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Commentary: Anticoagulation strategies: Awaiting a new paradigm

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In their article “Bioprosthetic Valves and Atrial Fibrillation: Direct Anticoagulants or Warfarin,” and Svensson and Kapadia¹ review the current state of anticoagulation therapy for patients with atrial fibrillation and bioprosthetic valves. They describe the well-known limitations of warfarin and discuss a promising future of direct oral anticoagulants. The unfortunate conclusion: “further investigations and more data are warranted.” It’s hard to wait. The data in regard to time in therapeutic range for warfarin are sobering. Even in a registry population, likely to be superior to the general population, only 59% of international normalized ratios are in the therapeutic range, and those at greatest risk seem to be the least likely to be in the therapeutic range.² To get to even that mediocre success rate requires frequent testing, manipulation of dosing regimens, and restrictive diets—it is cumbersome and frustrating for both patients and clinicians. The consequences of sub- and supratherapeutic anticoagulation can be devastating, making the suboptimal success rate even more concerning. If warfarin were to be reviewed as a new drug by the Food and Drug Administration today, it almost certainly would not be approved for clinical use in humans, given its unpredictability with regard to dose and response. And, according to the internet, warfarin is not even a good rat poison anymore: “the use of warfarin in rat poison is now declining because many rat populations have developed resistance to it and much better poisons are now available.”³ Of course, warfarin’s shortcomings cannot be used as an argument to approve novel agents in unproven circumstances. The prematurely terminated RE-ALIGN trial (Randomized, Phase

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CENTRAL MESSAGE

A new paradigm in anticoagulation for atrial fibrillation associated with valvular pathology with may be forthcoming.

II Study to Evaluate the Safety and Pharmacokinetics of Oral Dabigatran Etxilate in Patients after Heart Valve Replacement) demonstrated one direct oral anticoagulant’s shortcomings when compared against warfarin for patients with mechanical valves.⁴ The finding that warfarin is superior for mechanical valves, even with all its shortcomings, is certainly discouraging and raises concern over off-label use of alternative anticoagulants in unstudied postulations. Also of concern is the limited availability and prohibitive cost of direct oral anticoagulant reversal agents. So, while it may be hard to wait for further evidence, we are going to have to. As challenging as it may be, we are obligated to wait for validated data from randomized trials. Nevertheless, there may be a new paradigm ahead with agents that provide more predictable results and greater ease of use. Those of us in clinical practice who rely on safe anticoagulation for complex patients can hope for better days ahead.

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