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Conduction Heterogeneity

Impact of Underlying Heart Disease and Atrial Fibrillation

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ABSTRACT

OBJECTIVES The goal of this study is to investigate the impact of various underlying heart diseases (UHDs) and prior atrial fibrillation (AF) episodes on conduction heterogeneity.

BACKGROUND It is unknown whether intra-atrial conduction during sinus rhythm differs between various UHD or is influenced by AF episodes.

METHODS Epicardial sinus rhythm mapping of the right atrium, Bachmann's bundle (BB), left atrium and pulmonary vein area was performed in 447 participants (median age: 67 [interquartile range (IQR): 59 to 73] years) with or without AF undergoing cardiac surgery for ischemic heart disease, (ischemic and) valvular heart disease, or congenital heart disease. Conduction times (CTs) were defined as Δ local activation time between 2 adjacent electrodes and used to assess frequency (CTs $\geq$ 4 ms) and magnitude of conduction disorders (in increments of 10 ms).

RESULTS When comparing the 3 types of UHD, there were no differences in frequencies and magnitude of CTs at all locations ($p \geq 0.017$ and $p \geq 0.005$, respectively). Prior AF episodes were associated with conduction slowing throughout both atria (14.9% [IQR: 11.8 to 17.0] vs. 12.8% [IQR: 10.9 to 14.6]; $p < 0.001$). At BB, CTs with magnitudes ≥30 ms were more common in patients with AF (n = 56.2% vs. n = 36.0%; $p < 0.004$).

CONCLUSIONS UHD has no impact on the frequency and severity of conduction disorders. AF episodes are associated with more conduction disorders throughout both atria and with more severe conduction disorders at BB. The next step will be to determine the relevance of these conduction disorders for AF development and maintenance.

Intra-atrial conduction is determined by membrane properties, tissue structure and wavefront geometry (1). If there is a loss of cell-to-cell communication, resulting in enhanced non-uniform anisotropy, the wavefront geometry will be distorted, leading to conduction disorders and eventually to arrhythmias, such as atrial fibrillation (AF) (2,3).

A prior epicardial mapping study in patients with Wolff-Parkinson White syndrome with nondilated atria and without a history of AF demonstrated that the free wall of the right atrium (RA) was activated by a single broad activation wave without any areas of conduction disorders (4). Knowledge of the prevalence and severity of conduction disorders caused by structural remodeling during sinus rhythm is the first step in the detection of the arrhythmogenic substrate associated with development of AF. Various underlying heart diseases (UHDs) cause structural remodeling of the atria, and arrhythmias are therefore frequently observed in these patients. Conduction

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disorders in patients with valvular heart disease (VHD) may be solely due to pressure and/or volume overload (5). In patients with ischemic heart disease (IHD), conduction disorders leading to arrhythmias are, for example, caused by inflammation, atherosclerosis, and myocardial infarction (6–8). In patients with uncorrected congenital heart disease (CHD), conduction disorders are the result of abnormal anatomy, altered hemodynamics, and longstanding pressure and/or volume overload (9).

AF is the most common arrhythmia that itself induces both electrical and structural remodeling (10,11). Prolonged P-wave duration, as an indicator of intra-atrial conduction delay, predicts AF recurrences (12). Previous mapping studies using specific cutoff values for conduction times (CTs) demonstrated in a small number of patients that AF episodes resulted in more conduction delay and conduction block during sinus rhythm. However, these studies were limited to the pulmonary vein area (PVA) and Bachmann's bundle (BB) (13,14). So far, differences in the prevalence and severity of conduction disorders during sinus rhythm between patients with and without AF episodes, including all local CTs, throughout the RA, BB, PVA, and left atrium (LA) have not been reported.

For identifying the arrhythmogenic substrate underlying AF and the causal relation between UHD and AF, it is essential to understand conduction characteristics between various UHDs and a history of AF during sinus rhythm. We hypothesize that structural and electrical remodeled atria not only contain more, but also more severe conduction disorders during sinus rhythm. The aims of this study were therefore: 1) to distinguish conduction disorders between patients with IHD, (ischemic and) VHD (iVHD), and CHD; and 2) to determine the influence of AF episodes on conduction heterogeneity across the epicardial atrial surface in a large cohort of patients.

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METHODS

STUDY POPULATION. The study population consisted of participants undergoing open-heart surgery. Indications for surgery were either CHD, IHD, aortic- or mitral valve disease, or the combination of IHD and VHD. Additionally, patients were categorized into groups according to those: 1) with or without a history of AF; and 2) IHD, CHD, or iVHD patients without an AF history. The latter group is combined because previous epicardial mapping studies found no differences in total activation time and patterns of activation between patients with VHD and the combination of ischemic and VHD (15,16). This study is approved by the institutional Medical Ethical Committee (MEC 2010-054, MEC 2014-393) (17,18). Preceding the surgical procedure, written informed consent was obtained from all patients. Clinical data were extracted from electronic patient files.

MAPPING PROCEDURE. High-resolution epicardial mapping during sinus rhythm was performed during open-heart surgery before extracorporeal circulation (19). A detailed description of the method is provided in the Supplemental Methods. When patients were in AF, electrical cardioversion to sinus rhythm was performed before the mapping procedure. Mapping was conducted by shifting the 128- or 192-electrode array (interelectrode distance 2 mm) in a systemic order along predefined sites covering the epicardial surface of both atria (**Figure 1**, upper left panel), including RA (from the cavo-tricuspid isthmus up to the RA appendage, perpendicular to the caval veins), PVA (from the sinus transversus, alongside the borders of the pulmonary veins towards the atrioventricular groove), LA (from the lower border of the left pulmonary vein along the left atrioventricular groove towards the LA appendage), and BB (from the tip of LA appendage behind the aorta towards the superior cavo-atrial junction).

