Original Article

Should We Always Perform TEE Before Direct Current Cardioversion?

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Abstract

Background and objectives: Spontaneous or intended conversion of atrial fibrillation (AF) to sinus rhythm is associated with a short-term increase from baseline risk of clinical thromboembolism. Guidelines suggest performing cardioversion without prior execution of trans esophageal echo (TEE) if the patient has completed a month of anticoagulation with warfarin (in the therapeutic international normalized ratio range) or non-vitamin K antagonist oral anticoagulants (NOACs).

Methods: We performed TEE echo in 100 consecutive patients taking NOACs or warfarin for 1 month or more, to see if there was evidence of left arterial appendage thrombi or extremely low flow velocity (<40 cm/s) that can increase risk of ischemic events after cardioversion.

Results: Even in patients with correct anticoagulation therapy, thrombi can be found in the left atrial appendage. For this reason, until further data are present, we suggest executing TEE before direct current cardioversion. Moreover, NOAC was shown to be safe for use before cardioversion. The only exception was with rivaroxaban, so we suggest further analysis with larger samples to determine the mechanisms underlying this finding.

Conclusions: Even if cardioversion can be performed without prior TEE after 1 month of anticoagulation therapy, we think that (except in patients with very low risk of thrombosis) it is preferable to execute this exam before trying to restore sinus rhythm.

Introduction

All patients with atrial fibrillation (AF) have an increased risk of embolization compared to those without.[1] There is an exponential increase from the baseline risk in the immediate postcardioversion period, whether planned or spontaneous.[2] Most embolic events occur within 10 days of cardioversion for both warfarin and non-vitamin K antagonist oral anticoagulants (NOACs).[2–5] Patients undergoing cardioversion of AF for a duration of more than 48 hours represent a particularly high-risk group (compared to AF for a shorter duration), with an embolic risk from as low as 1% to as high as 5% in the first month in the absence of anticoagulation.[2–4,6–8] This rate is substantially higher than the rate that would be calculated for the general population of patients with AF, in whom the yearly rate ranges from 1.3% and 5.1% (or higher), depending on age and additional comorbidities.

There is an incremental increase from the baseline risk in the immediate postcardioversion period, whether planned or spontaneous. Most embolic events occur within 10 days of cardioversion for both vitamin K antagonists and non-vitamin K antagonist oral anticoagulants. Approximately 13% of patients with new-onset AF (depending on risk factors and length of AF) will have evidence of a left atrial thrombus on trans esophageal echo (TEE).[9–11] The prevalence is increased in high-risk patients with mitral stenosis (33% in one series),[12] left ventricular systolic dysfunction, enlargement of the left atrium or left atrial appendage, or spontaneous echo contrast.

The risk of thromboembolism after cardioversion can be diminished to less than 1% (during the 4 weeks after cardioversion) by the use of a month of antithrombotic therapy prior to and extending for 1 month after cardioversion or by the use of shorter term precardioversion antithrombotic therapy with screening TEE and with

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Abbreviations: AF, atrial fibrillation; NOAC, non-vitamin K antagonist oral anticoagulants; TEE, trans esophageal echo.
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concomitant full anticoagulation at the time of cardioversion[11] and extending 1 month after cardioversion. Prospective studies have demonstrated that the risk of clinical stroke or systemic embolism ranges from 0% to 0.9% if preceded by a month of anticoagulation with warfarin or one of the NOACs,[2–4,11] as compared with the retrospective data that have demonstrated 4% to 7% of non-anticoagulated patients will experience events.

American guidelines suggest that a TEE-based approach be used only for symptomatic patients and for patients for whom there is a concern about a 3- to 8-week delay in cardioversion. Such a concern might arise from a preference to not have ongoing symptoms or a possible lower likelihood of successful cardioversion with a longer period of AF. Other individuals for whom this strategy may be reasonable include those at high risk of bleeding, as the TEE-guided approach shortens the total precardioversion anticoagulation time for those without thrombus, and those at highest risk for a cardioversion-related thromboembolic event, including individuals with prior thromboembolism and elderly women with diabetes and heart failure. Patients who require hospitalization are also candidates for this approach. This recommendation for a limited use of the TEE-based approach is based on concerns about cost, morbidity, and the possibility of worse outcomes with this approach.

The 2016 European Society of Cardiology guideline for the management of AF, contrasting the American ones, recommends TEE-guided precardioversion more than anticoagulation-guided cardioversion.[12,13] But, both guidelines state that TEE is not necessary in patients with 4 or more weeks of effective anticoagulation, if they have not presented with cardiac failure or very high thrombotic risk.

