Atrial fibrillation in adult congenital heart disease

Puzzling with the pieces

Zwijnenburg, Roxanne D.; de Groot, Natasja M.S.

DOI
10.1016/j.hrthm.2023.05.024

Publication date
2023

Document Version
Final published version

Published in
Heart Rhythm

EDITORIAL COMMENTARY

Atrial fibrillation in adult congenital heart disease: Puzzling with the pieces

Roxanne D. Zwijnenburg, MD, MSc,*† Natasja M.S. de Groot, MD, PhD*‡

*From the *Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands, †Department of Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands, and ‡Department of Department of Microelectronics, Signal Processing Systems, Faculty of Electrical Engineering, mathematics and computer sciences, Delft University of Technology, Delft, The Netherlands.*

Atrial fibrillation (AF) in adult congenital heart disease (ACHD) is the main reason for hospitalization and responsible for a 5-fold higher all-cause death.[1] Once AF in patients with ACHD develops, there may be a fast progression from paroxysmal to (long-standing) persistent or permanent AF in a time period as short as only 3 years after the first documented AF episode.[2]

Hence, early diagnosis and subsequently effective treatment of AF is the next challenge in the management of the population with ACHD. To which degree AF-related triggers, arrhythmogenic substrates, and risk factors between patients with ACHD and the general population can be compared is largely unknown.[3]

In this issue of *Heart Rhythm Journal*, Wu et al[4] investigate a cohort consisting of 2350 patients ACHD and nearly 350,000 patients without congenital heart disease who developed new-onset AF. In this elegant study, they demonstrated an increasing incidence of AF with age in both populations, but with a 20-fold and 10-fold higher incidence in the ACHD group between 50 and 54 years and between 55 and 59 years, respectively. Additionally, a higher risk of AF was found in patients with atrial pathology or right-sided lesions. Traditional AF risk factors were present in both populations.

The authors concluded that aging was a common risk factor in both populations, but the age of onset of AF in ACHD was 30 years earlier than in the non-ACHD group. This observation is in line with other reports of early AF onset in patients with ACHD; for example, Teuwen et al[2] demonstrated in 199 patients with ACHD that the first documented AF episode occurred at the age of 49 $\pm$ 17 years.

As also acknowledged by the authors, there are some limitations that need to be addressed in future studies. Electrocardiograms (ECGs) were not available for review, and the accuracy of the diagnosis of AF is therefore unknown. It is unclear whether the diagnosis was a computer-generated interpretation of the ECG or whether health care providers evaluated the ECG themselves. However, 10% of the ECGs demonstrating AF are misdiagnosed when using built-in ECG analysis software.[5] Misclassification may occur when, for example, other irregular rhythms such as frequent ectopy are present. It has been demonstrated that atrial ectopy is indeed more frequent in patients with ACHD than in those without ACHD and may lead to overestimation of AF when using built-in ECG analysis software. On the contrary, underestimation of AF may have occurred as prolonged continuous rhythm monitoring was not performed. If this would be the case, the actual number of patients with AF would even be higher.

An innovative and emerging technology to accurately predict and detect AF is artificial intelligence (AI). Compared with a consensus committee of expert cardiologists, an AI algorithm had a 15% higher sensitivity (71% vs 86%) to detect AF.[6] Interestingly, most AI algorithms developed so far use either ventricular and signal features and not atrial features to discriminate AF from sinus rhythm. As sinus rhythm ECGs are necessary to train AF detection algorithms, a dedicated ACHD algorithm should be constructed as the population with ACHD typically has more complex sinus rhythm ECGs. The population presented in this study would be suitable for the development of such an AI algorithm. A dedicated ACHD algorithm could then be implemented in wearable devices and used for screening of AF. Given the size of the study population and the clinical data including follow-up available, the presented population with ACHD could also be used to develop an AI-based prediction model.

