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ORIGINAL ARTICLE

Heterogeneity in Conduction Underlies Obesity-Related Atrial Fibrillation Vulnerability

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BACKGROUND: Obese patients are more vulnerable to development of atrial fibrillation but pathophysiology underlying this relation is only partly understood. The aim of this study is to compare the severity and extensiveness of conduction disorders between obese patients and nonobese patients measured at a high-resolution scale.

METHODS: Patients (N=212) undergoing cardiac surgery (male:161, 63±11 years) underwent epicardial mapping of the right atrium, Bachmann bundle, and left atrium during sinus rhythm. Conduction delay (CD) was defined as interelectrode conduction time of 7 to 11 ms and conduction block (CB) as conduction time ≥12 ms. Prevalence of CD/CB, continuous CDCB (cCDCB), length of CD/CB/cCDCB lines, and severity of CB were analyzed.

RESULTS: In obese patients, the overall incidence of CD (3.1% versus 2.6%; P=0.002), CB (1.8% versus 1.2%; P<0.001), and cCDCB (2.6% versus 1.9%; P<0.001) was higher and CD (P=0.012) and cCDCB (P<0.001) lines are longer. There were more conduction disorders at Bachmann bundle and this area has a higher incidence of CD (4.4% versus 3.3%, P=0.002), CB (3.1% versus 1.6%, P<0.001), cCDCB (4.6% versus 2.7%, P<0.001) and longer CD (P<0.001) or cCDCB (P=0.017) lines. The severity of CB is also higher, particularly in the Bachmann bundle (P=0.008) and pulmonary vein (P=0.020) areas. In addition, obese patients have a higher incidence of early de-novo postoperative atrial fibrillation (P=0.003). Body mass index (P=0.037) and the overall amount of CB (P=0.012) were independent predictors for incidence of early postoperative atrial fibrillation.

CONCLUSIONS: Compared with nonobese patients, obese patients have higher incidences of conduction disorders, which are also more extensive and more severe. These differences in heterogeneity in conduction are already present during sinus rhythm and may explain the higher vulnerability to atrial fibrillation of obese patients.

VISUAL OVERVIEW: A visual overview is available for this article.

Key Words: atrial fibrillation ■ body mass index ■ cardiac electrophysiology ■ incidence ■ obesity

Obesity is a rampant epidemic and a well-established, highly prevalent risk factor for atrial fibrillation (AF).[1] The mechanisms by which obesity contributes to AF development include associated risk factors (eg, diabetes mellitus, hypertension, hyperlipidemia, and coronary artery disease) and atrial substrate modifiers[2] (eg, epicardial fat infiltrations, atrial fibrosis, and enhanced local inflammation because of increased adipocytokines and proinflammatory cytokines).

Previous human and experimental studies have reported on the relationship between the presence of epicardial adipose tissue and atrial electropathology.[3–6] In a 26 patients study group, Mahajan et al observed global reduction in conduction velocity in obese patients examined by endocardial electroanatomic mapping during sinus rhythm (SR). In the ovine experimental model of chronic obesity, endocardial electroanatomic mapping showed slowed and heterogenous conduction, an

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WHAT IS KNOWN?

- Obesity is a rampant epidemic and a well-established, highly prevalent risk factor for atrial fibrillation.
- Endocardial electroanatomic mapping of limited atrial regions showed that obesity is associated with slowed and heterogenous conduction and global reduction in conduction velocity during sinus rhythm.

WHAT THE STUDY ADDS?

- High-resolution epicardial mapping of the entire atrial surface shows that obese patients have an overall higher incidence and severity of conduction abnormalities, particularly in the Bachmann Bundle area.
- In addition, obese patients have a higher incidence of early de-novo postoperative atrial fibrillation, body mass index, and the overall amount of conduction block being independent predictors for incidence of early postoperative atrial fibrillation.

Nonstandard Abbreviations and Acronyms

AF	atrial fibrillation
BB	Bachmann Bundle
BMI	body mass index
CD	conduction delay
CB	conduction block
cCDCB	continuous conduction delay conduction block
EPoAF	early postoperative atrial fibrillation
OR	odds ratio
PV	pulmonary vein
RA	right atria
SR	sinus rhythm

increased incidence of complex fractionated electrograms (e-grams) and an increased voltage heterogeneity with reduction of voltages in the posterior left atrial wall.[4] In progressive weight gain ovine models,[5] conduction velocities and conduction heterogeneity indices assessed during pacing cycle at different cycle lengths from 4 directions[5] revealed that increasing adiposity was associated with the extent of conduction slowing and conduction heterogeneity.[5]

As data on atrial conduction properties in obese humans is scarce,[3] the aim of this study is to compare the severity and extensiveness of conduction disorders in both atria between obese patients and matched nonobese patients measured at high resolution scale during SR.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The study population consisted of adult patients scheduled for elective cardiac surgery for coronary artery disease, either isolated or in combination with aortic (coronary artery disease+aortic valve disease) or mitral (coronary artery disease+mitral valve disease) valve disease, isolated aortic (aortic valve disease) or mitral valve disease or correction of congenital heart defects. Patients with congenital heart defects disease included atrial septal defects (70%), partial anomalous pulmonary venous return (11%), ventricular septal defects (5%), total anomalous pulmonary venous return (5%), and transposition of the great vessels (5%).

Exclusion criteria were history of AF, prior ablation of atrial tachyarrhythmias, severe renal failure, atrial pacing and patients requiring mechanical or inotropic support. The population was divided into 2 categories: (1) obese patients (body mass index [BMI] ≥30) and (2) nonobese patients (BMI<30).

This study was conducted as part of 2 prospective observational projects including Quest for Arrhythmogenic Substrate of Atrial fibrRillation (QUASAR, MEC 2010-054) and Hsf1 activators lower cardiomyocyte damage toward a novel approach to REVERSE atrial fibrillation (HALT & REVERSE, MEC 2014-393). Both projects were approved by the local ethics committee of the Erasmus Medical Centre and adhere to the Declaration of Helsinki principles. Accordingly, written consent was obtained from the participating patients before surgical intervention.

