Review



Practical guide to choosing dabigatran 150 mg twice daily or apixaban 5 mg twice daily for patients with atrial fibrillation

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Abstract

Based on previous reports, we propose a practical guide to choose dabigatran 150 mg twice daily or apixaban 5 mg twice daily for patients with atrial fibrillation. We recommend the use of dabigatran 150 mg twice daily for patients with atrial fibrillation who have a high risk of embolism (e.g., ischemic stroke on other oral anticoagulants, presence of left atrial appendage thrombus) and a low risk of bleeding. However, the prevalence of such patients with atrial fibrillation is considered low because patients with atrial fibrillation with a high risk of embolism usually have a high risk of bleeding. In most other patients with atrial fibrillation, the use of apixaban 5 mg twice daily should be considered.

Key words: apixaban, atrial fibrillation, dabigatran, direct oral anticoagulants (DOACs)

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Introduction

Dabigatran, apixaban, rivaroxaban, and edoxaban are direct oral anticoagulants (DOACs) that have been shown to prevent embolisms in patients with atrial fibrillation (AF) in large clinical trials, with each investigating over 10,000 patients. Among the 4 DOACs, dabigatran 150 mg twice daily is the sole drug shown to be superior to warfarin for preventing ischemic stroke in patients with AF^{1} . In addition, only dabigatran 150 mg twice daily and apixaban 5 mg twice daily have been shown to be superior to warfarin for preventing "stroke or systemic embolic events" in patients with $AF^{1,2}$. On the other hand, the risk of gastrointestinal bleeding with dabigatran 150 mg twice daily is higher than that with warfarin¹). The benefit in terms of ischemic

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stroke prevention with dabigatran 150 mg twice daily is in exchange for a higher risk of gastrointestinal bleeding.

Based on these results, previous reports on choices of DOACs for patients with AF described that the use of dabigatran 150 mg twice daily should be considered in patients with AF with high embolic and low bleeding risk^{3–6)}. For other patients with AF, apixaban can be most widely used for its safety profile^{3, 4)}. However, there is no practical guide to choose dabigatran 150 mg twice daily or apixaban 5 mg twice daily for patients with AF. Herein, we propose a practical guide focused on choices of these agents for patients with AF.

Indications of DOACs for Patients with AF

In patients with non-valvular AF, evaluation using the $CHADS_2$ (Congestive heart failure, Hypertension, $Age \ge 75$, Diabetes, Stroke [doubled]) score or CHA_2DS_2 -VASc (Congestive heart failure, Hypertension, $Age \ge 75$ [doubled], Diabetes, Stroke [doubled]), Vascular disease, Age 65–74, Sex category [female]) score is recommended for the prediction of stroke risk⁷. In addition, evaluation using the HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile International Normalized Ratio (INR), Elderly (Age ≥ 65), Drugs/

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Table 1 Practical guide to choosing dabigatran 150 mg twice daily or apixaban 5 mg twice daily for patients with atrial fibrillation

Dabigatran 150 mg twice daily is recommended for patients meeting the following 2 criteria:

- 1. High risk of embolism.
- (e.g., ischemic stroke on warfarin, apixaban, rivaroxaban, or edoxaban^{3, 5)}; presence of left atrial appendage thrombus⁴⁾; or CHADS₂ scores \geq 5⁶⁾)
- 2. Low risk of bleeding. (age <75 years, no previous gastrointestinal bleeding, HAS-BLED scores ≤2, and creatinine clearance >50 mL/min)

Apixaban 5 mg twice daily should be considered for other patients.

CHADS₂: Congestive heart failure, Hypertension, Age \geq 75, Diabetes, Stroke [doubled]; CHA₂DS₂-VASc: Congestive heart failure, Hypertension, Age \geq 75 [doubled], Diabetes, Stroke [doubled], Vascular disease, Age 65–74, Sex category [female]; HAS-BLED: Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile International Normalized Ratio (INR), Elderly (Age \geq 65), Drugs/alcohol concomitantly.

alcohol concomitantly) score is recommended for the prediction of bleeding risk⁷.

In Japanese guidelines⁸, the use of dabigatran or apixaban is recommended for patients with AF with CHADS₂ scores ≥ 1 . Asian and European guidelines describe that the use of DOACs should be considered for patients with AF with CHA₂DS₂-VASc scores ≥ 1 for males or ≥ 2 for females^{7, 9}. American guidelines recommend the use of DOACs for patients with AF with CHA₂DS₂-VASc scores ≥ 2 for males or ≥ 3 for females¹⁰.

HAS-BLED scores \geq 3 suggest a high risk of bleeding, but do not preclude the use of DOACs⁷). Such patients should undergo regular review and follow-up of the modifiable bleeding risk factors⁷).

Practical Guide to Choosing Dabigatran 150 mg Twice Daily or Apixaban 5 mg Twice Daily for Patients with AF

Based on previous reports³⁻⁶, we recommend the use

of dabigatran 150 mg twice daily for patients with AF who have a high risk of embolism (e.g., ischemic stroke on warfarin, apixaban, rivaroxaban, or edoxaban^{3, 5}; presence of left atrial appendage thrombus⁴; or CHADS₂ scores \geq 5⁶) and a low risk of bleeding (age <75 years, no previous gastrointestinal bleeding, HAS-BLED scores ≤ 2 , and creatinine clearance >50 mL/min) (Table 1). However, the prevalence of such patients with AF is considered low because patients with AF with a high risk of embolism usually have a high risk of bleeding¹¹). In most other patients with AF, the use of apixaban 5 mg twice daily should be considered (Table 1). Unlike apixaban, dabigatran has no indications for venous thromboembolism and cannot be crushed and delivered via feeding tubes³. However, dabigatran has the only approved antidote, idatucizumab. Direct head-to-head comparison of DOACs in the future may clarify the best anticoagulation therapy for patients with AF.

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References

- 1. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009; 361: 1139–1151. [Medline] [CrossRef]
- Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011; 365: 981–992. [Medline] [CrossRef]
- 3. Shields AM, Lip GY. Choosing the right drug to fit the patient when selecting oral anticoagulation for stroke prevention in atrial fibrillation. J Intern Med 2015; 278: 1–18. [Medline] [CrossRef]
- 4. Schaefer JK, McBane RD, Wysokinski WE. How to choose appropriate direct oral anticoagulant for patient with nonvalvular atrial fibrillation. Ann Hematol 2016; 95: 437–449. [Medline] [CrossRef]
- 5. Weitz JI, Eikelboom J. Incorporating edoxaban into the choice of anticoagulants for atrial fibrillation. Thromb Haemost 2016; 115: 257–270. [Medline] [CrossRef]
- 6. Barnes GD, Kurtz B. Direct oral anticoagulants: unique properties and practical approaches to management. Heart 2016; 102: 1620–1626. [Medline] [CrossRef]
- 7. Chiang CE, Okumura K, Zhang S, *et al.* 2017 consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. J Arrhythm 2017; 33: 345–367. [Medline] [CrossRef]
- 8. JCS Joint Working Group Guidelines for Pharmacotherapy of Atrial Fibrillation (JCS 2013). Circ J 2014; 78: 1997–2021. [Medline] [CrossRef]
- 9. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace

2016; 18: 1609–1678. [Medline] [CrossRef]

- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm 2019; 16: e66–e93. [Medline]
- 11. Deitelzweig SB, Jing Y, Swindle JP, *et al.* Reviewing a clinical decision aid for the selection of anticoagulation treatment in patients with nonvalvular atrial fibrillation: applications in a US managed care health plan database. Clin Ther 2014; 36: 1566–1573.e3. [Medline] [CrossRef]