium, and high afterload states. Traditional risk factors for heart failure in the general population, including systemic hypertension, diabetes, obesity, and coronary artery disease, are emerging as risk factors in people with CHD as they age. While this suggests that morbidity, mortality, and healthcare resource utilization associated with HF in CHD may be modifiable, the burden and impact of HF across the lifespan remains under-explored among individuals with CHD.[6,7] Thus, identifying the risk factors and comorbidities associated with CHD, particularly those which can be prevented or reversed, is of critical importance. To this end, we report a population-based multi-site cross-sectional study of HF in adolescents and adults with CHD. We explore the association of HF and prevalence of modifiable cardiovascular risk factors as well as healthcare resource utilization.

METHODS

This study received approval from institutional review boards for each study site; and was reviewed by the United States Centers for Disease Control and Prevention (CDC) and conducted consistent with applicable federal law and CDC policy (see e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq).

Surveillance cohort

In this cross-sectional observational surveillance project, population-based healthcare data and vital records were obtained from a network comprised of five surveillance sites for individuals who had a healthcare encounter with an eligible CHD code between 2011 and 2013.[8] These sites included (1) the state of Colorado, (2) five counties in Georgia, (3) the state of North Carolina, (4) 11-counties in New York, and (5) the state of Utah. Case inclusion criteria were (1) presence of an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code for CHD (745.xx-747.xx), and (2) ages 11–64 years of age at first CHD encounter during the study period. The age range inclusion criteria were based on the lowest and highest age for which data were universally available across all sites. Exclusion criteria were (1) presence of an ICD-9-CM code for atrial septal defect/patent foramen ovale (745.5) in isolation,[9] and (2) other non-specific CHD codes as previously defined.[8] To define age-dependent differences in outcomes, we stratified analyses by adolescent (11–17 years of age) and adult (18–64 years of age) cohorts. This was based on the frequent use of 18 years of age to demarcate pediatric-vs adult-centered outcomes and as well as CHD practice guidance which uses this age to distinguish pediatric/adolescent-vs adult-specific care.[6,10]

Study definitions

CHD diagnoses were grouped by lesion severity including severe, shunt, valve, or shunt + valve, based on previous methodologies established by the CDC.[8,11,12] (Supplementary

Table 1). These categories, have been previously shown to have prognostic relevance and are used to study outcomes in CHD.[13] HF was defined using ICD-9-CM code 428.x in one of the following: (1) cardiologist-provided encounter, (2) an inpatient encounter, (3) two unique HF codes in an outpatient encounter, or (4) one unique HF code in at least 2 encounters. Comorbidities were defined using ICD-9-CM codes for coronary artery disease, genetic syndromes, pulmonary hypertension, CHD surgery complications, systemic hypertension, obesity, percutaneous coronary intervention, stroke, coronary artery bypass surgery, pulmonary embolus, diabetes mellitus, chronic renal disease, endocarditis, myocarditis, cardiac arrhythmias, implantable cardioverter defibrillator (ICD), and pacemaker (Supplementary Table 2). For non-cardiac birth defects, cases were cross-referenced in the North Carolina Department of Health and Human Services Birth Defects Monitoring Program, which tracks birth defects across the state of North Carolina, and non-cardiac birth defects were identified by ICD-9 code and manually curated to exclude cardiac diagnoses and non-specific codes. Length of follow-up time was determined based on time from index to final encounter within the study period (2011–2013). Encounters and admissions were defined as previously described.[8] Briefly, all available healthcare encounters, including those unrelated to CHD, were captured over the 3-year surveillance period. Healthcare encounters were categorized as inpatient, emergency department, or outpatient visits. Multiple visits on the same day were counted as one visit and was coded using the following hierarchy: (1) inpatient, (2) emergency department, and (3) outpatient. Cardiac procedures, imaging studies, and electrophysiology procedures were defined by ICD-9-CM and CPT procedure codes (Supplementary Table 3).