Epicardial High-Resolution Mapping

Epicardial high-resolution mapping was performed during open chest cardiac surgery after sternotomy and before connecting the patient to the cardiopulmonary bypass circulation.[6,7] A bipolar pacemaker wire was placed at the right atrial free wall to serve as a temporal reference electrode. The indifferent electrode was a steel wire attached to thoracic subcutaneous tissue.[6] The mapping procedure was performed using 16 mm width electrode arrays containing either 128 or 192 unipolar electrodes (2.0-mm interelectrode distance) with diameters of 0.65 and 0.45 mm, respectively.[7]

Epicardial mapping during SR was conducted following a predefined mapping scheme as shown in Figure I in the Data Supplement (left upper panel), approaching the entire epicardial surface of the right atrium (RA), Bachmann Bundle (BB), and LA.[6] As previously described,[6–8] the electrode array was shifted along the imaginary lines with a fixed orientation at each position. Mapping of the RA started at the cavo-tricuspid isthmus and continued perpendicular to the caval veins toward the RA appendage. BB was mapped starting at the tip of the LA appendage across the roof of the LA, behind the aorta toward the superior cavo-atrial junction.[7] Mapping of the LA was performed from the lower margin of the left inferior pulmonary vein (PV) along the left atrioventricular groove towards the LA appendage.[6] The PV area was mapped from the sinus transversus fold, in between the right and left PV toward the left atrioventricular groove.[7]

From every atrial mapping site, 5 seconds of SR were recorded, including surface ECG (lead I), a bipolar reference electrogram, a calibration signal with an amplitude of 2 mV and 1000 ms and unipolar epicardial electrograms. Recordings were sampled with a rate of 1 kHz, amplified (gain:1000),

filtered (bandwidth: 0.5–400 Hz), converted from analog to digital (16 bits) and stored on a hard disk.

Analysis of Mapping Data

Figure I in the Data Supplement shows all mapping locations, including BB, RA1-4, LA1-2, PVR, and PVL on a schematic posterior view of the atrial surface. Colour-coded local activation maps during SR were constructed by annotating the steepest negative deflection of atrial electrograms with a minimum slope threshold of 0.05 mV/ms. The ratio of threshold amplitude to noise amplitude was set at 2. Atrial extrasystolic beats were excluded.

Differences in local activation times (local conduction delay) were calculated between neighbouring electrodes (adjacent right and lower) resulting in 2 conduction delays per electrode (Figure I in the Data Supplement left lower). As previously described, conduction delay (CD) and conduction block (CB) were defined as differences in local activation time (ΔCT) between adjacent electrodes of 7 to 11 and ≥12 ms, respectively.[9–12] This finding corresponds to effective conduction velocities of 17 to 29 cm/s for CD and <17 cm/s for CB, respectively. Lines of CD, CB, and continuous CDCB (cCDCB) were defined as uninterrupted series of, respectively, interelectrode CD, CB, or a combination of CD and CB. Lengths of these lines were measured and analyzed as the median length of lines per patient as well as length of the longest line per patient. Incidence of CD and CB are expressed as a percentage of the total available number of interelectrode connections. Therefore, the percentage of CD/CB per mapping location was calculated using the following formulas[6]:

$$\%CD = \frac{\text{Number of CT} \geq 7\text{ ms}}{\text{Total number of CT}} \text{ and } \%CB = \frac{\text{Number of CT} \geq 12\text{ ms}}{\text{Total number of CT}}$$

Difference in severity of CB between obese and nonobese patients was investigated by calculating median CTs derived from all values for conduction time ≥12 ms per electrode in every patient separately.

Early De-Novo Postoperative AF

Early de-novo postoperative (EPoAF) was defined as the incidence of at least one AF episode with a duration of minimum 30 seconds during the first 5 postoperative days. EPoAF was confirmed by ECG, continuous rhythm monitoring, or patient discharge letters and clinical notes.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics 24 software (Corp, Armonk, NY software). Propensity score matching analysis was performed using logistic regression, cases being randomly assigned to controls based on the nearest neighboring propensity score (match tolerance 0.05). Data were tested using Shapiro-Wilk test of normality. Continuous, normally distributed data are expressed as mean±SD and skewed data as median and range (minimum-maximum). Student *T*-test was used to compare normally distributed continuous variables, while skewed parameters were compared using Mann-Whitney *U* test. Comparisons between related skewed variables were performed using Wilcoxon test. Categorical variables were compared using χ^2 test and are presented as percentages. Bonferroni correction was used for multiple comparisons. Pearson correlation test was used to evaluate the linear relationship between variables. Possible predictors for EPoAF were manually entered in a multivariate binary logistic regression based on *P* value (≤0.15) in univariate analysis or clinical relevance. A 2-sided *P*-value of <0.05 was considered statistically significant.

RESULTS

Study Population

Baseline characteristics of both the obese (N=106, 64±10 years; 78 (74%) male) and nonobese group (N=106, 62±12; 83 [78%] male) are presented in Table 1. Clinical characteristics between the obese and nonobese group only differed in BMI (32.9±2.9 versus 25.4±2.4). Coronary artery bypass grafting was the main surgical procedure performed in both groups (obese patients: 70 [66%] and nonobese patients: 64 [60%]).

Mapping Data

The total number of recording sites (electrodes) in the obese group was 202 304 (1909±320.6 electrodes/patient) and 200 192 in the nonobese group (1889±310.7 electrodes/patient, *P*=0.411). After exclusion of 0.65% of mapping sites due to poor signal-to-noise ratios, respectively, 1333 (12.5±4.2 per patient) and 1321 (12.4±4.1 per patient) mapping locations were available for further analysis (*P*=0.617).

