Direct oral anticoagulants versus vitamin K antagonists for left ventricular thrombus: a systematic review and meta-analysis


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Introduction: Left ventricular thrombi (LVTs) increase the risk of stroke and systemic embolism and are commonly seen after acute myocardial infarction. While vitamin K antagonists (VKAs) are the recommended first-line treatment for LVT, direct oral anticoagulants (DOACs) are being used as an alternative. However, the comparative efficacy and safety of DOACs and VKAs in LVT treatment are unclear.

Purpose: We conducted a systematic review with meta-analysis to evaluate the impact of DOACs compared with VKAs therapy in patients with LVT.

Methods: PubMed, Embase, and Cochrane were systematically searched for studies that compared DOACs versus VKAs and reported efficacy and safety endpoints. We performed meta-analyses with fixed or random effect models based on the level of heterogeneity determined by the Cochrane Q-test and I² statistics.

Results: Three randomised controlled trials (RCTs) and 29 cohort studies were included, with 4,400 patients assigned to either DOACs (1,307 patients) or VKAs (3,093 patients). Our findings indicate that DOACs therapy did not significantly reduce stroke/systemic embolic events (OR 0.90; 95% CI 0.65-1.26; p=0.54; I²=33%), stroke (OR 0.90; 95% CI 0.59-1.36; p=0.60; I²=7%), systemic embolic events (OR 0.65; 95% CI 0.39-1.06; p=0.08; I²=0%), thrombus resolution (OR 1.11; 95% CI 0.92-1.33; p=0.27; I²=0%), minor bleeding (OR 0.68; 95% CI 0.39-1.18; p=0.17; I²=0%), major bleeding (OR 0.84; 95% CI 0.47-1.49; p=0.54; I²=16%), or all-cause mortality (OR 1.01; 95% CI 0.75-1.36; p=0.97; I²=0%) compared to VKAs. However, DOACs therapy was associated with a statistically significant reduction in any bleeding (OR 0.72; 95% CI 0.55-0.96; p=0.02; I²=0%) and clinically relevant bleeding (OR 0.62; 95% CI 0.41-0.92; p=0.02; I²=0%) compared to VKAs therapy. Our subgroup analysis of patients treated with apixaban revealed no significant differences between DOACs and VKAs therapies for stroke, clinically relevant bleeding, and all-cause mortality. Conversely, rivaroxaban therapy was associated with a statistically significant reduction in systemic embolic events and clinically relevant bleeding compared to VKAs therapy.

Conclusion: DOACs therapy was not associated with reduced efficacy and safety endpoints compared to VKAs therapy, except for fewer haemorrhagic events. Rivaroxaban therapy had a significant reduction in systemic embolic and hemorrhagic events. These findings support the superiority of DOACs over VKAs therapy for LVT.
PRISMA Flow-Chart

Identification

Pubmed search: 108 results
Embase search: 234 results
Cochrane search: 24 results

Records identified in database search: 366 results

Duplicate reports (n = 138)

Number screened: 228 results

Excluded by title/abstract (n = 188)

Full-text reviewed: 40 results

Full-text articles excluded after applying inclusion and exclusion criteria (n = 12):
- Ineligible study design (n = 5)
- Overlapping populations (n = 2)
- Others (n = 5)

Studies identified through backward snowballing (n = 4)

Included

32 included RCTs in the qualitative synthesis

32 included RCTs in quantitative synthesis (meta-analysis)
  - 3 Randomized Controlled Trials
  - 29 Cohort Studies (non-randomized)
Forest plot of odds ratios (OR) for left ventricular thrombus outcomes
A comparison of direct oral anticoagulants (DOACs) and vitamin K antagonists (VKA)

- **Outcome**: Stroke/Systemic Embolism
  - Rivaroxaban: 4158 (94.5), 393 (8.9)
  - Edoxaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.9 (0.65-1.26), 0.91 (0.6-1.2), 0.65 (0.39-1.06)
  - P-Value: 0.54, 0.1, 0.08
  - I²: 33%, 7%, 0%

- **Outcome**: Stroke
  - Rivaroxaban: 1626 (37), 393 (8.9)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.9 (0.59-1.36), 0.91 (0.6-1.2), 0.65 (0.39-1.06)
  - P-Value: 0.6, 0.92, 0.08
  - I²: 7%, 1%, 0%

- **Outcome**: Systemic Embolism
  - Rivaroxaban: 1434 (32.6), 393 (8.9)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.9 (0.37-4.61), 0.38 (0.15-0.92)
  - P-Value: 0.44, 0.03
  - I²: 34%, 0%

- **Outcome**: Thrombus Resolution
  - Rivaroxaban: 2601 (59.1), 393 (8.9)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 1.11 (0.92-1.33), 1.51 (0.96-2.37)
  - P-Value: 0.27, 0.07
  - I²: 0%

- **Outcome**: Any Bleeding
  - Rivaroxaban: 3213 (73), 314 (7.1)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.72 (0.55-0.96), 0.62 (0.41-0.92)
  - P-Value: 0.02, 0.02
  - I²: 0%

- **Outcome**: Clinically Relevant Bleeding
  - Rivaroxaban: 2785 (63.3), 330 (7.0)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.26 (0.07-0.97), 0.2 (0.02-1.92)
  - P-Value: 0.04, 0.16
  - I²: 0%

- **Outcome**: Minor Bleeding
  - Rivaroxaban: 884 (20.1), 251 (5.7)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.68 (0.39-1.18), 1.56 (0.52-4.82)
  - P-Value: 0.17, 0.41
  - I²: 0%

- **Outcome**: Major Bleeding
  - Rivaroxaban: 1097 (24.9), 330 (7.5)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 0.84 (0.47-1.49), 0.29 (0.08-1.12)
  - P-Value: 0.54, 0.07
  - I²: 16%

- **Outcome**: All-Cause Mortality
  - Rivaroxaban: 1708 (38.8), 314 (7.1)
  - Apixaban: 142 (3.2), 59 (1.3)
  - OR (95% CI): 1.01 (0.75-1.36), 0.67 (0.15-3.06)
  - P-Value: 0.97, 0.6
  - I²: 0%