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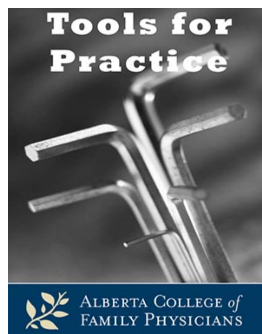
Reviewed: February 9, 2015
Evidence Updated: Context
Bottom Line: Updated to remove uncertainty around cost effectiveness and myocardial infarction
First Published: January 4, 2011



Dabigatran versus Warfarin in Atrial Fibrillation

Clinical Question: What are the benefits and risks of dabigatran (Pradaxa®) compared to warfarin, in patients with atrial fibrillation?

Bottom-line: Dabigatran offers some advantages over warfarin (example ~0.6%/year fewer strokes), but benefits decline as warfarin time in INR range improves. If using Dabigatran 150mg bid is generally recommended.

Evidence:

- Randomized Controlled Trial (RCT)[1,2] of 18,113 patients given dabigatran 110 mg BID or 150 mg 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 $CHADS_2$ 2.1. INR in range 64% of time for warfarin patients.
    - Dabigatran 150mg BID versus warfarin (events per year):
        - Dabigatran improved primary outcome (1.1% vs. 1.7%), Number Needed to Treat (NNT)=167.
        - Dabigatran improved net benefit (6.9% vs. 7.6%), NNT=137.
        - 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 110 mg BID vs. 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.
    - More patients stopped dabigatran (21%) than warfarin (17%) at two years.
    - Early RCT of dabigatran versus warfarin was too short (12 weeks) with too few patients (502) to assess meaningful clinical outcomes.[3]

Context:

- Potential risk of myocardial infarction: Number Needed to Harm ~400-500/year.[4,5]
- Dabigatran increases the risk of bleeding and thromboembolism in mechanical heart valves.[6]
- Benefits of dabigatran over warfarin declined (or disappeared) the more INR was in range (in the warfarin group).[7]
- Prescribing considerations:[8,9]
    - Dabigatran contraindicated: Creatinine clearance (CrCl) <30 ml/minute, patients on ketoconazole.
    - Drug interactions can occur with P-glycoprotein inhibitors (including verapamil, amiodarone, and quinidine).
    - Dabigatran 150 mg 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.
- Cost effectiveness analysis suggest dabigatran 150 mg is cost effective.[10,11]

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