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Editorial

National Consensus on the Diagnosis, Risk Stratification and Treatment of Patients with Pulmonary Embolism: An Update☆

Actualización del Consenso nacional sobre el diagnóstico, estratificación de riesgo y tratamiento de los pacientes con tromboembolia de pulmón

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In December 2013, the journal Archivos de Bronconeumología published the National consensus on the diagnosis, risk stratification and treatment of patients with pulmonary embolism.[1] This consensus represented a landmark in our specialty by bringing together the views of 6 different scientific societies (SEPAR, SEMI, SETH, SEMES, SEC and SEACV) on pulmonary embolism (PE).

During the compilation of the consensus document, several studies were completed and published on the use of direct oral anticoagulants: dabigatran (a thrombin inhibitor), rivaroxaban, apixaban and edoxaban (factor Xa inhibitors). These anticoagulants have all been approved by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the Spanish Agency of Medicines and Medical Devices (AEMPS) for the treatment of deep vein thrombosis (DVT) and PE, and for the prevention of recurrent DVT and PE in adults. In this editorial, we will analyze the design and the results of the pivotal clinical trials, and update our recommendations on anticoagulant treatment for PE.

In a pooled analysis of 2 clinical trials which evaluated rivaroxaban in the acute and long-term treatment (e.g. during the first 3, 6 or 12 months) of DVT and PE (58%), the efficacy of rivaroxaban was found to be similar to that of standard treatment (parenteral anticoagulation overlap therapy followed by vitamin K antagonists) (hazard ratio [HR]: 0.87; 95% confidence interval [CI]: 0.66–1.19), with a 50% reduction in major bleeding (HR: 0.54; 95% CI: 0.37–0.79).[2] Rivaroxaban is administered orally (previous parenteral anticoagulation is not required) at doses of 15 mg twice a day for 3 weeks, followed by 20 mg once a day.

The AMPLIFY trial evaluated the efficacy and safety of apixaban in the treatment of 5395 patients with DVT or PE (34%) in the first 6 months after a thrombotic event.[3] The efficacy of apixaban was similar to that of standard treatment (relative risk [RR]: 0.84; 95% CI: 0.60–1.18) with a statistically significant reduction in major bleeding (RR: 0.31; 95% CI: 0.17–0.55) and clinically relevant non-major bleeding (RR: 0.48; 95% CI: 0.38–0.60). Apixaban is administered orally (previous parenteral anticoagulation is not required) at doses of 10 mg twice a day for the first 7 days, followed by 5 mg twice a day. For extended treatment (e.g., beyond the first 3–6 months), a dose of 2.5 mg twice a day is recommended.

Clinical trials RECOVER and RECOVER II, which included 5107 patients with DVT and/or PE (31%) who were treated with low-molecular-weight heparin or unfractionated heparin during the first 5–11 days, compared the efficacy and safety of dabigatran 150 mg twice a day with warfarin for 6 months.[4] The results of these studies demonstrated non-inferiority for recurrent thrombotic events (HR: 1.09; 95% CI: 0.76–1.57) and for major bleeding (HR: 0.73; 95% CI: 0.48–1.11), and a significant reduction of 30% for all bleeds (HR: 0.70; 95% CI: 0.61–0.79).

The Hokusai-VTE randomized clinical trial, which included 4921 patients with DVT and 3319 with PE who had received heparin for a median period of 7 days, compared the efficacy and safety of edoxaban 60 mg/day (30 mg in patients with creatinine clearance 30–50 ml, weight ≤60 kg, or concomitant use of potent P-glycoprotein inhibitors) with warfarin for 3–12 months.[5] Edoxaban was not inferior to warfarin for the primary efficacy outcome (incidence of fatal or non-fatal recurrent thrombotic event) (HR: 0.89; 95% CI: 0.70–1.13). The incidence of major or clinically relevant non-major bleeding was significant lower in the group which received edoxaban (HR: 0.81; 95% CI: 0.71–0.94).

No studies have been designed to directly compare direct oral anticoagulants with agents of the same class:

- For acute and long-term treatment (e.g., first 3–6 months) of non-cancer patients with PE, we suggest the use of rivaroxaban or apixaban over vitamin K antagonists.
- For long-term treatment (e.g., first 3–6 months) of non-cancer patients with PE who have received an initial period of at least

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5 days of parenteral anticoagulation, we suggest the use of dabigatran or edoxaban over vitamin K antagonists

Conflict of interests

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