Methods

This study was designed to see if TEE is really useless in patients who are treated with an anticoagulation strategy before cardioversion. Moreover, we also analyzed a subpopulation with TEE-guided cardioversion to point out differences between warfarin and NOAC. A total of 120 patients with persistent or permanent AF were analyzed, including 100 with 4 weeks or more of anticoagulation therapy (most were candidates for ablation of AF) and 20 with more than 3 days of the NOAC and TEE strategy. TEE was performed in all patients, in order to examine for left atrial appendage thrombi. If thrombi were present, cardioversion was delayed. We also analyzed the presence of spontaneous echo contrast of high grade and left arterial appendage flow velocity.

Concerning anticoagulation, patients were randomized to receive either warfarin (60 patients) or NOACs (60 patients, including 20 receiving rivaroxaban, 18 receiving dabigatran, and 22 receiving apixaban). We had no patients taking edoxaban because the sample was collected before edoxaban was approved in Italy (representing a limitation of the study). Patients with AF that presented at less than 48 hours were excluded from our study; in such cases, we proceed directly to cardioversion, according to guidelines.

To our knowledge, proinflammatory status can modify the outcomes and the sinus rhythm restoration; for this reason, proinflammatory status was assessed by biochemistry (dosing C-reactive protein and lactic acid dehydrogenase), and no relevant alteration were found.[14]

Study limitations

The study was monocentric and has a small number of patients; more data are needed to confirm our findings. Moreover, it will be important to have a group of patients assume edoxaban, although the drug was not available in Italy when we performed the study.

Results

Left atrial appendage thrombi were found in 7 patients of the 120 total patients, and these patients included 3 who were taking warfarin and 3 who were taking rivaroxaban. No thrombi were found in the dabigatran-treated and apixaban-treated groups. Four patients with thrombi were switched to apixaban for 3 weeks; TEE was then performed, showing thrombus resolution in all four. Two patients continued to take rivaroxaban, and only one of them achieved thrombus resolution.

We also analyzed spontaneous echo contrast and mean left arterial appendage velocity, and found that the NOAC group had higher velocity and less spontaneous echo contrast (again, with the rivaroxaban group representing the exception, having velocity and echo contrast similar to the warfarin group). The evaluation was completed in all patients, with a CT scan using multiplanar and 3D reconstruction to assess the shape of the left atrial appendage and the presence of anomalies in the pulmonary vein. We followed up patients for 6 months after the cardioversion; there were not any thrombotic events during the follow-up.

Future research directions/prospective/prediction

Today, direct oral anticoagulants have a central role in the prevention of embolic risk for patients in AF, but little experience is published regarding their use before planned direct current cardioversion. Moreover, there are not any direct comparisons between them. We hope that our study, even as it involved a small number of patients, prompts further comparisons and analysis, in particular in a comprehensive trial with all the new anticoagulants. We are sure that, with the progressive experience worldwide, we can better handle the very subtle pre- and postcardioversion period, avoiding performance of TEE when it is not strictly necessary. In the future, we hope to enlarge our study with more patients and to include edoxaban, which was authorized for use in Italy after our study ended. We expect to discover that not all of the direct oral anticoagulants are good for use in this setting of patients; but such a finding will not be the defeat of a drug but a victory for the safety of patients.

Conclusions

Guidelines and appropriate use criteria state that TEE-guided direct current cardioversion should be avoided for patients that are taking 4 weeks of warfarin or other anticoagulant.[13] They approve its use for patients who have other indications to perform the TEE (*e.g.*, prior to AF ablation). By analyzing a population of 120 patients we were able to show that NOACs (except for rivaroxaban, for which we propose further analysis with bigger samples) are better than warfarin (i.e. no thrombi detected in the dabigatran and apixaban group, and higher flow velocity and less spontaneous echocontrast). Our analysis indicated that thrombi can be present even after 4 weeks of appropriate anticoagulation therapy. Therefore, we suggest that TEE is a good resource in centers with sufficient expertise in this examination technique.

Our study provides insight into answering the question of

whether the novel anticoagulants are better than warfarin for patients with AF; this question is a complex one. The NOACs overcome the need for routine blood monitoring, and the trial results have been encouraging overall and across important subgroups. Across four large studies with different populations of patients with AF, the direct thrombin and factor Xa inhibitors have been shown to have a more favorable bleeding profile than warfarin and are at least as efficacious. While it is difficult to understand why a practitioner would start warfarin in a new patient without a contraindication to a NOAC, switching to a newer agent may not be necessary for the patient in whom the international normalized ratio has been well controlled with warfarin. In addition, although the newer anticoagulants have a more rapid onset and termination of anticoagulant action than warfarin does, agents to reverse the effect of the drugs are still under development and are not routinely available. So, while a new era of anticoagulation is emerging, the decision to use a novel agent versus warfarin must be an individual one. Our opinion is when we start anticoagulation in a patient for the first time, an NOAC should be preferred because of efficacy, safety and easy management.[15]

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study design (PC, GG), performance of experiments (PC, GG, EC), analysis and interpretation of data (PC, EC), manuscript writing (PC), critical revision (PC), statistical analysis (PC, EC), critical funding (SN), administration (SN).

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