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First Evidence of Atrial Conduction Disorders in Pediatric Patients With Congenital Heart Disease

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ABSTRACT

This study sought to investigate whether pediatric patients with congenital heart disease (CHD) already have atrial conduction disorders early in life. The authors conducted first-in-children epicardial mapping in 10 pediatric patients with CHD undergoing primary open heart surgery. Areas of conduction delay (CD) and block (CB) were present in all patients and were particularly observed at Bachmann's bundle (CD: 4.9%; CB: 2.3%), followed by the right atrium (CD: 3.7%; CB: 1.6%) and, to a lesser degree, the left atrium (CD: 1.8%; CB: 1.0%). Conduction abnormalities may by aggravated over time (e.g., aging, residual lesions, or valvular dysfunction), predisposing these patients to atrial arrhythmias early in life. (J Am Coll Cardiol EP 2020;6:1739–43) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Abnormalities in myocardial conduction play a crucial role in both the genesis and perpetuation of tachyarrhythmias. In patients with congenital heart disease (CHD), chronic volume and/or pressure overload is an important contributor to structural remodeling giving rise to atrial conduction abnormalities (1). An inevitable consequence of this aging population is the rising number of patients with CHD presenting with complex atrial tachyarrhythmias such as atrial fibrillation. Prior studies have shown that acute atrial stretch causes atrial conduction abnormalities (2,3). It is therefore likely that even relatively short-lasting volume/pressure overload early after birth causes atrial conduction abnormalities that might persist beyond CHD repair, predisposing these patients to arrhythmias later in life.

At present, it is unknown whether, and to what extent, pediatric patients with CHD already have atrial conduction disorders early in life. To investigate the early effects of short-lasting volume/pressure overload on atrial conduction properties, we conducted epicardial high-density mapping in pediatric patients with CHD undergoing primary open heart surgery.

METHODS: EPICARDIAL HIGH-DENSITY MAPPING APPROACH

Parents gave informed consent to participate in the study protocol approved by the local ethics

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

BB = Bachmann's bundle
CB = conduction block
CD = conduction delay
CHD = congenital heart disease
CT = conduction time
LA = left atrium
RA = right atrium
SR = sinus rhythm

committee (MEC-2019-0543) of the Erasmus Medical Center Rotterdam. Epicardial mapping of the right atrial (RA) appendage, intercaval region, Bachmann's bundle (BB), left atrial (LA) appendage, and pulmonary vein region was performed before commencement of extracorporeal circulation (**Central illustration, A**) (4). A custom-made electrode array (192 electrodes; electrode diameter: 0.6 mm; interelectrode distance: 2.1 mm) was used to record unipolar electrograms during sinus rhythm (SR). Local activation maps were constructed by annotating the steepest negative deflection. Because of a lack of any reference values and to be consistent with previous epicardial mapping studies, conduction delay (CD) and block (CB) were defined as local conduction time (CT) differences of, respectively, 7 to 11 ms and ≥12 ms between adjacent electrodes, corresponding with effective conduction velocities of 17 to 29 cm/s for CD and <17 cm/s for CB (4). The amount of CD and CB was calculated as a percentage of the total mapping area.

STUDY POPULATION. Our study population consists of 10 pediatric patients with CHD (median age: 6 months; range 3 to 43 months; female: n = 5) scheduled for repair of an atrial septal defect type II (n = 1), ventricular septal defect (n = 7; 3 of them also have an atrial septal defect type II, and 2 have a patent foramen ovale), complete atrioventricular septal defect (n = 1), and sinus venosus defect (n = 1). Perimembranous and malalignment outlet ventricular septal defect were present in 6 patients and 1 patient, respectively. None of the patients had a history of atrial tachyarrhythmias.

