Safety and efficacy of dabigatran versus warfarin in patients undergoing catheter ablation of atrial fibrillation: a systematic review and meta-analysis


CRD summary
This review indicated that dabigatran for catheter ablation in patients with atrial fibrillation had a similar incidence of thromboembolic events and major bleeding to that of warfarin, with low event rates overall. The observational nature of nearly all the studies in the review, coupled with the few events, mean that the authors' conclusions should not be seen as definitive.

Authors' objectives
To compare the efficacy and safety of dabigatran, with that of warfarin, for patients undergoing catheter ablation for atrial fibrillation.

Searching
MEDLINE, EMBASE, and The Cochrane Library were searched in April 2013; search terms were reported. There were no restrictions on publication status. To identify further relevant studies the reference lists of identified studies were checked, and relevant experts were contacted.

Study selection
Controlled studies of patients with atrial fibrillation who were treated either with warfarin or dabigatran, before undergoing catheter ablation, were eligible. Studies had to compare warfarin versus dabigatran, or dabigatran twice daily at 110mg versus 150mg. Studies had to report all of the following outcomes: major bleeding, thromboembolism, and all-cause mortality (specific definitions were provided). Studies had to follow up patients until at least the time of their hospital discharge.

In the included studies, the mean patient age ranged from 59 to 67 years. Approximately one fifth of participants were female. Where reported, the ejection fraction (for the left ventricle) ranged from 55% to 64%, and the percentage of patients with paroxysmal atrial fibrillation ranged from 46 to 83.

Three reviewers selected studies; agreement was needed for a study to be included.

Assessment of study quality
Study quality was evaluated using the Delphi Consensus criteria for randomised controlled trials, and a modified Newcastle–Ottawa Quality Assessment Scale for case-control studies (producing a score out of 9).

Three reviewers performed the assessments; all three had to agree on the final classification.

Data extraction
The data were extracted to obtain risk ratios, with 95% confidence intervals. The authors did not state how many reviewers extracted the data.

Methods of synthesis
Meta-analyses were performed to pool the risk ratios with 95% confidence intervals, using a random-effects model. Heterogeneity was assessed using $I^2$ and Cochran's Q. Publication bias was assessed using funnel plots.

Sensitivity analyses were performed to examine the effects of: trials whose patients were treated with uninterrupted warfarin, prospective studies, investigations published as full texts, studies whose follow-up was at least 30 days, and studies in which five of the nine items on the Delphi Consensus criteria, for randomised controlled trials, and the modified Newcastle–Ottawa Quality Assessment Scale, for case–control studies, were deemed satisfactory.

Results of the review
Fourteen studies were included (4,782 patients; range 54 to 999). Ten studies were retrospective. Of the four prospective studies, one was randomised (satisfying five Delphi criteria). Most of the non-randomised studies scored 6 or 7 out of 9 (range 3 to 7). Five studies were reported only as conference abstracts. Follow-up ranged from hospital discharge to three months.

No significant differences were found between patients treated with dabigatran and those treated with warfarin for thromboembolic events (RR 1.78, 95% CI 0.66 to 4.80; six of the 14 studies had no events; $I^2$=0) and major bleeding (RR 1.07, 95% CI 0.51 to 2.26; four of the 14 studies had no events; $I^2$=41%). Dabigatran was associated with significantly fewer minor bleeding events, compared with warfarin (RR 0.65, 95% CI 0.45 to 0.93; 13 studies; $I^2$=26%).

No significant differences were found between the 110mg dose and the 150mg dose of twice daily dabigatran for major bleeding (RR 0.19, 95% CI 0.01 to 3.18) and thromboembolism (RR 0.72, 95% CI 0.04 to 12.98). There was a difference in minor bleeding: more events were observed with the 110mg dose, and the difference was statistically significant (RR 3.60, 95% CI 1.96 to 6.62). The numbers of studies for these analyses were not stated.

No deaths were reported. Funnel plots did not suggest that the pooled results were affected by publication bias. The sensitivity analysis results were broadly similar to those of the main analyses (except that the minor bleeding results were not significant). The results for the management of peri-procedural bridging anticoagulation were reported.

**Authors' conclusions**

For patients with atrial fibrillation, undergoing catheter ablation, the analysis indicated that dabigatran had a similar incidence of thromboembolic events and major bleeding to that of warfarin, with low event rates overall.

**CRD commentary**

The review addressed a clear question and was supported by reproducible eligibility criteria. Efforts to identify published and unpublished studies were undertaken, using several methods; it was unclear whether any language restrictions were imposed. Suitable methods were used to reduce the risk of reviewer error and bias throughout the review, except for data extraction where the methods were not clear.

Study quality was assessed and the results were used in the sensitivity analyses. Only one of the studies was randomised. Appropriate methods were used to pool the data and to assess and investigate heterogeneity.

The observational nature of nearly all the studies in this review, coupled with the few events, mean that the authors' conclusions should not be seen as definitive.

**Implications of the review for practice and research**

**Practice:** The authors stated that creatinine clearance and bleeding risk should be taken into account when choosing the dabigatran dosage. For patients with normal renal clearance, the best option might be dabigatran suspension on the morning of the procedure, or the night before, but always less than 24 hours before the procedure. There could be a rationale for restarting dabigatran three-to-four hours after ensuring haemostasis, considering its short half-life and rapid onset of action.

**Research:** The authors stated that further prospective randomised studies were needed to confirm their findings, and to clarify which peri-procedural regimen could minimise the risk of thromboembolic complications with dabigatran.

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**Bibliographic details**


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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.