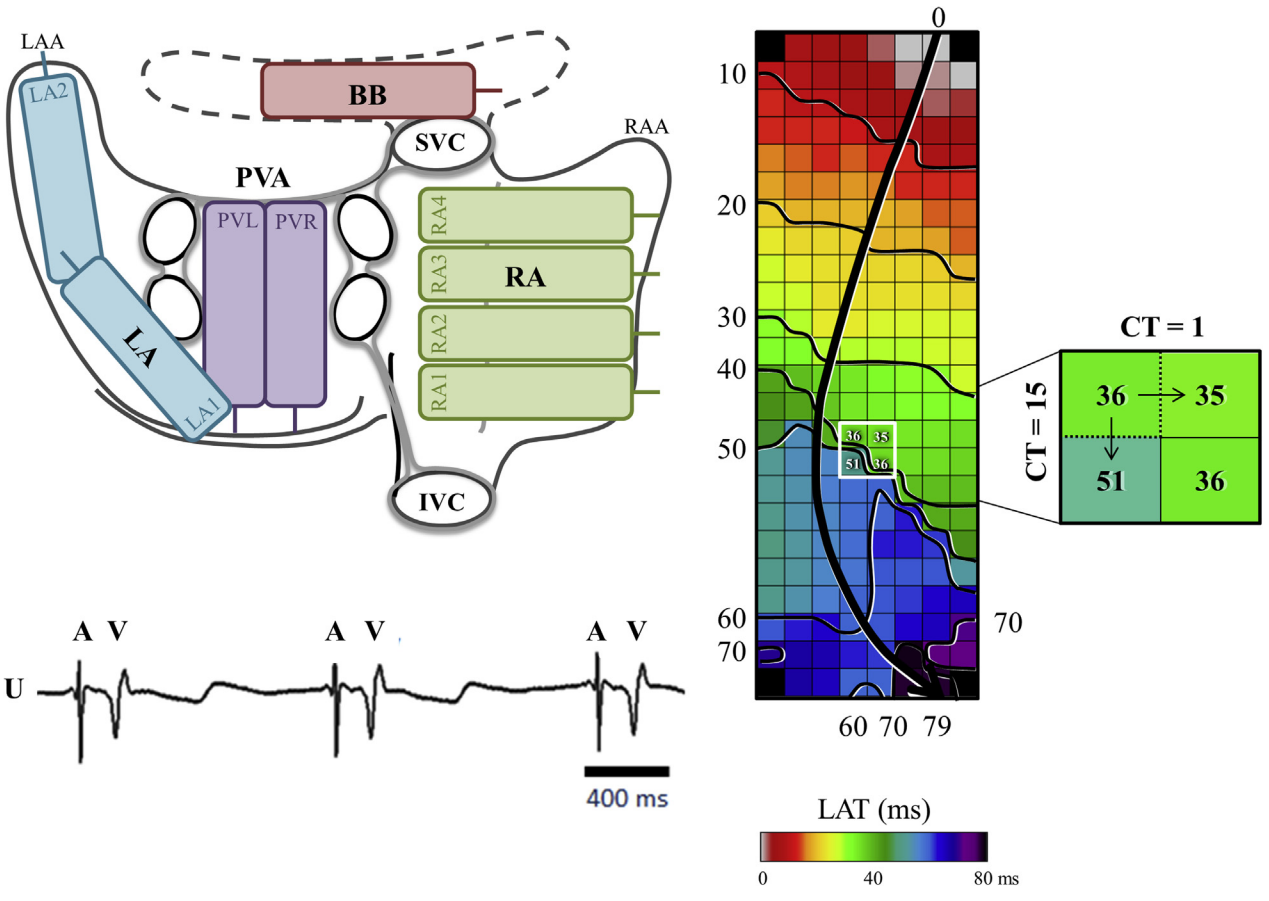
MAPPING DATA ANALYSIS. The steepest negative slopes of all atrial potentials were automatically annotated. For each electrode, the local activation time was determined and color-coded activation maps were reconstructed as shown in the right side of **Figure 1**. As previously described in a number of mapping studies, inter-electrode CTs were calculated by subtracting the local activation time of each electrode from the adjacent right and lower electrode (**Figure 1**, right) (13,14). The 90th percentile of all CTs was 4.7 ms (4.0 to 5.7 ms) and CTs <4 ms are therefore considered as normal atrial conduction. The frequency of CTs was analyzed per patient as the median proportion of CT ≥4 ms. The magnitude of CTs was defined as the size of inter-electrode differences in milliseconds and expressed as the percentage of patients with different magnitudes of CTs. The magnitude of CTs was analyzed in 10-ms increments.

STATISTICAL ANALYSIS. All data were tested for normality. Skewed continuous data were expressed as median (interquartile range [IQR]); comparison of continuous data between UHD was performed using the Kruskal-Wallis test and comparison of continuous data between patients with and without AF was

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
BB = Bachmann's bundle
CHD = congenital heart disease
CT = conduction time
iVHD = (ischemic and) valvular heart disease
IHD = ischemic heart disease
LA = left atrium
PVA = pulmonary vein area
RA = right atrium
UHD = underlying heart diseases

FIGURE 1 Methods of Epicardial Mapping



The upper left panel shows mapping sites on a schematic posterior view of the atria. **The lower left panel** shows unipolar electrogram recordings during 5 s of sinus rhythm. **The right panel** shows a color-coded activation map with isochrones **(black lines)** drawn at 10ms. The **black arrow** indicates the main wave direction. An example of determining conduction times (CTs) by subtracting the local activation time (LAT) of each electrode is shown next to the activation map. A = atrial signal; BB = Bachmann's bundle; IVC = inferior vena cava; LA = left atrium; LAA = left atrial appendage; PVA = pulmonary vein area; PVL = left pulmonary vein; PVR = right pulmonary vein; RA = right atrium; RAA = right atrial appendage; SVC = superior vena cava; U = unipolar electrogram recordings; V = ventricular signal.

