



Editorial

Risk profiling in atrial fibrillation: Value of assessment of vascular blush

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Atrial fibrillation (AF) is the most common sustained arrhythmia and is associated with significant morbidity, increased risk of stroke, reduced quality of life, and increased mortality [1]. Concomitant risk factors such as hypertension, obesity, metabolic syndrome and increased aging lead to structural remodelling processes in the atria [2–6] which contribute to the progressive nature of AF and the reduced efficacy of standard antiarrhythmic pharmacological and catheter-based rhythm control strategies in patients with more progressed AF-substrates [7,8].

Several studies have shown that common cardiovascular risk factors, which are highly prevalent in AF patients, are associated with impaired endothelial function [9,10]. Endothelial dysfunction is associated with increased risk of incidental AF and poor outcomes post AF ablation [9,10]. Additionally, dysfunctional endothelium has been suggested to be involved in the progressive atrial arrhythmogenic remodelling process in patients with hypertension [9] and also reflects vascular and systemic inflammation [11] with atrial inflammatory signalling being very recently discovered to be upregulated and casually contributing AF pathophysiology [12]. Interestingly, markers of endothelial dysfunction appear to be reversible, if sinus rhythm can be maintained in AF patients [10].

Mechanistically, the endothelium regulates the vascular response to stress through a combination of dilators including nitric oxide that downregulates adhesion molecules and modulate inflammatory and oxidative stressors. Dysfunctional endothelium promotes thrombogenicity and activates platelets resulting in increased risk of left atrial thrombus formation and may contribute to atrial remodelling in AF [13]. As the atrial remodelling process precedes the clinical manifestation of AF and stroke, a characterization and assessment of endothelial dysfunction may help to assess the progression of atrial cardiomyopathy and stroke risk [14] and might permit early initiation of up-stream therapy to prevent or even reverse the structural and electrophysiological changes in the atrium. Given the previously documented impact of risk factor management in the secondary prevention of AF, [15] a better assessment and characterization of the progression of the early preclinical AF substrate including the endothelial function measurements, can potentially allow a more informed and individualized primary prevention strategy in AF. Despite a clear association between endothelial dysfunction and AF, the best way to assess endothelial function in AF patients remains unclear. Non-invasive

approaches have been introduced to assess endothelial function by indirect estimates of vascular reactivity to flow and pressure wave pulsatility.

In this issue of the Int J Cardiol Heart Vasc, Kobayashi et al. [16] examined the association between AF recurrence and vascular endothelial function in ninety-nine consecutive AF patients who underwent catheter ablation. Endothelial function was assessed by peripheral arterial tonometry (PAT) using the natural logarithmic transformation of reactive hyperaemia peripheral arterial tonometry index (LnRHI) calculated and measured by the EndoPAT system. They found, that decreased LnRHI was associated with AF recurrence after catheter ablation and prolonged AF duration.

The study suggested endothelial dysfunction and vascular physiology in patients with AF, which correlated with the development and maintenance of AF. However, the findings have to be treated with caution. The technique used to assess endothelial function in this study has been developed for measurements during sinus rhythm and has never been validated in AF patients. Due to a high beat-to-beat pulse variability during AF, these methodologies may carry certain limitations, particularly if the measurements are just performed for 5 min, where rate control and beat-to-beat intervals may be highly variable. Additionally, the inter- and intra-observer variability was not reported in this study. The role of pharmacological treatment influencing endothelial function (particularly blockers of the renin angiotensin aldosterone system) has not been specifically investigated and, as recognized by the authors, the used patient cohort includes patient with persistent AF and even long-standing persistent AF being treated with various rhythm control strategies to help restore sinus rhythm which makes the interpretation of the results difficult.

Despite some limitations, the work by Kobayashi et al. [16] has provided further insights in the role of vascular functional assessment with the goal to characterize the overall burden of cardiovascular risk factors and degree of atrial remodelling predictive of AF outcomes. In addition to the assessment of the progression of atrial cardiomyopathy, quantification and characterization of endothelial function may help to monitor the effect of interventions (e.g. risk factor modification) and may even represent an interesting target in the treatment of AF substrate. Further, appropriately designed studies are required to explore the impact of vascular remodelling in better characterization of sub-clinical and

established end organ injury, e.g. atrial cardiomyopathy. However, particularly in the case of AF, validation studies are necessary to assure, that PAT or other techniques such as flow mediated vascular dilatation (FMD) are able to assess endothelial function in patients with AF with a good reproducibility and operator independence. This will facilitate assessment of endothelial function in the routine cardiovascular risk stratification in clinical management of AF patients. Finally, intervention studies are required to determine whether endothelial dysfunction represents a modifiable arrhythmogenic risk factor or a risk marker in conjunction with concomitant risk factor burden.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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