Statistical analysis

Individuals with HF at any point during the study period were compared to individuals without HF for all analyses. Outcomes of interest in this analysis were survival and cardiac transplant; comorbidities; and healthcare utilization including encounters, hospital admissions, imaging procedures, non-invasive electrophysiology procedures, cardiac/vascular procedures and surgeries, and invasive electrophysiology procedures. Prevalence of coronary artery disease, hypertension, obesity, and diabetes (Types 1 or 2), and death during the surveillance period (2011–2013) were compared by HF status using multivariable log-linear Poisson regression with robust covariance estimation to obtain adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) controlling for age, sex, and CHD severity. Median values of continuous variables were computed together with 25th and 75th interquartile range. Adjusted PR was depicted using forest plots with corresponding 95% CI. Statistical significance was set to $P < 0.05$. Analyses were conducted by the North Carolina site and were independently validated by the New York site.

RESULTS

Prevalence of heart failure among CHD survivors

The 5-site cohort was comprised of 25,343 individuals with an eligible CHD code. Among this cohort, HF was recorded in 2481 (9.8%) individuals among 7362 (2.2%) adolescents (ages 11–17) and 17,981 (12.9%) adults (ages 18–64) (Table 1). The HF prevalence for both adolescents and adults at each individual study site is summarized in Supplementary

Table 4. As frequency of HF increased markedly with age from 2.0% among individuals 11–15 years to 25.4% among those 61–64 years (Supplementary Fig. 1), we divided the cohort into adolescent and adult cohorts for further analyses. Within the adolescent cohort, there were marginal differences in sex, age, race, and ethnicity between those with and without HF (Table 1). Interestingly, we found a slightly higher proportion of females than males among the adolescent HF cohort (51.5% vs 48.5, respectively) which switched to a higher proportion of males compared to females among the adult HF cohort (54.4% vs 45.6, respectively). Further, among the adult cohort, those with HF were more commonly Black compared to those without HF (20.7% vs 10.7%, respectively). The proportion of individuals with HF was highest among the severe CHD category in both adolescent and adult cohorts (4.8% and 17.2%, respectively). In addition, HF among the valve group was higher in the adult cohort compared to the adolescent cohort (12.2% vs 1.1%, respectively). These findings are summarized in Supplementary Table 5. In both cohorts, individuals with HF had more follow-up time during the surveillance period compared to those without HF (Supplementary Table 6).

Impact of heart failure on survival among individuals with CHDs

HF was associated with increased mortality and frequency of cardiac transplant (Table 2). Among adolescents with CHD, those with HF had a markedly higher prevalence of death compared to those without HF (aPR = 19.6, 95% CI [10.4, 36.9]). Similarly, adults with CHD with HF had a 6.1 times greater risk of death during the surveillance period [4.9, 7.6] compared to those without HF. The aPR of cardiac transplant among adolescents and adults was 27.5 [17.6, 42.9] and 6.8 [5.0, 9.4], respectively, compared to their counterparts without HF.

HF was associated with higher healthcare resource utilization during the 3-year surveillance period (Table 3). Adolescents and adults with CHD and HF had a higher median [25th, 75th] number of encounters than their counterparts without HF (42 [16,79] vs 8 [3,18] and 28 [11,62] vs 9 [4,24], respectively) and admissions (6 [3,12] vs 0 [0, 0] and 3 [1,7] vs 0 [0, 2], respectively). In addition, those with HF had a higher median number of encounters with cardiac imaging procedures (7 [3,13] vs 1 [0, 2] and 1 [0, 3] vs 0 [0, 1], respectively) and non-invasive electrophysiology procedures (8 [4,17] vs 2 [1,3] and 5 [2,9] vs 2 [1,4], respectively). Further, there were a higher number of encounters with cardiovascular interventions and procedures among those with HF compared to those without HF, including cardiac/vascular procedures and surgeries (2 [0, 5] vs 0 [0, 0] and 1 [0, 2] vs 0 [0, 0], respectively) and invasive electrophysiology procedures (0 [0, 1] vs 0 [0, 0] and 0 [0, vs 0 [0, 0], respectively).

