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[Intervention Review]

# Anticoagulation for people with cancer and central venous catheters

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## ABSTRACT

### Background

Central venous catheter (CVC) placement increases the risk of thrombosis in people with cancer. Thrombosis often necessitates the removal of the CVC, resulting in treatment delays and thrombosis-related morbidity and mortality. This is an update of the Cochrane Review published in 2014.

### Objectives

To evaluate the efficacy and safety of anticoagulation for thromboprophylaxis in people with cancer with a CVC.

### Search methods

We conducted a comprehensive literature search in May 2018 that included a major electronic search of Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid), and Embase (Ovid); handsearching of conference proceedings; checking of references of included studies; searching for ongoing studies; and using the 'related citation' feature in PubMed. This update of the systematic review was based on the findings of a literature search conducted on 14 May 2018.

### Selection criteria

Randomized controlled trials (RCTs) assessing the benefits and harms of unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), vitamin K antagonists (VKA), or fondaparinux or comparing the effects of two of these anticoagulants in people with cancer and a CVC.

### Data collection and analysis

Using a standardized form, we extracted data and assessed risk of bias. Outcomes included all-cause mortality, symptomatic catheter-related venous thromboembolism (VTE), pulmonary embolism (PE), major bleeding, minor bleeding, catheter-related infection, thrombocytopenia, and health-related quality of life (HRQoL). We assessed the certainty of evidence for each outcome using the GRADE approach ([Balslem 2011](#)).

## Main results

Thirteen RCTs (23 papers) fulfilled the inclusion criteria. These trials enrolled 3420 participants. Seven RCTs compared LMWH to no LMWH (six in adults and one in children), six RCTs compared VKA to no VKA (five in adults and one in children), and three RCTs compared LMWH to VKA in adults.

### LMWH versus no LMWH

Six RCTs (1537 participants) compared LMWH to no LMWH in adults. The meta-analyses showed that LMWH probably decreased the incidence of symptomatic catheter-related VTE up to three months of follow-up compared to no LMWH (risk ratio (RR) 0.43, 95% confidence interval (CI) 0.22 to 0.81; risk difference (RD) 38 fewer per 1000, 95% CI 13 fewer to 52 fewer; moderate-certainty evidence). However, the analysis did not confirm or exclude a beneficial or detrimental effect of LMWH on mortality at three months of follow-up (RR 0.82, 95% CI 0.53 to 1.26; RD 14 fewer per 1000, 95% CI 36 fewer to 20 more; low-certainty evidence), major bleeding (RR 1.49, 95% CI 0.06 to 36.28; RD 0 more per 1000, 95% CI 1 fewer to 35 more; very low-certainty evidence), minor bleeding (RR 1.35, 95% CI 0.62 to 2.92; RD 14 more per 1000, 95% CI 16 fewer to 79 more; low-certainty evidence), and thrombocytopenia (RR 1.03, 95% CI 0.80 to 1.33; RD 5 more per 1000, 95% CI 35 fewer to 58 more; low-certainty evidence).

### VKA versus no VKA

Five RCTs (1599 participants) compared low-dose VKA to no VKA in adults. The meta-analyses did not confirm or exclude a beneficial or detrimental effect of low-dose VKA compared to no VKA on mortality (RR 0.99, 95% CI 0.64 to 1.55; RD 1 fewer per 1000, 95% CI 34 fewer to 52 more; low-certainty evidence), symptomatic catheter-related VTE (RR 0.61, 95% CI 0.23 to 1.64; RD 31 fewer per 1000, 95% CI 62 fewer to 51 more; low-certainty evidence), major bleeding (RR 7.14, 95% CI 0.88 to 57.78; RD 12 more per 1000, 95% CI 0 fewer to 110 more; low-certainty evidence), minor bleeding (RR 0.69, 95% CI 0.38 to 1.26; RD 15 fewer per 1000, 95% CI 30 fewer to 13 more; low-certainty evidence), premature catheter removal (RR 0.82, 95% CI 0.30 to 2.24; RD 29 fewer per 1000, 95% CI 114 fewer to 202 more; low-certainty evidence), and catheter-related infection (RR 1.17, 95% CI 0.74 to 1.85; RD 71 more per 1000, 95% CI 109 fewer to 356; low-certainty evidence).

