Background—The arrhythmia burden in tetralogy of Fallot, types of arrhythmias encountered, and risk profile may change as the population ages.

Methods and Results—The Alliance for Adult Research in Congenital Cardiology (AARCC) conducted a multicenter cross-sectional study to quantify the arrhythmia burden in tetralogy of Fallot, to characterize age-related trends, and to identify associated factors. A total of 556 patients, 54.0% female, 36.8 ± 12.0 years of age were recruited from 11 centers. Overall, 43.3% had a sustained arrhythmia or arrhythmia intervention. Prevalence of atrial tachyarrhythmias was 20.1%. Factors associated with intraatrial reentrant tachycardia in multivariable analyses were right atrial enlargement (odds ratio [OR], 6.2; 95% confidence interval [CI], 2.8 to 13.6), hypertension (OR, 2.3; 95% CI, 1.1 to 4.6), and number of cardiac surgeries (OR, 1.4; 95% CI, 1.2 to 1.6). Older age (OR, 1.09 per year; 95% CI, 1.05 to 1.12), lower left ventricular ejection fraction (OR, 0.93 per unit; 95% CI, 0.89 to 0.96), left atrial dilation (OR, 3.2; 95% CI, 1.5 to 6.8), and number of cardiac surgeries (OR, 1.5; 95% CI, 1.2 to 1.9) were jointly associated with atrial fibrillation. Ventricular arrhythmias were prevalent in 14.6% and jointly associated with number of cardiac surgeries (OR, 1.3; 95% CI, 1.1 to 1.6), QRS duration (OR, 1.02 per 1 ms; 95% CI, 1.01 to 1.03), and left ventricular diastolic dysfunction (OR, 3.3; 95% CI, 1.5 to 7.1). Prevalence of atrial fibrillation and ventricular arrhythmias markedly increased after 45 years of age.

Conclusions—The arrhythmia burden in adults with tetralogy of Fallot is considerable, with various subtypes characterized by different profiles. Atrial fibrillation and ventricular arrhythmias appear to be influenced more by left- than right-sided heart disease. (Circulation. 2010;122:868-875.)
arrhythmia burden in adults with tetralogy of Fallot by determining the prevalence of sustained arrhythmias and associated interventions, characterizing trends, and identifying associated clinical and echocardiographic features.

Methods

Patient Population
The study population comprised adults (≥18 years of age) with surgical repair of tetralogy of Fallot or pulmonary atresia with ventricular septal defect, identified by the following 11 participating AARCC centers: Oregon Health and Science University, Portland; University of California, Los Angeles; University of Washington, Seattle; Montreal Heart Institute, University of Montreal, Quebec, Canada; Boston Adult Congenital Heart Service, Children’s Hospital Boston, Boston, Mass; Ohio State University, Columbus; University of Colorado, Denver; Medical College of Wisconsin, Milwaukee; Columbia University, New York, NY; Hershey Medical Center, Pennsylvania State University, Hershey; and University of Pennsylvania, Philadelphia. Patients were required to have had an echocardiogram and outpatient visit within 2 years preceding data collection, conducted between September 2007 and October 2008. Patients were excluded if they had complex coexisting congenital abnormalities or uninterpretable echocardiographic images.

Study Design
A multicenter retrospective cross-sectional study was conducted with standardized reassessment of previously performed echocardiographic studies. Demographic, clinical, and echocardiographic data were collected on preprinted case report forms. Deidentified data were sent to a single center for consolidation and review for internal consistency and validity. Data quality checks consisted of identifying and tracking missing, incomplete, or inconsistent information. Illegible data, invalid formats, and invalid codes were flagged. Data queries were issued to clarify and resolve discrepancies on a per-patient basis. The study was submitted to and approved by each participating site’s Institutional Review Board.

Demographic and Clinical Data
Details relative to demographic variables, comorbidities, anatomy, surgical history, catheter interventions, medical therapy (ie, angiotensin-converting enzyme inhibitors, β-blockers, aspirin, digoxin, diuretics, anticoagulants, and antiarrhythmic agents), and arrhythmias were collected. Demographic variables included date of birth, sex, height, weight, body surface area, and blood pressure. Overweight was defined as body mass index ≥25 kg/m²; obesity was defined as body mass index ≥30 kg/m². Comorbidities incorporated atherosclerotic risk factors (eg, prior and current smoking history, dyslipidemia, hypertension, diabetes mellitus, and known coronary artery disease). Anatomic and surgical characteristics included pulmonary atresia, side of the aortic arch, number and type of prior palliative shunts, transannular patches, and conduits. Main categories for catheter procedures were balloon valvuloplasty, stents, atrial and ventricular septal defect closures, and percutaneous coronary interventions.

