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EFFICACY AND SAFETY OF DIRECT ORAL ANTICOAGULANTS VERSUS VITAMIN K ANTAGONISTS FOR LEFT VENTRICULAR THROMBUS: AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS

ADDITIONAL MATERIALS

Subgroup analysis depending on the DOAC class

We compared separately the use of each DOAC (rivaroxaban/apixaban/dabigatran/edoxaban) with VKA. Unfortunately, only rivaroxaban and apixaban data were available for the outcomes of interest, and no information was provided for dabigatran and edoxaban in the studies included in the meta-analysis.

For example, data on the number of thromboembolic and hemorrhagic complications of rivaroxaban were available in three studies [17, 18, 31]. There was a total 2 (2% of 100 patients) and 11 (10.4% of 106 patients) thromboembolic events in the rivaroxaban group and the VKA group, respectively. Rivaroxaban statistically significantly (4.8-fold, compared to VKA) reduced the risk of thromboembolic complications (OR 0.21; 95% CI: 0.05–0.83; $p=0.03$).

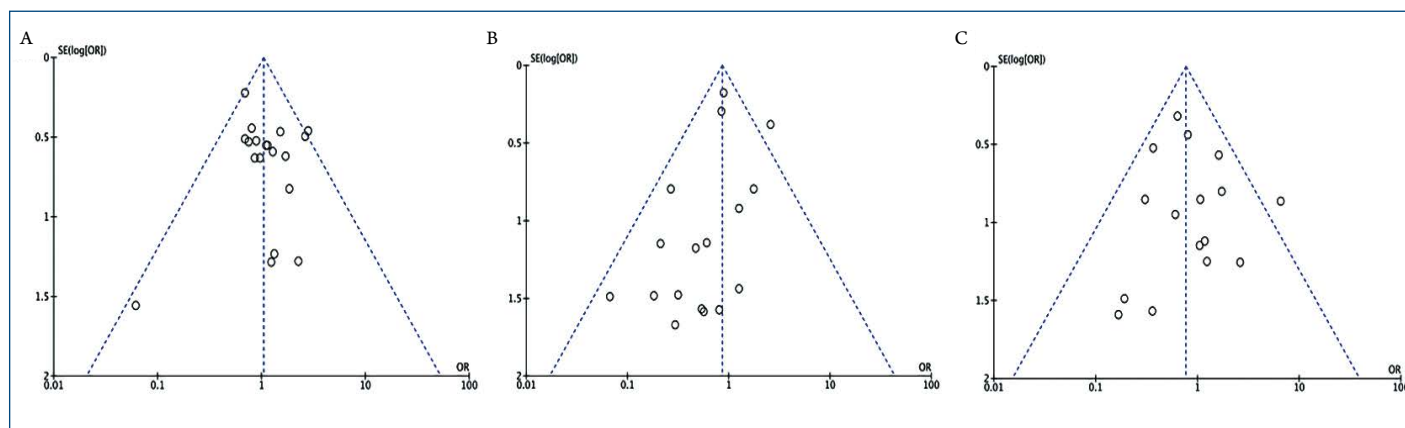
The heterogeneity test was not significant, $p=0.34$, $I^2=7\%$ (Figure 3A). There was a total 6 (6% of 100 patients) and 10 (9.4% of 106 patients) hemorrhagic events in the rivaroxaban group and the VKA group, respectively. The pooled analysis comparing rivaroxaban to VKA showed no statistically significant differences in hemorrhagic events (OR 0.60; 95% CI: 0.21–1.71; $p=0.34$). The heterogeneity test was not significant,

$p=0.37$, $I^2=0\%$ (Figure 3B). Information on the frequency of thrombus resolution was available for rivaroxaban in five studies [17, 18, 22, 25, 31]. There were 102 (79.7% of 128 patients) and 148 (71.2% of 208 patients) patients with thrombus resolution in the rivaroxaban group and the VKA group, respectively. The meta-analysis showed that there was no statistically significant difference in the frequency of LV thrombus resolution between the DOAC group and the VKA group (OR 1.44; 95% CI: 0.83–2.48; $p=0.20$). The heterogeneity test was not significant, $p=0.18$, $I^2=36\%$ (Figure 3C).

