INESSS
LE SAVOIR PREND FORME

APRIL 2019

Use of direct oral anticoagulants and warfarin in the context of atrial fibrillation and venous thromboembolism

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Direction du médicament

Québec

This is the English summary of the guidance entitled Usage des anticoagulants oraux directs et de la warfarine dans le contexte de la fibrillation auriculaire et de la thromboembolie veineuse - Revues systématiques - published in April 2019.

The complete version of this guidance (in French) is available on the website of INESSS in the Publications section.

Membres de l'équipe projet

Auteurs principaux
Frédéric St-Pierre, Ph. D.
Ann Lévesque, Ph. D.

Collaborateurs internes
Gabriel Carpentier, Ph. D.
Éric Plante, Ph. D.
Mélanie Turgeon, M. Sc.

Coordonnatrice scientifique
Mélanie Tardif, Ph. D.

Directrice
Sylvie Bouchard, B. Pharm., D.P.H., M. Sc., MBA

Repérage d'information scientifique et soutien documentaire
Mathieu Plamondon, M.S.I.
Flavie Jouandon

Soutien administratif
Ginette Petit

SUMMARY – STATES OF KNOWLEDGE

Introduction

Between 2011 and 2014, the Institut national d'excellence en santé et en services sociaux (INESSS) published two clinical tools for supporting clinicians in their decision-making regarding oral anticoagulation therapy in patients with atrial fibrillation (AF): an optimal use guide (OUG) on dabigatran anticoagulation therapy and a decision support tool concerning the differential choice of oral anticoagulant (warfarin, dabigatran, rivaroxaban and apixaban) in the context of AF.

However, there have been a number of changes since then, including Health Canada's approval of idarucizumab (in 2016), a specific antidote that neutralizes the effect of dabigatran, and edoxaban (in 2017), a direct oral anticoagulant (DOAC), like dabigatran, rivaroxaban and apixaban. Furthermore, changes were made to the DOAC coverage criteria in Québec's public prescription drug insurance plan (PPDIP), and CoaguChek XS PT TEST® test strips, which are used for international normalized ratio (INR) monitoring in patients treated with a vitamin K antagonist (VKA), are now covered by this plan.

Given these changes, it was necessary to completely revamp the clinical tools published in the area of AF, in addition to justifying the addition of a new OUG on DOACs and warfarin in the context of venous thromboembolism (VTE).

Methods

To gather the scientific evidence needed to create the OUGs, four systematic reviews (SRs) were conducted. The first two concerned, respectively, the efficacy and safety of DOACs compared to those of VKAs in preventing stroke and systemic embolism in patients with AF, and in treating VTE and preventing recurrences. They were supplemented with an SR on the efficacy and safety of VKA anticoagulation therapy self-monitoring and self-management compared to those of a follow-up provided at a clinic by a health professional (standard follow-up) in preventing thromboembolic events and death, and another SR on those of idarucizumab in neutralizing the anticoagulant effect of dabigatran.

The scientific data search was conducted in several databases and was limited to items published in French or English between 2012 to 2018. The bibliographies in the selected publications were searched as well. Two reviewers independently evaluated the methodological quality of the selected publications using grids validated and recognized for each type of publication. The results were extracted by an evaluator using preestablished grids and were then validated by a second evaluator and presented in the form of a narrative synthesis. The scientific evidence for each outcome of interest examined was assessed according to four predetermined criteria (methodological quality, consistency, clinical impact of the intervention, and generalizability).

Results

First, the results of the selected studies show that DOACs are at least as effective and safe as warfarin in preventing stroke and systemic embolism in patients with AF. A reduction in the risk of intracranial bleeding is generally observed with most DOACs compared to warfarin, but this is accompanied, in certain cases, by an increased risk of gastrointestinal bleeding. These findings apply to most of the populations studied, with the exception of individuals who have undergone bariatric surgery, those who are severely overweight (a body weight > 120 kg or a body mass index (BMI) > 40 kg/m^2) and those with a ClCr of 15 to 30 mL/min, on whom the data are insufficient for drawing a conclusion.

