Biomarkers in Atrial Fibrillation; From Pathophysiology to Diagnosis and Treatment

Atrial fibrillation (AF) is a frequent cardiovascular entity (almost 33 million subjects worldwide suffering from different forms of this entity) especially in developed countries [1] accompanied by poor quality of life and posing significant morbidity and mortality which may explain the increasing amount of research on ion and cells mechanisms, the identification of electric circuits and the introduction of novel pharmaceutical and invasive strategies.

Despite the advancements in diagnostic strategies, the recognition of the multiple wavelet hypothesis and rotors as sources of AF, the introduction of invasive strategies targeting specifically the generation of AF and the introduction of improve anticoagulant strategies we are far away from a treatment highly efficient since the best results for example of AF ablation reach only 60-70% success rate [2].

Therefore, there are gaps in evidence such as the basic pathophysiologic mechanisms underlining ion channels alterations, re-entry circuits and electrical remodeling, the identification of the patients best responsible to atrial fibrillation ablation, the selection of the optimum anti-arrhythmic management in each case and risk categorization of the patients concerning stroke risk, bleeding risk and recurrence of atrial fibrillation.

As the role of biomarker in the research relative to AF initiation and progression and in the management of clinical AF episodes is limited we believe that further insights into the role of specific biomarkers can be proved usefully in the understanding and management of this entity. In this thematic issue, we will discuss the role of biomarkers in the pathophysiology of AF, in prognosis, in the risk stratification for stroke and bleeding and in treatment strategies and in specific comorbidities associated with AF.

This special issue contains 13 review articles. The first 4 articles focus on the underlying pathophysiologic mechanism of AF [3-6]. The following 4 reviews present the possible role of biomarkers under specific circumstances [7-10]. Finally the prognostic role of biomarkers is presented in the last 5 articles [11-15]. All these issues are supported by appropriate illustrations and tables.

The role of inflammation in several cardiovascular diseases has been revealed over 3 decades ago which continues to focus interest since the modification of inflammatory cataract appeals as an attractive alternative therapeutic approach. The association of inflammation with AF seems to be bidirectional (AF may initiate the inflammatory cataract and a pro-inflammatory status precipitates episodes of AF). The purpose of the first article [3] is to examine this association and present data how biomarkers such as C reactive protein, Interleukin-1 and tumor necrosis factor are implicated in the genesis and perpetuation of AF.

Redox stress has been revealed as a significant factor affecting not only atherosclerosis progression and heart failure but several comorbidities. Formation of superoxide, hydroxyl radicals and peroxynitrate may cause oxidative modification of proteins and mitochondrial DNA damage, leading to cellular death and altered ion channels function. Under these circumstances, electrical properties of myocardial cells are modified and oxidative stress is implicated in the genesis of AF as it is presented in the second review of this issue [4].

The role of atrial fibrosis and remodeling has for long been recognized as a pathophysiologic mechanism of AF. Dilaveris et al. [5] focus on the underlying mechanisms of extracellular remodeling and present useful data how biomarkers can be used to monitor and evaluate the extent of remodeling and the prognostic yield of these biomarkers in the treatment strategies.

The role of small non-coding RNAs (microRNAs) has been recently revealed. They can orchestrate many biologic processes and organ functions. Their role in cardiovascular system focus is on the research interest in the setting of AF specific MicroRNAs as presented by Briasoulis et al. [6] which can not only be used to further understand pathophysiologic mechanisms but also to identify subjects prone to develop AF.
Atrial fibrillation is associated with several comorbidities. The specific issues raised when AF coexist with aortic stenosis, heart failure, hypertension and metabolic syndrome which are examined in the following 4 review articles. Toutouzas et al. [7] give insights in the interaction between AF and aortic valve stenosis and focus on the biomarkers that can be used to determine the prognosis of arrhythmias in patients after transcatheter aortic valve implantation. The close interrelationship between AF and heart failure is well established. In the following review [8], the significant role of a set of biomarkers in the prognosis of HF and atrial fibrillation is presented and the article focuses on the mechanistic links between raised natriuretic peptides and altered myocardial cell electrical properties which may precipitate in the episodes of AF. The prevalence of AF is increased in patients with hypertension and may further deteriorate patients’ functional status or may lead to clinical evident heart failure. Tsioufis et al. [9] present the biomarkers involved in the atria electrical remodeling in patients with hypertension and they propose a combination of multiple indices to effectively detect both AF and adverse characteristics of high risk patients with hypertension. Metabolic syndrome is an entity that encompasses a cluster of derangements such as obesity, hypertension, diabetes mellitus and dyslipidemia which may further deteriorate cardiac function and may adversely impact atrial remodeling and electrophysiologic properties. Vlachopoulos et al. [10] provide the most recent data concerning the link of these entities with the biomarkers associated with maladaptive changes in atrial remodeling.

Unfortunately, AF may cause significant complications in morbidity and mortality especially when it causes stroke or hemorrhage. Several prognostic models are used the last years in cardiovascular patients. A series of biomarkers are examined by Mazaris et al. [11] for their effort to support the clinician’s prognosticability while the additive prognostic value of biomarkers in determining the stroke risk is examined in a review article by Ioannou et al. [12]. In an interesting review, Sideris et al. [13] focus on the prognostic ability of biomarkers in the bleeding risk and how they can be used to altertherapeutic decisions.

The last two review articles covered two interesting issues. Development of atrial fibrillation after cardiac surgery may complicate post cardiac surgery period and may need specific treatment. Manfrini et al. [14] focus on the biomarkers which can be used to determine prognosis and identify patients needing preventing strategies. Finally Tsiachris et al. [15] examine how biomarkers can be used in atrial fibrillation ablation. Since results of atrial fibrillation are modest achieving a success rate of 60-70%, the identification of best candidates for this invasive strategy is of importance since it may change treatment decisions. The additive prognostic information obtained by the use of specific biomarkers is examined in this review as well as the role of biomarkers in the monitoring of AF recurrence.

REFERENCES


---

**Dr. Dimitris Tousoulis, MD, PhD, FACC, FESC**  
*Guest Editor*  
Vasilissis Sofias 114, TK115 28  
Hippokration Hospital, Athens  
Greece  
Tel: +30-213-2088099  
Fax +30-213-2088676  
E-mail: drtousoulis@hotmail.com