A Comparison Between Dabigatran and Warfarin on Time to Elective Cardioversion

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Abstract

Objective: To evaluate the use of dabigatran versus warfarin on time to elective direct current cardioversion (DCCV).

Methodology: This retrospective observational study was conducted at a single Veterans Affairs hospital in the Southwestern region of the U.S. Patients with atrial fibrillation or atrial flutter who were initiated on either warfarin or dabigatran prior to DCCV were reviewed. The time to cardioversion was compared between warfarin and dabigatran, as well as costs of therapy, rescheduling rates, and adverse events.

Results: Out of 258 patients reviewed, a total of 68 patients were included in the study. All patients were male with an average age of 68 years (SD=8.6). A total of 38 patients (56%) received dabigatran and 30 patients (44%) received warfarin. Patients in both groups had a median CHADS2 and HASBLED score of 2. The median number of days to cardioversion was 34.5 (range=22-148) for dabigatran compared to 66.5 (range=32-183) for warfarin (p<0.01). Total costs of anticoagulation for warfarin averaged $183.50 (SD=95.02) from initiation of anticoagulation to the end of the required four week period following cardioversion, whereas dabigatran costs averaged $193.20 (SD=59.38). Three patients (10%) in the warfarin group had DCCV rescheduled compared to none in the dabigatran group. There was one bleeding event in the warfarin group and no thromboembolic events in either group.

Conclusion: The use of dabigatran prior to elective DCCV results in a significant decrease in number of days from initiation of anticoagulation to cardioversion as compared to warfarin, with a minor increase in total costs.

Background

Rhythm control with direct current cardioversion (DCCV) is a commonly used strategy in the treatment of atrial fibrillation (AF). Factors favoring rhythm control include young age, first episode of AF, difficulty in achieving rate control, persistent symptoms despite rate control, tachycardia induced cardiomyopathy, and patient preference. Both the current CHEST and AHA/ACC/HRS guidelines recommend therapeutic anticoagulation for a minimum of three weeks before and four weeks after cardioversion for patients with AF or atrial flutter. In studies with warfarin, the risk of thromboembolic events following DCCV was significantly reduced with appropriate anticoagulation. However, interactions with diet and other drugs, frequent blood tests for monitoring, and INRs outside of therapeutic range can result in rescheduling and delay DCCV, making warfarin less desirable to use. A meta-analysis to assess the quality of warfarin control in atrial fibrillation patients found INRs within therapeutic range only 55% of the time. The approval of new agents in the class of direct oral anticoagulants (DOACs) in recent years has expanded options for patients undergoing cardioversion. Dabigatran (Pradaxa®) was the first DOAC approved in 2010 for stroke prophylaxis in patients with non-valvular atrial fibrillation. DOACs are an attractive option overcoming the limitations of warfarin as they do not require INR monitoring.

There is limited literature comparing the use of warfarin to dabigatran for anticoagulation associated with cardioversion, although the 2012 CHEST guidelines recommend dabigatran as an option for anticoagulation prior to DCCV. The Veterans Affairs (VA) criteria for dabigatran use, last updated in December 2014, lists warfarin as the standard of care for anticoagulation associated with cardioversion. This study intended to evaluate if dabigatran reduces the number of days from start of anticoagulation to cardioversion in our veteran population. Additionally, this study sought to observe rescheduling rates, adverse outcomes such as thromboembolic and bleeding events, and compare costs of anticoagulation between the two groups.

Key Words:
Cardioversion, DCCV, Dabigatran, Warfarin, Anticoagulation.
Results

Out of 258 patients reviewed, a total of 68 patients fulfilled the inclusion criteria and were included in the analysis. Patients were all male with a median age of 68 years (Table 1). The median CHADS\textsubscript{2} score was 2 and the median HASBLED score was 2. The median time from initiation of anticoagulation to cardioversion for all patients was 44 days.

A total of 30 patients (44%) received warfarin and 38 patients (56%) received dabigatran. In the warfarin group, the time from initiation of anticoagulation to cardioversion was significantly longer than dabigatran (median 67 vs. 35 days; p<0.01). There were no thromboembolic events in either anticoagulation group. There was one bleeding event in the warfarin group manifested by hematuria resulting in hospitalization and discontinuation of warfarin prior to completing four weeks of anticoagulation after cardioversion. There were no bleeding events in the dabigatran group. Three patients (10%) in the warfarin group had their cardioversion rescheduled (p=0.08).

Two of these three patients had documented subtherapeutic INRs resulting in rescheduling of the cardioversions.