performed by using the Mann-Whitney U test. Categorical data are expressed as absolute numbers (percentages) and analyzed with chi square or Fisher exact test if appropriate. Bonferroni correction was applied for comparison of the UHD ($p < 0.0083$ [i.e. 0.05/6]), divided into 3 categories: IHD, iVHD, and CHD ($p < 0.017$ [i.e., 0.05/3]). Furthermore, a $p < 0.0125$ (0.05/4) was considered statistically significant for the comparison of anti-arrhythmic drug usage. Overall, a $p < 0.05$ was considered statistically significant. For other comparisons that require correction for multiple testing, corrected p values will be reported. Statistical analysis was performed with SPSS version 24 (IBM Corporation, Armonk, New York).

RESULTS

CHARACTERISTICS OF PARTICIPANTS. Baseline characteristics of the study population are shown in Table 1. Participants either had no history of AF (n = 372, 83.2%), paroxysmal AF (n = 52, 11.6%), persistent AF (n = 21, 4.7%), or longstanding persistent AF (n = 2, 0.4%). Patients without a history of AF were younger than patients with a history of AF (median age: 67 [interquartile range (IQR): 58 to 77] years vs. 70 [range 65 to 77] years, respectively; $p < 0.001$). The comparison of UHD included IHD (n = 219, 58.9%), iVHD (n = 121, 32.5%), and CHD (n = 32, 8.6%). A history of AF was associated with LA

TABLE 1 Characteristics of Participants

	Total Group (n = 447)	No History of AF (n = 372)	AF (n = 75)	p Value
Age, yrs	67 (59-73)	67 (58-72)	70 (65-77)	<0.001
Male	325 (72.7)	280 (75.3)	45 (60.0)	0.007
BMI, kg/m^2	27.0 (24.7-30.2)	27.1 (24.9-30.4)	26.9 (24.0-29.6)	0.22
Underlying heart disease				<0.001
AVD	60 (13.4)	42 (11.3)	18 (24.0)	<0.0083*
AVD and IHD	48 (10.7)	41 (11.0)	7 (9.3)	0.67
IHD	238 (53.2)	219 (58.9)	19 (25.3)	<0.0083*
CHD	40 (8.9)	32 (8.6)	8 (10.7)	0.57
MVD	36 (8.1)	19 (5.1)	17 (22.7)	<0.0083*
MVD and IHD	25 (5.6)	19 (5.1)	6 (8.0)	0.41
Echocardiography				
LVF				0.08
Normal	344 (77.0)	283 (76.1)	61 (81.3)	
Mild dysfunction	79 (17.1)	71 (19.1)	8 (10.7)	
Moderate dysfunction	20 (4.5)	16 (4.3)	4 (5.3)	
Severe dysfunction	4 (0.9)	2 (0.5)	2 (2.7)	
Dilated LA >45 mm	98/284 (34.5)	63/224 (28.1)	35/60 (58.3)	<0.001
Medication				
Antiarrhythmic drugs				0.006
Class I	2 (0.4)	1 (0.3)	1 (1.3)	0.31
Class II	284 (63.5)	239 (64.2)	54 (60.0)	0.49
Class III	23 (5.1)	5 (1.3)	18 (24.0)	<0.0125*
Class IV	19 (4.3)	1 (4.6)	2 (2.7)	0.75
Digoxin	11 (2.5)	3 (0.8)	8 (10.7)	<0.0125*

Values are median (interquartile range) or n (%). *Bonferroni correction was applied.

AF = atrial fibrillation; AVD = aortic valve disease; BMI = body mass index; CHD = congenital heart disease; IHD = ischemic heart disease; LA = left atrium; LVF = left ventricular function; MVD = mitral valve disease; UHD = underlying heart disease.

enlargement (58.3%; $p < 0.001$). Sinus rhythm cycle length during epicardial mapping did not differ between the 3 UHD (IHD median (IQR) time: 901 [range: 762 to 1023] ms; iVHD median (IQR) time: 835 [range: 721 to 999] ms; CHD median (IQR) time: 866 [range: 734 to 963] ms; $p = 0.09$) or patients with and without an history of AF (874 [753 to 1,065] ms vs. 876 [750 to 1,012] ms, respectively; $p = 0.46$).

