Anthropometric parameters and AF outcomes: a path to precision medicine

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Anthropometric parameters, such as obesity, are a well-established risk factor for the development of atrial fibrillation (AF). Indeed, this importance has been reflected in the most recent European Society of Cardiology (ESC) guidelines for AF[1]. However, there remains a gap in our understanding of how body shape and composition influences outcomes following the development of AF.

Boriani et al.[2] address this in an article published in the Journal, where they describe a large observational study exploring how differences in baseline anthropometry may be associated with differences in outcome in patients with AF. Specifically, they looked at height, weight, body mass index (BMI), body surface area (BSA) and lean body mass (LBM) in an unselected population of individuals with recent AF. We congratulate the authors as it is one of the first studies to focus on these parameters and allow us to contextualise the role of such characteristics in clinical practice.

Across 10220 patients, they consistently found that the lowest tertile of each parameter was associated with worse all-cause survival independent of sex. Other findings showed that patients in the lowest tertile for weight, BMI, BSA and LBM were less likely to be on indicated antithrombotic therapy and tended to be of an older demographic, often with multiple comorbidities. The underlying reason for this requires further exploration in clinical practice to ensure disparities in anticoagulation are addressed. Multivariable cox regression suggested that in women in the highest tertile of weight and BSA had improved MACE outcomes, whilst for men this association was seen in the highest tertiles of BSA and LBM. Disentangling this obesity paradox, whereby the improved outcomes in the obese is countered by an increased risk for the development of AF, will be clinically important.

This observational study has many strengths, one being that it includes a large unselected population of over ten thousand people and the provision of a useful clinical stratification, by splitting each parameter into tertiles. Crucially, the lowest tertile component has not been very well studied in existing literature.

In view of the differences in anthropometry between men and women, the group chose to separately analyse the two sexes. Discrepancies in AF outcomes between men and women have been previously reported, with mortality and stroke risk being higher in women[3]. Whilst this study did not identify a sex

related disparity in outcome, there were differences in the impact of anthropometric parameters between the sexes. In men, the Kaplan-Meier curves for all of the parameters suggested a better outcome with higher values of the parameter. This relationship was more complicated in women, with minimal separation of the survival curves in middle and highest tertiles. It is unclear why such a disparity exists identifying an area for future research.

Furthermore, the probable role of frailty as an explanation for the worse outcomes in the lowest tertiles requires exploration. Frailty is a complex, multi-system clinical syndrome which is gaining significant influence across multiple cardiac conditions and outcomes. Not unexpectedly, studies suggest that more frail individuals with AF have increased mortality and stroke risk[4,5]. Clinical phenotyping studies of frailty have emphasised the importance of advancing age, sarcopenia and low physical activity in the development of frailty[6]. Boriani et al. found that patients in the lowest tertiles in each of their investigated parameters were older and with more comorbidities. Moreover, it is self-evident that patients with sarcopenia will have lower body weights and BMI, and that low physical activity will result in reduced lean body mass. Are the worsened outcomes, seen in the lowest tertiles, reflecting a frailer individual? And should such individuals be managed differently? In this context, the addition of other parameters such as handgrip could have been particularly useful in identifying the sarcopenic or frail individuals.

The other component of the worsened outcomes in some of the lowest tertile groups was that these individuals were less likely to be prescribed indicated antithrombotic therapy. It is plausible that this prescribing reticence reflects concerns about antithrombotic therapy in the frail population[7]. This includes worries about falls risk and bleeding complications in more frail individuals. However, the most recent literature suggests a net-clinical benefit for anticoagulant therapy for frail patients with AF[8], highlighting a vital need for better understanding of this prescribing discrepancy.

Current literature with the REVERSE-AF[9] and LEGACY-AF[10] studies have implicated obesity as a modifiable risk factor for AF related symptoms, time in AF and risk of conversion to a permanent AF phenotype. However, it appears as if baseline obesity in this cohort of AF patients is associated with an improved prognosis. This is also alluded to in the ESC guidelines, which cites a meta-analysis based on the oral anticoagulant trials[11]. In this study, patients with an elevated BMI also tended to be younger.

This mirrors findings across other studies of the obesity paradox in AF. Since younger patients are at an inherently reduced risk of major adverse outcomes and death, it seems likely that this is at least contributing to the apparent paradox highlighting another area for future research.

This well-conducted observational study helps remind clinicians that there is work to be done in improving outcomes for AF patients. Whilst antithrombotic therapy has helped to address stroke outcomes, and there is much interest in preventing the development of AF, improving other outcomes in patients with established AF has been less well studied. The next step is to identify whether precision medicine, incorporating anthropometric parameters will help address disparities in outcome, and whether modern scores for need of anticoagulation and prediction of AF, might benefit from including them.

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