Thromboprophylaxis in cancer patients with central venous catheters: a systematic review and meta-analysis
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CRD summary
The review concluded that thromboprophylaxis had no significant effect on the risk of catheter-related thrombosis or bleeding in cancer patients. The authors' conclusions broadly reflected the evidence presented and appear likely to be reliable, although they appeared a little too definitive considering the authors' recommendations and the variable trial quality.

Authors' objectives
To determine the risks and benefits of primary thromboprophylaxis with anticoagulants in cancer patients with central venous devices.

Searching
MEDLINE and Cochrane Central Register of Controlled Trials (CENTRAL) databases and Google Scholar were searched without language restrictions to June 2006; search terms were reported. Reference lists of included studies were searched.

Study selection
Randomised controlled trials (RCTs) of the efficacy of primary thromboprophylaxis (low dose warfarin 1mg/day, unfractionated heparin or low molecular weight heparin) compared with placebo, no treatment or a different regimen for prevention of catheter-related thrombosis and systemic embolisation in cancer patients with central venous devices were eligible. Studies could be of patients with haematological or solid tumours. Only the first period of crossover studies was included. Studies of heparin flushes or heparin-bonded catheters alone were excluded.

Most of the included trials used superior vena cava catheters (type of catheter varied) and half of the studies used additional heparin flushes. Catheter thrombosis was diagnosed using contrast venography in all trials except one. Duration of treatment ranged from six to 16 weeks. Catheter thrombosis, bleeding and thrombocytopenia were the main outcomes assessed. Warfarin was the intervention used in half the trials; other studies evaluated enoxaparin, dalteparin and unfractionated heparin. Half of the studies used placebo as a comparator, three studies used no treatment and one compared warfarin with nadroparin.

It appeared that two reviewers independently assessed studies.

Assessment of study quality
Study quality was evaluated by assessing the criteria: allocation concealment; blinding of participants, investigators and outcome assessors; use of intention-to-treat data; and completeness of follow-up.

Two reviewers independently assessed study quality. Discrepancies were resolved via a third reviewer.

Data extraction
Data on numbers of events per patient were extracted in order to calculate relative risks (RR) with 95% confidence intervals (CI).

Two reviewers independently extracted data. Discrepancies were resolved via a third reviewer.

Methods of synthesis
Meta-analyses were performed to calculate pooled relative risks and their 95% CIs using a random-effects model.
Heterogeneity was assessed using $X^2$ and $I^2$ tests.

**Results of the review**

Eight RCTs were included (n=1,428, range 29 to 439 participants). Methods for allocation concealment were unclear in all studies. Four trials were reported as using complete blinding. Three trials analysed data for the intention-to-treat population. No studies reported on losses to follow-up. Duration of follow-up ranged from eight weeks after catheter removal to six months.

There were no statistically significant differences in the risk of catheter-related thrombosis for warfarin versus placebo or no treatment (RR 0.75, 95% CI 0.24 to 2.35, $I^2$=70%; three RCTs, n=425), heparin versus placebo or no treatment (RR 0.46, 95% CI 0.18 to 1.20, $I^2$=60%; four RCTs, n=886) or warfarin, unfractionated heparin or low-molecular-weight heparin versus placebo or no treatment (RR 0.59, 95% CI 0.31 to 1.13, $I^2$=58%; seven RCTs, n=1,311).

There were no significant differences between any treatments in terms of risk of overall bleeding (five studies) and risk of thrombocytopenia in the four RCTs that compared heparin with placebo.

**Authors’ conclusions**

In cancer patients with central venous devices, thromboprophylaxis has no significant effect on the risk of catheter-related thrombosis or bleeding. Use of primary thromboprophylaxis in cancer patients with central venous catheters did not cause any harm, but provided no benefit.

**CRD commentary**

The review addressed a clear question supported by appropriate inclusion criteria. Two databases and an internet search were used to identify studies in any language. It appeared that no explicit attempts were made to identify unpublished studies, so it was possible that some relevant trials were missed. Suitable methods were used to minimise the possibility of reviewer error and bias during the review processes. Study quality was evaluated, although no assessment was made of methods of randomisation (or whether groups were similar at baseline). Appropriate methods were used to pool data, although the authors’ decision to pool studies of no treatment with studies that used placebo appeared questionable. Heterogeneity was assessed and possible causes of heterogeneity were discussed. The authors noted that since confidence intervals were wide and heterogeneity was detected, they could not exclude the possibility of some benefit from coagulation.

The authors’ conclusions broadly reflected the evidence presented and appear likely to be reliable, although they appeared a little too definitive considering the authors’ recommendations and the variable trial quality.

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

**Practice:** The authors stated that universal use of anticoagulants as antineoplastic therapy or anticoagulation in all cancer patients could not be recommended until additional RCTs confirmed that the benefits of anticoagulation outweighed the risks.

**Research:** The authors stated that future RCTs needed to be adequately powered to detect differences in both short- and long-term outcomes. Future studies should have adequate follow-up periods to detect differences between symptomatic and asymptomatic central venous catheter thrombosis and should use a standardised definition of catheter-related thrombosis.

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**Bibliographic details**

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.