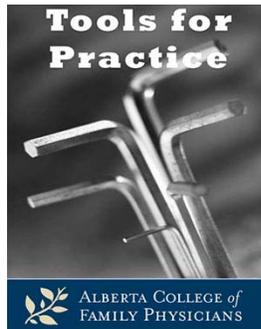


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Dabigatran versus Warfarin in Atrial Fibrillation

Clinical Question: What are the benefits and risks of dabigatran (Pradax) (a direct thrombin inhibitor), compared to warfarin, in patients with atrial fibrillation?

Evidence:

Randomized Controlled Trial (RCT)¹ of 18,113 patients given dabigatran 110mg BID or 150mg BID, or warfarin. Primary outcome: stroke or systemic embolism. Net benefit outcome: stroke, systemic or pulmonary embolism, MI, death or major hemorrhage.

- 63% male, mean age 71 years, mean CHADS₂ 2.1 (INR in range 64% of time for warfarin patients).
- After initial publication, additional events, mainly major bleeds and myocardial infarctions, were reported (included below where possible)²
- **Dabigatran 150mg BID versus warfarin (events per year):**
 - Dabigatran improved primary outcome (1.1% vs 1.7%), NNT (number needed to treat) 167, statistically significant (SS)
 - Dabigatran improved net benefit (6.9% vs 7.6%), NNT 137 (SS)
 - No difference in death or major bleed, but trend favoured dabigatran
 - Dabigatran had non-statistically significant increase in myocardial infarctions (0.8% vs 0.6%)
- **Dabigatran 110mg BID versus warfarin (events per year):**
 - No difference in primary outcome, death, myocardial infarction or net benefit
 - Dabigatran had fewer major bleeds (2.9% vs 3.6%) NNT 143, (SS)
- More patients stopped dabigatran (21%) than warfarin (17%) at 2 years (SS)
- Early RCT of dabigatran versus warfarin was too short with too few patients to assess meaningful clinical outcomes.³

Context:

- Difference in outcomes between dabigatran and warfarin depend on success of warfarin management (time INR in range)
 - Benefits of dabigatran over warfarin declined (or disappeared) the more INR was in range (in the warfarin group)⁴
- Prescribing considerations^{5,6}
 - Dabigatran contraindicated: Creatinine clearance (CrCl) <30 ml/minute, patients on ketoconazole
 - Drug interactions can occur with P-glycoprotein inhibitors (including verapamil, amiodarone, & quinidine)

- Dabigatran 150mg BID recommended but consider 110 mg BID for patients >80 years, or patients >75 years old with risk factors for bleeding, diminished renal function (CrCl 30 – 50 ml/ minute)
- If switching from warfarin to dabigatran, do when INR <2.0
- While a cost effectiveness analysis exists, application to Canada is uncertain.⁷

Bottom-line: Dabigatran offers some advantages over warfarin, but the benefits decline as warfarin management (time INR in range) improves. If using dabigatran, 150 mg bid is generally recommended (see above possible exceptions). Risk of myocardial infarction and cost effectiveness remain uncertain.

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