Heterogeneity in Conduction

Areas of CD and CB were present in all patients. Figure 1 depicts examples of CD/CB maps obtained from a typical obese and nonobese patient constructed from respectively RA, BB, LA, and PV. These maps clearly show that there are not only more CD or CB lines in the obese patient, but that these CD/CB lines are also longer. The upper panel of Figure 2 shows that obesity is indeed associated with higher incidences (3.1% [0.0–20.4] versus 2.6% [0.0–10.9], *P*=0.002) and longer lengths (3.3 mm [2.0–12.0] versus 3.0 mm [2.0–9.0], *P*=0.012) of CD lines.

The middle panel of Figure 2 shows that though the length of CB lines were similar between obese (5 mm [2.0–42.0]) and nonobese patients (4.8 mm [2.0–26.0]), (*P*=0.059), there was a higher incidence of CB lines (1.8% [0.0–25.1] versus 1.2% [0.0–12.6]), *P*<0.001 in the obese group. In addition, the incidence of cCDCB was also higher in obese (2.6% [0.0–39.8] compared with nonobese patients (1.9% [0.0–17.9], *P*<0.001) as shown in the lower panel of Figure 2. Again, these lines were also longer (14 mm [4.0–83]) versus 13.6 mm [4.0–116.0], *P*<0.001).

Table 1. Patient Characteristics

	Obese Patients BMI ≥30 (N=106)	Nonobese Patients BMI <30 (N=106)	*P* Value
Age, y	63.5±9.6	62.3±11.8	0.742
Male sex, N (%)	78 (74)	83 (78)	0.521
BMI	32.9±2.9	25.4± 2.4	<0.001
Risk factors, N (%)			
Hypertension	65 (61.3)	60 (56.6)	0.577
Diabetes mellitus	37 (35)	25 (23.5)	0.096
Dyslipidemia	44 (41.5)	42 (39.6)	0.889
Left ventricular function			0.357
Normal (EF >55%)	84 (79.2)	83 (78.3)	
Mild impairment (EF 46%–55%)	21 (19.8)	18 (17)	
Moderate impairment (EF 36%–45%)	1 (0.9)	3 (2.8)	
Severe impairment (EF <35%)	0 (0)	2 (1.9)	
Left atrial dilatation, N (%; LA diameter, ≥45 mm)	15 (14.1)	16 (15)	0.679
Preoperative medication, N (%)			
Antiarrhythmic drugs			
Class II	46 (68.6)	59 (66.2)	0.863
Class IV	2 (3)	4 (4.4)	0.467
ACE inhibitors	42 (62.6)	49 (55)	0.412
Surgical procedure, N (%)			0.277
CABG	70 (66)	64 (60.3)	
AVD	10 (9.4)	12 (11.3)	
MVD	2 (1.8)	7 (6.6)	
CABG+AVD	15 (14.1)	11 (10.3)	
CABG+MVD	3 (2.8)	1 (0.9)	
CHD	6 (5.6)	11 (10.3)	

Statistically significant values ($P<0.05$). ACE indicates angiotensin-converting enzyme; AVD, aortic valve disease; BMI, body mass index; CABG, coronary artery bypass grafting; CHD, congenital heart disease; EF, ejection fraction; and MVD, mitral valve disease.

Predilection Sites for Conduction Abnormalities

Regional differences in incidences of CD, CB, and cCDCB lines for the obese and nonobese groups separately are demonstrated in Figure 3 and summarized in Table 2. In both groups, conduction abnormalities were observed at all atrial sites but preferentially at BB. The upper panel of Figure 3 shows that the incidence of CD lines at BB was significantly higher in the obese group (4.4% [0.3–20.4] versus 3.3% [0.0–10.9], $P=0.002$) and these lines were also longer (4.0 mm [2.0–8.0] versus 3.0 mm [2.0–9.0], $P<0.001$). In the LA area, obese patients also had a higher incidence of CD lines (2.5% [0.0-9.1] versus 2.0% [0.0–8.6], $P=0.047$), but the length of CD lines was not different between the 2 groups.

Predilection sites for CB lines are depicted in the middle panel of Figure 3. Though the lengths of CB lines were similar between obese and nonobese patients within all atrial areas, obese patients had significantly higher incidences of CB lines at BB (3.1% [0.0–25.1] versus 1.6% [0.0–12.6], $P<0.001$) and RA (2.6% [0.0–18.1] versus 2.0% [0.0–11.7], $P=0.049$). Furthermore, as shown in the lower panel of Figure 3, incidences of cCDCB lines (4.6% [0.0–39.8] versus 2.7% [0.0–17.9], $P<0.001$) at BB were higher and lengths of these lines were longer (16.0 mm [6.0–83.0] versus 14.0 mm [6.0–116.0] $P=0.017$) in the obese patients.

Heterogeneity in Conduction in Coronary Artery Bypass Grafting Patients

Areas of CD and CB were present in all coronary artery bypass grafting patients. Higher incidence of CD was observed in obese (3.2% [0.0–20.4]) compared with nonobese patients (2.6% [0.0–9.4], $P=0.003$) along with longer lines of CD (obese 3.5 mm [2.0–12.0] versus nonobese 3.0 mm [2.0–9.0]; $P=0.003$). There was also an increase in CB incidence in obese (1.6% [0.0–25.1]) versus nonobese patients (1.1% [0.0–12.6], $P=0.003$). Significantly higher incidences of CD were observed in obese patients at BB (3.3% [0.0–20.4] versus 2.2% [0.0–9.4]; $P<0.001$) and LA (3.3% [0.4–11.0] versus 2.5% [0.1–6.4]; $P=0.012$), with longer CD lines at LA (4.0 mm [2.0–9.0] versus 3.2 mm [2.0–8.0]; $P=0.013$). Obese patients also had higher incidences of CB at BB (1.6% [0.0–25.1] versus 1.0% [0.0–7.2]; $P=0.006$) and LA (1.7% [0.0–16.0] versus 1.1% [0.0–8.1]; $P=0.020$).

