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Trends in Cardiovascular Medicine

journal homepage: www.elsevier.com/locate/tcmEditorial commentary: Sex, strokes and atrial fibrillation[☆]

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Stroke prevention in both men and women is of utmost importance in the treatment of atrial fibrillation. The paper “Stroke risk in female patients with atrial fibrillation (AF): Relationship to current guideline recommendations” by Nielsen et al. in this month’s issue of *Trends in Cardiovascular Medicine* compares the North American to the European guidelines [1]. The authors stated that both guidelines recommend using the CHA₂DS₂-VASc (Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, previous Stroke/transient ischemic attack, Vascular disease, Age 65–74 years, Sex category) score to assess the risk of stroke [2,3]. Both guidelines have identical recommendations for patients with CHA₂DS₂-VASc score of 0 and ≥ 3 . Where the guidelines differ are in their recommendations for those with CHA₂DS₂-VASc score of 1 and 2. One notable difference is that the use of aspirin is not recommended by the European guidelines for any score. Females with a CHA₂DS₂-VASc score of 2 may be considered for oral anticoagulation by the European guidelines whereas the North American guidelines recommend oral anticoagulation.

The authors question the North American guidelines’ recommendation to consider the use of oral anticoagulation or aspirin in female patients whose only risk factor is sex. This is a IIB, level C recommendation which indicates that the evidence is less well established and its usefulness is unclear or unknown [2]. In comparison, the European guidelines recommend no therapy for the female patients with the same score [3].

The C statistic for CHA₂DS₂-VASc score is only 0.6–0.7 which leaves room for improvement [4,5]. The Nielsen et al. article highlights the need for continued efforts to improve the ability to predict strokes in patients with AF. While the CHA₂DS₂-VASc score improves upon the older CHADS₂ score by identifying those patients at the lowest and highest risk for stroke [5,6], the differences between American and European guidelines underscore the fact that more data are required in cases when female sex is the only risk factor.

Two of the same authors (Nielsen and Lip) recently investigated the role of female sex in the risk of stroke in patients with AF [7]. They analyzed nearly 240,000 newly diagnosed AF patients (48.7% females) and examined whether female sex is a stroke risk modifier rather than an independent risk factor within the CHA₂DS₂-

VASc score. They found that the excess female sex-related risk of stroke was seen only if there were other CHA₂DS₂-VASc risk factors, especially if they had ≥ 2 concomitant non-gender CHA₂DS₂-VASc risk factors. They believe that a revision of the American guidelines should be considered to reflect that low risk females should not be offered any oral anticoagulation or aspirin. The efficacy of aspirin has been proven to be inferior to oral anticoagulants [8] yet women are often treated with aspirin [9]. Their study adds valuable evidence that is lacking in this patient population.

Nielsen et al. also raise an additional significant point that AF patients are undertreated for stroke prevention. Under-utilization of anticoagulation occurs not only in the United States but globally [10,11]. In the National Cardiovascular Data Registry’s Practice Innovation and Clinical Excellence Registry of outpatients with AF, less than half of CHA₂DS₂-VASc score ≥ 4 patients were receiving oral anticoagulants [10]. In addition, women were significantly less likely to receive oral anticoagulants at all levels of the CHA₂DS₂-VASc score and more likely to receive aspirin [9]. In contrast, the global anticoagulant registry in the FIELD (GARFIELD)-AF registry showed no significant difference in the overall rate of anticoagulant use between women (60.8%) and men (60.9%) [12].

Further studies are needed to improve the predictability of strokes in women with low CHA₂DS₂-VASc, but more importantly additional efforts are needed to improve the utilization of effective therapies in patients with high risk for strokes, as they benefit the most. These efforts could include increased healthcare provider education about the benefits of oral anticoagulation, greater insurance coverage of the novel anticoagulants, and shared decision making [13]. The Class I, level of Evidence C recommendation by the American guidelines is that antithrombotic therapy should be based on shared decision making with discussion of risks of stroke and bleeding with the patient, taking into consideration the patient’s preferences. This recommendation had no references hence the low level of evidence. In an effort to improve this level of evidence, the American Heart Association partnered with the Patient-Centered Outcomes Research Institute to form two Decision-making and Choices to Inform Dialogue and Empower A-Fib Patients (DECIDE) Centers at a cost of about \$10 million. These DECIDE centers will test and deliver shared decision-making tools for clinicians and patients to use together to determine which treatment options will work best to provide the desired outcomes for each individual patient [14]. Perhaps this effort would improve the outcomes for both women and men with AF and provide much needed data for patients with low CHA₂DS₂-VASc scores.

[☆] Authors have no conflict of interest and no funding was provided for this publication.

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