Arrhythmia-Related Data
Arrhythmia-related data included current rhythm (eg, sinus, atrial tachyarrhythmia, junctional, atrial and/or ventricular pacing) and most recent QRS duration. Data were collected on sustained arrhythmias since 18 years of age that were documented electrocardiographically (ie, by 12-lead ECG, rhythm strip, ambulatory ECG recording, or implantable cardiac device). Site investigators reviewed source data to classify arrhythmias as atrial fibrillation (AF), intraaortic reentrant tachycardia (IART) including typical atrial flutter, ectopic atrial tachycardia, other forms of supraventricular tachycardia (eg, accessory pathway mediated and atrioventricular nodal reentrant tachycardia), ventricular tachycardia (VT), and ventricular fibrillation (VF). Catheter ablation procedures were tabulated, along with targeted arrhythmias. Because nonautomatic focal atrial tachycardia is indistinguishable from IART by noninvasive means, nonautomatic focal atrial tachycardia confirmed by electrophysiological testing was considered a subcategory of IART in inferential analyses. Pacemaker data included type of device (ie, single chamber, dual chamber, or biventricular) and indication (ie, sinus node dysfunction, atrioventricular block, or tachycardia/bradycardia syndrome). The presence of an implantable cardioverter-defibrillator (ICD) and its indication (ie, primary or secondary prevention) were noted.

Echocardiographic Data
Echocardiographic parameters were reviewed and reassessed with a standardized protocol and uniform definitions. Left ventricular (LV) internal dimensions (diastole and systole) and wall thickness were determined in parasternal long-axis views. Right ventricular (RV) outflow length (diastole) was obtained at the level of the aortic valve in parasternal short-axis views and RV long-axis length (diastole and systole) and inlet diameter (diastole) in apical 4-chamber views. Right and left atrial enlargement was categorized as present or absent, according to recommendations from the American Society of Echocardiography on chamber quantification. Atrioventricular valve closure and ejection times were measured for both ventricles, permitting tabulation of myocardial performance indexes. Color, continuous-wave, and pulsed-wave Doppler data for all valves were recorded. Pulmonary valve regurgitation was quantified as absent, mild (regurgitant jet width/RV outflow diameter <30%), no diastolic reversal in main or branch pulmonary arteries by color or pulsed-wave Doppler), moderate (regurgitant jet width/RV outflow tract diameter 30% to 49%), no diastolic reversal in branch pulmonary arteries), or severe (regurgitant jet width/RV outflow tract diameter ≥50%, diastolic flow reversal in branch pulmonary arteries). Other forms of valve dysfunction were categorized according to established criteria.

Estimates of LV ejection fractions were based on all available echocardiographic data, as per standard practice. RV systolic function was assessed by visual estimation as normal (ejection fraction ≥50%) or mildly (ejection fraction 40% to 49%), moderately (ejection fraction 30% to 39%), or severely (ejection fraction <30%) impaired. Pulsed-wave Doppler assessment of mitral inflow E and A velocities and tissue Doppler assessment of lateral mitral annulus was used to assess diastolic function. Diastolic dysfunction was defined as a priori lateral mitral annulus a’ velocity greater than e’ velocity (indicating decreased LV compliance) and/or an E/e’ ratio >10 (indicating elevated LV filling pressures).

Data Analysis
Continuous variables are summarized by mean±SD or median and interquartile range (25th and 75th percentiles), depending on normality of distribution. Categorical variables are represented by frequencies and percentages. Factors associated with IART/AF and VT/VF were assessed by logistic regression. Variables with values of P<0.2 in individual analyses were considered in multivariable automated stepwise models (P=0.05 for entry and P=0.1 for removal). Association between the E/e’ ratio and ventricular arrhythmias was further characterized by considering receiver-operating characteristics. In exploratory posthoc analyses, the E/e’ value with the greater discriminatory potential was selected on the basis of the Youden index (1-(false-positive rate)+(false-negative rate)). Two-tailed values of P<0.05 were considered statistically significant. Analyses were performed with SAS software version 9.2 (SAS Institute Inc, Cary, NC).