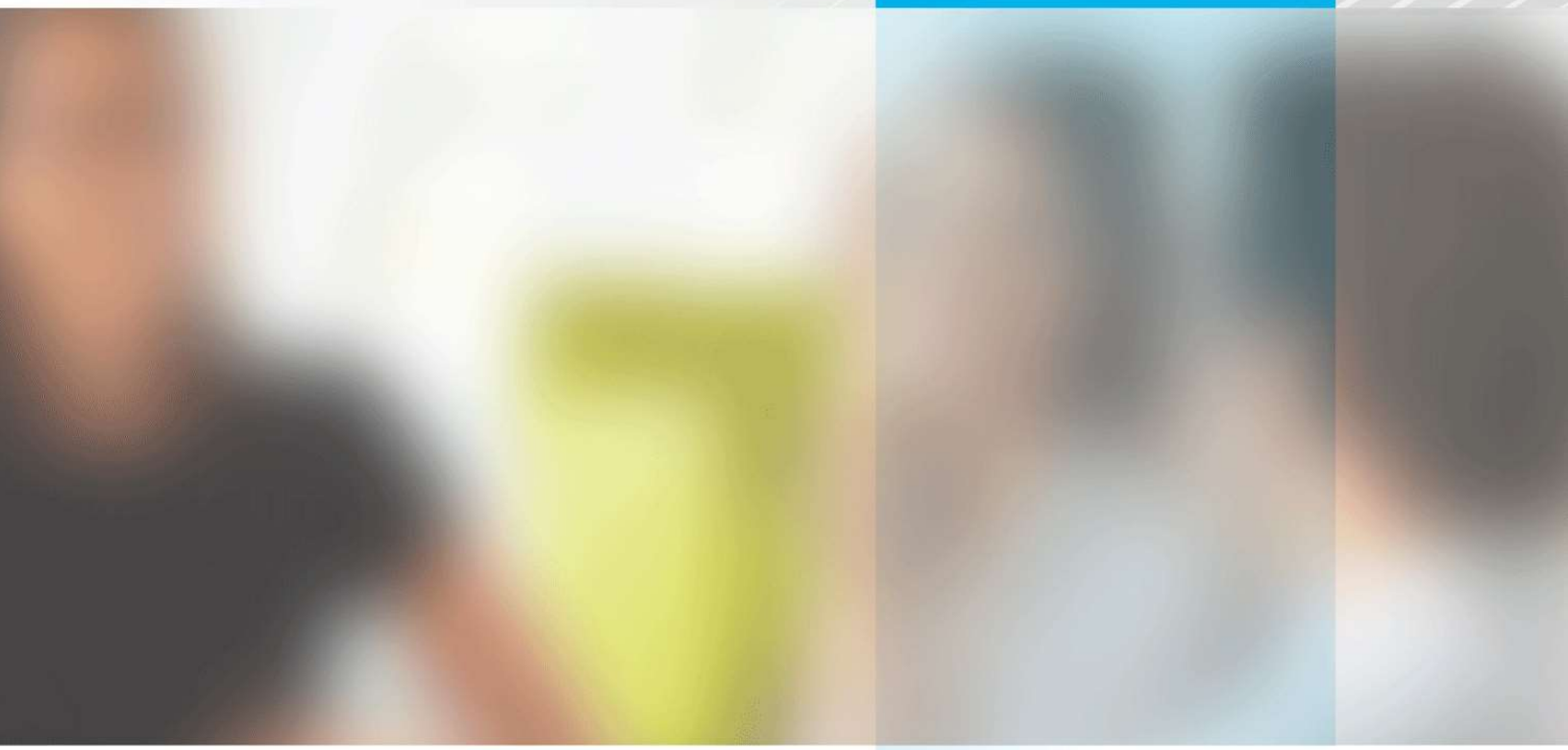
Findings similar to those for AF can be drawn from the selected studies on the treatment of VTE and the prevention of recurrences. Furthermore, these studies show that edoxaban and rivaroxaban are at least as effective as the low-molecular-weight heparins (LMWHs) in treating VTE and preventing recurrences in cancer patients, and they show an equivalent (rivaroxaban) or greater (edoxaban) risk of major bleeding that seems to be associated with the presence of gastrointestinal cancer. However, the data were insufficient for drawing any conclusions regarding the efficacy of DOACs in patients with a ClCr of 15 to 50 mL/min. As well, no conclusions can be drawn regarding patients with antiphospholipid syndrome because of the paucity of the available data on this subject and especially because of the heterogeneity of the medical problems that make up the clinical presentation of this syndrome. However, several of these safety analyses are based mainly on data obtained in an AF context, given the lower incidence of this type of event in a VTE context.

In other respects, the results of the studies selected for this SR report show that self-monitoring improves the efficacy of VKA anticoagulation therapy relative to the standard follow-up, i.e., that provided by a health professional at a clinic or hospital, by reducing the risk of thrombotic events without altering the treatment's safety profile. A similar conclusion can be drawn from the results regarding VKA anticoagulation therapy self-management, the difference being that the risk of all-cause mortality with such therapy is also lower compared to the standard follow-up.

Lastly, idarucizumab seems effective in neutralizing the effect of dabigatran in patients with uncontrolled or potentially fatal bleeding or whose condition requires emergency surgery, although no conclusion regarding its safety can be drawn.

Conclusions

The results presented in this SR report provided the necessary scientific data for developing recommendations presented in the OUGs on the use of DOACs and warfarin in the contexts of AF and VTE, notably, in certain specific populations. These SRs have also shed light on certain populations for which there is very little data available on the use of DOACs and that could benefit from more extensive clinical research, notably, individuals with a high body weight (> 120 kg), those who have undergone bariatric surgery and those with antiphospholipid syndrome.



Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec