Low-voltage potentials contribute to postoperative atrial fibrillation development in obese patients

Corina Schram-Serban, DVM,* Mathijs S. van Schie, MSc,* Paul Knops, BSc,* Charles Kik, MD,† Ad J.J.C. Bogers, MD, PhD,† Natasja M.S. de Groot, MD, PhD*

From the *Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands, and †Department of Cardiothoracic Surgery, Erasmus Medical Center, Rotterdam, The Netherlands.

BACKGROUND Obesity predisposes to the development of atrial fibrillation (AF); however, the pathophysiology underlying this relation is only partly understood.

OBJECTIVE As low-voltage areas are considered indicators of the arrhythmogenic substrates promoting AF, our study aimed to compare the extensiveness of atrial low-voltage areas between obese and non obese patients by using high-resolution epicardial mapping in order to identify predilection sites of low-voltage areas.

METHODS A total of 430 patients (131 (30%) obese and 299 (70%) nonobese) were matched resulting in 212 patients (body mass index [BMI] ≥30 kg/m²; n = 106; BMI <30 kg/m²; n = 106) undergoing cardiac surgery (mean age 63 ± 11 years; 161 male). All patients underwent epicardial mapping of the right atrium, Bachmann bundle (BB), and left atrium during sinus rhythm. Low-voltage potentials were defined as potentials with peak-to-peak amplitudes below the fifth percentile of all potential amplitudes obtained from nonobese patients.

RESULTS Compared with nonobese patients, obese patients have potentials with lower voltages (median of medians) (4.5 mV [0.4–16.2 mV] vs 5.5 mV [0.8–18.0 mV]; P < .001), especially at BB (4.1 mV [0.4–12.3 mV] vs 6.2 mV [1.0–14.3 mV]; P < .001) and left atrium (5.1 mV [0.5–10.1 mV] vs 6.2 mV [0.8–15.9 mV]; P = .003). The percentage of low-voltage potentials was higher in obese (median 3.6% [0.0%–77.1%]) than in nonobese (median 2.3% [0.0%–57.9%]) patients (P < .001), again at BB (obese: 2.9% [0.0%–7.7%] vs nonobese: 0.9% [0.0%–42.0%]; P < .001).

CONCLUSION Obesity may predispose to an overall decrease in atrial voltage and a higher percentage in low-voltage potentials. BB was a predilection area for low voltage within the atria of obese patients.

KEYWORDS Obesity; Epicardial mapping; Low-voltage; Early postoperative atrial fibrillation; Sinus rhythm

Introduction

Obesity is a well-established independent risk factor for the most common type of arrhythmia—atrial fibrillation (AF).1–3 In obese patients, risk factors (eg, hypertension [HT], diabetes mellitus, hyperlipidemia [HL], and coronary artery disease [CAD]) and atrial substrate alterations4 (epicardial fat infiltrations, atrial fibrosis, and enhanced local inflammation due to increased adipocytokines and proinflammatory cytokines) are related to AF development.

Previous experimental and human studies have reported the association between the presence of epicardial adipose tissue (EAT) and atrial electrophathology.4,5

In a previous study, we showed that obese patients undergoing cardiac surgery have higher incidences of conduction disorders than do nonobese patients, making them more vulnerable to developing early postoperative AF (EPoAF).6

In 16 obese patients, Mahajan et al7 observed lower regional mean voltages of bipolar electrograms recorded during sinus rhythm (SR) in the posterior and inferior left atrial (LA) walls as compared with 10 nonobese patients.

In the ovine experimental model of chronic obesity,8 there was an increased voltage heterogeneity with the reduction of voltages in the posterior LA wall in addition to the increased incidence of complex fractionated electrograms and heterogeneous conduction.

As low-voltage areas are considered to be indicators of the arrhythmogenic substrates promoting AF in patients with a...
history of AF, low-voltage areas in the LA are targeted in addition to pulmonary vein (PV) isolation to prevent AF recurrences. It is unknown whether this approach is also suitable for obese patients, as they may have a more extensive arrhythmogenic substrate. So far, it is unknown whether and to what extent voltage distributions differ between nonobese and obese patients and whether there is a larger amount of low-voltage areas in the latter group.

The aim of our study was to compare the extensiveness and severity of atrial low-voltage areas identified during SR between obese and matched nonobese patients measured at a high-resolution scale.