Data completeness was as follows: presence of arrhythmias and devices, 100%; QRS duration, 94.4%; anatomic/surgical characteristics, 98.9%; medical therapy, 98.2%; comorbidities, 97.2%; and echocardiographic variables, >96%, except for diastolic dysfunction, for which 321 patients (57.7%) had interpretable studies. The potential effect of missing diastolic dysfunction data on the effect estimate for VT/VF was explored in a sensitivity analysis. Expected exposure counts were assigned to excluded patients with and without VT/VF at a ratio equal to complete cases. Newly classified subjects were added to the nonmissing cohort. The proportion of exposed patients in the missing cohort with VT/VF was then sequentially

Khairy et al Arrhythmias in Tetralogy of Fallot 869
decreased by moving 1 count from exposed to unexposed categories while simultaneously increasing by 1 count the number of exposed versus unexposed subjects in the missing cohort without VT/VF. After each iteration, the newly classified cohort was aggregated with complete cases for derivation of an odds ratio (OR) and 95% limits. Sample size calculations were based on an initially projected estimate of 385 patients to provide 95% confidence intervals (CIs) ranging from 3.0% to 24.3% for arrhythmia point prevalence values between 10% and 25%. For arrhythmia prevalence rates ranging from 15% to 85%, the achieved sample size of 556 patients provided >80% statistical power to detect OR ≥2.06, ≥1.91, and ≥1.85 for potential risk factors present in 20%, 30%, and 40% of the study population, respectively.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Characteristics of the Study Population
A total of 556 patients, 54.0% female, were recruited, 8.1% of whom had pulmonary atresia. The median time interval from echocardiography to clinical assessment was 17.0 days (2.0 to 64.0 days). Mean age at the time of study was 36.8±12.0 years, with a body mass index of 26.0±6.8 kg/m². Patients had a mean of 2.5±1.5 cardiac surgeries, with prior palliative shunts in 46.6%, pulmonary transannular patches in 80.4%, RV-to-pulmonary-artery conduits in 10.9%, and pulmonary shunts in 46.6%, pulmonary transannular patches in 80.4%, and 1.5 cardiac surgeries, with prior palliative surgeries. At the last follow-up visit, pharmacological therapy in 102 patients (18.3%) had implanted IART or AF (N=81), or none of these arrhythmias (n=408) are summarized in Table 1.

Arrhythmia Burden
Overall, 43.3% (95% CI, 39.3 to 47.5%) of patients had at least 1 type of clinically sustained arrhythmia, an implanted cardiac arrhythmia device, or transcatheter ablation. Table 2 summarizes the prevalence of sustained tachyarrhythmias and arrhythmia interventions. The following 48 arrhythmia substrates were targeted by ablation therapy in 40 patients (7.2%): IART (n=27), nonautomatic focal atrial tachycardia (n=3), AF (n=1), accessory pathway-mediated tachycardia (n=2), atrioventricular nodal reentrant tachycardia (n=4), automatic ectopic atrial tachycardia (n=2), and VT (n=9). In addition, 20 patients (3.5%) had surgical atrial maze procedures, and 10 (1.8%) had operative VT ablation performed concomitant with pulmonary valve replacement surgery.

Implantable Cardiac Rhythm Devices
Overall, 102 patients (18.3%) had implanted cardiac rhythm devices, with pacemakers in 44 (7.9%) and ICDs in 58 (10.4%). Data on primary pacemaker indications were complete in all patients and consisted of sinus node dysfunction in 8 (18.2%), atrioventricular block in 29 (65.9%), and tachycardia/bradycardia syndromes in 7 (15.9%). ICD indications were available in 46 patients (79.3%), with primary and secondary prevention indications in 27 (58.7%) and 19 (41.3%) patients, respectively. For patients with primary prevention indications, the QRS was ≥180 ms in 10 (37.0%), LV ejection fraction was <35% in 4 (14.8%), and moderate or severe systolic RV dysfunction was present in 14 (51.9%). Twelve of 27 patients (44.4%) with primary prevention indications later experienced clinical ventricular tachyarrhythmias. Of all implanted devices, 33.3% were single chamber, 61.8% were dual chamber, and 4.9% were biventricular.

