Initiation of warfarin is associated with decreased mortality in patients with infective endocarditis: a population based cohort study

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Background: The use of warfarin as an anticoagulant to prevent thromboembolism in setting of infective endocarditis (IE) remains controversial due to increased bleeding risks.

Purpose: To study the risks of stroke, mortality and bleeding in warfarin users compared with non-use.

Methods: Patients aged 18 or older and diagnosed with IE in our city between January 1st 1997 and August 31st 2020 were included. Patients with use of any anticoagulant 30 days before IE diagnosis were excluded. Patients initiated on warfarin within 14 days of IE diagnosis and patients without warfarin use were matched using propensity scores (1:1 ratio). The study outcomes were ischemic stroke, all-cause mortality, intracranial hemorrhage, and gastrointestinal bleeding. Cox proportional hazards regression was used to determine the hazard ratios [95% confidence intervals (CIs)] for the predictors of study outcomes at the end of 90-day follow up.

Results: The matched cohort consisted of 675 warfarin users (57.0% male, age 59±16 years, mean CHA2DS2-VASc score: 1.42±1.72) and 675 warfarin non-users (53.5% male, age 61±19 years, mean CHA2DS2-VASc score: 1.58±1.76). Warfarin use was not associated with ischemic stroke risk (Hazard ratio: 1.04 [95% CI, 0.70-1.53]), but was associated with a 50% decreased risk of all-cause mortality (HR: 0.50 [0.39-0.65]). In terms of bleeding risk, intracranial hemorrhage occurred in 36 (5.3%) warfarin users and in 29 (4.3%) patients warfarin non-users, and gastrointestinal bleeding occurred in 27 (4.0%) warfarin users and in 26 (3.9%) warfarin non-users.

Conclusions: Warfarin use is associated with decreased risks of mortality but similar risks of ischemic stroke compared with non-use of warfarin in patients with IE.
Figure 1: Study flow chart

7054 patients with a diagnosis of infective endocarditis from January 1, 1997 to August 31, 2020 recruited from all Hong Kong public hospitals

1027 patients excluded:
- 861 patients with use of anticoagulants within 30 days prior to IE diagnosis
- 166 patients aged under 18 years

6027 patients
- 1284 with warfarin use
- 4743 patients without warfarin use

550 patients with warfarin use after 14 days since infective endocarditis diagnosis excluded

5477 patients
- 734 with warfarin use within 14 days of infective endocarditis diagnosis
- 4743 patients without warfarin use

4127 excluded (not successfully matched for 1:1 propensity score matching)

1350 patients successfully matched
- 675 with warfarin use within 14 days of infective endocarditis diagnosis
- 675 patients without warfarin use
**Figure 2: Kaplan-Meier survival curves of study outcomes stratified by warfarin initiation**

- **90-day ischemic stroke risk**: HR 1.04 (95% CI 0.70 - 1.53) (p = 0.88)
- **90-day all-cause mortality risk**: HR 0.50 (95% CI 0.39 - 0.65) (p = 0.0001)
- **90-day intracranial hemorrhage risk**: HR 1.25 (95% CI 0.77 - 2.04) (p = 0.37)
- **90-day gastrointestinal bleeding risk**: HR 1.04 (95% CI 0.60 - 1.78) (p = 0.9)

Kaplen Meier curves of study outcomes