**Methods**

**Study population**

The study population consisted of adult patients scheduled for elective cardiac surgery for CAD, either isolated or in combination with aortic (CAD + AVD) or mitral (CAD + MVD) valve disease, isolated AVD or MVD, or correction of congenital heart defects. Exclusion criteria were history of AF, prior ablation of atrial tachyarrhythmias, severe renal failure, atrial pacing, and patients requiring mechanical or inotropic support. Patients with sleep apnea were not included in the study. The population was divided into 2 categories: (1) the study group: obese patients (body mass index [BMI] ≥30 kg/m²) and (2) the control group: nonobese patients (BMI <30 kg/m²).

This study was conducted as part of 2 prospective observational projects including Quest for Arrhythmogenic Substrate of Atrial fibrillation (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 Center 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 before connecting the patient to cardiopulmonary bypass circulation. 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. 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.

Epicardial mapping during SR was conducted following a predefined mapping scheme as shown in Figure 1 (upper left panel), approaching the entire epicardial surface of the right atrium (RA), Bachmann bundle (BB), and LA. As previously described, the electrode array was shifted along imaginary lines with a fixed orientation at each position.

**Figure 1** Epicardial mapping during SR. The upper left panel shows the projection of the 192-unipolar electrode array on a schematic posterior view of the atria. The upper right panel shows epicardial unipolar potentials recorded during 3 seconds of SR at BB and the corresponding color-coded voltage map. The lower left panel shows typical examples of 9 unipolar potentials. The lower panel shows potential voltage defined as the peak-to-peak amplitude of the steepest deflection. A = atrial potential; BB = Bachmann bundle; LA = left atrium; LAT = local activation time; PV = pulmonary vein; RA = right atrium; SR = sinus rhythm; V = ventricular potential; VCI = vena cava inferior; VCS = vena cava superior.
Mapping of the RA began at the cavotricuspid isthmus and continued perpendicular to the caval veins toward the RA appendage. BB was mapped beginning at the tip of the LA appendage across the roof of the LA, behind the aorta toward the superior cavoatrial junction. Mapping of the LA was performed from the lower margin of the left inferior PV along the left atrioventricular groove toward the LA appendage. The PV area was mapped from the sinus transversus fold in between the right and left PVs toward the left atrioventricular groove.

From every atrial mapping site, 5 seconds of SR were recorded, including surface electrocardiogram (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

Semiautomatic analysis of unipolar electrogram morphology was performed using Python 3.6 software. Recording sites with ≥25% excluded or missing electrograms, injury potential electrograms, and premature atrial complexes or aberrant beats were excluded from the analysis. Local activation time was established by marking the steepest negative slope of an atrial deflection, with a minimum slope threshold of 0.05 mV/ms. The amplitude threshold was set at 2 times the signal noise level. All signal markings were manually checked and corrected by a consensus of 2 investigators.

Unipolar electrogram voltage was defined as the peak-to-peak amplitude of the steepest deflection. Unipolar electrograms with peak-to-peak amplitudes below the fifth percentile of all deflection amplitudes obtained from nonobese patients were known as low-voltage potentials.

### Evaluation of EPoAF

Rhythm was continuously monitored in all patients during the first 5 postoperative days. EPoAF was defined as the incidence of at least 1 AF episode with a duration of minimum 30 seconds. EPoAF was also confirmed by documentation in patient discharge letters and clinical notes.

### Statistical analysis

The analysis data set consisted of age- and sex-matched pairs of an obese patient and a nonobese counterpart. We constructed a propensity score for this purpose by using logistic regression, whereas the nearest nonobese neighbor (match tolerance 0.05) was linked to an obese patient. Following this approach, we were able to create 106 matched pairs.
starting from a larger (430 patients) pool of obese (131 patients) and nonobese (299 patients) patients.

We described and analyzed baseline characteristics of patients that compose the analysis data set. Normality of continuous data was first evaluated using the Shapiro-Wilk test, and continuous data are described as mean ± SD or median (minimum-maximum). Differences between obese and nonobese patients were evaluated using the Wilcoxon signed-rank test. Categorical data are described as number and percentage, whereas differences between obese and nonobese patients were evaluated using the McNemar test.

Conditional binary logistic regression was performed to determine the predictors of EPoAF. In univariable analysis, we considered the following potential predictors: HT, HL, diabetes mellitus, LA enlargement (LAE), BMI, AVD, AVD + coronary artery bypass grafting (CABG), CABG, MVD, MVD + CABG, median voltage, and percentage of low voltage. Multivariable analysis was performed following the 1 in 10 rule and on the basis of their association in the univariable analysis (2-sided P value of <.05). We did not apply a model reduction strategy, while 2-sided P values of .05 were considered statistically significant.

