Outcomes With Novel Oral Anticoagulants in Obese Patients who Underwent Electrical Cardioversion for Atrial Tachyarrhythmias

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The efficacy of novel oral anticoagulants (NOACs) in severely obese patients is uncertain as volume of distribution is related to weight, and few such patients were enrolled in the pivotal trials. As the month after direct-current cardioversion (DCCV) for atrial fibrillation and atrial flutter is a high-risk period for stroke, we sought to evaluate the safety of performing DCCV in obese patients on NOAC. All patients who underwent DCCV after ≥3 weeks of NOAC or therapeutic warfarin treatment without a previous transesophageal echocardiogram over a 3-year period at a single center were included. Obesity groups were defined as normal (body mass index [BMI] < 25), overweight (BMI 25 to <30), class 1 obesity (BMI 30 to <35), class 2 obesity (BMI 35 to <40), and class 3 or severe obesity (BMI ≥ 40). The primary end point was stroke at 30 days. Of 761 patients, 73 were severely obese, 78 class 2 obese, 197 class 1 obese, 254 overweight, and 159 in the normal weight group. Average age 66.4 ± 10.3 years and 32.5% women. Mean CHA_2DS_2-VASc score was 2.6 ± 1.6, and 78.9% were on NOACs with no differences in groups. There were no strokes in the severely obese group, and 1 each in class 2 obesity and normal weight (p = 0.3). In conclusion, there was a low rate of stroke in all weight classes after DCCV in patients taking NOACs and warfarin. NOAC use in severely obese patients who underwent DCCV appears safe even in the absence of transesophageal echocardiogram. **(Am J Cardiol 2018;00:1−4)**

Novel oral anticoagulants (NOACs) have become widely adopted in patients with nonvalvular atrial fibrillation (AF).[1] Variations in the volume of distribution of these fixed-dose drug regimens at extremes of body weight raise some pharmacokinetic concerns, particularly the potential for lower drug concentrations and shorter half-lives, resulting in underdosing.[2] However, few patients at very elevated weights were included in the original NOAC trials for either nonvalvular AF or prevention of venous thromboembolism.[3−5] Current cardiology guidelines do not discuss changes in use of NOACs in obese patients, whereas the hematology guidelines recommend against the use of NOACs in patients with body mass index (BMI) >40 or weight >120 kg, as well as checking drug-specific serum levels, but evidence for this strategy remains limited.[2,6] Electrical cardioversion (direct-current cardioversion [DCCV]) is associated with an elevated risk of stroke or thromboembolism within the first 30 days due to the potential for dislodging a thrombus formed in the static left atrium or left atrial appendage, or formation of a thrombus as a result of left atrial stunning after restoration of sinus rhythm.[7,8] This risk of thromboembolism is mitigated either by ensuring 3 to 4 weeks of therapeutic anticoagulation before DCCV or by utilizing transesophageal echocardiography (TEE) to evaluate for left atrial or left atrial appendage thrombus. The purpose of this study is to evaluate the safety of NOACs for stroke prevention in AF in obese patients in the peri-DCCV period without previous TEE.

Methods

A retrospective analysis was performed on 1386 elective DCCVs done at a single medical center (Northwestern Memorial Hospital) from January 2015 to September 2017. Of these, 761 were performed without TEE guidance and included in the present study. All 761 patients had at least 3 weeks of NOAC or therapeutic warfarin treatment before DCCV. Decisions regarding selection of anticoagulant were at the discretion of the treating physician.

The DCCVs were performed in a noninvasive procedure room by either a credentialed advanced practice provider or cardiology fellow under the supervision of an attending electrophysiologist.[9] After a standard history and physical and informed consent, Quik-Combo pads were applied to the patient in the anterior-posterior orientation and connected to a biphasic defibrillator. An anesthesiologist provided Monitored Anesthesia Care with deep sedation for each procedure. Synchronized cardioversion was performed with initial shock at 200 J for AF, 100 J for atrial flutter, and 50 J for atrial tachycardia. In the case of immediate return of AF, a second shock was performed, with increasing energy (up to 360 J for AF). Subsequent shocks or use of ibutilide was at the discretion of the attending electrophysiologist.

Obesity groups followed the definitions from the Centers for Disease Control and Prevention and were classified as

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See page 4 for disclosure information.

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normal (BMI < 25), overweight (BMI 25 to <30), class 1 obesity (BMI 30 to <35), class 2 obesity (BMI 35 to <40), and class 3 or severe obesity (BMI ≥ 40).[10] The primary end point was stroke at 30 days. Additional analysis was done by weight class, defined simply as ≥ or <120 kg.

Continuous variables were expressed as mean ± standard deviation. A 1-way analysis of variance was used to compare >2 means, and student's *t* test was used to compare 2 continuous variables. Chi-square test was used to compare proportions. A p value of <0.05 was considered significant. In the case of non-normally distributed variables, nonparametric adjustment was done.

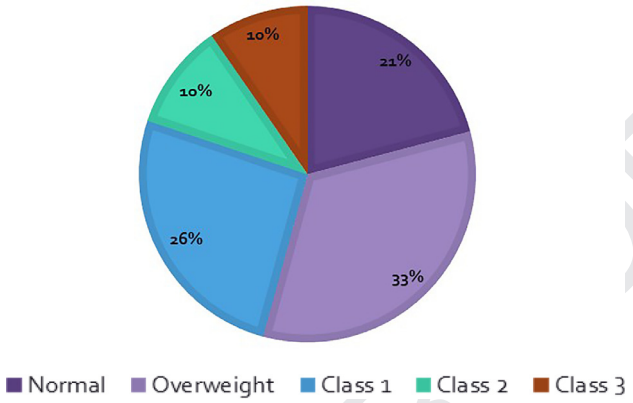

Figure 1. Distribution of BMI classifications.