Heart failure in CHD cases by presence of modifiable cardiovascular risk factors

We identified several cardiovascular risk factors that were associated with HF among both adolescents and adults with CHD. HF was associated with coronary artery disease (aPR 10.9 [6.3, 19.0] among adolescent CHD survivors and 3.0 [2.8, 3.2] adult CHD survivors). Further coronary artery disease was not associated with specific underlying congenital heart lesions (Supplementary Tables 7, 8, respectively). Moreover, HF was associated with systemic hypertension (4.7 [3.6, 6.1] and 1.7 [1.6, 1.7]), obesity (2.1 [1.4, 3.2], 2.3 [2.1,

2.5]), and diabetes mellitus (5.3 [2.6, 11.0], 2.4 [2.2, 2.6]) in adolescents and adults, respectively, with CHD (Fig. 1). These associations held when stratified by type of CHD lesion for adolescent and adult CHD survivors, respectively (Supplementary Figs. 2, 3). In addition to these cardiovascular risk factors, we found an association between the presence of non-cardiac birth anomalies and HF among pediatric (aPR 1.8 [1.4, 2.6]) and adult (2.0 [1.8, 2.2]) CHD survivors (Supplementary Tables 9–12). Conversely, presence of a genetic syndrome was not associated with an increased prevalence ratio of HF in both cohorts (Fig. 1). Overall, these findings suggest that cardiovascular risk factors are associated with an increased risk of HF in both pediatric and adult survivors of CHD.

DISCUSSION

Rapid advancements in the early diagnosis, medical management, and surgical treatment of CHD have led to tremendous gains in survival of individuals with CHD. With these successes, there has been a shift in CHD mortality beyond early childhood.[13,14] Survival of infants with even the most severe forms of CHD approaches 90%, and 96% of newborns with CHD who survive the first year of life will be alive at 16 years of age.[15] As a result, an estimated 1.4 million adults and 1 million children in the US were living with CHD in 2010.[5] Many of these individuals with CHD require specialized and expensive health care services, and are at increased risk for poor outcomes driven, in large part, by the development of HF. HF is responsible for 25% of deaths among patients with CHD,[16,17] making HF the most common cause of death in both children.[18,19] and adults.[20] with CHD. Moreover, there is increasing evidence that the presence of HF maybe a valuable prognostic indicator of mortality, particularly in the adult CHD population.[21]

In this study, we present a large cross-sectional cohort involving linked outcomes data from five sites encompassing over 25,000 individuals with CHD across the lifespan (*Visual Abstract Figure*). We identified a high prevalence of HF among individuals with CHD: ~2% of adolescent CHD patients and ~13% of adult CHD patients. At the oldest age group (61–64 years of age), prevalence of HF was 25.4%. The association between HF and risk of death was particularly strong among adolescent patients—those with HF were 20 times more likely to die during the surveillance period compared to adolescent patients without HF. Among adults with CHD, the aPR for death was lower, but still considerable (~6). This trend is similar to a recent study from the Swedish National Patient Register and Cause of Death Register which identified an inversely correlated hazard ratio of death by age in individuals with CHD and HF, ranging from HR of 222 in pediatric individuals to 3.1 among individuals >80 years old.[22] Individuals with CHD who were Black were disproportionately represented in the adult HF population, comprising 20% of those with HF, compared to 10% of those without HF. This finding is consistent with the higher HF-related death rates and a higher rate of HF-related admissions seen in Black individuals without CHD. Further, we find subtle, yet statistically significant, differences in the predominance of HF among male and female individuals with CHD. Interestingly, there is a slight female predominance among adolescent CHD survivors with HF which flips to a slight male predominance among the adult population. Sex as a biological variable in HF development is well recognized, particularly in HF associated with ischemic heart disease.[23] while studies exploring HF in CHD have not consistently explore sex differences. Previous CHD registry outcomes

analysis has found that overall mortality among adult CHD survivors is unchanged between the sex; however, noted a higher median age of death in woman (~45 years) than men (43 years).[2] This places our study among the first to identify a sex-based difference in HF outcomes in the CHD population, both among adolescent and adult CHD survivors.

Our study finds that HF among individuals with CHD is associated with higher healthcare resource utilization regardless of age. This aligns with previous work which found that HF is the second most common cause of hospitalizations, behind arrhythmia, among individuals with CHD.[11,12] From 1998–2005, the number of hospitalizations for patients with CHD increased by 101% with rates up to 3-fold higher than those without CHD.[24] In our study, both adolescents and adults with CHD and HF had higher healthcare resource utilization than those without HF. Adolescents with HF had a 5-fold higher number of encounters and greater than a 6-fold higher number of admissions compared to those without HF. This increased healthcare utilization extended to cardiac imaging procedures (7-fold), electrophysiology procedures (7-fold), and surgeries/procedures (2-fold). These findings align with previous work, including a retrospective study of the Pediatric Health Information System database which found pediatric patients with CHD and acute HF incurred 6-fold hospital costs compared to those without HF.[25] Collectively, our findings, as well as others, suggest that HF in individuals with CHD contributes heavily to healthcare utilization.

