Direct oral anticoagulants reduce the risk of dying from bleeding compared with vitamin K antagonists in patients with atrial fibrillation or venous thromboembolism

Question

In people with atrial fibrillation or venous thromboembolism, do direct oral anticoagulants reduce the risk of dying from bleeding compared with vitamin K antagonists (warfarin)?

The research

A summary of 11 studies published up to November 2014.

Who? The studies included more than 70,000 people with atrial fibrillation and more than 27,000 patients with venous thromboembolism. Patients with these conditions need medium to long-term anticoagulation.

What? The studies compared direct oral anticoagulants with warfarin.

<table>
<thead>
<tr>
<th>Direct oral anticoagulants</th>
<th>vs</th>
<th>Vitamin K antagonists</th>
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| • Pradaxa (dabigatran), a direct thrombin inhibitor  
• Eliquis (apixaban), Xarelto (rivaroxaban), and Savaysa (edoxaban), all factor Xa inhibitors | Mostly Coumadin (warfarin) |

What the researchers found

Most studies were moderate to high quality.

People with atrial fibrillation

Taking a direct oral anticoagulant instead of warfarin would prevent 2 deaths from bleeding in 1000 people over an average of 1 to 3 years.

People with venous thromboembolism
Taking a direct oral anticoagulant instead of warfarin would prevent 1 death from bleeding in 1000 patients over an average of 6 months.

The bottom line

In people with atrial fibrillation or venous thromboembolism, treatment with a direct oral anticoagulant instead of a vitamin K antagonist (warfarin) reduces the risk of dying from bleeding.

Summary of findings

**Direct oral anticoagulants vs vitamin K antagonists (warfarin) for atrial fibrillation or venous thromboembolism**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Rate of dying from bleeding</th>
<th>Number of studies and quality of the evidence</th>
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<tbody>
<tr>
<td>Patients with atrial fibrillation</td>
<td>0.27%</td>
<td>About 2 fewer people out of 1000 died from bleeding</td>
</tr>
<tr>
<td>Patients with venous thromboembolism</td>
<td>0.06%</td>
<td>About 1 less person out of 1000 had fatal bleeding</td>
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This Evidence Summary is based on the following systematic review:


**Effect of direct oral anticoagulants (DOACs) on death due to bleeding**

The incidence of venous thromboembolism (VTE) in Canada has been estimated at about 1 per 1000 patients. Assuming a population of about 35,000,000, there will be about 35,000 new cases of VTE per year in Canada, and about 35 deaths per year will be prevented by using direct oral anticoagulants (DOACs) rather than warfarin. From a population perspective, this is undoubtedly an important result. Assuming a cost of $600
for 6 months of treatment with a DOAC, the cost per life saved would be $600,000, and the overall cost to save 35 lives would be $21 million. This is valuable information for policy makers and those in charge of coverage decisions.

Of course, the effect of DOACs on VTE recurrence and overall mortality should also be assessed. In making decisions about treatment, particularly when a patient is paying for the medication, absolute numbers are even more important to consider. In patients with VTE, the risk of dying from bleeding is about 2 per 1000 patients treated, and the risk is reduced to 1 per 1000 with DOACs compared with warfarin. Is this worth $600 out of pocket? There is no right or wrong answer, and the need for monitoring and the potential drug and food interactions should weigh in on the decision. Certainly, the risk is not so high that a patient should lose his peace of mind if he cannot afford treatment with a DOAC. And what about the lack of an antidote to reverse the effect of DOACs when bleeding occurs—a key concern when making the decision to start DOAC therapy. Although reversal of DOACs might be more cumbersome, the overall mortality due to bleeding is lower with DOACs than with warfarin. Thus, reversal might not be such a big problem.

Doctor, what is my risk of dying from bleeding if I take a DOAC?

Your risk of dying from bleeding is very low: About 1 in 1000 patients taking a DOAC for 6 months to treat VTE will die by bleeding. This is about half the risk of bleeding you would be exposed to by taking warfarin, the only anticoagulant that was available until few years ago and still is a viable and much cheaper alternative.