Severity of Conduction Block

Figure 4 depicts differences in severity of CB (ΔCT ≥12 ms) between obese and nonobese patients. The upper panel shows that within the entire atria, CB with severities ≥15 ms occurs more frequently in obese patients with ($P=0.001$). In the lower panels, differences in severity of CB is shown for obese and nonobese patients for each of the 4 mapping locations separately; CB was significantly more severe in the obese patients at BB ($P=0.008$) and PV ($P=0.020$).

Incidence and Risk Factors for Early De-Novo PoAF

Figure II in the Data Supplement shows that the incidence of EPoAF was higher in the obese group (36% [N=38] versus 17% [N=18]; $P=0.003$). Univariate and multivariate predictors for EPoAF Table 3 with their respective odds ratio (OR) values and 95% CIs. Significant univariate predictive factors for incidence of EPoAF include HT (OR, 1.332; $P=0.004$), LAE (OR,

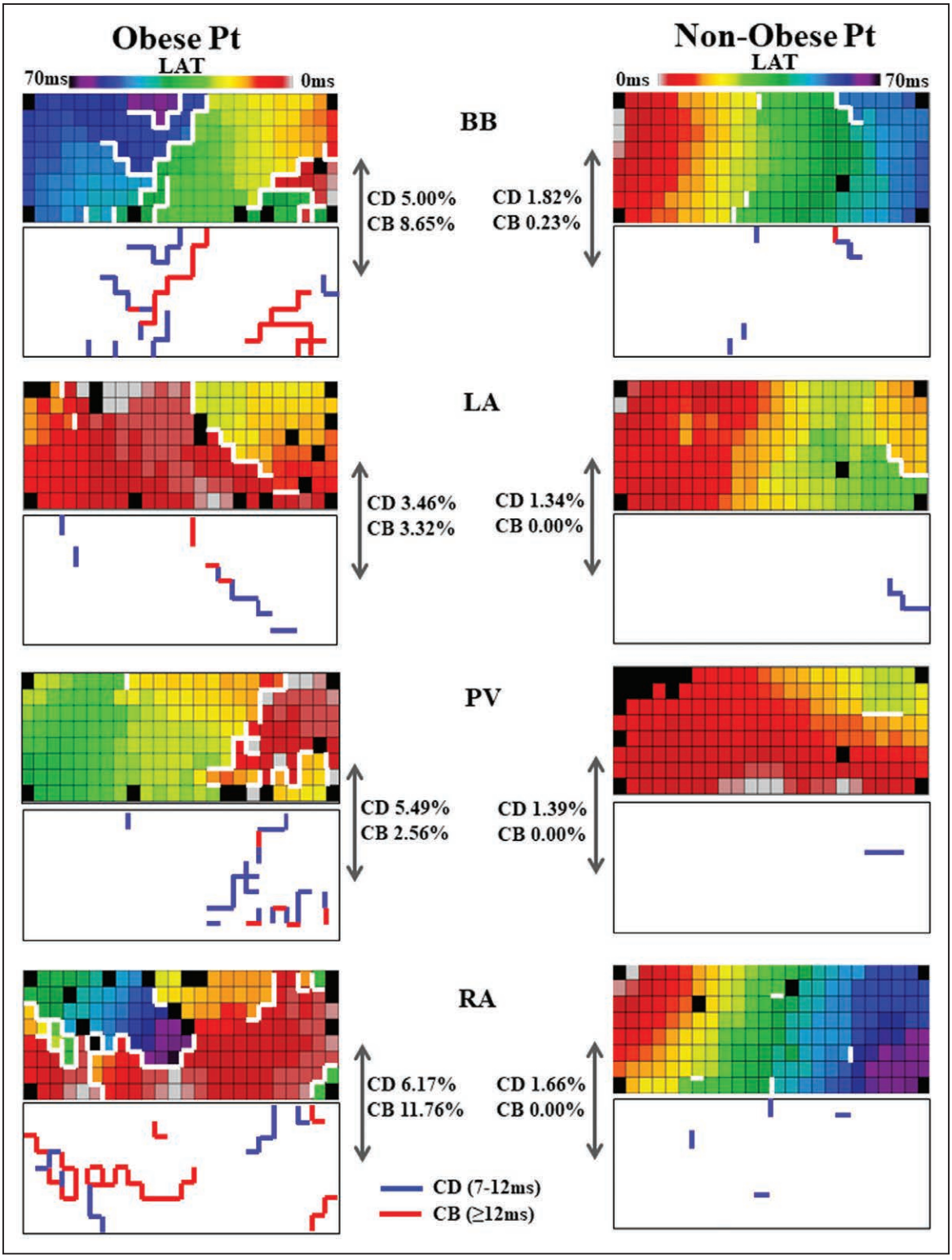

Figure 1. Examples of colour-coded activation maps show the distribution of lines conduction delay (CD; blue) and conduction block (CB; red) within predefined atrial areas from an obese patient (left) and a nonobese matched control patient (right). These maps show that there is an increase in both incidence and length of lines of CD and CB in the obese patient. The incidence of conduction abnormalities are expressed as percentage of CD and CB for every region separately. BB indicates Bachmann Bundle; CB, conduction block; CD, conduction delay; LA, left atria, LAT, local activation time; PV, pulmonary vein area; Pt, patient; and RA, right atria.