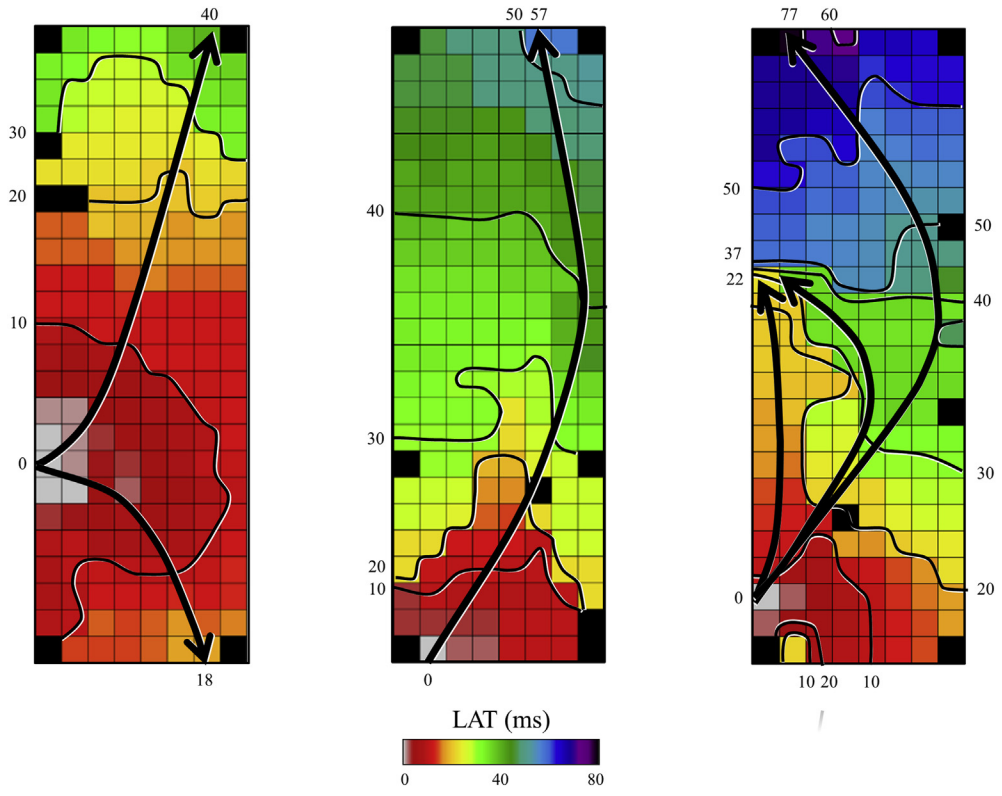
IMPACT OF UNDERLYING HEART DISEASES ON INTRA-ATRIAL CONDUCTION. Figure 2 shows 3 examples of color-coded activation maps. In the activation map on the left side of Figure 2, the SR wavefront does not encounter any areas of conduction delay. The middle activation map shows slightly more areas of conduction delay represented by crowding of isochrones in the lower right part, whereas in the activation map on the right side of Figure 2, a large area of conduction delay is present in the middle left part of the activation map. In these 3 activation maps, CTs ≥12 ms are 0.3%, 2.1%, and 5.9%, respectively. When comparing the 3 UHDs, there were no differences in frequencies of CTs ≥4 ms (all locations, $p \geq 0.017$).

IMPACT OF VARIOUS UHDs ON THE SEVERITY OF CONDUCTION DISORDERS. Each patient in both groups had at least a CT ≥16 ms. Magnitudes of CTs were comparable between patients with IHD, iVHD, and CHD throughout both atria (Bonferroni corrected $p \geq 0.005$) and at each location separately (RA: $p \geq 0.005$, BB: $p \geq 0.004$, LA: $p \geq 0.006$, PVA: $p \geq 0.008$, all Bonferroni corrected).

IMPACT OF AF HISTORY ON INTRA-ATRIAL CONDUCTION. The upper panel of Figure 3 shows 2 typical examples of color-coded activation maps obtained from a patient without AF and with AF. As shown in the CT maps, there is only 1 small area of conduction slowing with a CT of 7 ms (left panel) in the patient without AF, whereas the patient with AF has multiple areas of CTs ranging from 7 to even 30 ms (right panel) (11.8% vs. 0.3%).

An AF history was associated with slowing of conduction; the maximum CT (IQR) for patients in the AF group ranged from 40 to 66 ms (median: 54 ms), whereas in patients in the no-AF group, the maximum CT ranged from 33 to 54 ms (median: 45 ms) ($p = 0.006$).

FIGURE 2 Color-Coded Activation Maps Showing Conduction Disorders



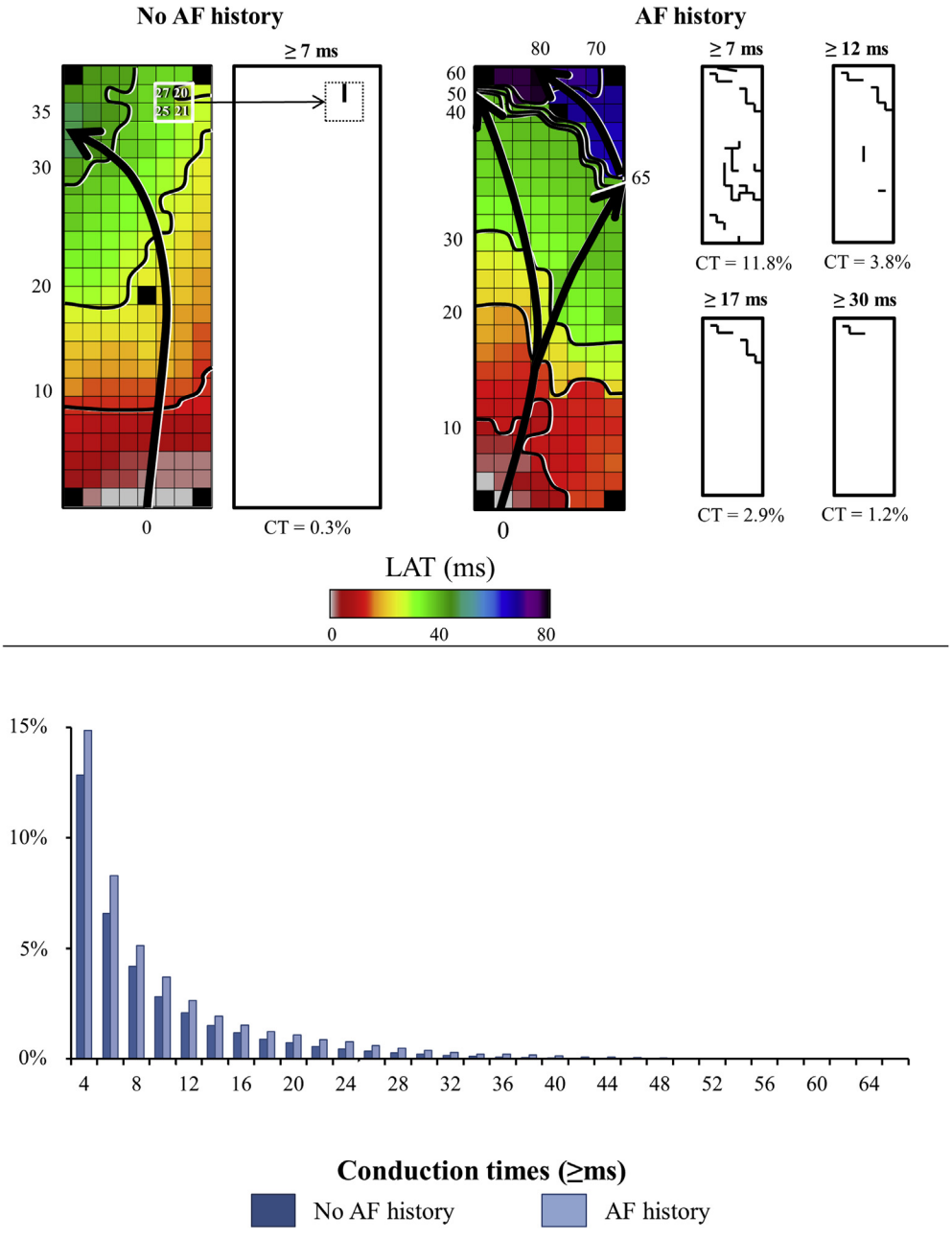
Examples of color-coded activation maps. In the **left** activation map, the sinus rhythm wavefront propagates and encounters only 1 small area of conduction delay. The **middle** activation map has slightly more areas of conduction delay represented by crowding of isochrones in the lower right part of the activation map, whereas in the **right** activation map a large area of conduction delay is present in the middle left part of the activation map. Isochrones are drawn at 10ms. The **black arrow** indicates the main trajectories of activation. Abbreviation as in Figure 1.

