



## Editorial

## The continuing gender gap in cardiovascular disease: What are we missing in clinical practice?



Gender differences in diagnostics and treatment of cardiovascular conditions has been a topic of discussion for a long time and evidence has demonstrated significant variance in care and treatment approaches as well as associated outcomes between men and women. Naturally, substantial biologic gender differences and sociocultural impact contribute to these differences, however the call for more personalised models of care, focussing on the gender-specific differences in symptom pattern, and the required optimal timing of diagnosis and treatment, is far from being optimal in clinical practice and differences in diagnosis and management in cardiovascular conditions persists.

Atrial Fibrillation (AF) is the most prevalent cardiac arrhythmia which increases with age and an increasing burden of risk factors such as hypertension, obesity and obstructive sleep apnoea (OSA) [1]. In a recent publication in this Journal, Lin et al., investigated the association between AF burden and OSA and the differences in clinical characteristics between women and men with AF and OSA [2]. The study demonstrated a significant correlation between these conditions, only in men, for which the authors provided several potential reasons related to the cardiovascular system. Beyond these potential explanations, they interestingly also outlined potential gender-related reasons. Whilst women generally show lower OSA severity compared to men, this study demonstrated similar OSA severity in women and men with both AF and OSA. Interestingly, women were on average seven years older compared to men with moderate-to-severe OSA. Given that the risk of OSA increases with age, specifically in women after menopause (e.g. a 7% increase each year after menopause) [3], would explain why women typically experience symptoms of OSA at an older age compared to men. Indeed, the study by Lin et al observed similar OSA severity and patient characteristics (except for age) in women and men, but with women showing a lower AF burden, potentially due to a later onset of AF in women. This leads us to ask, should we assess women's AF burden differently from men?

Besides the fact that OSA management is often sub-optimal in clinical practice, a recent European survey of health care professionals demonstrated the lack of structured integration of OSA assessment in the work-up of AF [4]. Interestingly the survey did not incorporate any sex-specific details related to OSA nor to AF, which confirms the gender divide, whilst available evidence reports on significant sex-related differences in epidemiology, pathophysiology, and clinical presentation. Also, generally women present with AF at an older age and may be more symptomatic compared to men but the symptom scores in use may not be sensitive enough for females and despite the disease severity, the disease burden is just not being picked up. Given that women with AF have a greater stroke severity and associated disability than men, female gender has been long identified as a risk factor for stroke and as such

incorporated in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score to determine the yearly risk of stroke and associated necessity for oral anticoagulant treatment [1]. It may be that female gender (as a separate risk factor) needs to be considered in other assessment tools as well. Integrated cardiovascular care models have been advocated to provide personalised and individualised treatment in patients with cardiovascular conditions, necessitating a whole of systems approach [5]. Moreover, international practice guidelines for the management of AF state that sex-related differences should be considered in personalized, individual, patient-centred AF approaches in clinical practice, and that integrated models of care should be considered in the treatment of patients with AF to improve outcomes [1,6]. Obviously this implies important implications for clinical practice [7], and is a crucial evolution towards tailored precision medicine. However, besides gender as a risk factor in stroke assessment and treatment, no sex-specific recommendations on AF or OSA management are provided. In fact, there is only one specific sex-related recommendation stating that 'women with symptomatic paroxysmal or persistent AF should be offered timely access to rhythm control therapies, including AF catheter ablation, when appropriate for medical reasons (Class IIa, Level of Evidence B) [1].

The paper by Lin et al, provides crucial clinical implications addressing the current gaps in sex-specific and personalised AF care. Multiple interventions have been undertaken to improve clinical practice potentially including dedicated pathways to provide personalised care which would increase awareness of risk factor management. OSA screening and assessment requires a team approach and seamless collaboration between sleep and AF specialists to reduce fragmentation, and thus calls for a redesign and reform of clinical practice [8]. Dedicated pathways for multidisciplinary, integrated OSA and AF pathways have been suggested [9] and have demonstrated good outcomes in terms of improving lead time to diagnosis and improved structured management of OSA as an integrated part of AF treatment [10]. Moreover, international AF practice guidelines have defined the fusion of crucial fundamentals forming the integrated approach [7]. Although this includes a specific focus on patient-centred care incorporating patient preferences, there is no focus on sex-specific patient characteristics. This raises the issue whether clinical AF practice needs a risk stratification score to further establish AF precision medicine. In other words, similarly to stroke risk assessment, is there a need for an overall AF assessment incorporating sex-specific components? If we are to implement individualised treatment, we need to ensure that the assessment and risk scores we apply are sensitive to females. It is only by doing this will we truly address the gender gap that currently remains in clinical practice.

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