Modifiable cardiovascular risk factors offer an opportunity to mitigate the development of HF in patients with CHD. Recent studies have found a clear link between risk factors, such as hypertension, and the development of HF and premature mortality in people with CHD. For example, among adults with CHD and concomitant HF, the baseline 5-fold rate of mortality nearly doubled to ~10-fold in the presence of systemic hypertension.[26] Most salient from our study is the finding of cardiovascular disease risk factors in pediatric patients with CHD which mirrored, or even exceeded, that of adults. Adolescents with CHD and HF had ~10 times the prevalence of coronary artery disease compared to those without HF, while the same aPR in adults was ~3. Further, systemic hypertension, obesity, and diabetes mellitus were 2–5 times higher among adolescents with HF, with approximately a 2-fold increase of these risk factors seen among adults. An association between CHD and the development of cardiovascular disease has been well-established in the literature. As an example, the adjusted relative risk of coronary artery disease was 1.5 compared to individuals without CHD in a recent study including a combined cohort of 684,000 CHD cases.[27] This suggests that patients with CHD may be predisposed to cardiovascular disease, and our findings suggest that these same risk factors are associated with HF development. Further, the impact of these risk factors is greater among adolescents but is present throughout the lifespan. Should our findings be replicated in other independent studies, this would provide a pathway for reducing the mortality and healthcare costs associated with HF among people with CHD through control of cardiovascular risk factors. For example, there has traditionally been a hesitancy of many providers to allow CHD survivors, particularly adolescents and young adults, to engage in strenuous physical exercise and competitive sports. Recently, there has been an evolution towards encouraging exercise and even sports participation among the vast majority of CHD survivors while under appropriate cardiology care.[28,29] Encouraging the safe liberalization of physical activity, exercise, and sports participation may be one way in which HF, and the resultant morbidity and mortality, might

be reduced. This represents one of a myriad of potential approaches to reducing the factors which predispose to HF in CHD. Ultimately, management of these risk cardiovascular risk factors could be pursued throughout the lifespan to optimally reduce mortality, morbidity, and healthcare costs associated with HF in CHD.

LIMITATIONS

The cross-sectional nature of this study limits our ability to determine temporality of events, such as heart failure diagnosis and cardiovascular risk factors. Moreover, diagnoses of HF that were made after the study period or made before the study period which resolved and not noted as a diagnosis during the study period, would not have been consistently captured. Identification of comorbidities by administrative code data, which may be non-specific, is also a limitation. For example, we are unable to explore associations between specific forms of CHD and these risk factors. In addition, findings are cross-sectional and observational in nature and purely associative rather than causal. This study did not include children <11 years of age with CHD, a patient population that may have more serious forms of CHD associated with HF than this older cohort.

CONCLUSIONS

In this population-based study, over 1 in 50 adolescents and 1 in 8 adults with CHD had HF documented during the 3-year surveillance period. HF at any age was associated with increased mortality and healthcare resource utilization. We also identified several potentially modifiable cardiovascular comorbidities associated with HF. Prevention and management of cardiovascular risk factors such as diabetes, obesity, and hypertension in CHD patients of all ages may reduce morbidity and mortality associated with HF.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

FUNDING

This project was supported by Centers for Disease Control and Prevention (CDC, Atlanta, Georgia, United States) and CHD Lifespan project and support from the CDC NU50DD004933-03-00. A.P.L. is supported by National Institutes of Health (R01-HL160654, R01-HL166217), Doris Duke Charitable Foundation (CSDA-2020098), John Taylor Babbitt Foundation, The Hartwell Foundation, Additional Ventures, Y.T. and Alice Chen Pediatric Genetics and Genomics Research Center.

DATA AVAILABILITY

The data that support the findings of this study are available from the study sites, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the investigator site and CDC.

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IMPACT:

- Five sites in the United States linked population-based healthcare data and vital records to establish surveillance network for identifying the factors which influence congenital heart disease (CHD) outcomes.
- Survivors of CHD frequently develop heart failure across the lifespan.
- Over 1 in 50 adolescent and 1 in 8 adult survivors of CHD have heart failure which is associated with increased mortality compared to CHD survivors without heart failure.
- Heart failure development is associated with potentially modifiable cardiovascular risk factors such as hypertension, coronary artery disease, and diabetes.
- Controlling modifiable cardiovascular risk factors may serve to lower the risk of heart failure and mortality in survivors of congenital heart disease of all ages.

