



HAS-BLED SCORE: LIMITATIONS DUE TO UNDERESTIMATION OF BLEEDING RISK IN THE ELDERLY

Gülistan Bahat, Birkan İlhan, Mehmet Akif Karan

Istanbul Üniversitesi, İstanbul Tıp Fakültesi, İç Hastalıkları AD, Geriatri Bölümü

Atrial fibrillation (AF) is the most prevalent sustained arrhythmia associated with a significant increased risk of ischemic stroke. It is a global healthcare problem with evidence suggesting an increasing prevalence and incidence worldwide.¹ The prevalence of AF is greater in older subjects. 70% of AF is reported in ≥ 65 years-old and 45% in ≥ 75 years.² On the other hand, the age itself is a well-identified risk factor amplifying the risk of stroke associated with AF. The higher prevalence and higher negative impact of the problem in the aged population makes AF a huge geriatric problem.

Current recommendations are to consider oral anticoagulation (OAC) for all AF patients with a CHA₂DS₂VASc score of 1 or higher.^{3,4} In conjunction with the CHA₂DS₂VASc score, the HAS-BLED bleeding score is recommended for use to weigh the risk of thrombosis against the risk of bleeding.^{4,5} Recently HAS-BLED scoring system has been criticized for its tendency in misinterpretation by end-users leading overestimation of bleeding risk in the real life settings.⁶ In his editorial, Gulec reported that in a national quiz for cardiology trainees to test their knowledge of the current practice guidelines, the HAS-BLED question was answered correctly by only 4.5% of trainees. The very highly prevalent wrong answers were in the favor of overestimation of the HAS-BLED bleeding risk. Accordingly, he noted that, one can easily overestimate the bleeding risk, especially in certain type of patients with stage 1 hypertension and/or mild to moderate renal/liver dysfunction in the real life settings.

Aging is well-known with its detrimental effects on the skeletal muscle content. Sarcopenia is the decrease in skeletal muscle mass and function. It is a well-known and prevalent problem of the older people with prevalences of $>50\%$ in men and 30% in women > 80 years in different studies.^{7,8} Additionally, malnutrition is another well-known and prevalent geriatric syndrome associated with ageing. The prevalence of malnutrition across settings and countries is reported 22.8% in a

multinational study having a mean age of 82.3 years and it can definitely decrease the muscle mass further.⁹

The acronym HAS-BLED represents each of the bleeding risk factors and assigns 1 point for the presence of each of the following: hypertension, abnormal renal and/or liver function (1 point each), previous stroke, bleeding history or predisposition, labile international normalized ratios, elderly, and concomitant drugs and/or alcohol excess.⁵ The maximum score is 9. The score ≥ 3 points suggests a high risk of bleeding, where caution and regular observation of the patient is recommended.⁴ Renal failure is a prevalent problem in the aged population. Using GFR estimated by the modified Modification of Diet in Renal Disease (MDRD) study equation among participants in the NHANES III study, 38% of individuals >70 years, even without hypertension or diabetes, had estimated GFRs <60 mL/min.¹⁰ By comparison, such low values were seen in only 0.7% of such participants between 20-39 years of age. Also, using the Cockcroft-Gault method among nearly 100,000 subjects >20 years of age (11), $>80\%$ of those >70 years had a calculated clearance of <60 mL/min. In HAS-BLED scoring system, 'abnormal renal function' is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥ 200 $\mu\text{mol/L}$ (2.24 mg/dL) by the developers. However, individuals with significant variations in dietary intake i.e. vegetarian diet, diminished protein intake or reduction in muscle mass i.e. malnutrition, muscle wasting, produce lower amounts of creatinine than the general population leading to decreased serum creatinine levels.¹² Accordingly, having well prevalent problems of sarcopenia and malnutrition, the success of "serum creatinine" -of its own- to predict renal function decreases with ageing. Seemingly normal serum creatinine levels are found in many older people with renal insufficiency.¹³ Rather than serum creatinine level itself, the prediction of GFR via Cockcroft-Gault formulation, creatinine clearance by 24 hr urine collection is much more appropriate in the older people. Accordingly, US Food and Drug Administration (FDA) recommend to pharmaceutical industries to use an estimating equation, rather than serum creatinine alone. On the other hand, a measured creatinine clearance would be better for patients at the extremes of muscle mass and/or low protein diet rather than estimation equations that use the serum creatinine.^{12,14} Hence, the definition of 'abnormal renal function' as serum creatinine ≥ 200 $\mu\text{mol/L}$ (2.24 mg/dL) leads to underestimation of the bleeding risk via the HAS-BLED scoring system in the older population.

Last but not the least; falls are another very prevalent problem in the older people. The incidence of falls increases with age and varies according to living setting. 30-40% of community-dwelling people >65 years fall each year, the prevalence increasing to about 50% for those >80 years.^{15,16} Not surprisingly, fall is a major factor contributing to the bleeding risk associated with OAC. HAS-BLED scoring system does neither consider the fall history nor increased fall risk in the older population. We suggest that non-consideration of falls is another factor limiting the utility of HAS-BLED in predicting bleeding risk in favor of underestimation.

The HAS-BLED scheme was developed by using the Euro Heart Survey data on AF.¹⁷ It was validated in a European cohort as well as an anticoagulated AF trial cohort, where it performed at least as good as other published bleeding risk stratification schemes.^{5,18} However, these studies have an estimated mean age 66.7 years, 66.1 years and 71 years -at most-.^{5,17,18} Furthermore, they all did not consider the frailty in the elderly participants which is associated with more prevalent malnutrition, sarcopenia, any adverse results and falls.¹⁹

Elderly constitute a rather heterogeneous population and study recommendations could only be generalized to a given population if the given study participants are real and good representative of the population they recommend for. Departures from representativeness are amplified with increasing age. Progressively older adults, who do participate in studies, may be progressively less representative of the group they are intended to reflect-as more non-representatively vigorous and robust. Consequently, the older the age, the greater the disparity may be between what is recommended based on 'evidence' and what is best for the patient.²⁰ Accordingly, similar to the problem and our subsequent conclusion on hypertension study analyses of the elderly, the results from these AF surveys could not be generalized to the elderly due to under-representation of frail or medically compromised patients that are rather prevalent in this age group.²¹

In conclusion, we suggest that HAS-BLED score has 2 main limitations: Consideration of the serum creatinine level -in its own- as marker of renal function and non-consideration of falls. These problematic aspects that shall limit the utility of HAS-BLED scoring system making it an under-estimating tool for bleeding risk in the older people.

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