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REVIEW

Effective diagnosis and treatment of pulmonary embolism: Improving patient outcomes

Des changements dans le diagnostic et la thérapeutique pour améliorer le pronostic de l'embolie pulmonaire

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Summary Pulmonary embolism can be life threatening and difficult to diagnose as signs and symptoms are not specific. European guidelines recommend stratification of pulmonary embolism by risk of early mortality. Patients with suspected pulmonary embolism should be assessed for clinical probability of pulmonary embolism using a validated risk score. A low or intermediate clinical probability plus a negative high-sensitivity D-dimer test excludes pulmonary embolism. Anticoagulation is indicated in patients with a positive multidetector computed tomography or high-probability lung scan. An important part of the management of patients with pulmonary embolism has traditionally been anticoagulant treatment with parenteral heparins and oral vitamin K antagonists. Although effective, this dual-drug approach is associated with limitations. Direct oral anticoagulants that may overcome some of these problems have been tested in phase III clinical trials for the treatment of venous thromboembolism. Of these, rivaroxaban and apixaban have demonstrated non-inferiority to standard therapy when given as single-drug approaches for venous thromboembolism treatment, and provided

Abbreviations: CI, Confidence interval; CrCl, Creatinine clearance; CT, Computed tomography; DVT, Deep vein thrombosis; GARFIELD, Global Anticoagulant Registry in the FIELD; HR, Hazard ratio; LMWH, Low-molecular-weight heparin; OAC, Oral anticoagulant; PE, Pulmonary embolism; RIETE, Registro Informatizado de Pacientes con Enfermedad TromboEmbólica; VKA, Vitamin K antagonist; VTE, Venous thromboembolism.

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significant reductions in major bleeding rates. Dabigatran and edoxaban were non-inferior to standard therapy when given as part of a dual-drug approach after initial parenteral anticoagulation, and reduced clinically relevant bleeding rates. There may be a benefit to extended anticoagulation with direct oral anticoagulants for the prevention of recurrent venous thromboembolism. Registry studies will provide more information on the use of these agents in real-world populations. Accurate diagnosis and risk stratification of patients with pulmonary embolism, together with simplified anticoagulation therapy, is likely to improve outcomes.

MOTS CLÉS
Traitement anticoagulant ;
Diagnostic ;
Embolie pulmonaire

Résumé L'embolie pulmonaire est une pathologie potentiellement létale et est difficile à diagnostiquer. Les signes et les symptômes de l'embolie pulmonaire ne sont pas spécifiques. Les recommandations européennes recommandent de stratifier les malades selon leur risque de mortalité. La probabilité clinique de l'embolie pulmonaire doit être évaluée à l'aide d'un score devant toute suspicion clinique d'embolie pulmonaire. Une probabilité clinique faible ou intermédiaire associée à un taux de D-dimère normal élimine le diagnostic. Le diagnostic est affirmé par l'angioscanner thoracique ou la scintigraphie pulmonaire. Le traitement initial associe traditionnellement une héparinothérapie parentérale et un antagoniste de la vitamine K. Ce traitement est efficace mais comporte certains inconvénients. Des inhibiteurs oraux directs de la coagulation, qui pourraient limiter ces inconvénients, ont été testés dans de grands essais de phase III. Parmi eux, le rivaroxaban et l'apixaban administrés dès l'inclusion ont démontré leur non-infériorité par rapport au traitement standard en termes d'efficacité tout en obtenant une réduction des hémorragies majeures. Le dabigatran et l'edoxaban sont également non inférieurs au traitement standard après un traitement parentéral initial et sont également associés à une réduction des saignements cliniquement significatifs. La prolongation du traitement au-delà de six mois en cas de thrombose non provoquée pourrait être associée à une réduction des récidives. Des études de registres devraient apporter des informations sur l'utilisation de ces nouvelles molécules en situation de soin courant. Un diagnostic rigoureux, associé à une stratification du risque et à un traitement anticoagulant simplifié devraient permettre une amélioration du pronostic de l'embolie pulmonaire.

Introduction

Pulmonary embolism (PE) is a relatively common disease, with an incidence ranging from 60 to 112 per 100,000 inhabitants of the United States [1], and is the third most common cause of death among patients with cardiovascular diseases [2]. Patients are at particular risk in the acute stage of the disease, with 30-day mortality rates in excess of 15% for PE associated with shock and/or hypotension [3]. PE is difficult to diagnose because of the wide range of presentations of the disease. Among those patients who die of PE, 94% do so before diagnosis [4]. The mainstay of treatment for most patients with PE is anticoagulation, and the risk of death is much reduced in optimally anticoagulated patients. The recurrence rate of venous thromboembolism (VTE) after stopping anticoagulant treatment varies with the cause of the disease and is much higher in patients with unprovoked VTE than in patients with VTE provoked by a major transient risk factor [5]. Duration of anticoagulant treatment is tailored to the risks of VTE recurrence and bleeding for each individual patient [3,6].

Treatment of PE has predominantly involved the use of low-molecular-weight heparins (LMWHs), unfractionated heparin or fondaparinux in combination with vitamin K antagonists (VKAs) [3,6]. However, this dual-drug approach is associated with some limitations, including the need to co-administer the parenteral agent and VKA concurrently for several days at the start of treatment, and the subsequent need for regular coagulation monitoring and dose adjustments during VKA monotherapy. The recently developed direct oral anticoagulants circumvent some of these limitations, and several have completed large phase III clinical trials in the treatment of acute VTE. In Europe, only rivaroxaban is currently approved for the treatment and secondary prevention of deep vein thrombosis (DVT) and PE. In the USA, rivaroxaban and, more recently, dabigatran have been approved for VTE treatment.

This review covers the diagnosis and treatment of PE, focusing on data for direct oral anticoagulants.

Clinical presentations of PE

Most patients with suspected PE present with some degree of chest pain and dyspnoea, a frequent cause of referral to the emergency department. These symptoms are non-specific and can be confused with other differential diagnoses, such as acute coronary syndromes, exacerbation of chronic obstructive pulmonary disease or pneumonia [7]. The most specific symptoms of PE—haemoptysis and calf