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ORIGINAL ARTICLE

Novel Oral Anticoagulants in Direct Current Cardioversion for Atrial Fibrillation

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Background For some patients with atrial fibrillation, direct current cardioversion (DCCV) is one strategy that can be used to establish sinus rhythm but appropriate anticoagulation is mandatory to prevent thromboembolic events. Historically, patients were anticoagulated with warfarin with bridging with unfractionated or low molecular weight heparin, however, recently novel oral anticoagulants (NOACs), apixaban, dabigatran and rivaroxaban have become more popular. Despite the increase in use, real world data on safety and efficacy is limited.

Methods We retrospectively analysed patients that underwent DCCV at Wollongong Hospital from 1 January 2014 to 30 June 2016 and compared peri-procedural anticoagulation with warfarin and the three NOACs. Patients were treated with at least 24 hours of anticoagulation before and at least four weeks after the procedure unless contraindication developed. All patients underwent transoesophageal echocardiography prior to cardioversion regardless of anticoagulation type or duration. Patients with left atrial or left atrial appendage thrombus did not undergo cardioversion. We analysed the utilisation rates of NOACs and compared the incidence of post procedural ischaemic strokes and major bleeding events at eight weeks follow-up.

Results Over the study period, 284 patients underwent DCCV; 109 (38.4%) patients were anticagulated with warfarin and 175 (61.6%) with one of the three NOACs; 77 (27.1%) with apixaban, 60 (21.1%) with rivaroxaban and 38 (13.4%) with dabigatran. Patients treated with warfarin were on average older (71.3 +/−9.7 vs. 65.2 +/− 12.9; p value, 0.0005) with more cardiac risk factors including documented heart failure with reduced ejection fraction (39.4% vs. 22.9%; p value, 0.0032), medically treated hypertension (76.1% vs. 48.6%; p value, 0.0001) and peripheral vascular disease (31.2% vs. 12.1%; p value, 0.0004). The NOACs were more frequently used in patients with lower CHA_2DS_2-VASc scores; 179 patients had a score ≤ 3 with 52 (29.1%) patients treated with warfarin and 127 (70.9%) treated with a NOAC (p value, 0.0001). In our cohort, the use of NOACs increased over the study period from 45.6% in 2014 to 82.8% in 2016. There was a low incidence of ischaemic stroke and bleeding events in both groups, 1.8% versus 0.6% (p value, 0.5607) and 3.6% versus 1.7% (p value, 0.4343) respectively. In the NOAC group, 95 of the 174 patients were anticoagulation-naïve and anticoagulated for less than five days; in comparison to longer duration therapy there was no difference in ischaemic stroke and bleeding events.

Conclusion In our institution, the use of NOACs in electrical cardioversion increased significantly over the study period and in our experience, they appear to be as safe as warfarin with low rates of ischaemic stroke and major bleeding. In addition, a short duration NOAC strategy was comparable to longer duration therapy.

Keywords Atrial fibrillation • Novel oral anticoagulants • Warfarin • Direct current cardioversion procedures

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Introduction

Non-valvular atrial fibrillation (NVAF) is the most common atrial arrhythmia affecting one in four adults over the age of 65 [1]. In selected individuals, direct current cardioversion (DCCV) is a safe and effective strategy for restoring sinus rhythm but in patients without therapeutic anticoagulation the risk of post-procedural thromboembolic events ranges from 5–7% [2,3]. For patients with atrial fibrillation longer than 48 hours or unknown duration, two anticoagulation strategies are recommended: long duration therapy with therapeutic anticoagulation for three weeks before and four weeks after cardioversion and short duration therapy supplemented by transoesophageal echocardiography excluding left atrial and/or left atrial appendage thrombus [4]. Historically, patients were anticoagulated with warfarin but recent *post hoc* analyses of the RE-LY, the ARISTOTLE, and the ROCKET-AF trials have suggested that all three NOACs are suitable and safe alternatives [5–7]. Two prospective clinical trials have demonstrated the safety and efficacy of rivaroxaban as peri-procedural therapy for patients undergoing DCCV [8,9]. In addition, recent studies have suggested dabigatran and rivaroxaban are safe for short duration therapy [10,11].