RESULTS

Figure 1A shows signs of RA dilatation on an apical 4-chamber echocardiographic view and lead II from the surface electrocardiogram from a patient with an atrial septal defect type II. Color-coded activation maps of the RA are shown in **Figure 1B**. The SR wave front originates from the superior part of the RA, from where it spreads to the surrounding area in a radial fashion. Areas of CD and CB were found at both the superior and inferior RA, indicated by, respectively, crowding of the isochrones and thick black lines (CT: >7 ms). **Figure 1C** shows signs of LA dilatation on an apical 4-chamber echocardiographic view and lead V1 from the surface electrocardiogram in a 2-year-old patient with a perimembranous ventricular septal defect. As shown in the **Figure 1D**, areas of conduction abnormalities are present in different parts of BB. The **Central Illustration, B**, shows the relative frequency distribution of CTs for all patients specified per atrial region. Areas of CD and CB were present in all patients and were particularly observed at BB (CD: 4.9%; CB: 2.3%), followed by the RA (CD: 3.7%; CB: 1.6%) and, to a lesser degree, in the LA (CD: 1.9%; CB: 1.0%). The amount of CD and CB in the entire atria ranged from 1.8% to 4.9% and 1.0% to 2.3%, respectively. The highest CTs measured at the RA, BB, and LA were, respectively, 44, 25, and 23 ms. Conduction abnormalities in patients with an isolated atrial septal defect type II (n = 2) or ventricular septal defect (n = 2) were more pronounced at the RA (1.9%; maximal CT: 34 ms) and BB (2.1%; maximal CT: 17 ms), respectively. Post-operative atrial arrhythmias were not observed in the study population.

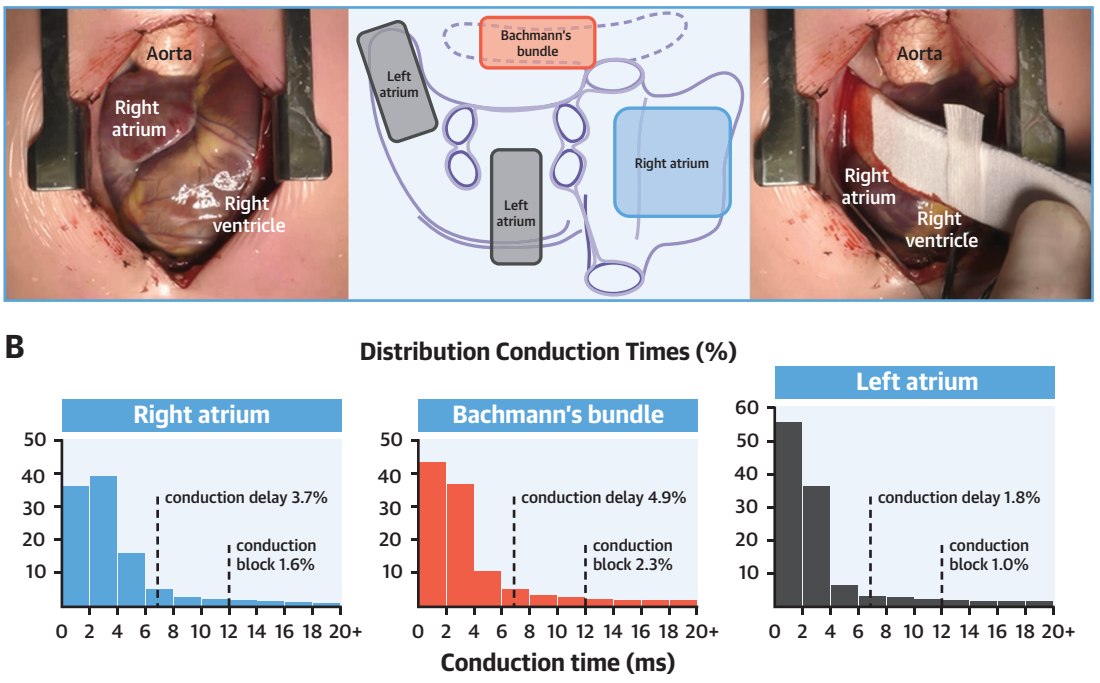
DISCUSSION

In this first-in-children epicardial mapping study, we demonstrated, for the first time that conduction abnormalities are already present early after birth in pediatric patients with CHD without history of atrial tachyarrhythmias. In general, slowing of conduction was more pronounced at the RA (maximal CT: 44 ms) and BB (maximal CT: 25 ms).

Recently, Rouatbi et al. (5) investigated structural myocardial changes in the RA tissue of pediatric patients with an atrial septal defect and demonstrated that myocardial damage and fibrotic tissue are already present early in life. In line with these findings, we now provide the first evidence of conduction abnormalities in this population.