Statistical analysis was performed using IBM SPSS Statistics version 24 (IBM Corporation, Armonk, NY). Bonferroni correction was used to control for family-wise error when comparing voltage characteristics for the 4 atrial locations (a P value of <.0125 was considered significant). The Pearson correlation test was used to evaluate the linear relationship between electrophysiological parameters including median voltage and percentage of low voltage and conduction delay (in percentage), conduction block (CB) (in percentage), continuous conduction delay conduction block (in percentage), conduction delay lines (in millimeters), CB lines (in millimeters), and continuous conduction delay conduction block lines (in millimeters) in obese and nonobese patients separately. The data were collapsed from all the values per patient, extracting the median voltage and the median percentage per location and per patient. A 2-sided P value of <.05 was considered statistically significant.

Results

Study population

The baseline characteristics of both the obese (n = 106; mean age 64 ± 10 years; 78 male [74%]) and the nonobese (n = 106; mean age 62 ± 12 years; 83 male [78%]) group are presented in Table 1. Clinical characteristics between these groups differed only in BMI (32.9 ± 2.9 kg/m² vs 25.4 ± 2.4 kg/m²; P < .001). CABG 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 was 202,304 in the obese group (1909 ± 321 electrodes per patient) and 200,192 in the nonobese group (1889 ± 311 electrodes per patient; P = .411). After exclusion of 0.65% of the mapping sites because of electrograms with poor signal-to-noise ratios, 1333 (12.5 ± 4.2 per patient) and 1321 (12.4 ± 4.1 per patient) (P = .617) mapping locations were available for analysis.

Differences in unipolar voltage distribution

Figure 2 shows the median voltage of the entire atria for each individual obese and nonobese patients. The left panel shows that voltages were lower in obese than in nonobese patients (4.5 mV [0.4–16.2 mV] vs 5.5 mV [0.8–18.0 mV]; P < .001). The right panel shows that for potentials within the fifth percentile, the median amplitude was significantly lower in obese (median 1.3 mV [0.1–6.8 mV]) than in nonobese (median 1.6 mV [0.2–8.6 mV]) patients (P < .001).
significantly lower in obese (median 1.3 mV [0.1–6.8 mV]) than in nonobese (median 1.6 mV [0.2–8.6 mV]) patients ($P < .001$).

**Regional heterogeneity in unipolar voltages**

Regional differences in unipolar voltages between obese and nonobese patients are depicted in Figure 3 and summarized in Online Supplemental Table 1. As demonstrated in the upper panel, obese patients have significantly lower unipolar voltages, specifically at BB (obese: median 4.1 mV [0.4–12.3 mV] vs nonobese: median 6.2 mV [1.0–14.3 mV]; $P < .001$) and LA (obese: median 5.1 mV [0.5–10.1 mV] vs nonobese: 6.2 mV [0.8–15.9 mV]; $P = .003$).

Similarly, as shown in the lower panel of Figure 3, the fifth percentile of unipolar voltages was also significantly

![Figure 3](https://example.com/figure3.png)

**Figure 3** Graphic representation of differences in median and P5 voltage between obese and nonobese patients. The areas that are significantly different between obese and nonobese patients are highlighted in red. The upper panel shows a significantly lower median voltage in obese than in nonobese patients, particularly at BB ($P < .001$) and LA ($P = .003$). The lower panel shows that obese patients also have a significantly lower P5 voltage mainly at BB ($P < .001$) and LA ($P = .009$). Statistical significance: $P < .0125$. BB = Bachmann bundle; P5 = fifth percentile; Pt. = patient.
lower in obese than in nonobese patients at BB (obese: 1.1 mV [0.1–5.0 mV] vs nonobese: 1.9 mV [0.3–8.7 mV]; \(P < .001\)) and LA (obese: 1.3 mV [0.2–7.9 mV] vs nonobese: 1.7 mV [0.2–4.9 mV]; \(P = .009\)).

Spatial distribution of unipolar low-voltage potentials

Low-voltage areas were observed in all nonobese and obese patients. Figure 4 depicts examples of color-coded unipolar voltage maps obtained from typical obese and nonobese patients that were recorded from the RA, BB, LA, and PV. Although these maps demonstrate that there is a wide variation in unipolar voltages throughout the entire atrial surface in both the obese and the nonobese patient, the extent of low-voltage areas is higher in the obese patient. The cutoff value for low-voltage areas, defined as the fifth percentile of all unipolar voltages in nonobese patients, was 0.833 mV. Figure 5 shows incidences of low-voltage potentials within the entire atria for obese and nonobese patients separately. There was a significantly higher incidence of low-voltage potentials in obese (median 3.6% [0.0%–77.1%]) than in nonobese (median 2.3% [0.0%–57.9%]) patients (\(P < .001\)).