The warfarin group had more pharmacist visits (median 8 vs. 2; p<0.01) and technician visits (median 3.5 vs. 2; p<0.01). Medication costs were higher for patients receiving dabigatran than warfarin (median $141.90 vs. $4.83; p<0.01). However, the total costs of anticoagulation, which included drug costs, pharmacist and technician time, and lab costs, averaged $183.50 for warfarin and $193.20 for dabigatran (p<0.01; Table 2). Patients on warfarin had an average of 11 INRs checked from initiation of anticoagulation to the end of the required four week period following cardioversion.

Discussion

The results of this study show that in patients with AF or atrial flutter undergoing DCCV for restoration of sinus rhythm, dabigatran significantly reduces the number of days from initiation of anticoagulation to cardioversion compared to warfarin. Both groups in this study had similar background characteristics such as mean age, male gender, and CHADS\textsubscript{2} or HASBLED scores. These results were similar to those of a study from another VA health system which found that dabigatran significantly reduced the median number of days to cardioversion by 33 days and had similar overall costs compared to warfarin.\textsuperscript{8} Similar conclusions were also made in a limited number of studies using non-veteran populations.\textsuperscript{7,8} One of these studies concluded that dabigatran improves the efficiency of an elective DCCV service by significantly lowering the rates of rescheduling compared with warfarin (9.7% vs. 34.4%) and reduces the time between initial assessment and DCCV by an average of 22 days.\textsuperscript{8} In addition to the obvious improvements in efficiency, these findings have a meaningful impact on clinical practice as studies have suggested that success of electrical cardioversion is inversely related to duration in AF.\textsuperscript{9} Reasons observed for rescheduling in the warfarin group included subtherapeutic INRs and patient unavailability. The rescheduling rate in the warfarin group of our study was lower than those found by other studies previously mentioned,\textsuperscript{6,8} which may be a result of different scheduling procedures between health care systems. Another reason may be a selection bias since several patients were included in the dabigatran group that had been converted from warfarin due to variable or subtherapeutic INRs. For these patients, measuring rates of rescheduling in this study did not adequately capture the delays in cardioversion related to subtherapeutic INRs.

There were no statistically significant differences in thromboembolism and bleeding events in this study, which has been
demonstrated in previous studies. A large post-hoc analysis of the RE-LY study demonstrated that dabigatran appeared no worse than warfarin for thromboembolic and bleeding outcomes in patients undergoing both electrical and pharmacologic cardioversion. Another retrospective analysis confirmed no statistically significant differences in thromboembolic and bleeding events with dabigatran versus warfarin. A meta-analysis comparing all DOACs, including dabigatran, rivaroxaban, apixaban, and edoxaban, to warfarin for cardioversion found no significant differences in thromboembolism, stroke, or major bleeding between groups.

The numbers of technician and pharmacist encounters documented in 15-minute increments were significantly fewer in the dabigatran group due to absence of INR monitoring. The total cost for warfarin therapy was slightly lower than the total cost for dabigatran therapy. However, the cost analysis did not factor in phlebotomist costs or indirect costs such as the patients’ time off work and travel costs for INR monitoring. Also, additional pharmacist time was probably required to review technician notes and telephone calls, and this was not measurable through chart review. As a result, the actual total costs of warfarin are likely higher than estimated, and the minor increase in cost of dabigatran found in this study is negligible when considering other factors.

This study is especially meaningful for the VA health care systems which are focused on improving timely access to care. Measures that will achieve clinical goals in a shorter time frame and reduce rescheduling rates are needed. Utilizing dabigatran in place of warfarin in the appropriate patients will achieve the goal of cardioversion in a shorter amount of time, reduce patient visits, travel costs, phlebotomist and pharmacist time, and rescheduling, thereby increasing available appointments in VA hospitals and improving efficiency and access to care.

The major limitation of this study is that it is a retrospective, single-center study with a small sample size. Many patients were excluded because they were already established on anticoagulation for a period of time prior to the decision to perform elective cardioversion, or they received TEE-based cardioversion. A lengthy time period of 61 months was required to obtain sufficient data, and many of the warfarin patients in this sample had cardioversion prior to the availability of dabigatran at the studied facility.

Conclusions

Dabigatran significantly decreases the number of days from initiation of anticoagulation to cardioversion, as compared to warfarin, with a minor increase in total costs. Implementation of dabigatran as the preferred agent in VA and other health care systems may improve timely access to care and make elective cardioversion services more efficient.

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References