The lower panel of Figure 3 shows the frequency of CTs between 4 and 66 ms measured from both atria in the entire study population. Patients with AF had more CTs ≥4 ms compared to patients without AF (14.9% [11.8 to 17.0] vs. 12.8% [10.9 to 14.6], $p < 0.001$). These differences in CT incidences became even more pronounced at CTs ≥6 ms. Comparing the frequency of CTs for each location separately showed that at BB, LA, and PVA, slowing of conduction (CT ≥4 ms) occurred more frequently in patients with AF (BB: 20.5% [14.0% to 26.2%] vs. 15.2% [11.8% to 19.5%], $p < 0.001$; LA: 10.0% [7.0% to 13.3%] vs. 9.0% [6.5% to 11.9%], $p = 0.045$; PVA: 13.4% [9.0% to 17.6%] vs. 10.9% [8.4% to 14.1%], $p = 0.001$). No differences in the amount of CTs ≥4 ms were found at RA ($p > 0.05$).

IMPACT OF AF HISTORY ON THE SEVERITY OF CONDUCTION DISORDERS. Figure 4 shows the magnitude of CTs in patients with and without an AF history for the entire study population (upper panel). Each patient in both groups had at least a CT ≥16 ms. A considerable overlap in magnitude of CTs between patients with and without a history of AF is observed up to a CT ≥50 ms. However, more patients with AF had prolonged CTs ≥50 ms compared to patients without AF (CTs ≥50 ms: n = 54.7% vs. n = 34.4%, Bonferroni corrected $p < 0.004$).