As for apixaban, only three studies [19, 22, 25] contained data on the frequency of thrombus resolution and only one [19] contained data on thromboembolic and hemorrhagic events, which is why we performed only a pooled analysis of the differences in the frequency of thrombus resolution.

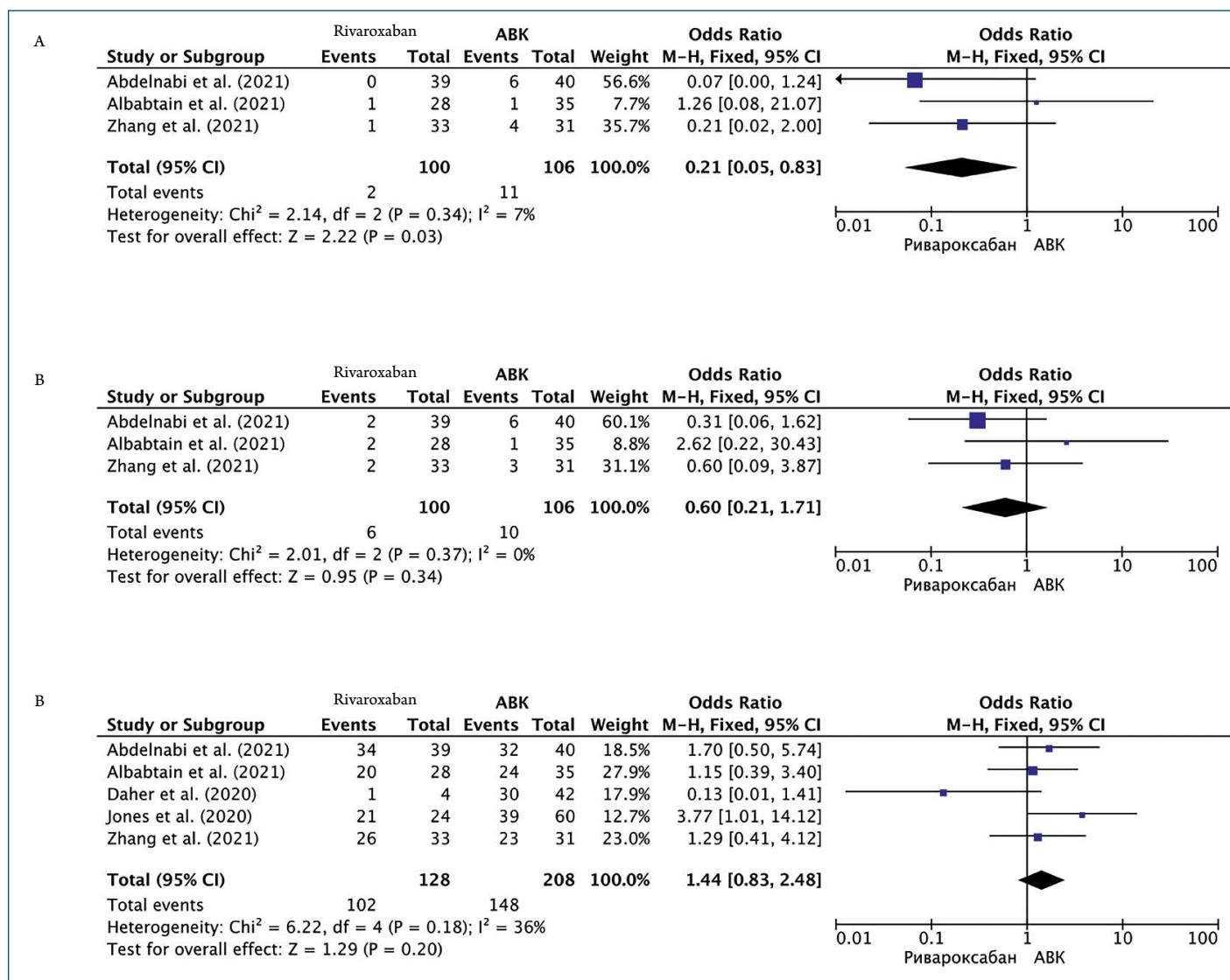
There were 42 (93.3% of 45 patients) and 84 (70.6% of 119 patients) patients with thrombus resolution in the apixaban group and the VKA group, respectively. Thus, there were statistically significantly more (4.88 times) cases of thrombus resolution in the apixaban group than in the VKA group (OR 4.88; 95% CI: 1.37–17.30; $p=0.01$). The heterogeneity test was not significant, $p=0.77$, $I^2=0\%$ (Figure 4).