Predilection sites for low-voltage potentials

Figure 6 depicts the spatial distribution of low-voltage potentials for every atrial location separately; corresponding values are summarized in Online Supplemental Table 1. Although percentages of low-voltage potentials were similar between obese and nonobese patients within the majority of atrial locations, there was a significantly higher percentage of...
low-voltage potentials at BB in obese (2.9% [0.0%–77.1%]) than in nonobese (0.9% [0.0%–42.0%]) patients ($P < .001$).

**Correlations between heterogeneity in conduction and potential voltages**

In our previous article, we have shown that heterogeneity in conduction was higher in obese patients, thus increasing their vulnerability toward AF. Therefore, we wanted to assess the relationship between potential voltages including the extent of low-voltage areas and conduction abnormalities. Correlations between potential voltages and various conduction parameters for all patients obese and nonobese patients separately are summarized in Online Supplemental Table 2. Most correlations were weak to moderate, though significant. The highest correlation coefficient was observed between the percentage of low-voltage potentials and the percentage of CB (entire population: $\rho = 0.442$, $P < .001$; obese group: $\rho = 0.473$, $P < .001$; and nonobese patients: $\rho = 0.381$, $P < .001$).

**Risk factors for EPoAF**

As shown in our previous article, the incidence of EPoAF in our population was higher in obese (36%; $n = 38$) than in nonobese (17%; $n = 18$) patients ($P = .003$). Univariable and multivariable predictors of EPoAF with their respective odds ratio [OR] (95% confidence interval) are summarized in Table 2. Significant univariable predictive factors for the incidence of EPoAF include HT (OR 1.559; $P = .004$), LAE (OR 1.908; $P = .008$), BMI (OR 1.084; $P < .001$), MVD (OR 3.013; $P = .039$), MVD + CABG (OR 9.159; $P < .001$), and percentage of low-voltage potentials (OR 1.023; $P = .002$). In the multivariable analysis, percentage of low-voltage potentials was the only significant electrophysiological parameter for the development of EPoAF (OR 1.023; $P = .002$). Other significant associations between clinical parameters and the incidence of EPoAF include HT (OR 2.496; $P < .001$), LAE (OR 1.890; $P = .020$), and BMI (OR 1.058; $P = .028$).

**Discussion**

**Key findings**

This study compared the magnitude and spatial distribution of unipolar voltages between obese and nonobese patients. Obesity is associated with lower unipolar voltages, particularly at BB and LA. Low-voltage areas were predominantly found at BB. Moderate correlations were observed between voltage characteristics and conduction abnormalities in both obese and nonobese patients. In addition, both BMI

---

**Figure 6** Graphic representation of the relative distribution of low-voltage potentials within different atrial areas. Although there were a higher percentage of low-voltage potentials within all atrial areas, BB was the only region where the differences between obese and nonobese patients were significant ($P < .001$). Statistical significance: $P < .0125$. BB = Bachmann bundle; LA = left atrium; Pt. = patient; PV = pulmonary vein; RA = right atrium.
and percentage of low-voltage areas were independent predictors for the development of EPoAF.

Obesity and voltage characteristics

Previous studies have shown the link between obesity and development of AF; however, the underlying electrophysiological mechanism are still incompletely understood.\(^\text{13,14}\) BMI has been associated with an increased amount of pericardial and epicardial fat.\(^\text{15,16}\) EAT, through its paracrine effect, contributes to the development of atrial interstitial fibrosis.\(^\text{17}\)

In a study conducted by Mahajan et al,\(^\text{2}\) low atrial voltages were observed in the posterior and inferior LAs. These areas were adjacent to the posteriorly located fat pad in obese patients undergoing electroanatomic mapping during SR before AF ablation.\(^\text{2}\) In our study population, consisting of patients without a history of AF, we observed that obesity was associated with a higher incidence of low-voltage potentials, particularly at BB. BB is the preferential interatrial connection ensuring biatrial synchronous contraction.\(^\text{18}\) This observation suggests that deposition of EAT may be more pronounced at BB. Indeed, Saremi et al\(^\text{19}\) demonstrated that in some patients BB is replaced by fat.