Our aim was to assess the safety and efficacy of NOACs compared to warfarin in patients undergoing DCCV. In addition, we report the results of short duration (less than five days) NOAC therapy.

Methods

Setting

The procedural database at The Wollongong Hospital was retrospectively reviewed for all DCCV procedures performed between 1 January 2014 and 30 June 2016. Results were analysed by two independent physicians. All patients were treated with at least 24 hours of anticoagulation before and at least four weeks post procedure unless contraindication developed. All patients underwent a transoesophageal echocardiogram prior to cardioversion regardless of anticoagulation type and duration to exclude patients with left atrial and/or left atrial appendage thrombus.

Procedure, Endpoints and Definitions

The electronic medical record for each patient was reviewed and data on type of anticoagulant, length of therapy, age, sex, risk factors and CHA_2DS_2-VASc score was obtained (The CHA_2DS_2-VASc score is a clinical predictor of ischaemic stroke in patients with atrial fibrillation and ranges from 0 to 9). We compared the incidence of post procedural ischaemic stroke and major bleeding events between warfarin and the three NOACs. We defined ischaemic stroke according to the World Health Organization as new focal neurological disturbance of cerebral function lasting more than 24 hours or leading to death after DCCV. We defined major bleeding events according to The International Society on Thrombosis and Haemostasis (ISTH) criteria as bleeding that was clinically overt and associated with a fall in haemoglobin level of at least 20 g/L; or led to a transfusion of a minimum of two units of erythrocytes; or was retroperitoneal, intracranial or in another critical site; or was associated with mortality [12]. Second, we assessed the safety of short duration NOAC therapy in anticoagulation-naive patients. Short-term NOAC therapy was defined as anticoagulation treatment less than five days. Patients were followed up for a minimum of eight weeks as established by previous investigators studying embolic and bleeding events post procedure.

Statistical Analysis

Categorical variables are expressed as numbers and percentages and continuous variables as median with standard deviation (SD). Statistical analysis was performed using SPSS software for Mac v. 22 (IBM, NY, USA) and p values of less than 0.05 were considered significant.

Results

Clinical Characteristics and Anticoagulation Utilisation Trends

During the study period from 1 January 2014 to 30 June 2016, 284 patients with NVAF underwent DCCV; characteristics were comparable between groups and are shown in Table 1. Warfarin was used in 109 (38.4%) patients and NOACs in 175 (61.6%), 77 (27.1%) apixaban, 60 (21.1%) rivaroxaban and 38 (13.4%) dabigatran. Patients treated with warfarin were older (71.3+/−9.7 vs. 65.2 +/− 12.9; p value, 0.0005) with more risk factors including heart failure with reduced ejection fraction (39.4% vs. 22.9%; p value, 0.0032), medically treated hypertension (76.1% vs. 48.6%; p value, 0.0001) and vascular disease (31.2% vs. 12.1%; p value, 0.0004) (Table 2). Novel oral anticoagulants utilisation increased over the study period with 45.6% in 2014, 73.0% in 2015 and 82.8% in 2016 (Figure 1). In particular, apixaban utilisation increased from 12.5% in 2014 to 44.3% in 2016. Novel oral anticoagulants were most frequently utilised in patients with lower CHA_2DS_2-VASc scores; 179 patients had a score ≤ 3 with 52 (29.1%) patients treated with warfarin and 127 (70.9%) treated with a NOAC agent (p value, 0.0001) compared to 105 patients had a score ≥ 4 with 57 (52.3%) patients treated with warfarin and 48 (45.7%) treated with a NOAC agent (p value, 0.2695) (Figure 1) (Figure 2).

Ischaemic Strokes and Major Bleeding Events

In our cohort, there was a low frequency of ischaemic strokes and major bleeding events with no statistically significant difference between the warfarin and NOAC groups (Table 2). The incidence of ischaemic stroke in the warfarin group was

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