Electrical cardioversion is commonly performed in patients with symptomatic or hemodynamically unstable atrial fibrillation (AF). The associated risk of a periprocedural embolic event after cardioversion has significantly decreased from an estimated 5%–7% to approximately 1% with the use of uninterrupted anticoagulation. The introduction of direct oral anticoagulants (DOACs) over the past decade has greatly simplified periprocedural anticoagulation management by eliminating the need for intravenous heparin and avoiding delay and/or need for transesophageal echocardiography (TEE) in patients with subtherapeutic or variable international normalized ratio levels with vitamin K antagonist (VKA) treatment.

DOACs have been proven in randomized controlled trials (RCTs) to be as good as, if not better than, VKA prevention of thromboembolic events in patients with AF. Post hoc subgroup analyses of the pivotal DOAC trials in patients who underwent cardioversion demonstrated feasibility and safety in this setting as well. These trials were later followed by 3 specific prospective RCTs designed to assess the safety and efficacy of DOAC treatment in the context of cardioversion, each of which confirmed DOACs as viable alternatives to VKA therapy in the pericardioreversion period.

Current Food and Drug Administration labeling recommends DOAC dose reduction in the setting of renal dysfunction as well as advanced age and low body weight. The safety and efficacy of reduced-dose DOACs, when appropriately indicated, were reported in the major RCTs and have become a mainstream treatment for these specific populations. However, suboptimal DOAC adherence as well as frequent inappropriate underdosing (dose reduction without a clear indication) may expose patients to excess stroke risk in the particularly high-risk period post cardioversion. What data exist on the safety of treatment with reduced-dose DOACs in the vulnerable period after electrical cardioversion?

The post hoc analyses of the cardioversions in the RE-LY trial demonstrated a numerically higher number of patients with stroke or systemic embolism in those receiving 110 mg of dabigatran than in those receiving the 150 mg dose, although this difference did not reach statistical significance. We are unaware of any data on the use of dabigatran 75 mg twice daily. Similarly, the post-hoc analysis of ENGAGE AF-TIMI 48 revealed stroke or systemic emboli following cardioversion in 2 patients on reduced-dose edoxaban as compared with no events in patients on high-dose edoxaban or warfarin. No dose-specific results were reported for reduced-dose rivaroxaban or apixaban in the post hoc analyses of ROCKET-AF and ARISTOTLE trials, respectively.

Of the 3 RCTs designed to assess the safety of DOAC use in cardioversion, none reported any specific results on reduced-dose DOACs. Only the Edoxaban vs. warfarin in subjectS UndeRgoing cardioVension of atrial fibrillation (ENSURE-AF) study separately reported outcomes for patients with reduced creatinine clearance who were presumably taking reduced-dose edoxaban; these patients had fewer events than did those on warfarin (Table 1).

While several additional retrospective or single-center studies have addressed treatment with DOACs for cardioversion, the only study that specifically assessed differences between reduced- and high-dose DOACs is a single-center study in which all patients presenting for cardioversion underwent TEE with documentation of spontaneous echo contrast and thrombus formation. They found a statistically significant increase in spontaneous
The most significant adverse event after cardioversion is stroke or systemic embolism. This risk is highest in the first 7–10 days after cardioversion, presumably as atrial mechanical function recovers. The safety of reduced-dose DOACs (particularly in patients without a firm indication) in this period represents an important knowledge gap. We are in need of more robust data in the form of a prospective trial or comparative effectiveness study to address the safety of appropriately reduced-dose DOACs in the setting of cardioversion. Until this is available, it may be reasonable to consider using a short pericardioversion course of full-dose DOACs with or without TEE in particularly high-risk patients (Figure 1) and take this opportunity to revisit and adjust the dose as indicated.

References