Journal of Cardiology 66 (2015) 361–369

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Review

Obesity and atrial fibrillation: A comprehensive review of the pathophysiological mechanisms and links

Christos A. Goudis (MD)[a], Panagiotis Korantzopoulos (MD, PhD)[b,*], Ioannis V. Ntalas (MD)[b], Eleftherios M. Kallergis (MD, PhD)[c], Dimitrios G. Ketikoglou (MD, PhD)[d]

[a] Department of Cardiology, General Hospital of Grevena, Grevena, Greece
[b] First Department of Cardiology, University of Ioannina Medical School, Ioannina, Greece
[c] Department of Cardiology, University Hospital of Heraklion, Heraklion, Greece
[d] Department of Cardiology, Interbalkan Medical Center, Thessaloniki, Greece

ARTICLE INFO

Article history:
Received 25 December 2014
Received in revised form 15 March 2015
Accepted 2 April 2015
Available online 7 May 2015

Keywords:
Obesity
Epicardial adipose tissue
Atrial fibrillation
Atrial remodeling

ABSTRACT

Obesity is a worldwide health problem with epidemic proportions that has been associated with atrial fibrillation (AF). Even though the underlying pathophysiological mechanisms have not been completely elucidated, several experimental and clinical studies implicate obesity in the initiation and perpetuation of AF. Of note, hypertension, diabetes mellitus, metabolic syndrome, coronary artery disease, and obstructive sleep apnea, represent clinical correlates between obesity and AF. In addition, ventricular adaptation, diastolic dysfunction, and epicardial adipose tissue appear to be implicated in atrial electrical and structural remodeling, thereby promoting the arrhythmia in obese subjects. The present article provides a concise overview of the association between obesity and AF, and highlights the underlying pathophysiological mechanisms.

Contents

* Corresponding author at: Department of Cardiology, University Hospital of Ioannina, 45110 Ioannina, Greece. Tel.: +30 2651045654; fax: +30 2651007017.
E-mail addresses: p.korantzopoulos@yahoo.gr, pkorantz@cc.uoi.gr (P. Korantzopoulos).

http://dx.doi.org/10.1016/j.jjcc.2015.04.002
0914-5087/

Introduction

Atrial fibrillation (AF) is the commonest arrhythmia in clinical practice and is associated with increased cardiovascular morbidity and mortality [1,2]. Obesity represents a novel risk factor for AF associated with a 50% increased incidence [3]. Even though the pathophysiological substrates and links implicating obesity in AF occurrence are not completely understood, various comorbidities as well as ventricular adaptation and epicardial adipose tissue appear to play a crucial role (Fig. 1). This article provides a comprehensive and critical overview of the mechanisms facilitating AF initiation and perpetuation in obese subjects.

Obesity as a risk factor for atrial fibrillation

A mounting body of evidence indicates an association between obesity and AF [3–17]. Indeed, obese individuals have an almost 50% increased risk for AF compared to nonobese [3,4]. Specifically, Wang et al. observed a 4% increase in AF risk per 1-U increase in body mass index (BMI), at a mean follow-up of 13.7 years [3]. The Danish Diet, Cancer, and Health Cohort Study indicated a higher risk of AF associated with increased anthropometric measurements such as height, weight, BMI, hip circumference, and waist circumference, as well as with increased bioimpedance-derived measures of body fat mass, body fat percentage, and lean body mass [7]. It has also been reported that overweight and obese young men have more than a 2-fold risk of AF compared with young men of normal weight [16], while obesity is an independent risk factor for AF among young and essentially healthy fertile women despite the low incidence of the arrhythmia [11]. Resistin, a hormone that is abundantly secreted from lipid cells, is linked to type 2 diabetes and obesity. Obese people appear to have higher resistin levels compared to healthy subjects and this increase correlates with BMI [18]. Furthermore, patients with paroxysmal and persistent AF were found to have higher resistin levels compared to controls [18]. In cardiothoracic surgery cohorts, the risk for postoperative AF in obese patients is also increased compared to nonobese [19,20], and this risk increases progressively with rising BMI [20]. In a recent meta-analysis, Hernandez et al. showed that obese patients undergoing cardiac operations have a modestly higher risk of postoperative AF, whereas the association between obesity and postoperative AF does not vary by the type of cardiac operation [21]. Several studies have also reported that BMI independently predicts progression from paroxysmal to permanent AF [22–24]. In women without AF at baseline increasing adiposity was preferentially associated with the early development of non-paroxysmal AF [23]. Additionally, for people whose initial AF episode terminates, the benefits of lowering BMI may include a lower risk for future development of permanent AF [24]. In this context, Guglin et al. demonstrated that obesity is associated with a higher recurrence rate and greater burden of AF compared to nonobese patients [25]. After multivariate analysis it was demonstrated that left atrial (LA) size but not BMI was an independent predictor of recurrence and AF burden, but given the correlation between LA size and BMI the effects of increased BMI on atrial size possibly reflect the atrial remodeling observed in this setting [25]. Another recent meta-analysis reported that elevated BMI is significantly associated with AF recurrence after pulmonary vein isolation [26]. Interestingly, BMI has been incorporated in validated risk scores for AF developed in community-based cohorts [27–29]. Therefore, the impact of increased BMI on AF risk appears to be well established.