Risk analysis for comorbidities could not be performed because of missing data on traditional risk factors. Hypertension, diabetes mellitus, and obesity are in the general population related to a higher incidence of AF. As life expectancy is increasing, "normal" comorbidities are also likely present in aging patients with ACHD.[7,8]

But are traditional risk factors also applicable for the much younger population with ACHD? Wu et al[4] clearly stated that

Funding Sources: The authors have no funding sources to disclose. Disclosures: The authors have no conflicts of interest to disclose. **Address reprint requests and correspondence:** Dr Natasja M.S. de Groot, Unit Translational Electrophysiology, Department of Cardiology, Erasmus Medical Center, Doctor Molewaterplein 40, 3015 GD Rotterdam, The Netherlands. E-mail address: n.m.s.degroot@erasmusmc.nl.

 https://doi.org/10.1016/j.hrthm.2023.05.024

AF starts at a younger age when a patient suffers from congenital heart disease, with an annual risk of 1.3 and 2.9 per 1000 between 25 and 29 years and between 35 and 39 years, respectively. Traditional risk factors are usually not commonly present in young patients with ACHD. Hence, the contribution of traditional risk factors in the pathophysiology of AF in patients with ACHD is therefore most likely small. We must therefore consider that other factors play a more crucial role in the development of AF, such as atrial scars, frequent atrial ectopy, altered cardiac hemodynamic, and the presence of a more extensive arrhythmogenic substrate.[2,9] In 573 patients with ACHD, it was indeed shown that an association between increased atrial ectopy frequency and a higher risk of AF development exists. Interestingly, Wu et al also found that AF was related with right-sided defects, indicating that in patients with ACHD not only the left atrium is involved in the pathophysiology of AF. This observation is supported by the outcomes of several mapping studies in patients with ACHD demonstrating extensive conduction abnormalities in the right atrium and right atrial localized areas of conduction abnormalities, giving rise to AF, which terminated when this region was isolated by radiofrequency ablation.[10,11]

The study of Wu et al[4] provides novel insights into AF development in patients with ACHD by contrasting AF development across varying age groups between the population with ACHD and the general population and relating it with traditional and ACHD-specific risk factors. Their observations emphasize the importance of prevention and early detection of AF in young patients with ACHD.

References

1. Mandalenakis Z, Rosengren A, Lappas G, et al. Atrial fibrillation burden in young patients with congenital heart disease. Circulation 2018;137:928–937.
2. Teuwen CP, Ramdjan TT, Götte M, et al. Time course of atrial fibrillation in patients with congenital heart defects. Circ Arrhythm Electrophysiol 2015; 8:1065–1072.
3. Teuwen CP, Ramdjan TTTK, de Groot NMS. Management of atrial fibrillation in patients with congenital heart defects. Expert Rev Cardiovasc Ther 2015; 13:57–66.
4. Wu M-H, Chiu S-N, Tseng W-C, et al. Atrial fibrillation in adult congenital heart disease and the general population. Heart Rhythm 2023;20:1248–1254.
5. Hwan Bae M, Hoon Lee J, Heon Yang D, et al. Erroneous computer electrocardiogram interpretation of atrial fibrillation and its clinical consequences. Clin Cardiol 2012;35:348–353.
6. Hannun AY, Rajpurkar P, Haghpanahi M, et al. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med 2019;25:65–69.
7. Labombarda F, Hamilton R, Shohoudi A, et al. Increasing prevalence of atrial fibrillation and permanent atrial arrhythmias in congenital heart disease. J Am Coll Cardiol 2017;70:857–865.
8. Warnes CA, Liberthson R, Danielson GK, et al. Task Force 1: the changing profile of congenital heart disease in adult life. J Am Coll Cardiol 2001; 37:1170–1175.
9. Teuwen CP, Korevaar TIM, Coolen R, et al. Frequent atrial extrasystolic beats predict atrial fibrillation in patients with congenital heart defects. Europace 2018;20:25–32.
10. Houck C, Lanters EAH, Heida A, et al. Conduction disorders in patients with congenital heart disease and right atrial volume overload: an intraoperative epicardial mapping study. Eur Heart J 2019;40:600–601.
11. De Groot NMS, Blom NA, van der Wall EE, et al. Different mechanisms underlying consecutive, postoperative atrial tachyarrhythmias in a Fontan patient. Pacing Clin Electrophysiol 2009;32:E18–E20.