11-2017

Elective Direct Current Cardioversion for Patients with Atrial Fibrillation: A Registry Analysis of Adverse Events and Recurrence

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Background

Synchronized direct current cardioversion (CV) is a common treatment for atrial fibrillation (AF) if primary treatment with anti-arrhythmic drugs fails. However, direct current CV, without pretreatment precautions, is associated with an increased risk of embolic stroke, presumably due to dislodgement of intracardiac thrombi. In order to prevent such complications, patients are typically treated with systemic anticoagulants for at least 3 weeks prior to cardioversion. (1)

Warfarin has historically been the standard for anticoagulant treatment in AF. Warfarin reduces the risk of embolic stroke by 66% in AF patients. In addition, warfarin is relatively inexpensive and unaffected by renal function, which makes it a popular anticoagulant drug. (2)

Direct oral anticoagulants (DOACs such as apixaban, dabigatran, rivaroxaban and edoxaban) are becoming more prevalent in use. DOACs directly inhibit clotting factors instead of targeting Vitamin K as warfarin does. Apixaban, rivaroxaban and edoxaban are reversible inhibitors of Factor Xa. Dabigatran is a reversible inhibitor of thrombin.

DOACs are being increasingly used in place of warfarin to prevent embolic stroke in AF but there is limited data on their efficacy and safety in the setting of elective CV for AF, particularly compared to warfarin.

Hypothesis

Our hypothesis was that DOACs are not inferior to warfarin in preventing adverse events and recurrent AF following elective CV. To test this, we analyzed 30-day outcomes from an ongoing three-year outpatient CV registry.

We sought to determine the following objectives:

- The rate of adverse events within 30 days following all cardioversions on patients treated with warfarin vs. DOACs.
- The rate of AF recurrence within 30 days post-cardioversion in patients on warfarin vs. DOACs.

Methods

Patient charts from the ongoing registry (May 2013 – May 2016) of elective synchronized direct current CV at Parkview Heart Institute were analyzed. The elective distinction was made in order to exclude CVs done in emergency situations or in situations where the patient could be at risk for other comorbidities; thus, by only including outpatients, several confounding variables were avoided. Of significance, each CV was treated as a separate data point even if a given patient had multiple treatments. Multiple co-variants were examined and shown in Table 1.

Number of patients	519
Age (avg)	65 yrs
BMI (avg)	33.4
CHA_2DS_2-VASc Score (avg)	2.36
Cigarette Smoker	279
Diabetes	126
Hypertension	417
Hypercholesterolemia	211
Prior Stroke	44
Maze Procedure	33
Maze Procedure	131
Prior Ablation	80
Current ASA therapy	201
Duration of anticoag pre procedure (avg)	79.7 days

Table 1: Clinical Characteristics

Results Analyzed for warfarin vs. DOACs	P-value	Significant Difference
Adverse Events	0.6103	No
Atrial Fibrillation Recurrence	0.5419	No

Table 2: Table showing outcomes surveyed concerning the rate of adverse events (defined as Stroke, Intracranial Hemorrhage, and ISTH Major Bleeding) within 30 days following CV and the rate of recurrence of atrial fibrillation within 30 days following CV.

Subject	Anticoagulant	Aspirin Use?	CHA_2DS_2-VASc Score	Pre-operational TEE?	Adverse Event
X	Warfarin	No	3	No	Stroke
Y	Dabigatran	Yes	4	No	Stroke
W	Apixaban	No	3	Yes	Splenic Infarct
V	Warfarin	No	5	Yes	Intracranial Hemorrhage
U	Rivaroxaban	No	2	No	Rectal Bleed

Table 3: List of patients that experienced an adverse event within 30 days of their elective cardioversion. Arbitrary letters were used to de-identify the patients' data. Of significance, 4/5 patients with an adverse event were not on Aspirin (P-value = 0.1875 using a binomial distribution). In addition, 3/5 of the patients with adverse events suffered from embolic events while 2/5 suffered from hemorrhagic events.

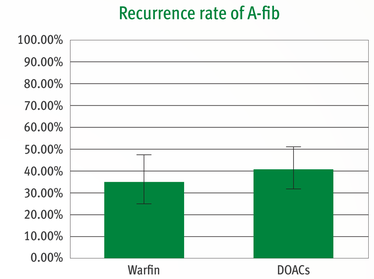

Figure 1: Graph showing the insignificant difference in the recurrence rate of A-fib for patients on Warfarin vs. DOACs.

Results

Overall, 960 CVs were surveyed, but 441 were excluded from the study using the criteria listed above (Note that 13/226 pre-procedural TEEs showed intracardiac thrombus and thus their data were excluded from the study because no CV was performed). Two main outcomes were surveyed, with regards to the adverse event rate for patients within 30 days following CV, which are shown in Table 2. For the purpose of this study, adverse events were defined to include both bleeding and embolic events regardless of their difference in pathology (Table 3).

Adverse events and recurrence of AF after 30 days were not considered in this study in order to ensure that any complications observed were likely due to the CV itself and not any other disease states, accidents or complicating conditions.

A two-tailed Fischer Exact Test was not able to show a relationship of dependence between treatment type (warfarin vs. DOACs) and frequency of adverse events (P-value = 0.6103). Specifically, 2/137 patients on warfarin experienced adverse events within 30 days, whereas 3/382 patients on DOACs experienced adverse events within 30 days. Due to the low occurrence rates seen in this study, the statistical power of this test (found by simulation, using 10,000 data sets) was found to be only ~0.087.

Likewise, a two sided 2 sample z test for proportions was not able to show a significant difference between the rate of recurrence of atrial fibrillation for warfarin vs. DOACs within 30 days following cardioversion (P-value = 0.5419). Specifically, 41/130 (31.5%) of patients on warfarin experienced a recurrence of AF within 30 days, whereas 116/336 (34.5%) of patients on DOACs experienced a recurrence within 30 days. The statistical power of this test was found to be 0.095.

Conclusions

Cardioversions at Parkview Hospital were found to be safe. The rate of adverse events within 30 days following cardioversion was found to be only 5/519 (0.963%). However, the rate of atrial fibrillation recurrence within 30 days was found to be 157/466 (33.7%).

No significant relationship of dependence was seen between treatment type (warfarin vs. DOACs) and adverse event rate within 30 days. Due to the very low occurrence rate of adverse events, the statistical power of this analysis was quite low. Likewise, no significant relationship of dependence was seen between treatment type and recurrence of AF within 30 days.

Discussion

Since the emergence of DOACS in 2010, several large randomized controlled trials have demonstrated their efficacy and safety in preventing embolic stroke in AF. Subset analyses of patients undergoing CV during these studies have not shown a significant difference in outcomes between patients randomized to DOACs versus warfarin. (3) A recent study demonstrated significantly less adverse events using treatment with apixaban compared to treatment with heparin/vitamin K antagonists in AF patients undergoing scheduled cardioversion. (4) None of these studies examined the incidence of AF recurrence following CV in either treatment type.

Our study adds important real-world data applicable to this common clinical setting and provides additional support for the continued use of DOACs in place of warfarin for anticoagulation prior to CV. It is becoming increasingly evident that providers can be comfortable using DOACs prior to CV without the fear of lessened efficacy or safety.

References

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Disclosures

Emily Keltner, MA – Zoll, Charles Wong BS – None, Christopher Davis MD – None, Aaron Becker BA – None, William Wilson, MD – None