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Commentary

How to treat left ventricular thrombi- warfarin or direct oral anti-coagulants?

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Left ventricular (LV) thrombi are mostly associated with LV dysfunction which might be secondary to either ischemic, or more commonly with nonischemic cardiomyopathies. The pathogenesis of LV thrombi after acute myocardial infraction (AMI) involves same factors collectively known as Virchow's triad as they are for any venous/arterial thromboembolism including stasis of the blood because of LV regional wall akinesia or dyskinesia, endothelial and subendocardial injury caused by inflammatory changes after AMI, and hypercoagulability with increased concentrations of procoagulant proteins such as prothrombin and von Willebrand factor.

LV thrombi carry a significant risk of distal embolization, including stroke. Contrast echocardiography remains a cornerstone for the diagnosis of LV thrombus. Most commonly, LV thrombus is located within or adjacent to the LV apex associated usually with anterior wall MI, but may also occur in association with large basal inferolateral wall MI. Many a time, dislodging of the LV thrombus or its fragment is the cause of thrombo-embolic event.

Although we believe that LV thrombi are frequent and may be the cause of thrombo-embolic events, there are no clear-cut guidelines for the appropriate treatment, choice of therapeutic agent, and the duration of the treatment. ACCF/AHA 2013 STEMI guidelines and ESC 2012 guidelines have recommended anticoagulation with warfarin for a duration of 3–6 months in patients with AMI with LV ejection fraction ≤40% [1,2]. However, the efficacy of new direct oral anti-coagulants (DOACs) in the treatment of patients with LV thrombi has not been established. The meta-analysis by Sayed et al. [3] reported in this issue of the journal is timely. The meta-analysis showed no statistically significant difference in terms of mortality, stroke, or resolution of LV thrombi when DOACs were compared with use of warfarin. As expected, major bleeding episodes were significantly lower in patients receiving DOACs.

DOACs have gained popularity in almost all clinical scenarios in which long term anticoagulant is needed such as after venous thromboembolism and atrial fibrillation and when used off label in patients with anti-phospholipid syndrome and bioprosthetic valves. There are multiple reasons why physicians, and more importantly, patients choose DOACs over warfarin including lower incidence of major bleeding, ease of administration, no need for frequent blood tests for monitoring international normalized ratio (INR), fewer drug interactions, and freedom from dietary restrictions especially in patients with labile INR. Several studies have shown that DOACs are similar to warfarin in terms of efficacy and rates of total LV thrombus regression with fewer adverse effects and bleeding complications [4,5].

The optimal duration of such antithrombotic therapy in the treatment of patients with LV thrombi is also unknown, and treatment decision needs duration be individualized for each patient. We have learnt that the relative risk of bleeding and thrombosis in patients with intracoronary stent depends upon several factors including age, renal function, and other co- existent conditions. Lattuca et al. [5] observed total resolution of LV thrombus in two-thirds of patients within 3 months; however, only half of the patients were on full anticoagulation. In a recent retrospective study, Robinson et al. [6] observed that the use of DOACs for LV thrombus treatment was associated with a higher risk of systemic embolism compared with warfarin use, even after adjustment for other factors. However, this study used different DOACs including dabigatran, and did not measure bleeding rates and adherence to

Abbreviations: LV thrombus, Left ventricular thrombus; AMI, Acute Myocardial Infarction.

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medications.

There are some limitations of the meta-analysis by Sayed et al. [3]. First, the number of studies included in the meta-analysis had small sample size; second, the optimal duration of therapy cannot be determined from this meta-analysis.

It is of note that the role of cardiac magnetic resonance (CMR) imaging in the diagnosis and follow up has not been studied. Many consider CMR imaging, with cine-CMR and contrast-enhanced CMR (CE-CMR), to be the gold standard for diagnosis of LV thrombus. However, because of limited availability of CMR, contrast echocardiography remains the most practical. Overall, prospective randomized controlled trials are needed to be conducted to define appropriate management of this important condition.

In patients with LV thrombus, we suggest that DOACs are the appropriate therapy for patients with LV thrombus and repeat contrast echocardiography be performed 3–6 months after initiation of therapy with DOACs. If there is evidence of dissolution of LV thrombus and improvement of LV function, therapy may be discontinued. If LV thrombus persists at 3–6 months of therapy, change of agent or longer duration of treatment may be needed. While these suggestions for therapy are for patients with ischemic cardiomyopathy, optimal management of LV thrombus associated with non-ischemic cardiomyopathy such as dilated cardiomyopathy, Chagas disease and LV non-compaction cardiomyopathy may be similar.

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