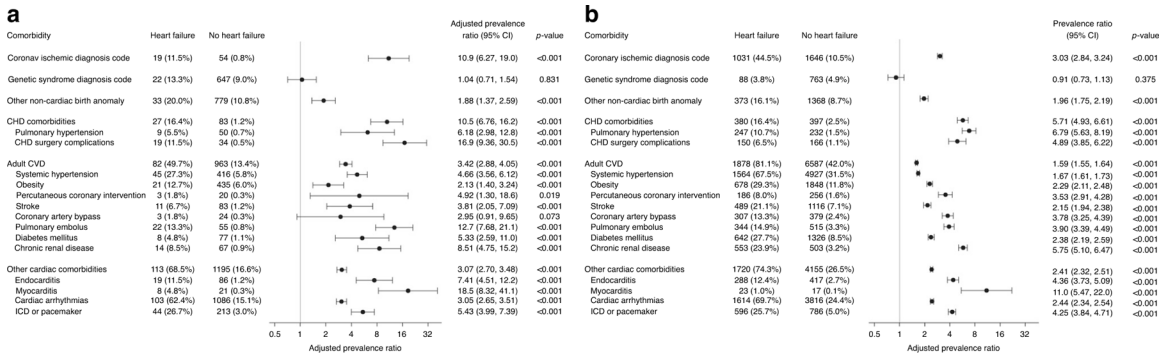

Fig. 1. Comorbidities associated with heart failure in children and adults with CHD.

a Forest plot of cardiovascular comorbidities for adolescent (11–17 years of age) patients with CHD and heart failure versus no heart failure. Prevalence ratios adjusted for age, sex, and CHD severity group, with corresponding 95% CI are shown. **b** Forest plot of cardiovascular comorbidities for adults (18–64 years of age) with CHD and heart failure versus no heart failure. Prevalence ratios adjusted for age, sex, and CHD severity group, with corresponding 95% CI are shown. CHD congenital heart disease, CVD cardiovascular disease, ICD implantable cardioverter defibrillator, CI confidence interval.

Table 1.

Patient characteristics in adolescents and adults with congenital heart disease.

Characteristic	Ages 11–17 Heart Failure[a] (*N* = 165)	Ages 11–17 No Heart Failure (*N* = 7197)	Ages 11–17 *p* value	Ages 18–64 Heart Failure[a] (*N* = 2316)	Ages 18–64 No Heart Failure (*N* = 15665)	Ages 18–64 *p* value
Sex			0.039			<0.001
Male	80 (48.5%)	4082 (56.7%)		1260 (54.4%)	7552 (48.2%)	
Female	85 (51.5%)	3115 (43.3%)		1056 (45.6%)	8107 (51.8%)	
Age at Index Encounter— years	14 (12, 16)	14 (12, 15)	0.006	48 (35, 58)	36 (25, 51)	<0.001
Race			0.139			<0.001
American Indian or Native Alaskan	2 (1.2%)	74 (1.0%)		19 (0.8%)	116 (0.7%)	
Asian	2 (1.2%)	129 (1.8%)		17 (0.7%)	285 (1.8%)	
Black or African American	29 (17.6%)	941 (13.1%)		480 (20.7%)	1678 (10.7%)	
Native Hawaiian or other Pacific Islander	0 (0.0%)	13 (0.2%)		2 (0.1%)	24 (0.2%)	
White	78 (47.3%)	3522 (48.9%)		1317 (56.9%)	9589 (61.2%)	
Multiracial	2 (1.2%)	17 (0.2%)		6 (0.3%)	32 (0.2%)	
Unknown	52 (31.5%)	2501 (34.8%)		475 (20.5%)	3941 (25.2%)	
Hispanic Ethnicity	22 (17.6%)[b]	923 (19.7%)[c]	0.648	237 (12.1%)[d]	1399 (11.8%)[e]	0.706

Values presented are counts(%) for categorical variables or median (25th, 75th) for continuous variables.

p values presented are Wilcoxon rank-sum test for continuous variables, Fisher exact test for dichotomous variables, or Chi-square test for categorical variables. Age ranges are inclusive, calculated at index encounter.