Our previous study showed relationships between conduction abnormalities and obesity.\(^\text{6}\) In this study, we demonstrated correlations between conduction abnormalities and low-voltage areas. This finding further supports the associations between obesity and electrophysiological abnormalities.

### Table 2

| Variable                  | OR   | 95% CI for OR | P   |
|---------------------------|------|---------------|-----|
| **Univariable analysis**  |      |               |     |
| HT                        | 1.559| 1.149–2.115   | .004|
| HL                        | 1.332| 0.991–1.792   | .058|
| DM                        | 1.126| 0.816–1.554   | .471|
| LAE                       | 1.908| 1.186–3.072   | .008|
| BMI                       | 1.084| 1.050–1.120   | <.001|
| AVD                       | 1.321| 0.487–2.061   | .219|
| AVD + CABG                | 1.486| 0.958–2.304   | .177|
| CABG                      | 1.114| 0.662–1.217   | .486|
| MVD                       | 3.013| 1.058–8.581   | .039|
| MVD + CABG                | 9.159| 2.925–28.679  | <.001|
| Median voltage            | 1.279| 0.822–2.938   | .552|
| Percentage of low voltage | 1.023| 1.008–1.038   | .002|
| **Multivariable analysis**|      |               |     |
| HT                        | 2.496| 1.519–4.102   | <.001|
| LAE                       | 1.890| 1.107–3.227   | .020|
| BMI                       | 1.058| 1.006–1.112   | .028|
| MVD + CABG                | 4.953| 1.344–18.256  | .016|
| Percentage of low voltage | 1.041| 1.017–1.064   | .001|

BMI was used as a continuous variable in the conditional univariable and multivariable binary logistic regression analysis.

AVD = atrial valve disease; BMI = body mass index; CABG = coronary artery bypass grafting; CI = confidence interval; DM = diabetes mellitus; EPOAF = early postoperative atrial fibrillation; HL = hyperlipidemia; HT = hypertension; LAE = left atrial enlargement; MVD = mitral valve disease; OR = odds ratio.

Significant P values are written in boldface.

Obesity, voltage characteristics, and EPoAF

Previous studies have shown that BMI, as a measure of adiposity, is a strong independent factor for both AF and EPoAF.\(^\text{14,20,21}\) In a meta-analysis focusing on patients without a history of AF, Phan et al\(^\text{22}\) demonstrated that obesity was associated with an increased risk of developing EPoAF. In our study, the multivariable analysis showed that a 1.058-unit increase in BMI resulted in a higher incidence of EPoAF (P = .028). Csige et al\(^\text{22}\) demonstrated that a 1-unit increase in BMI can increase the incidence of newly developed AF by 4%. Clinical factors including HT, HL, and LAE were also independently associated with the development of EPoAF. These findings were reported by prior studies.\(^\text{23}\)

Atrial fibrillation is a feature in obesity-related structural remodeling. Prior studies demonstrated relations between histological evidence of increased atrial fibrosis and indirect evidence of reduced endocardial atrial voltages.\(^\text{24}\) Development of obesity is associated with hypoxia of the expanded adipose tissue, resulting in adipose tissue fibrosis and production of various adipocytokines including transforming growth factor-β family.\(^\text{25}\) The combination between increased epicardial adiposity, atrial fibrosis, and altered 3-dimensional atrial architecture could be proarrhythmia with an increased likelihood of conduction heterogeneity that may sustain reentry.\(^\text{24}\) Our previous study has shown that the incidence of CB was an independent predictor for EPoAF occurrence.\(^\text{6}\) In this study, we found that the percentage of low-voltage potentials is also independently associated with the development of EPoAF in obese patients. The correlation between the 2 electrophysiological parameters could therefore potentially explain the higher risk of EPoAF development in obese patients.

Study limitations

Recordings of the interatrial septum could not be obtained during the closed beating heart epicardial mapping approach. Because of the invasive mapping approach, healthy patients could not be included. EAT, whenever present on the atria, was not dissected before myocardial sampling. Distribution of EAT could not be examined through imaging because of logistic reasons. Lipotoxicity of the underlying myocardial tissue was not assessed.