Atrial Tachyarrhythmias
Prevalence rates for atrial tachyarrhythmias are summarized in Table 2. Prevalence rates according to age are depicted in Figure 1. Factors associated with IART or AF are listed in Table 3. As summarized in Table 4, variables jointly associated with IART differed from those jointly associated with AF, except for number of cardiac surgeries, which was common to both. Of the 41 patients with AF, 38 (92.7%) had paroxysmal or persistent forms, whereas 3 (7.3%) had permanent AF. Figure 2 portrays the prevalence of atrial and ventricular arrhythmias according to number of cardiac surgeries. At the last follow-up visit, pharmacological therapy in patients with AF or IART included the following: β-blockers in 50 (56.2%), digoxin in 28 (31.5%), sotalol in 11 (12.5%), amiodarone in 7 (7.9%), class I antiarrhythmic agents in 2 (2.2%), dofetilide in 1 (1.1%), aspirin in 36 (40.4%), and anticoagulants in 30 (33.7%).

Ventricular Tachyarrhythmias
Clinical sustained VT occurred in 79 patients (14.2%). Associated variables are summarized in Table 5. The most common antiarrhythmic drug received was amiodarone (n=11, 13.6%), followed by sotalol (n=9, 11.1%) and class I agents (n=4, 4.9%). A 5-point increase in LV E/e′ was associated with a 1.9-fold higher prevalence of VT or VF (OR, 1.9; 95% CI, 1.3 to 2.9; P=0.002). Box plots of LV E/e′ ratios in patients with and without VT or VF are provided in Figure 3. The E/e′ ratio cutoff value yielding the greatest discriminatory potential, as identified by posthoc receiver-operating characteristics analysis, was 9.6 (Youden index, 0.28; OR, 3.9, 95% CI, 1.9 to 7.8; P<0.001).

For missing diastolic dysfunction data, systematically varying exposure prevalence among missing subjects revealed that substantial departures from expected values are required to render the OR nonsignificant. The lower 95% confidence limit would breach 1 if the exposure prevalence in missing cases with VT/VF decreased from 51.3% (as in the measured cohort) to 14.3% (P<0.001). This would require an OR of 0.5 (95% CI, 0.2 to 1.1) in missing cases, suggesting an inverse correlation between diastolic dysfunction and VT/VF. Such a substantial reversal in direction from data observed in 321 cases appears highly improbable.

Discussion
This large cross-sectional study quantified and characterized the high arrhythmia burden in adults with surgically repaired tetralogy of Fallot. The prevalence of sustained tachyarrhythmias increased with age, particularly for AF and ventricular arrhythmias.
These results are consistent with earlier studies in younger populations that reported a relatively quiescent period 10 to 15 years after corrective surgery, followed by a steady decline in freedom from atrial and ventricular arrhythmias. Moreover, these findings further extend observations from population studies based on administrative data that, although valuable, are inherently limited in their capacity to discriminate between arrhythmia subtypes.

The observed prevalence of atrial arrhythmias (20.1%) was modestly superior to ventricular arrhythmias (14.6%). Nevertheless, the single most common arrhythmia subtype was VT (14.2%), followed by IART (11.5%). An important point

| Table 1. Characteristics According to Whether Patients Had Atrial Arrhythmias (IART/AF), Ventricular Arrhythmias (VT/VF), or No Sustained Arrhythmias |
|-----------------------------------------------|-----------------|-----------------|-----------------|
| No Tachyarrhythmia (n=408) | IART/AF (n=89) | VT/VF (n=81) |
| Age, y | 34.4±10.4 | 46.7±13.7 | 40.5±13.0 |
| Female sex, n (%) | 229 (56.1) | 43 (48.3) | 35 (43.2) |
| Body mass index, kg/m² | 25.9±7.0 | 27.3±6.4 | 26.7±6.7 |
| Diabetes mellitus, n (%) | 7 (1.8) | 8 (9.2) | 7 (9.0) |
| Hypertension, n (%) | 35 (8.7) | 25 (29.4) | 17 (22.1) |
| Dyslipidemia, n (%) | 33 (8.3) | 18 (21.2) | 13 (16.9) |
| Smoking history, n (%) | 65 (18.1) | 11 (15.1) | 13 (17.8) |
| QRS duration, ms | 145±25 | 165±35 | 163±30 |
| Pulmonary atresia, n (%) | 32 (8.0) | 5 (7.9) | 11 (13.9) |