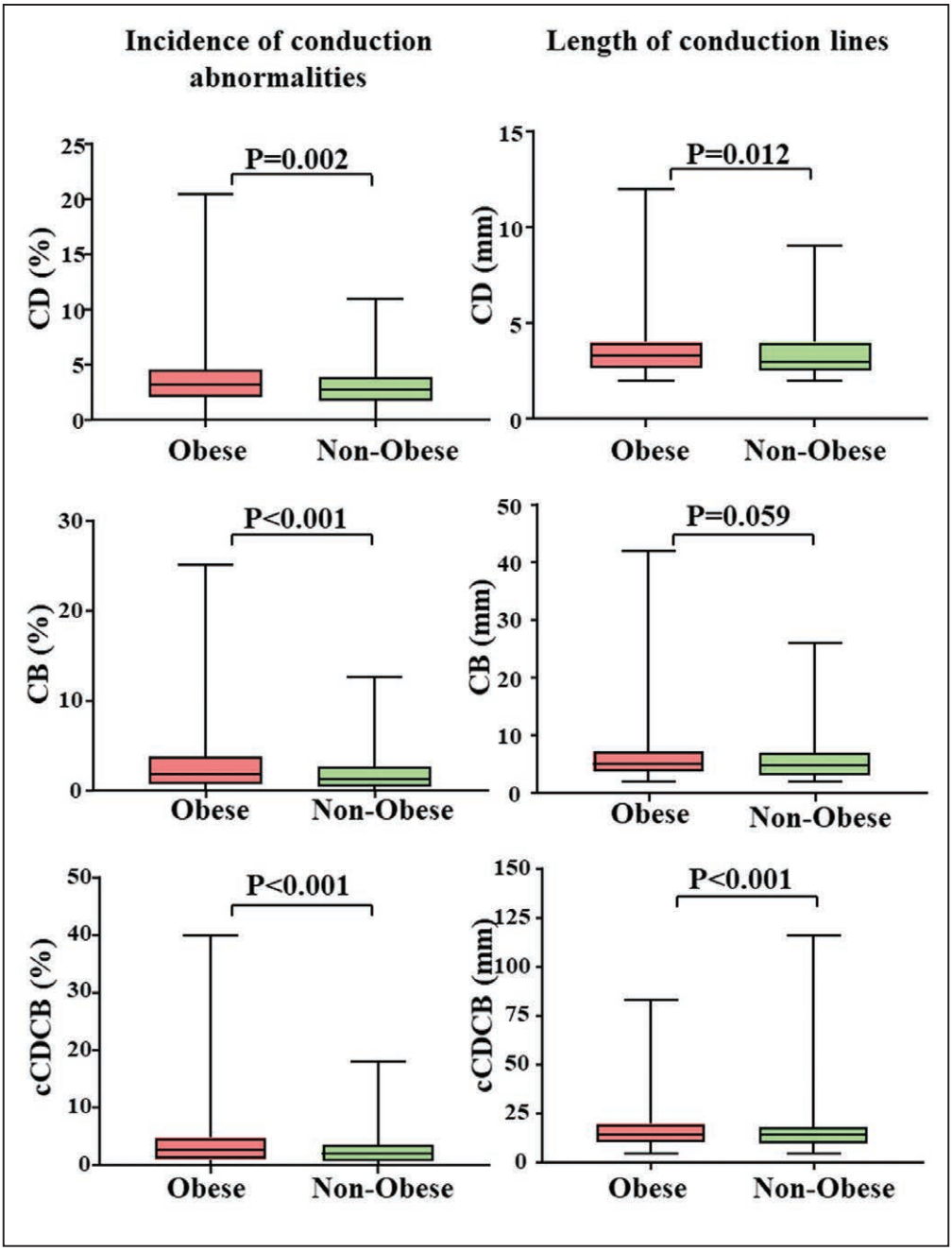

Figure 2. Graphs demonstrating the median and ranges (minimum-maximum) of the incidence (%) and length of conduction delay (CD), conduction block (CB), and continuous conduction delay conduction block (cCDCB) lines within the entire atria. Upper: there was not only a significant increase in the amount of CD in obese patients (*P*=0.002), but these CD lines of CD were also longer (*P*=0.012). The middle: obese patients had a significantly higher incidence of CB within the entire atria (*P*<0.001). Lower: both incidence and lines of continuous CDCB were significantly higher in obese compared with nonobese patients (*P*<0.001).

1.908; *P*=0.008), BMI (1.084; *P*<0.001), mitral valve disease (OR, 3.013; *P*=0.039), and coronary artery bypass grafting (OR, 9.159; *P*<0.001). Though none of the electrophysiological parameters showed any significant association with incidence of EPoAF in the univariate analysis, the multivariate model showed a significant relation between incidence of CB (OR, 1.307; *P*=0.012) and EPoAF. Other significant associations between clinical parameters and incidence of EPoAF include HL (OR, 2.921; *P*<0.001), LAE (OR, 2.302; *P*=0.008), and BMI (OR, 1.064; *P*=0.037).

DISCUSSIONS

Key Findings

This study compared the incidence, extensiveness, and severity of areas of CD and/or CB at the atrial epicardial