### LMWH versus VKA

Three RCTs (641 participants) compared LMWH to VKA in adults. The available evidence did not confirm or exclude a beneficial or detrimental effect of LMWH relative to VKA on mortality (RR 0.94, 95% CI 0.56 to 1.59; RD 6 fewer per 1000, 95% CI 41 fewer to 56 more; low-certainty evidence), symptomatic catheter-related VTE (RR 1.83, 95% CI 0.44 to 7.61; RD 15 more per 1000, 95% CI 10 fewer to 122 more; very low-certainty evidence), PE (RR 1.70, 95% CI 0.74 to 3.92; RD 35 more per 1000, 95% CI 13 fewer to 144 more; low-certainty evidence), major bleeding (RR 3.11, 95% CI 0.13 to 73.11; RD 2 more per 1000, 95% CI 1 fewer to 72 more; very low-certainty evidence), or minor bleeding (RR 0.95, 95% CI 0.20 to 4.61; RD 1 fewer per 1000, 95% CI 21 fewer to 95 more; very low-certainty evidence). The meta-analyses showed that LMWH probably increased the risk of thrombocytopenia compared to VKA at three months of follow-up (RR 1.69, 95% CI 1.20 to 2.39; RD 149 more per 1000, 95% CI 43 fewer to 300 more; moderate-certainty evidence).

## Authors' conclusions

The evidence was not conclusive for the effect of LMWH on mortality, the effect of VKA on mortality and catheter-related VTE, and the effect of LMWH compared to VKA on mortality and catheter-related VTE. We found moderate-certainty evidence that LMWH reduces catheter-related VTE compared to no LMWH. People with cancer with CVCs considering anticoagulation should balance the possible benefit of reduced thromboembolic complications with the possible harms and burden of anticoagulants.

## PLAIN LANGUAGE SUMMARY

### Blood thinners to prevent blood clots in people with cancer and central venous catheters

#### Background

A central venous catheter (CVC) is a tube that is inserted into a large vein to give fluids or medicines. CVC placement increases the risk of blood clots in people with cancer. This review evaluated the effectiveness and safety of blood thinning agents (anticoagulants) in people with cancer and a CVC.

#### Study characteristics

We searched the scientific literature for studies of anticoagulants in people with cancer and a CVC. The evidence is current to 14 May 2018.

#### Key results

We included 13 trials enrolling 3420 people with cancer and a CVC. Most trials included people with various types and stages of cancer. Seven studies compared injectable blood thinners to no anticoagulation, six studies compared blood thinner pills to no anticoagulation, and three studies compared injectable blood thinners to blood thinner pills. When considering people with cancer and a CVC, injectable blood thinners probably reduced the risk of CVC-related blood clots compared to no anticoagulation and probably increased the risk of thrombocytopenia (low levels of platelets in the blood, which causes bleeding into the tissues) compared to blood thinner pills.

#### Certainty of the evidence

When comparing injectable blood thinners to no anticoagulation, we judged the certainty of the evidence to be moderate for blood clot at the catheter site, low for mortality, infection at the catheter site and minor bleeding, and very low for major bleeding.

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When comparing blood thinner pills to no anticoagulation, we judged the certainty of the evidence to be low for mortality major and minor bleeding, premature catheter removal and catheter-related infection low, and very low for blood clot at the catheter site.

When comparing injectable blood thinners to blood thinner pills, we judged the certainty of the evidence to be low for mortality and blood clots in the limbs and very low for blood clot at the catheter site, major and minor bleeding.