Epicardial mapping in 31 adult patients with congenital heart disease (age 49 ± 14 years; 16% with a history of atrial fibrillation) also showed conduction abnormalities, particularly at the RA and BB rather than the LA (4). Comparison of mapping data derived from pediatric and adult CHD patients with respectively short- and long-term volume overload shows that areas of conduction abnormalities are less extensive and severe in pediatric CHD patients. At present, our data suggests that the duration of volume overload and increase in the amount and extent of conduction disorders go hand in hand. Over time, our CHD epicardial mapping dataset will enable us to investigate the characteristics of atrial conduction disorders from childhood to adulthood and to correlate these findings with clinical characteristics such as age and type of CHD.

CENTRAL ILLUSTRATION **First Evidence of Atrial Conduction Disorders in Pediatric Patients With Congenital Heart Disease**



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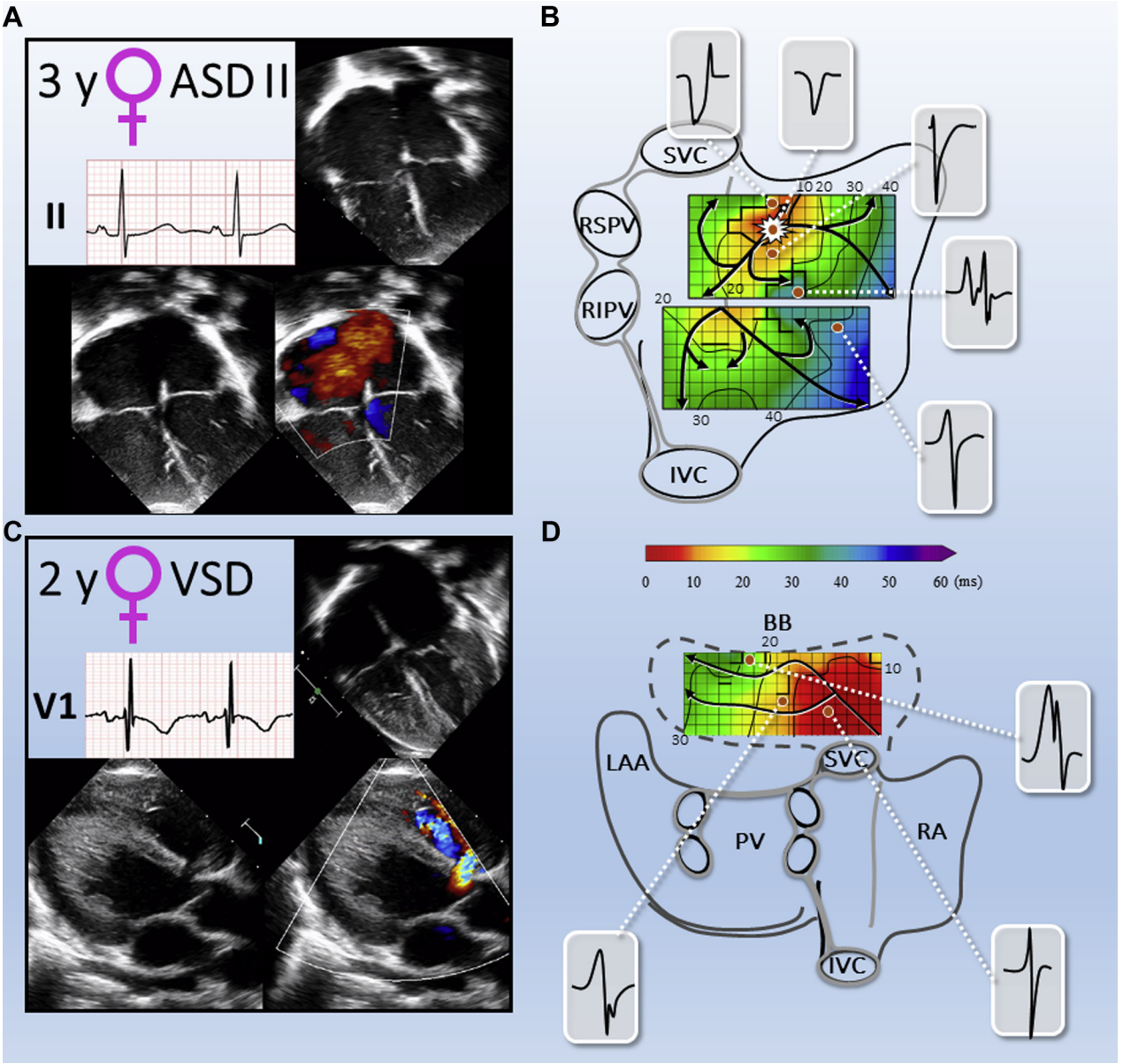
(A) Intraoperative images of the mapping procedure and a schematic overview of the mapping sites from a posterior view of the atria. **(B)** Spatial distribution of conduction times specified for each atrial region separately. Percentages of conduction delay and conduction block are depicted by **dashed lines**.