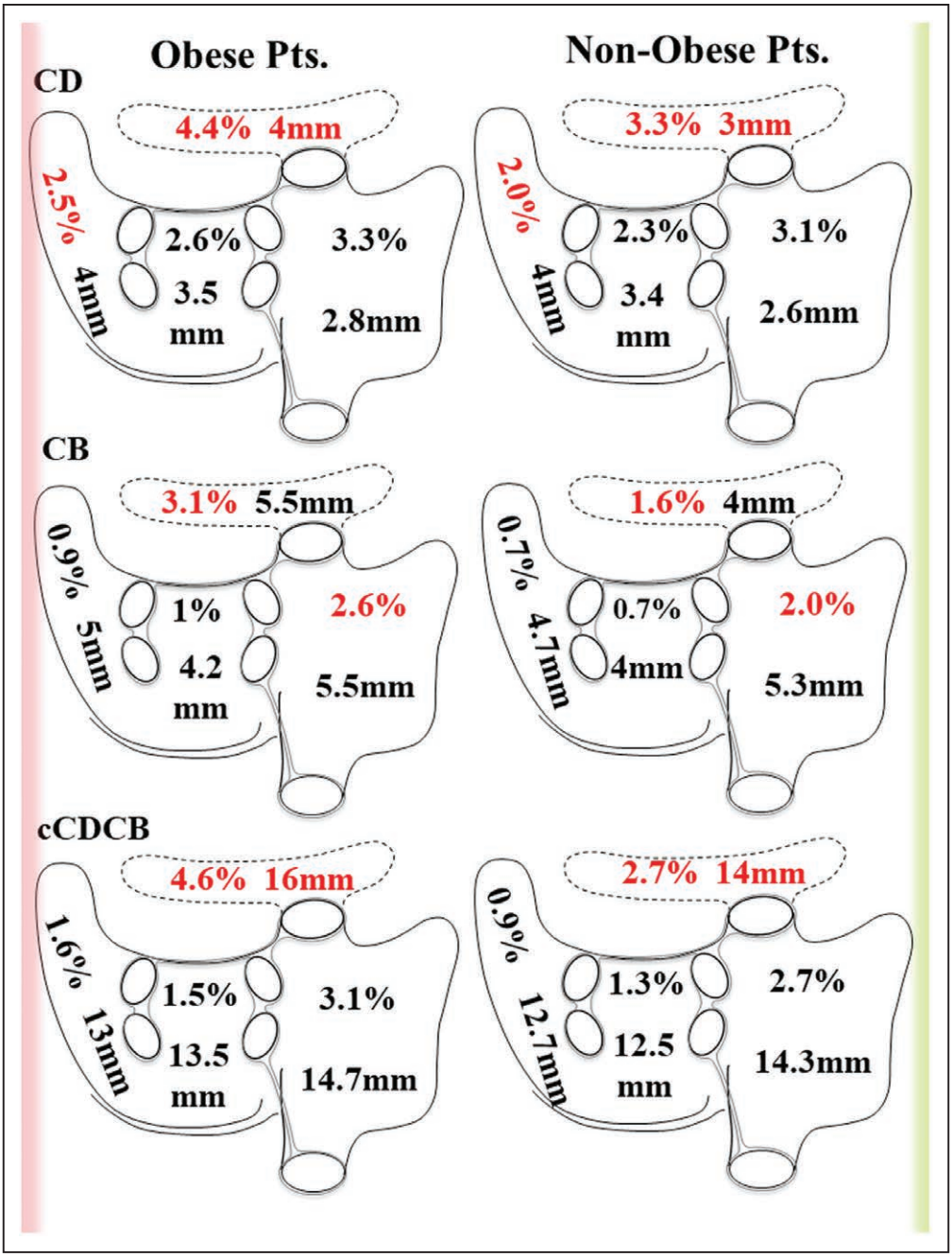

Figure 3. Distribution of incidences and lengths of conduction delay (CD), conduction block (CB), and continuous conduction delay conduction block (cCDCB) lines within predefined atrial mapping sites presented on a schematic posterior view of the atria.

The areas that are significantly different between obese and nonobese patients are highlighted in red. The upper shows that BB was a predilection site of higher incidences (P=0.002) and longer lines of CD (P<0.001) in obese patients. In these patients, the amount of CD was also significantly higher in the LA region (P=0.047). The middle panel demonstrates that the incidence of CB was significantly higher in obese compared with nonobese patients at Bachmann Bundle (BB; P<0.001) and right atria, respectively (P=0.049). The lower panel shows that BB is the only area with a higher incidence (P<0.001) and longer lines (P=0.017) of cCDCB in obese compared with nonobese patients.

surface during SR between obese and nonobese patients without previous history of AF measured at high resolution scale. In obese patients, the overall incidence of CD, CB, and cCDCB is higher and CD and cCDCB lines are longer. There are more conduction disorders at BB and this area has higher incidences of CD, CB, cCDCB and longer CD or cCDCB lines. The severity of CB is also higher, particularly in the BB and PV areas. In addition, obese patients have a higher incidence of early de-novo postoperative atrial fibrillation. BMI and the overall amount of CB were independent predictors for incidence of early postoperative atrial fibrillation.

Table 2. Conduction Parameters Within Predefined Atrial Areas

Region	Conduction Parameter	Obese Patients	Nonobese Patients	*P* Value
BB	CD (%)	4.4 (0.3–20.4)	3.3 (0.0–10.9)	0.002
	CB (%)	3.1 (0.0–25.1)	1.6 (0.0–12.6)	<0.001
	cCDCB (%)	4.6 (0.0–39.8)	2.7 (0.0–17.9)	<0.001
	Length of CD lines, mm	4.0 (2.0–8.0)	3.0 (2.0–9.0)	<0.001
	Length of CB lines, mm	5.5 (2.0–23.0)	4.0 (2.0–23.0)	0.190
	Length of cCDCB lines, mm	16.0 (6.0–83.0)	14.0 (6.0–116.0)	0.017
	ΔCT, ms	15.1 (12.0–43.0)	14.2 (12.0–39.0)	0.008
RA	CD (%)	3.3 (0.5–13.0)	3.1 (0.3–10.2)	0.422
	CB (%)	2.6 (0.0–18.1)	2.0 (0.0–11.7)	0.049
	Continuous cCDCB (%)	3.1 (0.0–23.7)	2.7 (0.0–15.4)	0.088
	Length of CD lines, mm	2.8 (2.0–5.3)	2.6 (2.0–5.1)	0.543
	Length of CB lines, mm	5.5 (2.0–19.6)	5.3 (2.0–22.5)	0.453
	Length of cCDCB lines, mm	14.7 (5.3–42.7)	14.3 (4.0–47.2)	0.309
	ΔCT, ms	17.9 (12.3–43.0)	17.0 (12.0–42.0)	0.070
LA	CD (%)	2.5 (0.0–9.1)	2.0 (0.0–8.6)	0.047
	CB (%)	0.9 (0.0–15.2)	0.7 (0.0–5.7)	0.186
	cCDCB (%)	1.6 (0.0–9.8)	0.9 (0.0–6.5)	0.211
	Length of CD lines, mm	4.0 (2.0–9.0)	4.0 (2.0–8.2)	0.666
	Length of CB lines, mm	5.0 (2.0–24.7)	4.7 (2.0–26.0)	0.763
	Length of cCDCB lines, mm	13.0 (4.0–36.2)	12.7 (5.0–46.0)	0.757
	ΔCT, ms	14.7 (12.0–45.0)	14.1 (12.0–38.0)	0.650
PV	CD (%)	2.6 (0.0–11.0)	2.3 (0.0–10.7)	0.554
	CB (%)	1 (0.0–13.2)	0.7 (0.0–8.7)	0.281
	cCDCB (%)	1.5 (0.0–16.0)	1.3 (0.0–9.8)	0.459
	Length of CD lines, mm	3.5 (2.0–12.0)	3.4 (2.0–8.0)	0.806
	Length of CB lines, mm	4.2 (2.0–42.0)	4.0 (2.0–18.0)	0.259
	Length of cCDCB lines, mm	13.5 (4.0–77.0)	12.5 (4.0–33.5)	0.315
	ΔCT, ms	14.5 (12.0–43.0)	13.5 (12.0–36.0)	0.020