Surgical characteristics

| Prior palliative shunt, n (%) | 186 (45.6) | 43 (48.3) | 39 (48.1) |
| Age at corrective surgery, y* | 5.0 (2.5, 7.0) | 9.0 (5.0, 17.9) | 6.1 (3.0, 11.0) |
| Transannular patch, n (%) | 282 (81.5) | 54 (77.1) | 47 (71.2) |
| RV-to-pulmonary-artery conduit, n (%) | 38 (11.2) | 5 (7.9) | 9 (14.5) |
| Pulmonary valve replacement, n (%) | 142 (34.8) | 54 (50.7) | 58 (71.6) |
| Cardiac surgeries, n | 2.2±1.3 | 3.3±2.0 | 3.3±1.8 |

Echocardiographic parameters

| LV ejection fraction, % | 59±7 | 53±12 | 54±10 |
| LV end-diastolic dimension, mm | 45.6±5.7 | 49.7±7.8 | 49.0±7.5 |
| LV end-systolic dimension, mm | 30.9±6.1 | 34.8±9.2 | 34.9±8.5 |
| LV myocardial performance index | 0.43±0.26 | 0.43±0.25 | 0.48±0.27 |
| At least moderate MR, n (%) | 4 (1.0) | 6 (6.7) | 1 (1.2) |
| Left atrial enlargement, n (%) | 59 (14.8) | 35 (41.2) | 23 (28.8) |
| LV diastolic dysfunction, n (%) | 54 (22.1) | 11 (23.9) | 20 (51.3) |
| RV long-axis length, cm | 8.9±1.7 | 9.0±2.0 | 9.1±1.8 |
| RV outflow diameter, cm | 3.3±0.9 | 3.7±1.1 | 3.6±0.9 |
| RV myocardial performance index | 0.19±0.10 | 0.23±0.11 | 0.24±0.10 |
| RV dysfunction (moderate/severe), n (%) | 49 (12.0) | 25 (28.0) | 19 (23.4) |
| Right atrial enlargement n (%) | 190 (48.5) | 71 (82.6) | 55 (68.8) |
| At least moderate PR, n (%) | 208 (51.9) | 37 (42.0) | 22 (27.2) |
| At least moderate TR, n (%) | 44 (10.8) | 29 (32.6) | 21 (25.9) |

Medical therapy, n (%)

| ACE inhibitor | 40 (10.0) | 29 (32.0) | 21 (26.3) |
| β-blocker | 76 (19.0) | 50 (56.8) | 46 (58.2) |
| Aspirin | 92 (22.9) | 36 (40.4) | 26 (32.5) |
| Digoxin | 22 (5.5) | 28 (32.6) | 14 (17.9) |
| Diuretic | 36 (9.0) | 40 (45.5) | 23 (29.1) |
| Anticoagulation | 7 (1.7) | 30 (33.7) | 8 (9.9) |

MR indicates mitral regurgitation; PR, pulmonary regurgitation; TR, tricuspid regurgitation; and ACE, angiotensin-converting enzyme. No tachyarrhythmia denotes absence of clinically sustained IART, AF, VT, and VF.

*Nonnormally distributed continuous variables are summarized by median and interquartile range (25th and 75th percentiles).
is that AF was uncommon and far less prevalent than IART in patients <45 years of age (Figure 1). However, the prevalence of AF exceeded that of IART after 55 years of age. These diverging trends suggest that determinants of IART likely differ from AF, a hypothesis further corroborated by multivariable regression analyses. Whereas both forms of arrhythmia were more common in patients with extensive cardiac surgery, as reflected by the number of interventions, additional jointly associated variables revealed disparate profiles. IART in tetralogy of Fallot is predominantly a right-sided arrhythmia that, perhaps not surprisingly, was jointly associated with right atrial dilation. The identified association between hypertension and IART merits further study. Although pathophysiological mechanisms remain unclear, hypertension is commonly associated with cardiac arrhythmias in patients with and without underlying structural heart disease.