Pathophysiological links between obesity in atrial fibrillation

Clinical correlates between obesity and atrial fibrillation

Several potential mechanisms link obesity and AF (Fig. 1). Common pathophysiological pathways appear to be operative in obesity, AF, and specific clinical conditions such as hypertension, diabetes mellitus (DM), metabolic syndrome (MS), coronary artery disease, and obstructive sleep apnea (OSA).

Hypertension

An increasing body of evidence supports the concept that hypertension is an important risk factor for AF [5,30–33], increasing the risk of the arrhythmia by almost 2-fold [34]. Hypertension causes reduction of left ventricular (LV) compliance, diastolic dysfunction, and LV hypertrophy (LVH). LVH increases LV stiffness, wall stress and filling pressure, decreases coronary flow reserve, and activates the sympathetic nervous system as well as the renin–angiotensin–aldosterone system (RAAS) [35,36]. The mechanisms involved in hypertension-associated AF include triggering activity, atrial electrical and structural remodeling, and inflammation. Stretch impulses depolarize the myocyte membrane within milliseconds and induce after-polarizations, which produce

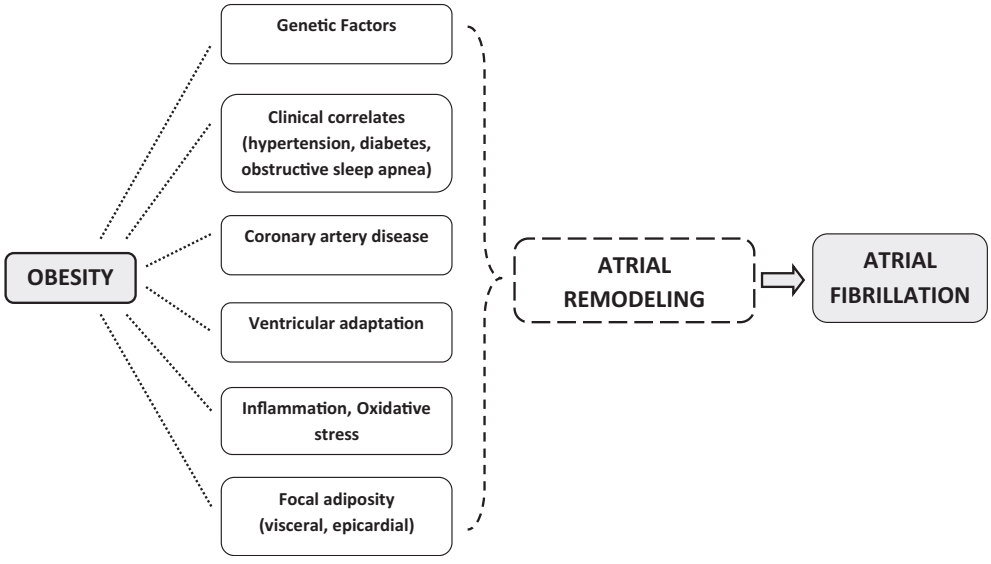

Fig. 1. Graphical depiction of pathophysiological links between obesity and atrial fibrillation.