Figure 1. Funnel plot for (A) thrombus resolution, (B) thromboembolism, (C) bleeding in the DOAC group versus the VKA group



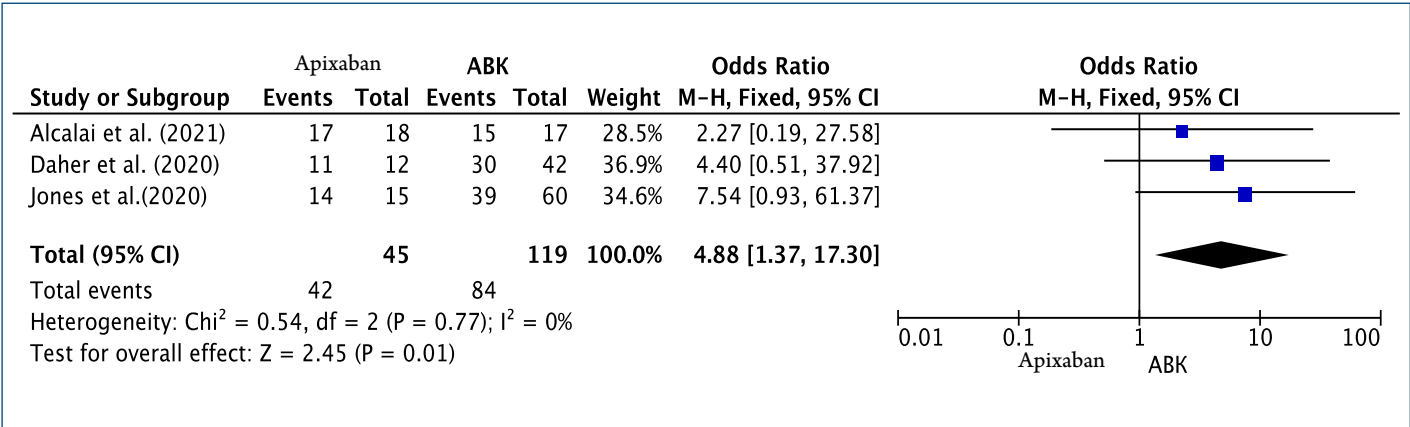
DOAC, direct oral anticoagulant; VKA, vitamin K antagonist; SE, standard error; OR, odds ratio.

Figure 3. Forest plot of odds ratio (logarithmic scale) for (A) thromboembolic risks, (B) hemorrhagic complications and (C) thrombus resolution during apixaban therapy compared to VKAs



The center of each line represents the OR for each study, and the ends of the horizontal lines represent 95 % CI. The solid vertical line is the OR equal to 1. VKA, vitamin A antagonist; OR, odds ratio; CI, confidence interval.

Figure 4. Forest plot of odds ratio (logarithmic scale) for thrombus resolution during apixaban therapy compared to VKAs



The center of each line represents the OR for each study, and the ends of the horizontal lines represent 95 % CI. The solid vertical line is the OR equal to 1. VKA, vitamin A antagonist; OR, odds ratio; CI, confidence interval.

Scheme 1. Flowchart for the selection of studies included in the review