In contrast, AF was associated predominantly with markers of left-sided heart disease, ie, lower LV ejection fraction and left atrial dilation. Relationships between left atrial enlargement, LV dysfunction, and AF are well recognized in other forms of heart disease. The association between older age and AF is also established in patients without tetralogy of Fallot, with demonstrated cellular electrophysiological changes that include shortened action potential duration, decreased capacity of the action potential to adapt to heart rate, and increased

![Figure 1. Prevalence of tachyarrhythmias in surgically repaired tetralogy of Fallot according to age. Shown are prevalence rates for IART, AF, IART or AF, and VT or VF by age category. The graph was generated with Excel 2008 for Mac (version 12.2.4) with automated Bezier curve functions that soften jagged edges without altering data points.](image-url)
spatial variability of repolarization. However, the steep rise in prevalence of AF appears to occur considerably earlier in patients with tetralogy of Fallot (ie, ≥45 years of age) than in the general population (ie, ≥65 years of age), with a prevalence exceeding 30% in those ≥55 years of age. Predictably, AF will continue to increase in prevalence with the aging population.

The high prevalence of ventricular arrhythmias is consistent with and further expands on prior observations. Indeed, VT accounted for the large majority of ventricular arrhythmias. Macreorrrent substrates for monomorphic VT are well characterized. The lack of association between severe pulmonary regurgitation and ventricular arrhythmias may be explained largely by an older study population, 43% of whom had pulmonary valve replacement. The strong correlation between QRS duration and clinical sustained VT has withstood the test of time and is further validated by our analysis. The association between number of cardiac surgeries and ventricular arrhythmias is likewise not surprising, especially considering that prior palliative shunts has previously been independently associated with inducible ventricular arrhythmias and appropriate ICD shocks in tetralogy of Fallot.

To the best of our knowledge, the association between LV diastolic dysfunction and ventricular arrhythmias identified by exploratory multivariable analyses is a novel finding that merits particular attention. It supports results from a multi-center study that identified elevated LV end-diastolic pressure (≥12 mm Hg) as the most powerful predictor of appropriate shocks in ICD recipients with tetralogy of Fallot. Reasons why LV diastolic dysfunction is strongly associated with ventricular arrhythmias remain speculative. It may be that LV diastolic dysfunction reflects, in part, LV systolic dysfunction, which has previously been linked to sudden death in tetralogy of Fallot, in addition to comorbidities such as diabetes mellitus, hypertension, hypercholesterolemia, and obesity and increased RV afterload. The latter may contribute to the complex pathophysiology of RV failure, particularly in the setting of pulmonary regurgitation with chronic volume overload. Diastolic dysfunction has been independently associated with ventricular arrhythmias and mortality in other disease states such as chronic renal failure, sickle cell anemia, and post–coronary bypass surgery.
surgery. The value of LV diastolic dysfunction in risk stratifying patients with tetralogy of Fallot remains to be demonstrated. Nevertheless, identification of a noninvasive means of assessing LV diastolic dysfunction associated with ventricular arrhythmias represents a promising avenue to explore further. To that end, the ratio of early transmural flow velocity (E) to early diastolic mitral annular velocity (e'), a Doppler-derived index of LV filling pressure, was a powerful predictor of ventricular arrhythmias. Posthoc analyses supported an E/e' ratio of 10 as a practical cutoff value for risk stratification.

In addition to the high prevalence of sustained tachyarrhythmias, implantable cardiac rhythm devices were present in 18.3% of patients, with ICDs in 10.4%. Defibrillators were implanted for primary prevention in 58.7% and secondary prevention in 41.3%, a distribution pattern consistent with the multicenter ICD experience (ie, primary prevention, 56.2%; secondary prevention, 43.8%). The present study was not designed to assess rates of appropriate or inappropriate shocks or other ICD-related complications. It may be noted, however, that 44% of patients with primary prevention indications later experienced sustained ventricular tachyarrhythmias. Also noteworthy is the small proportion of devices (4.9%) with biventricular leads. Merits of cardiac resynchronization therapy in tetralogy of Fallot remain to be conclusively demonstrated.