Conclusion

Obesity may predispose to an overall decrease in atrial voltage and a higher percentage in low-voltage potentials. BB was a predilection area for low voltage within the atria of obese patients. However, whether obesity alone is responsible for low-voltage areas remains to be further investigated. In order to determine the impact of obesity-induced low-voltage areas during long-term clinical outcome, further prospective studies are mandatory.
Acknowledgments
We thank F.B.S. Oei, MD, J.A. Bekkers, MD, P.C. van de Woestijne, MD, W.J. van Leeuwen, MD, Y.J.H.J. Taverne, MD, PhD, O. Birim, MD, E.A.F. Mahtab, MD, M.W.A. Bekker, MD, and F.R.N. van Schaagen, MD, for their contribution to this work.

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2022.01.027.

References
1. Dublin S, French B, Glazer NL, et al. Risk of new-onset atrial fibrillation in relation to body mass index. Arch Intern Med 2006;166:2322–2328.
2. Mahajan R, Nelson A, Pathak RK, et al. Electroanatomical remodeling of the atria in obesity: impact of adjacent epicardial fat. JACC Clin Electrophysiol 2018;4:1529–1540.
3. Tedrow UB, Conen D, Ridker PM, et al. Heterogeneity in conduction disorders during sinus rhythm. Int J Cardiol 2017;249:220–225.
4. Teuwen CP, Ramdjan TT, Gotte M, et al. Time course of atrial fibrillation in patients with congenital heart defects. Circ Arrhythm Electrophysiol 2015;8:1065–1072.
5. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol 2007;49:565–571.
6. Wang TJ, Patise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. JAMA 2004;292:2371–2377.
7. Sons HU, Hoffmann V. Epicardial fat cell size, fat distribution and fat infiltration of the right and left ventricle of the heart. Anat Anz 1986;161:355–373.
8. Katririssi D, Sougiannis D, Giuzitzioglou E, Kourlabia G, Ellenbogen KA. Regional endocardial left atrial voltage and electrogram fractionation in patients with atrial fibrillation. J Cardiovasc Electrophysiol 2008;19:1254–1258.
9. Teuwen CP, Yaksh A, Teuwen CP, et al. Spatial distribution of conduction disorders during sinus rhythm. Int J Cardiol 2017;249:220–225.
10. Teuwen CP, Yaksh A, Lanters EA, et al. Relevance of conduction disorders in Bachmann’s bundle during sinus rhythm in humans. Circ Arrhythm Electrophysiol 2016;9:e003972.
11. Teuwen CP, Ramdjan TT, Gotte M, et al. Time course of atrial fibrillation in patients with congenital heart defects. Circ Arrhythm Electrophysiol 2015;8:1065–1072.
12. Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol 2007;49:565–571.
13. Wang TJ, Patise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. JAMA 2004;292:2371–2377.
14. Sons HU, Hoffmann V. Epicardial fat cell size, fat distribution and fat infiltration of the right and left ventricle of the heart. Anat Anz 1986;161:355–373.
15. Iacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Relation between epicardial adipose tissue and left ventricular mass. Am J Cardiol 2004;94:1084–1087.
16. Sugi I, Ujyoris D, Szabo Z, et al. The impact of obesity on the cardiovascular system. J Diabetes Res 2018;2018:3407306.
17. van Campenhout MJ, Yaksh A, Kik C, et al. Bachmann’s bundle: a key player in the development of atrial fibrillation? Circ Arrhythm Electrophysiol 2013;6:1041–1046.
18. Sarem F, Torrone M, Yashar N. Cardiac conduction system: delineation of anatomic landmarks with multidetector CT. Indian Pacing Electrophysiol J 2009;9:318–333.
19. Serbon C, Arinze JT, Starreveld R, et al. Time course of atrial fibrillation in patients with congenital heart defects. Circ Arrhythm Electrophysiol 2015;8:1065–1072.
20. Munger TM, Dong YX, Masaki M, et al. Electrophysiological and hemodynamic characteristics associated with obesity in patients with atrial fibrillation. J Am Coll Cardiol 2012;60:851–860.
21. Phan K, Kluoong JN, Xu J, Kanagaratnam A, Yan TD. Obesity and postoperative atrial fibrillation in patients undergoing cardiac surgery: systematic review and meta-analysis. Int J Cardiol 2016;17:49–57.
22. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Europace 2010;12:1360–1420.
23. Lau DH, Schotten U, Mahajan R, et al. Novel mechanisms in the pathogenesis of atrial fibrillation: practical applications. Eur Heart J 2016;37:1573–1581.
24. Sun K, Halberg N, Khan M, Magalang UJ, Scherer PE. Selective inhibition of hypoxia-inducible factor 1α ameliorates adipose tissue dysfunction. Mol Cell Biol 2013;33:904–917.