[a]Patients with at least one heart failure code in a cardiologist-provided encounter, at least one heart failure code in an inpatient encounter, two unique codes at an outpatient encounter, or one unique code at >1 encounters.

[b]Out of 125 adolescents with HF.

[c]Out of 4680 adolescents without HF.

[d]Out of 1959 adults with HF.

[e]Out of 11,850 adults without HF.

Table 2.

Prevalence of death and cardiac transplantation in adolescent and adult patients with and without heart failure.

	Ages 11–17				Ages 18–64			
	Heart Failure (*N* = 165)	**No Heart Failure (*N* = 7197)**	**Prevalence Ratio (95% CI)**	***p* value**	**Heart Failure (*N* = 2316)**	**No Heart Failure (*N* = 15,665)**	**Prevalence Ratio (95% CI)**	***p* value**
Death or Cardiac Transplant	39 (23.6%)	72 (1.0%)	23.7 (16.6, 33.8)	<0.001	282 (12.2%)	257 (1.6%)	6.2 (5.2, 7.4)	<0.001
Death	13 (7.9%)	29 (0.4%)	19.6 (10.4, 36.9)	<0.001	200 (8.6%)	176 (1.1%)	6.1 (4.9, 7.6)	<0.001
Cardiac Transplant[a]	28 (17.0%)	45 (0.6%)	27.5 (17.6, 42.9)	<0.001	93 (4.0%)	85 (0.5%)	6.8 (5.0, 9.4)	<0.001

Prevalence ratios adjusted for age at index encounter, sex, and congenital heart disease severity group. Values presented are counts (%) for categorical variables or median (25th, 75th) for continuous variables. Death or diagnosis/procedure code within the study period, 1 January 2011–31 December 2013.

CI confidence interval.

[a]Includes transplant status codes that reflect a history of transplant. Cardiac transplant diagnosis ICD-9 codes include 996.83, V42.1, Z94.1, T86.20, T86.21, T86.22, 998.83; and procedure codes include 00580, 00.93, 37.51, 33930, 33933, 33935, 33944, 33945, 02YA0Z0, 02YA0Z1.

Table 3.

Resource utilization in adolescent and adult patients with and without heart failure.

	Ages 11–17			Ages 18–64		
	Heart Failure (*N* = 165)	**No Heart Failure (*N* = 7197)**	***p* value**	**Heart Failure (*N* = 2316)**	**No Heart Failure (*N* = 15,665)**	***p* value**
Number of Encounters—median (Q1, Q3)	42 (16, 79)	8 (3, 18)	<0.001	28 (11, 62)	9 (4, 24)	<0.001
Number of Admissions—median (Q1, Q3)	6 (3, 12)	0 (0, 0)	<0.001	3 (1, 7)	0 (0, 2)	<0.001
Patients with at least one procedure[a]	165 (100.0%)	6452 (89.6%)	<0.001	2272 (98.1%)	13693 (87.4%)	<0.001
Number of Cardiac Imaging Procedures – median (Q1, Q3)	7 (3, 13)	1 (0, 2)	<0.001	1 (0, 3)	0 (0, 1)	<0.001
Number of Cardiac or Vascular Procedures/Surgeries – median (Q1, Q3)	2 (0, 5)	0 (0, 0)	<0.001	1 (0, 2)	0 (0, 0)	<0.001
Number of Electrophysiology Procedures– median (Q1, Q3)	7 (2, 16)	1 (0, 3)	<0.001	4 (1, 9)	1 (0, 2)	<0.001
Noninvasive—median (Q1, Q3)	8 (4, 17)	2 (1, 3)	<0.001	5 (2, 9)	2 (1, 4)	<0.001
Invasive—median (Q1, Q3)	0 (0, 1)	0 (0, 0)	<0.001	0 (0, 1)	0 (0, 0)	<0.001

Values presented are counts (%) for categorical variables or median (Q1, 25th percentile; Q3, 75th percentile) for continuous variables. Encounters include inpatient, outpatient, emergency room, mental health, outpatient, ambulatory, observation, and telemedicine visits.

[a]Procedures include cardiac imaging procedures, cardiac or vascular procedures/surgeries, and electrophysiology procedures as defined in Supplementary Table 3. For each procedure type, the number of encounters with at least one code for that procedure type is enumerated.