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Retrospective Evaluation of Oral Anticoagulant Therapy may not Reveal the Reality

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We have read the article published by Aslan et al with a great interest.[1] They reported a real-world experience with dabigatran compared to warfarin in patients with atrial fibrillation (AF). They have shown that both dabigatran doses (110 and 150 mg) were superior to warfarin in reducing ischemic stroke without an increase in bleeding rates. This is an interesting study. However, we want to mention minor criticism about this study from methodological aspects.

First, in the methods section, treatment duration <3 months was mentioned as an exclusion criterion for patients receiving dabigatran. On the other hand, the authors stated that the patients with treatment duration of at least ≥120 days were enrolled in the study. Thus, there were patients taking dabigatran for only 3 months which was shorter than 120 days. Ho et al have recently compared dabigatran with warfarin for stroke prevention in a cohort of real-world patients with AF.[2] Although these 2 studies were differently designed, we have some concerns regarding treatment duration, follow-up, and outcome periods in the article of Aslan and colleagues. In the article by Ho et al, the median duration of follow-up was 310 days, the outcome data were available for the whole period, and the treatment and follow-up duration were similar in both groups.[2] However, follow-up periods were different for dabigatran and warfarin groups in the current study. The median duration of the follow-up period was 15 months for warfarin but only 6 months for dabigatran. They also mentioned that the outcome data were limited to 6 months. It was unclear which time period (the first 6 months or the last 6 months) was chosen for outcome data.

Our second concern is about the evaluation method of anticoagulation intensity. A commonly used summary of the quality of warfarin anticoagulation is the linearly interpolated percent time in the therapeutic range (TTR). The TTR must be >65% for a better anticoagulation.[3] The following 3 different methods were identified for the measurement of TTR:

a. percentage of visits in range (Traditional Method);
b. percentage of visits in range on given date (Cross-Section Method); and
c. percentage of days in range (Rosendaal Method).

In this article, TTR was reported to be 32% but it is not clear which method was used to calculate TTR. Moreover, it was not clear whether this number "32%" was the mean TTR of the study patients or the percentage of patients with acceptable TTR (TTR > 65%).

Our last concern is about increased adverse cardiovascular events, in patients on warfarin therapy in the current study. Previous studies have shown that the warfarin was a useful drug for the management of patients with coronary artery disease.[4] Lip and colleagues stated that warfarin may result in a lower risk of myocardial infarction compared with other (nonwarfarin) anticoagulants or an anticoagulant equivalent.[5] Recently, a meta-analysis of 14 randomized controlled trials provided that dabigatran was associated with a 34% increase in the risk of myocardial infarction. The risk was principally identified when warfarin was used as comparator.[6] In contrast to the above-mentioned literature, myocardial infarction rates were higher in the warfarin group in the study by Aslan et al. The authors accused low TTR rates for increased myocardial infarction and death in patients on warfarin therapy. However, the number of patients with coronary artery disease was not mentioned in table 1 which demonstrates the baseline characteristics of the study population. Although dabigatran might be expected to be noninferior to warfarin in patients with low TTR levels, increased myocardial infarction rates with warfarin is an unexpected result and should not be attributed to warfarin alone. In conclusion, retrospective analysis of oral anticoagulant therapies may not provide the real-world experience and may

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be in contradiction with prospective randomized controlled trials.

References

1. Aslan O, Yaylali YT, Yildirim S, et al. Dabigatran versus warfarin in atrial fibrillation: multicenter experience in Turkey [published online August 12, 2014]. *Clin Appl Thromb Hemost*. 2014. doi: 10.1177/1076029614546327.
2. Ho JC, Chang AM, Yan BP, et al. Dabigatran compared with warfarin for stroke prevention with atrial fibrillation: experience in Hong Kong. *Clin Cardiol*. 2012;35(12):E40-E45.
3. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace*. 2010;12(10):1360-1420.
4. Hurlen M, Abdelnoor M, Smith P, et al. Warfarin, aspirin, or both after myocardial infarction. *N Engl J Med*. 2002;347(13): 969-974.
5. Lip GY, Lane DA. Does warfarin for stroke thromboprophylaxis protect against MI in atrial fibrillation patients? *Am J Med*. 2010; 123(9):785-789.
6. Douxfils J, Buckinx F, Mullier F, et al. Dabigatran etexilate and risk of myocardial infarction, other cardiovascular events, major bleeding, and all-cause mortality: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc*. 2014; 3(3):e000515.