Risk of Renal Failure With the Non-Vitamin K Antagonist Oral Anticoagulants: Systematic Review and Meta-Analysis

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Abstract

Purpose

Vitamin K antagonists (VKA)-related nephropathy is a novel entity characterized by acute kidney injury related to International Normalized Ratio supratherapeutic levels. Non-vitamin K antagonists oral anticoagulants (NOACs) have a predictable dose-response relationship and an improved safety profile. We hypothesized that these drugs do not have an increased risk of incident renal failure, which may be detrimental for the use of NOACs.

Methods

Systematic review and meta-analysis of phase III randomized controlled trials (RCTs). Trials were searched through Medline, Cochrane Library and public assessment reports in August 2014. Primary outcome was renal failure. NOACs were evaluated against any comparator. Random-effects meta-analysis was performed by default, and pooled estimates were expressed as Risk Ratio (RR) and 95%CI. Heterogeneity was evaluated with I(2) test.

Results

Ten RCTs fulfilled inclusion criteria (one apixaban RCT, three dabigatran RCTs, and six rivaroxaban RCTs), enrolling 75 100 patients. Overall NOACs did not increase the risk of renal failure with an RR 0.96, 95%CI 0.88-1.05 compared with VKA or Low-molecular weight heparin (LMWH), without significant statistical heterogeneity (I(2) = 3.5%). Compared with VKA, NOACs did not increase the risk of renal failure (RR 0.96, 95%CI 0.87-1.07; I(2) = 17.8%; six RCTs). Rivaroxaban did not show differences in the incidence of renal failure compared with LMWH (RR 1.20, 95%CI 0.37-3.94; four trials), but there was an increased risk of creatinine elevation RR 1.25, 95%CI 1.08-1.45; I(2) = 0%.

Conclusions

NOACs had a similar risk of renal failure compared with VKA/LMWH in phase III RCTs. Post-marketing surveillance should be warranted.