P<0.05 statistically significant values. BB indicates Bachmann bundle; CB, conduction block; cCDCB, continuous conduction delay conduction block; CD, conduction delay; LA, left atrium; PV, pulmonary veins; and RA, right atrium.

Obesity and Conduction Abnormalities

Previous studies have shown the epidemiological link between obesity and AF; however, the underlying electrophysiological characteristics and mechanisms are yet to be defined.[13–15] BMI, as a measure of systemic adiposity is associated with an increase in the amount of pericardial and epicardial fat.[16,17] Through its paracrine effect, epicardial adipose tissue contributes to the development of atrial interstitial fibrosis.[18] Infiltration of myocardium with adipocytes along with fibrosis results in heterogenous atrial conduction caused by increased nonuniform anisotropy, which contributes to endo and epicardial electrical dissociation.[19–21] This process in turn favors development of atrial reentry and hence AF.[18]

Our study shows that the incidence and extent of atrial conduction abnormalities were significantly higher in obese compared with nonobese patients. Similar findings were presented by Magnani et al in a cross-sectional analysis to determine the association of obesity with P wave indices. Multivariable analysis of resting 12-lead ECG recordings showed significant progressive increases in PR interval, P wave maximum duration, and P wave terminal force in overweight and obese patients compared with the reference group.[22] All these findings support the involvement of obesity in evolvement of atrial electropathology including conduction abnormalities. Moreover, our study shows that BB was a predilection site for conduction disorders. BB, the preferential inter-atrial connection ensures bi-atrial synchronous contraction.[23] Depositions of epicardial adipose tissue in this region stimulates development of atrial interstitial fibrosis and therefore contribute to interatrial conduction abnormalities and subsequently promote the risk for arrhythmogenesis.[24] Though obesity was associated with a statistical higher incidence and extent of conduction abnormalities, the magnitude of differences between obese and nonobese patients remains relatively small. These findings may therefore be related to the large sample used in the comparison.