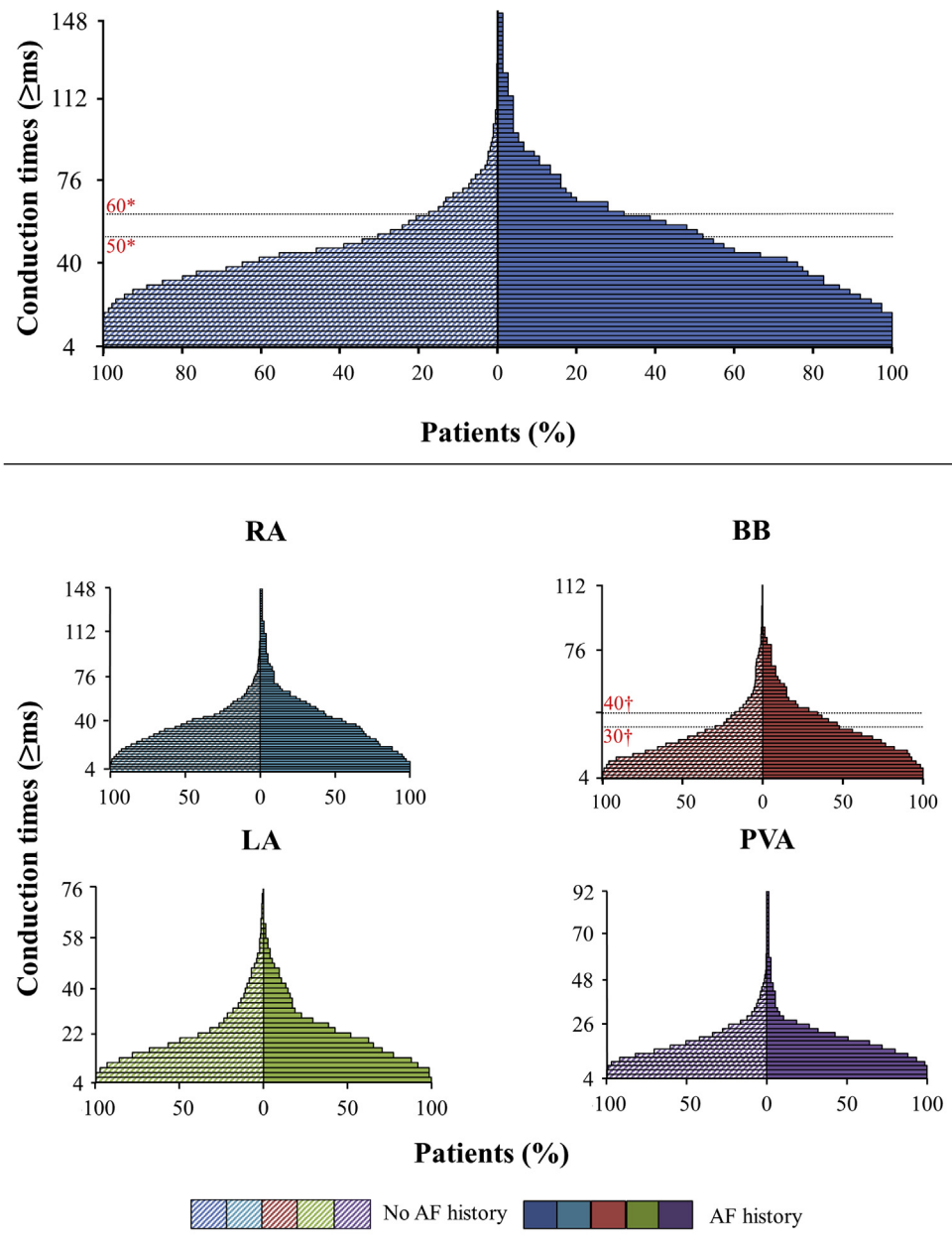
The lower panel of Figure 4 shows the magnitude of CTs in patients with and without an AF history for each separate location. In the RA, 1 patient had a CT of even 148 ms. Figure 5 shows the color-coded activation map of this specific patient including a CT map of ≥140 ms indicated by the thick black lines. Atrial electrograms (right panel) consist of long double potential reflecting the 2 wavefronts propagating along both sides of the line of block. As shown in the lower panel of Figure 4, the magnitude of CTs only differed at BB. At this site, more patients with AF had prolonged CTs (CT ≥30 ms: n = 56.2% vs. n = 36.0%, Bonferroni corrected $p < 0.004$). Overall, RA, PVA,

FIGURE 3 Frequency of Conduction Disorders in Patients With and Without AF



The **upper left panel** shows a color-coded activation map of a patient without AF. The sinus rhythm wavefront propagates without encountering any areas of conduction disorders. The **upper right panel** shows a color-coded activation map of a patient with AF and an area of conduction delay in the upper right part of the activation map reflected by crowding of isochrones. CT maps constructed using various CT values are depicted next to the corresponding activation map. Isochrones are drawn at 10ms. The **black arrows** indicate the main trajectories of activation. The **lower panel** shows bi-atrial relative frequency distribution of CTs between patients with and without an AF history. AF = atrial fibrillation; other abbreviations as in Figure 1.

FIGURE 4 **Severity of Conduction Disorders in Patients With and Without AF**



The **upper panel** shows magnitude of CTs measured in patients with and without an AF history for the entire study population. The **lower panel** shows magnitude of CTs measured in patients with and without an AF history for each location separately. The left side shows patients in the no-AF group, and the right side patients in the AF group. *Bonferroni corrected $p < 0.004$. †Bonferroni corrected 0.004. Abbreviations as in Figures 1 and 3.

and LA show no differences in magnitude of conduction disorders (RA: $p \geq 0.004$, LA: $p \geq 0.006$, PVA: $p \geq 0.006$, all Bonferroni corrected).

DISCUSSION

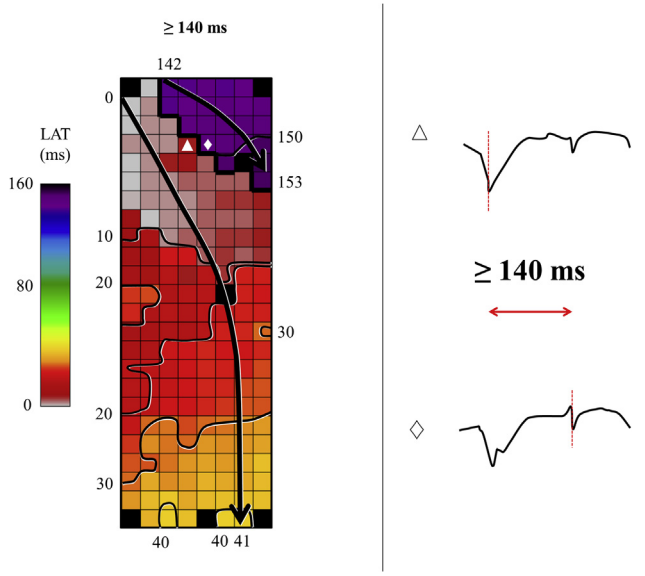
KEY FINDINGS. This high-resolution intra-operative mapping study during sinus rhythm is the first to investigate the impact of various UHD and prior AF episodes on epicardial atrial CTs throughout both atria (**Central Illustration**) . By comparing the 3 UHDs, the frequency and severity of conduction disorders did not differ. Patients with AF had more conduction disorders than patients without AF throughout both atria. More severe conduction disorders were found in patients with AF at BB.