Limitations

Except for the echocardiographic data that was reassessed with a standardized protocol to limit interobserver variability, data collection was retrospective. In particular, classification of arrhythmias was based on chart review, with confirmation by local site investigators. This process was subject to data quality and error checks but not blinded adjudication. The targeted study population consisted of patients currently followed up by a large sample of adult congenital heart centers, as opposed to an inception cohort of patients diagnosed with tetralogy of Fallot. Thus, the study was limited to adult survivors and not designed to capture sudden cardiac deaths. The cross-sectional analysis did not assess ventricular tachyarrhythmia cycle lengths or the extent to which arrhythmias were adequately controlled. Although the study design was deliberately selected to quantify prevalence rates, to assess multiple outcomes, and to identify associations, cause-and-effect relationships cannot be inferred.

Conclusions

The arrhythmia burden in adults with tetralogy of Fallot is considerable, with a high prevalence of sustained atrial and ventricular tachyarrhythmias and cardiac rhythm devices. Arrhythmia subtypes are characterized by different profiles. Although IART is the most common atrial arrhythmia overall, the prevalence of AF exceeds IART in older patients (≥55 years of age). Ventricular arrhythmias, like AF, increase with age and appear to be influenced more by left- than right-sided ventricular function. In particular, exploratory multivariable analyses revealed that LV diastolic dysfunction, as assessed by Doppler echocardiography, is associated with ventricular arrhythmias and should be considered in future attempts to refine risk stratification schemes.

Acknowledgments

We wish to thank Mary Beth Lee (University of Washington) for central data collection and database entry and Dawn Peters, PhD (Oregon Health and Science University), for statistical assistance. In addition, several individuals made significant contributions to data collection, including Susan Fernandes, PA-C (Children’s Hospital Boston); Elizabeth Crawford, RDMS (Children’s Hospital Boston); Annie Dore, MD; Lise-Andrée Mercier, MD; François Marcotte, MD, and Maude Bergeron, RN (Montreal Heart Institute); Matthew Page (University of California, Los Angeles); and Anisa Chaudry, MD (Hershey Medical Center, University of Pennsylvania). AARCC has benefited greatly from the scholarly contributions of Carole Warnes, MD (Mayo Clinic).

Sources of Funding

This study was supported by a Canada Research Chair in Electrophysiology and Adult Congenital Heart Disease (Dr Khairy), the Quebec Cardiovascular Research Network (Fonds de Recherche en Santé du Québec), and the Dunlevie Foundation.

Disclosures

None.

References


CLINICAL PERSPECTIVE

Tetralogy of Fallot is the most prevalent cyanotic heart defect. Successes from an early surgical era and continued advances in care have resulted in dramatic improvements in survival. However, postoperative sequelae are common, and arrhythmias are frequently encountered late after repair. The Alliance for Adult Research in Congenital Cardiology (AARCC) sought to quantify the arrhythmia burden in adults with tetralogy of Fallot by determining the prevalence of sustained arrhythmias and related interventions, characterizing trends, and identifying associated clinical and echocardiographic features. A total of 556 patients, 36.8±12.0 years of age, were enrolled from 11 centers. Overall, 43.3% experienced a sustained arrhythmia or had an arrhythmia intervention. The prevalence of atrial tachyarrhythmias was 20.1%, with intra-atrial reentrant tachycardia being the most common (11.5%). Associated factors were right atrial enlargement, hypertension, and number of cardiac surgeries. Prevalence of atrial fibrillation (7.4%) increased with age, becoming the most common atrial arrhythmia in adults ≥55 years of age. Associated factors included a lower left ventricular ejection fraction, left atrial dilation, and number of cardiac surgeries. Ventricular arrhythmias occurred in 14.6% and were associated with prior cardiac surgeries in addition to QRS duration and left ventricular diastolic dysfunction. In summary, this multicenter analysis revealed a considerable arrhythmia burden in adults with tetralogy of Fallot, with various arrhythmia subtypes characterized by different profiles. Ventricular arrhythmias, like atrial fibrillation, appear to be influenced more by left- than right-sided ventricular function. Left ventricular diastolic dysfunction should be considered in future studies on risk stratification for ventricular arrhythmias and sudden death.
Arrhythmia Burden in Adults With Surgically Repaired Tetralogy of Fallot: A Multi-Institutional Study

*Circulation*. 2010;122:868-875; originally published online August 16, 2010; doi: 10.1161/CIRCULATIONAHA.109.928481
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/122/9/868

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/