CONDUCTION ABNORMALITIES AT BACHMAN'S BUNDLE. Based on several epicardial mapping studies, conduction abnormalities at BB are considered to play an important role in atrial arrhythmogenesis (6). For the first time we demonstrate that conduction abnormalities are already present at BB in pediatric patients with CHD with RA and LA volume overload (7). The right side of BB is connected to the septum spurium, and the left side is attached to the left atrioventricular ring bundle, which continues into the posterior LA wall, including the pulmonary veins. Hence, from an anatomic point of view, BB is more attached to the LA than to the RA. Therefore, it is more likely that LA volume overload induces more stretch at BB than RA volume overload, eventually resulting in conduction abnormalities at BB.

ATRIAL CONDUCTION ABNORMALITIES: RESULT OF CONGENITAL HEART DISEASE OR A PHYSIOLOGICAL PHENOMENON? The observed atrial conduction abnormalities in our study might be a result of: 1) structural remodeling induced by short-lasting volume/pressure overload; 2) genetically determined (e.g., abnormalities in cell structures relevant for electrical conduction); or 3) a physiological phenomenon. Because of the invasive nature of our pediatric epicedial mapping technique, it is not possible to study atrial conduction properties or histology at different RA and LA regions in healthy control individuals. However, other histological (5) and epicardial mapping (8) studies substantiate that the presence of atrial conduction abnormalities in pediatric patients with CHD is presumably a result of CHD rather than a physiological phenomenon.

Structural remodeling underlies the development of conduction disorders. Because Rouatbi et al. (5) demonstrated that myocardial damage and structural remodeling are already present in a similar group of pediatric patients with CHD with RA volume overload who did not have surgery, it is most likely that atrial structural remodeling is also present in our cohort,

FIGURE 1 Linking Electrocardiographic and Echocardiographic Data With Characteristics of Epicardial Atrial Conduction



(Top) Signs of **(A)** right and **(B)** left atrial dilatation on different echocardiographic views and leads II and V_1 from the surface electrocardiogram. **(Bottom)** Color-coded activation maps of the **(C)** RA and **(D)** BB. The **arrows** display the main trajectories of the electrical wavefront. **Thick black lines** indicate areas of CD and CB (CT: >7 ms). ASD = atrial septal defect; BB = Bachmann's bundle; CB = conduction block; CD = conduction delay; CT = conduction time; IVC = inferior vena cava; LAA = left atrial appendage; PV = pulmonary vein region; RA = right atrium; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; SVC = superior vena cava; VSD = ventricular septal defect.

giving rise to conduction abnormalities. Previous epicardial mapping studies in 25 patients with Wolff-Parkinson-White syndrome showed smooth RA conduction without any areas of conduction disorders (8). None of these patients had a history of atrial fibrillation or atrial dilatation. Conduction times longer than 14 ms were not observed in these patients without structural heart disease. At present, there are no validated CT cutoff values for pediatric patients. To avoid overestimating areas of conduction

abnormalities, we used the same cutoff values as used in adult patients during SR. In our pediatric cohort, we observed CTs up to 44 ms, which are presumably a result of CHD rather than a physiological phenomenon.

STUDY LIMITATIONS. Because of the invasive nature of our mapping technique, we did not perform epicardial mapping in pediatric patients without structural heart disease for comparison. In addition, endocardial mapping is not possible with the present epicardial mapping approach.

CONCLUSIONS

Epicardial mapping in pediatric patients with CHD revealed that atrial conduction abnormalities are already present before surgical correction in their first year of life, primarily at the RA and BB. Over time, surgical scar tissue, aging, and volume/pressure overload from residual lesions or valvular dysfunction may aggravate these atrial conduction abnormalities, predisposing these patients to atrial arrhythmias early in life.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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