THE RELATION OF UHDs AND CONDUCTION DISORDERS. No differences were found in the frequency and severity of conduction disorders between patients with iVHD, IHD, and CHD. As mentioned earlier, all 3 UHDs are known to cause structural remodeling. In patients with IHD, conduction disorders leading to arrhythmias are, for example, caused by inflammation, atherosclerosis, and myocardial infarction (6–8). Additionally, both VHD and CHD are associated with atrial pressure and/or volume overload, leading to structural changes in the atria (5,20). Chronic atrial stretch in both groups eventually leads to conduction disorders because of increased interstitial connective tissue, fibrotic changes, and myocyte alterations (5,21,22). In patients with CHD, the pressure and/or volume overload usually extents for decades. Additionally, impaired electrical connections may be present because of the underlying congenital heart defect itself (20).

A previous mapping study by Mouws et al. (15) investigated conduction disorders across BB between patients with VHD and IHD in a smaller study population. They examined the frequency of CTs between 7 to 11 ms and ≥12 ms and also found that conduction disorders were equally present between IHD and VHD. Patients with CHD did not have the most or the most severe conduction disorder compared to VHD and IHD despite the long time-course of the disease. A possible explanation may be that in our study population, patients with CHD (median age (IQR) age: 52 (range: 41 to 61) years) were younger than patients with IHD an iVHD (median age (IQR) age: 67 (60 to 72) years, $p < 0.001$ and 70 (63 to 76) years, $p < 0.001$, respectively).

THE RELATION BETWEEN AF AND CONDUCTION DISORDERS. Our study showed that more conduction disorders were found in patients with AF.

FIGURE 5 Example of a Severe Conduction Disorder

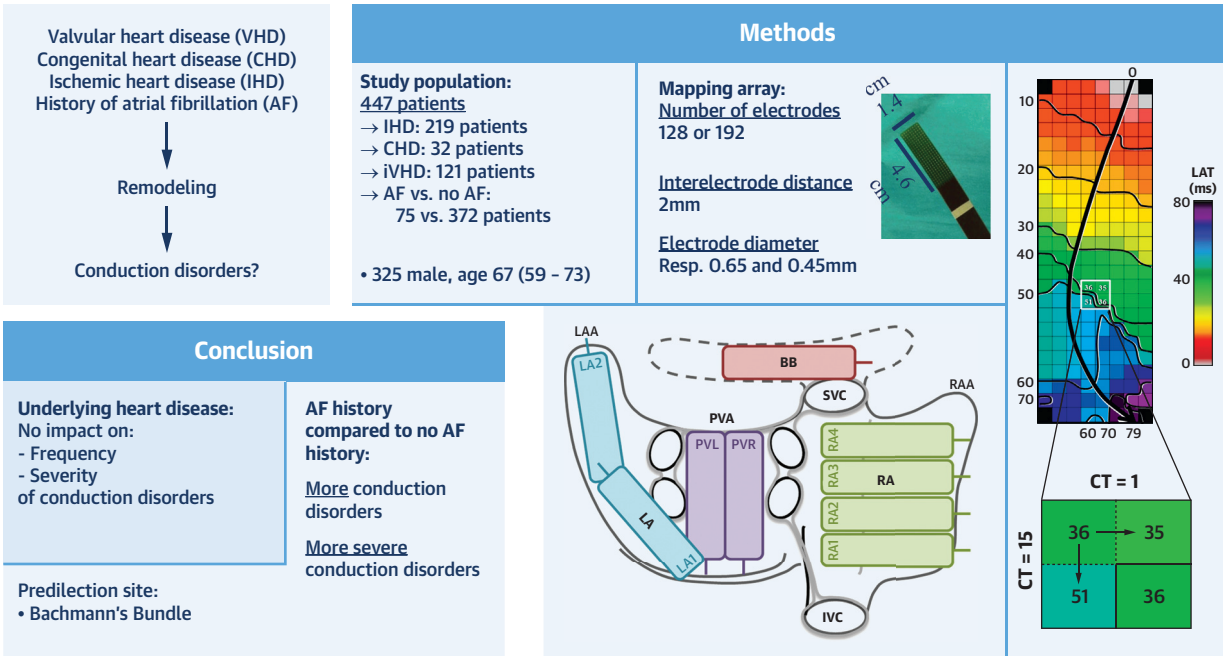


A color-coded activation map with a severe conduction delay of 140 ms indicated by the **thick black lines**. The corresponding atrial electrograms around this line of conduction block are depicted next to the activation map. There are 2 wavefronts propagating along the line of conduction block; 1 is propagating from the left upper corner at T = 0 ms ending in the right lower corner at T = 43 ms, and another propagating from the left upper corner at T = 142 ms to the right middle corner at T = 153 ms. Hence, there is a line of block of ≥140 ms. The recording shows a long double potential representing the 2 wavefronts that propagates along both sides of the line of block at different times. Isochrones are drawn at 10 ms. The **black arrow** indicates the main trajectories of activation. The **red dashed line** indicates the steepest negative deflection. Abbreviation as in **Figure 1**.

Previous studies have also demonstrated that patients with AF have more conduction disorders, but the study populations were smaller and only BB or PVA were investigated. Moreover, they measured differences in CTs ≥7 ms and/or ≥12 ms (13,14). At BB, Teuwen et al. (14) found an association between paroxysmal AF and a CT of ≥12 ms. Albeit, in this study merely 13 patients of 185 had a history of paroxysmal AF (14). Mouws et al. (13) showed that the prevalence of ≥12 ms at PVA is higher in patients with AF. Both studies at BB and PVA are consistent with our findings.

A previous mapping study by Lanters et al. (23) found that the prevalence of CTs ≥7 ms and ≥12 ms was low in patients without AF (1.4% [range: 0.2% to 4.0%] and 1.3% [range: 0.1% to 4.3%], respectively). Despite the low prevalence, a considerable intra-atrial variation already was found, with a predilection site at the superior intercaval region and to a lesser extent BB (23). However, the impact of prior AF episodes was not investigated. In our study, we compared the prevalence of intra-atrial conduction

CENTRAL ILLUSTRATION **The impact of Various Underlying Heart Diseases and Atrial Fibrillation Episodes on Conduction Heterogeneity**



Heida, A. et al. J Am Coll Cardiol EP. 2020;6(14):1844–54.