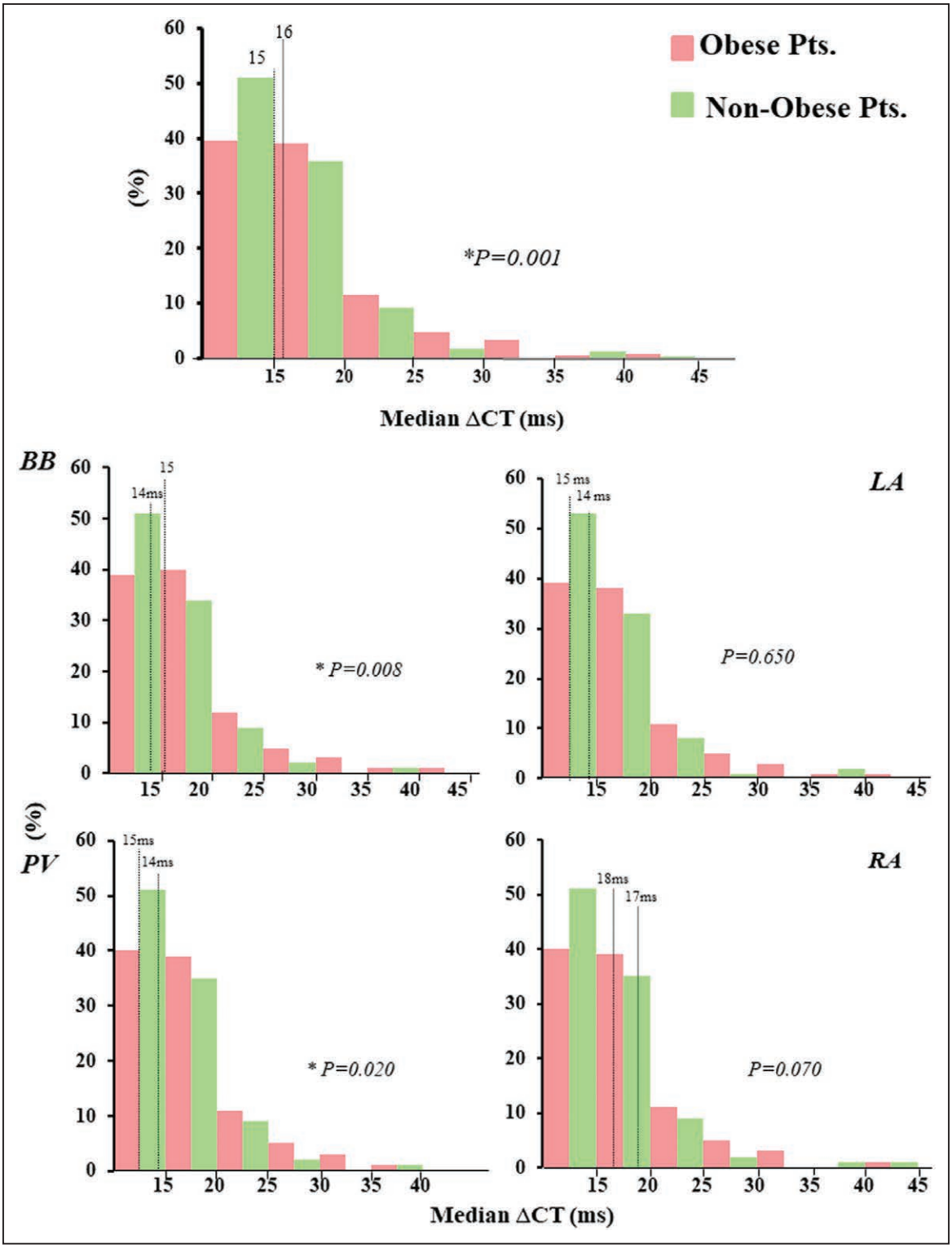

Figure 4. Bar graphs demonstrating the degree of severity of conduction block (CB).
The *y* axis represents the relative distribution of ΔCT (%), provided ΔCT ≥12 ms, for obese and nonobese patients separately. The *x* axis represents the median length of conduction time. The *P* value refers to the difference in median ΔCT between obese and nonobese patients. The upper panel shows a significant increase in median ΔCT (ms) in obese compared with nonobese patients. Severity of CB was also higher in obese patients particularly in Bachmann bundle (BB) and pulmonary vein (PV) area, as shown in left mid and lower panels, respectively. LA indicates left atrium; and RA, right atrium.

Table 3. Clinical and Electrophysiological Risk Factors for Incidence of EPoAF

Variables	OR	95% CI for OR	*P* Value
Univariate analysis			
HT	1.559	1.149–2.115	0.004*
HL	1.332	0.991–1.792	0.058
DM	1.126	0.816–1.554	0.471
LAE	1.908	1.186–3.072	0.008*
BMI	1.084	1.050–1.120	<0.001*
AVD	1.321	0.487–2.061	0.219
AVD+CABG	1.486	0.958–2.304	0.177
CABG	1.114	0.662–1.217	0.486
MVD	3.013	1.058–8.581	0.039*
MVD+CABG	9.159	2.925–28.679	<0.001*
CD%	1.021	0.953–1.093	0.562
CB%	1.026	0.973–1.083	0.339
Continuous CDCB%	1.003	0.960–1.047	0.906
CD lines	0.975	0.872–1.091	0.661
CB lines	1.012	0.977–1.048	0.493
Continuous CDCB lines	1.004	0.989–1.020	0.606
Multivariate analysis			
HT	1.551	0.915–2.627	0.103
HL	2.921	1.706–5.002	<0.001*
DM	1.667	0.979–2.838	0.060
LAE	2.302	1.243–4.261	0.008*
BMI	1.064	1.004–1.127	0.037*
MVD	1.110	0.321–3.846	0.869
MVD+CABG	4.146	0.958–17.938	0.057
CD%	1.026	0.832–1.264	0.814
CB%	1.307	1.060–1.613	0.012*
Continuous CDCB%	0.810	0.663–0.991	0.120
CD lines	0.872	0.693–1.096	0.239
CB lines	0.969	0.894–1.050	0.443
Continuous CDCB lines	1.023	0.984–1.063	0.248

AVD indicates atrial valve disease; BMI, body mass index; CABG, coronary artery bypass grafting; CB, conduction block; CD, conduction delay; DM, diabetes mellitus; EPoAF, early postoperative atrial fibrillation; HL, hyperlipidemia; HT, hypertension; LAE, left atrial enlargement; MVD, mitral valve disease; and OR, odds ratio.

*Statistically significant values ($P<0.05$).

Obesity, Conduction Abnormalities, and EPoAF

Previous studies have demonstrated that BMI, a measure of overall adiposity, is a strong independent associated factor with not only AF but also PoAF.[15,25–28] In a meta-analysis of the association between obesity and postoperative atrial fibrillation in patients without previous history of AF, Phan et al found that obesity was associated with a significant risk of postoperative atrial fibrillation. Moreover, Munger et al showed that obesity was associated with shorter effective refractory period (ERP) in the LA, proximal and distal PV in 63 patients with AF undergoing catheter ablation. In our study, we found that obese patients had a higher incidence of EPoAF. Multivariate analysis showed that a 1.064 unit increase in BMI resulted in a higher incidence of EPoAF ($P=0.037$). Previous studies demonstrated that 1-unit rise in BMI increases the frequency of newly developed AF by 4%.[18] Comparable to other studies, we also found other comorbidities contributing to development of EPoAF including incidence of mitral valve disease, hypertension, and left atrial enlargement.[29]

In our study, the incidence of CB in the entire atria independently predicted development of EPoAF. Karaca et al[30] investigated the value of interatrial conduction time for the prediction of EPoAF using intraoperative transoesophageal echocardiography and found a significant increase in EPoAF in patients with a longer interatrial conduction time. The observation in our study that obese patients had overall more conduction abnormalities than nonobese patients and both CB incidence and BMI were predictive of EPoAF suggests that obesity-related heterogeneity in conduction plays an important role in development of EPoAF.

Conclusions

Obesity may predispose to a larger incidence, extensiveness, and severity of CD and/or CB at the atrial epicardial surface during SR in patients without a history of AF. There were more conduction disorders at BB, and this area has a higher incidence of CD, CB, and cCDCB and longer CD and cCDCB lines. The severity of CB is also higher, particularly in the BB and PV areas. However, whether obesity alone is responsible for all the electropathological abnormalities remains to be further investigated. To determine the impact of obesity-induced atrial conduction abnormalities on long-term clinical outcome, further prospective studies are mandatory.

As experimental studies showed that the effect of obesity on atrial electropathology is reversible with weight control, further studies are needed to evaluate whether preventive lifestyle also reverses electropathology in humans.

Study Limitations

Recordings of the interatrial septum could not be obtained during closed beating heart epicardial mapping approach. Due to the invasive mapping approach, healthy patients could not be included.

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Disclosures

None.

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