Results

Of 761 patients included in this study, 159 were classified as normal by BMI, 254 in the overweight group, 197 patients in the class 1 obese group, 78 in class 2, and 73 in class 3 or severe obesity (Figure 1). There were just 3 patients who would be considered underweight by BMI and they were included with the normal group. Baseline characteristics are shown in Table 1. Of note, the obese patients were significantly younger, but without difference in CHA_2DS_2-VASc score (overall average 2.6 ± 1.6). There was no significant difference in individual anticoagulant choice by BMI class (Figure 2). Apixaban was the most commonly used anticoagulant in each class, followed by rivaroxaban. Together, apixaban and rivaroxaban accounted for 92.8% of the NOAC usage overall. When groups are separated by absolute weight (≥ or <120 kg), the higher weight group was more likely to be younger, male, have a lower CHA_2DS_2-VASc score, and a larger left atrium. There was no significant difference in the usage of each NOAC between the 2 weight groups (Table 2).

Two patients (0.26%) in the study had cardioembolic strokes after DCCV. One patient had a BMI of 38 (class 2 obesity) with a total weight of 100.6 kg; the other patient had a BMI of 22.5 (normal) with a total weight of 62 kg. Both patients had been taking apixaban before DCCV. Other adverse events were 2 episodes of bradycardia requiring medication intervention in the class 2 obesity group.

Discussion

In our study of 761 patients on NOACs who underwent DCCV without previous TEE, there was a very low rate of stroke in all weight classes and none in patients with BMI ≥40. These data suggest that NOAC use for stroke prevention in nonvalvular AF even in severely obese patients appears safe. The stroke rate of 0.26% is similar to that

Table 1
Baseline characteristics by body mass index (kg/m^2)

Variable	< 25	25 − < 30	30 − < 35	35 − < 40	≥ 40	p value
Age (Years)	71.6 ± 11.8	68.7 ± 11.0	67.2 ± 9.9	66.7 ± 9.2	62.0 ± 10.8	<0.01
Women	73 (45.9%)	53 (20.9%)	73 (37.2%)	23 (29.4%)	24 (32.9%)	0.03
Weight (kg)	67.9 ± 11.7	86.9 ± 11.7	98.5 ± 13.9	114 ± 16.0	131 ± 20.3	<0.01
CHA_2DS_2-VASc score	3.0 ± 1.7	2.5 ± 1.6	2.6 ± 1.7	2.7 ± 1.6	2.4 ± 1.4	0.04
Left ventricular ejection fraction (%)	53.1 ± 11.6	54.9 ± 10.8	54.0 ± 11.9	55.1 ± 10.2	52.4 ± 12.5	0.38
Left atrial diameter (cm)	4.2 ± 0.7	4.2 ± 0.7	4.3 ± 0.6	4.4 ± 0.7	4.5 ± 0.9	0.05
Presenting rhythm						
- Atrial fibrillation	105 (66.0%)	203 (79.9%)	161 (81.7%)	72 (92.3%)	69 (94.5%)	0.18
- Atrial flutter	51 (32.1%)	47 (18.5%)	35 (17.8%)	6 (7.7%)	3 (4.1%)	<0.01
- Atrial tachycardia	3 (1.9%)	4 (1.6%)	1 (0.5%)	0 (0%)	1 (1.4%)	0.19
Antiarrhythmic drug use						
- Any antiarrhythmic	99 (62.3%)	164 (64.5%)	121 (61.4%)	57 (73.1%)	48 (65.7%)	0.86
- Amiodarone	32 (20.1%)	56 (22.0%)	45 (22.8%)	31 (39.7%)	20 (27.4%)	0.05
- Dofetilide	12 (7.5%)	23 (9.0%)	12 (6.1%)	7 (9.0%)	7 (9.6%)	0.92
- Dronedarone	18 (11.3%)	28 (11.0%)	23 (11.7%)	5 (6.4%)	12 (16.4%)	0.33
- Flecainide	10 (6.3%)	20 (7.9%)	16 (8.1%)	4 (5.1%)	0 (0%)	0.08
- Propafenone	18 (11.3%)	19 (7.5%)	11 (5.6%)	4 (5.1%)	2 (4.1%)	0.27
- Sotalol	9 (5.7%)	18 (7.1%)	14 (7.1%)	6 (7.7%)	7 (9.6%)	0.86
Anticoagulation						
- Warfarin	48 (30.2%)	45 (17.7%)	41 (20.8%)	11 (14.1%)	15 (20.5%)	0.13
- Apixaban	59 (37.1%)	106 (41.7%)	89 (45.2%)	43 (55.1%)	36 (49.3%)	0.38
- Rivaroxaban	37 (23.3%)	91 (35.8%)	61 (31.0%)	19 (24.4%)	16 (21.9%)	0.26
- Dabigatran	13 (8.2%)	11 (4.3%)	6 (3.0%)	5 (6.4%)	6 (8.2%)	0.43
- Edoxaban	1 (0.6%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	