Intracranial hemorrhage risk with the new oral anticoagulants: a systematic review and meta-analysis

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Abstract
The new oral anticoagulants/non-vitamin K antagonists oral anticoagulants (NOACs) have recently reached the market and less is known about their safety in comparison to their efficacy. Therefore, we aimed to evaluate intracranial hemorrhage (ICH) risk with NOACs, the most feared adverse event of anticoagulation treatment. This is a systematic review and meta-analysis of phase III randomized controlled trials (RCTs) comparing NOACs versus any control and reporting ICH events. Studies were searched through Medline and Cochrane Library (April 2014). Reviews and reference lists were also screened. Random effects' meta-analysis was performed to derive pooled estimates expressed as relative risk (RR) and 95 % CI. Number needed to treat/harm (NNT/NNH) taking into account the baseline risk was also calculated. Heterogeneity was evaluated with I 2 test. 18 RCTs evaluating 148,149 patients were included. NOAC significantly reduced ICH risk compared to vitamin K antagonists (VKA) (RR 0.44; 95 % CI 0.36–0.54; I 2 = 37 %; NNT: 137 during 2 years) and to sequential treatment with low molecular weight heparin and VKA (RR 0.28; 95 % CI 0.12–0.65; I 2 = 0 %; NNT: 463 patients during 7 months). Compared to placebo, NOACs were associated with an increased ICH risk (RR 3.31; 95 % CI 1.59–6.90; I 2 = 0 %; NNH: 433 during 1 year). Results were similar for the different NOAC drugs and across the different clinical conditions. In patients requiring anticoagulation treatment, the risk of ICH is about half with the NOACs in comparison to standard antithrombotic treatment. This safer profile found in RCTs should be confirmed in real-world database studies.

Keywords
Intracranial hemorrhages, Anticoagulants, Meta-analysis