

Journal Watch

Parenteral anticoagulation for prolonging survival in patients with cancer who have no other indication for anticoagulation

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Reference: Parenteral anticoagulation for prolonging survival in patients with cancer who have no other indication for anticoagulation (Review). Copyright 2009 The Cochrane Collaboration. Published by John Wiley & Sons Ltd.

Abstract:

Background: Basic research and clinical studies have generated the hypothesis that anticoagulation may improve survival in patients with cancer through an antitumor effect in addition to the antithrombotic effect.

Objectives: To evaluate the efficacy and safety of heparin (including unfractionated heparin (UFH) and low molecular weight heparin (LMWH) and fondaparinux to improve survival of patients with cancer.

Search strategy: A comprehensive search for studies of anticoagulation in cancer patients including 1) A January 2007 electronic search of the following databases: Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and ISI the Web of Science; 2) Hand search of the American Society of Clinical Oncology and of the American Society of Hematology; 3) Checking of references of included studies; and 4) Use of "related article" feature in PubMed.

Selection criteria: Randomized controlled trials (RCTs) in cancer patients without clinical evidence of venous thromboembolism comparing UFH, LMWH or fondaparinux to no intervention or placebo and RCTs comparing two of the three agents of interest.

Data and collection analysis: Using a standardized form we extracted in duplicate data on methodological quality, participants, interventions and outcomes of interest including all cause mortality, venous thrombosis, symptomatic pulmonary embolism, major bleeding and minor bleeding.

Main results: Of the 3986 identified citations, five RCTs fulfilled the inclusion criteria. In all included RCTs the intervention consisted of heparin (either UFH or LMWH). The quality of the evidence was high for survival, low for major and minor bleeding and very low for DVT. Overall, heparin therapy was associated with a statistically and clinically significant survival benefit (hazard ratio=0.77; 95% CI:0.65 to 0.91). In subgroup analyses, patients with limited small cell lung cancer experienced a clear survival benefit (hazard ratio=0.56; 95% CI:0.38 to 0.83). The survival benefit was not statistically significant for either patients with extensive small cell lung cancer (hazard ratio=0.8; 95% CI:0.60 to 1.06) or patients with advanced cancer (hazard ratio=0.84; 95% CI:0.68-1.03). The increased risk of bleeding with heparin was not statistically significant (RR 1.78; 95% CI:0.73 to 4.38).

Author's conclusions: This review suggests a survival benefit of heparin in cancer patients in general, and in patients with small cell lung cancer in particular. Heparin might be particularly beneficial in patients with limited cancer or a longer life expectancy. Future research should further investigate the survival benefit of different types of anticoagulation (in different dosing, schedules and duration of therapy) in patients with different types and stages of cancer.

Strengths:

Type of study - Review of 5 RCTs

Specific inclusion and exclusion criteria used; two independent reviewers screened the studies

Very comprehensive search strategy and analyses, including subgroup analyses

Studies included compared LMWH and UFH at doses commonly used in our patient population

Long follow-up period in all studies, good rate of follow-up (lowest percentage of follow-up was 97%)

Three of the five studies had intention-to-treat analysis

Weaknesses:

Only 5 RCTs included, with a relatively small patient sample size (1189)

Some patients included in the studies had a previous history of VTE

Patients had multiple types of cancer and varying stages (heterogeneity among groups and studies)

None of the five studies used the same doses or duration of heparin anticoagulation

Relevance to Palliative Care:

Patients with cancer are at higher risk for developing co-morbid conditions such as deep venous thrombosis and pulmonary emboli. Depending on the stage of their disease, they may have limited physical activity or may even be bedridden; therefore, physicians, especially in the palliative care units, are often faced with the question of whether or not to initiate prophylactic therapy to prevent such conditions. Unfortunately, there are no strict guidelines related to heparin therapy in cancer patients with no other indication for anticoagulation. This systematic review addresses some of the concerns associated with heparin therapy, namely its effect on survival, reduction of DVTs and the risks of both major and minor bleeds, thereby allowing physicians and patients to make informed, evidence-based decisions regarding treatment.