It is unknown whether intra-atrial conduction during sinus rhythm throughout the atria differs between patients with various underlying heart diseases or is influenced by atrial fibrillation episodes **(left upper panel)**. This high-resolution epicardial mapping **(right panel)** revealed that atrial conduction is affected by prior AF episodes, particularly at BB **(lower left panel)**. BB = Bachmann's bundle; CT = conduction time; iVHD = (ischemic and) valvular heart disease; LA = left atrium; LAA = left atrial appendage; LAT = local activation time; PVA = pulmonary vein area; PVL = left pulmonary vein; PVR = right pulmonary RA = right atrium; RAA = right atrial appendage; SVC = superior vena cava.

between patients with and without AF at all regions. Patients with AF had more conduction disorders at BB and LA, and more severe conduction disorders at RA and BB compared to patients without AF.

A mapping study by Allessie et al. (24) investigated the electropathological substrate of AF by comparing patients with persistent AF (duration of >1 year) and induced AF. In this study, conduction block lines (CT ≥ 12 ms) in both AF groups changed continuously on a beat-to-beat basis throughout the atria (24). Furthermore, at the RA, longer lines of conduction block and a higher frequency of conduction block were found in patients with persistent AF compared to those with induced AF (24). This indicates that for AF maintenance both the frequency and severity of conduction disorders are important. Long lines of conduction block present during sinus rhythm result in large CTs because a wavefront takes longer to propagate around a line of conduction block and activate the other side. Thus, initiation of re-entry is facilitated as the likelihood of the rotating wavefront encountering excitable tissue increases. In our population, CTs were as large as 142 ms.

As previously described, the high-rate AF episode itself induces atrial remodeling on a structural and electrical level. Electrical remodeling is reversible within a week of sinus rhythm, unlike structural remodeling, which is still partially present after 4 months of sinus rhythm (11,25). Structural remodeling consists of atrial fibrosis, side-to-side cell uncoupling, or atrial enlargement (2,5,26). In our data, LA enlargement was more present in patients with AF compared to patients without AF. However, also UHDs such as VHD and CHD are as such well-known risk factors which contribute to the development of the arrhythmogenic substrate (27). In the present study we did not find any differences in UHDs between patients with VHD, CHD, and IHD.

BACHMANN'S BUNDLE AS A PREDILECTION SITE FOR CONDUCTION DISORDERS. Differences in

frequency and severity of conduction disorders in patients with AF were found at all locations, but particularly at BB. BB is an inter-atrial muscular bundle consisting of parallel arranged myocardial strands and myofibers connecting the right side to the septum spurium and the left side to the left atrioventricular ring, which continues into the posterior LA wall including the pulmonary veins (28). Hence, BB is more attached to the LA than to the RA and therefore considered more sensitive to LA overload. In our study, enlarged LA were more prevalent in patients with AF, which may explain why this is a predilection site for conduction disorders in patients with AF. Furthermore, because of its fiber orientation, BB is considered a highway for intra-atrial conduction (28,29). However, the fibers are not enclosed by a fibrous tissue sheet and therefore disrupt more easily by pressure and volume overload (30).

IMPACT OF SINO-ATRIAL NODE EXIT PATHWAYS ON CONDUCTION DISORDERS. During sinus rhythm, the activation origin is dynamic, as the impulse usually reaches the atrial myocardium via the superior exit pathway at higher heart rates and via the inferior pathway at slower heart rates (31). In our data, sinus rhythm frequencies varied between patients. With different heart rates, a different exit pathway may occur. This in turn may change the wavefront direction and possibly alter the amount of conduction disorders.

STUDY LIMITATIONS. There is a limited number of patients with CHD compared to IHD and iVHD. Comparison of CHD, IHD, and iVHD should therefore be interpreted with caution. The number of patients in the AF group is relatively small in comparison with the no-AF group as it was not always possible to electrically convert to stable sinus rhythm. Furthermore, patients with a history of AF had different degrees of electrical remodeling because sinus rhythm recordings in some patients were made immediately after electrical cardioversion, whereas others were in sinus rhythm for a longer period before recording all locations. Moreover, at different sinus rates, different exit pathways occur that can affect the CTs. Direction-dependent conduction disorders could be missed as we only analyzed sinus rhythm.

CONCLUSIONS

This high-resolution epicardial mapping study during sinus rhythm is the first to investigate the impact of various UHD and AF episodes on epicardial atrial CTs throughout both atria. By comparing the 3 UHDs, no differences were found in the frequency and severity of conduction disorders. The presence of AF episodes is associated with more conduction disorders throughout both atria and with more severe conduction disorders at BB. These findings indicate that atrial conduction is affected by prior AF episodes, particularly at BB, and is not affected by UHD. The next step will be to determine the relevance of these conduction disorders for AF development and maintenance.

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AUTHOR DISCLOSURES

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Knowledge of the prevalence and severity of conduction disorders caused by structural remodeling during sinus rhythm is the first step in detection of the arrhythmogenic substrate associated with development of AF. At present, it is unknown whether intra-atrial conduction during sinus rhythm throughout the atria differs between patients with various underlying heart diseases or is influenced by AF episodes.

TRANSLATIONAL OUTLOOK: Atrial conduction is affected by prior AF episodes, particularly at BB. These alterations may provide an arrhythmogenic substrate for AF development and maintenance. UHD does not affect atrial conduction.

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APPENDIX For an expanded Methods section and supplemental references, please see the online version of this paper.