Utility of direct oral anticoagulants for left ventricular thrombus: lessons to learn from a systematic review and meta-analysis?

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Introduction

Left ventricular thrombus (LVT) may occur in a variety of conditions including acute anterior wall myocardial infarction, cardiomyopathy with left ventricular ejection fraction of less than 50%, and apical wall motion abnormality. Left ventricular dysfunction with or without associated wall motion abnormality results in the stasis of blood which is a precursor for thrombus formation. With regard to the treatment of LVT, no formal guidelines exist for the use of direct oral anticoagulants (DOACs), and warfarin is typically endorsed.¹ Chen et al² performed a systematic review and meta-analysis on the use of direct oral anticoagulants versus vitamin K antagonist for patients with LVT. The main conclusion from this study is that direct oral anticoagulants had similar efficacy as vitamin K antagonists for the prevention of stroke, systemic embolism, thrombus resolution, and any bleeding risk. The use of DOACs, when compared with vitamin K antagonists for treatment of LVT, was associated with lower risk of stroke and clinically relevant bleeding.

The current study addresses an important and clinically relevant question regarding the use of DOACs for LVT. DOACs have been well validated for venous thromboembolism and atrial fibrillation but there is a paucity of data regarding their utility in LVT. The literature search for this review is limited to Embrace and PubMed. It would have been useful to use additional databases, for example, Web of Science, CINAHL, and Science Direct, to avoid risk of missing additional studies.³

Statistics quality assessment

Chen et al² state: “A fixed-effect model was applied if no significant heterogeneity was observed; otherwise, a random-effects model was used.” This approach is not consistent with what is generally considered to be a standard statistical practice in meta-analyses. For example, in one of the leading texts on meta-analysis, Borenstein et al⁴ state: “Some have adopted the practice of starting with a fixed-effect model and then switching to a random-effects model if the test of homogeneity is statistically significant. This practice should be discouraged because the decision to use the random-effects model should be based on our understanding of whether or not all studies share a common effect size, and not on the outcome of a statistical test (especially since the test for heterogeneity often suffers from low power).” Chen et al² could have provided better justification for using a fixed-effects model instead of a random-effects model. Similarly, their use of a fixed-effects model for their meta-analysis is not consistent with their use of random-effects meta-regression: “The random-effect meta-regression analyses were performed to determine whether age had an impact on various outcomes.” It should be noted that Chen et al² did not comment on the “file drawer problem” where unpublished negative studies may exist that were not included in the meta-analysis.

Suggestions for future studies

Despite certain limitations, this analysis opens doors for the use of DOACs in the management of LVT. Several unanswered questions, including efficacy of LVT dissolution, need to be better defined in randomized controlled trials. From a clinical standpoint, there is also a need to know the duration of anticoagulation therapy. We propose new studies with the addition of surrogate markers, for example, D-dimer, to better define clot dissolution. Plasma D-dimer has issues with modest specificity but has excellent sensitivity. It can also serve as a marker of clot dissolution within individual patients. We have used the D-dimer level to guide anticoagulation therapy in an elderly patient. Her D-dimer level normalized over the course of 3 months on
DOAC therapy.\textsuperscript{5} If future studies were to combine anatomic markers of LVT, with pathophysiologic elevation in plasma D-dimer levels, the treating physician could obtain evidence of efficacy with a specific therapeutic anticoagulant by measuring serial plasma D-dimer levels. If D-dimer levels fail to normalize, the patient could be switched to another anticoagulant. We have proposed such combined anatomic and pathophysiologic assessments in the management of left atrial appendage thrombus in patients with atrial fibrillation and possible embolic stroke.\textsuperscript{6}

**Summary** We are thankful to the authors for providing us with a comprehensive meta-analysis that increases all clinicians’ confidence in further evaluating the role of DOACs in the therapy of LVT. We also note that treatment with these agents is much easier to manage both for the patient and clinician and are generally associated with much less clinically relevant bleeding.

We congratulate the authors for taking a major step in defining the role of DOACs in patients with LVT. Their meta-analysis should serve as a background for a larger randomized controlled trial to evaluate efficacy and safety of DOACs in the treatment of patients with LVT.

**ARTICLE INFORMATION**

**DISCLAIMER** The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

**CONFLICT OF INTEREST** None declared.

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**HOW TO CITE** Robinson VJB, Sharma GK, Looney SW. Utility of direct oral anticoagulants for left ventricular thrombus: lessons to learn from a systematic review and meta-analysis? Pol Arch Intern Med. 2021; 131: 411-412. doi:10.20452/pamw.16009

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