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Implementation of a Procainamide-Based Cardioversion Strategy for the Management of Recent-Onset Atrial Fibrillation

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ABSTRACT
Atrial fibrillation/flutter (AF) remains the most common rhythm disturbance in adult patients presenting to emergency departments (EDs). Although pharmacologic cardioversion has been established as safe and effective in recent-onset AF, its use in U.S. EDs is uncommon. The purpose of this study was to assess the safety and efficacy of intravenous (IV) procainamide for pharmacologic cardioversion in patients presenting to the ED with AF of <48-hr duration. Patients presenting to the ED with recent-onset AF (<48 hr) undergoing a cardioversion strategy with IV procainamide from 2017 to 2019 were reviewed. Clinical outcomes assessed included rates of cardioversion, hospital admission, stroke, and return ED visits for arrhythmia or serious adverse events. A total of 64 patients received procainamide therapy—60.9% achieved cardioversion and 35.9% were admitted to the hospital. The mean dose was 1062.4 mg (12.1 mg/kg). No patients returned to the ED secondary to stroke and 9.4% experienced complications attributed to procainamide, the most common

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being hypotension. Within 30 days of therapy, 20.3% of patients returned to the ED secondary to arrhythmia recurrence. Patients experiencing cardioversion with procainamide were less likely to be admitted to the hospital (25.6% vs. 52.0%; $p = 0.04$) or receive a rate control agent (17.9% vs. 64.0%; $p = 0.001$). There was no significant difference in the rate of 30-day return between those who experienced pharmacologic cardioversion and those who did not ($p = 0.220$). The implementation of a procainamide-based acute cardioversion strategy for patients presenting to the ED with recent-onset AF resulted in a 60% cardioversion rate, which was associated with a significantly higher rate of discharge from the ED. Transient hypotension was the most common adverse event. Further investigation into ED-based protocols for management of recent-onset AF is necessary to better understand their safety and efficacy. **Key words:** arrhythmias, atrial fibrillation, atrial flutter, cardioversion, emergency medicine, procainamide

ATRIAL FIBRILLATION/FLUTTER (AF) is the most frequent cardiac rhythm disturbance for which patients present to the emergency department (ED) (January et al., 2014, 2019; McDonald, Pelletier, Ellinor, & Camargo, 2008). In patients with recent-onset AF and flutter (defined as symptomatic onset <48 hr), several studies have assessed and validated the safety of electrical and chemical cardioversion (Burton et al., 2004; Scheuermeyer et al., 2010, 2012; Stiell et al., 2007, 2010, 2017; Vinson, 2012; White, Heller, Kahoud, Slade, & Harding, 2015). Despite this, rate control continues to be the mainstay of therapy in the United States, where hospital admission rates of patients who present to the ED with AF are as high as 64%–76% (McDonald et al., 2008). By contrast, numerous Canadian and U.S. studies have demonstrated that acute cardioversion in patients with recent-onset AF results in admission rates as low as 3%–15%. Moreover, the use of acute pharmacologic cardioversion has consistently demonstrated less than 1% risk of 30-day stroke or life-threatening adverse effects (Scheuermeyer et al., 2012; Stiell et al., 2007, 2010, 2017; Vinson, 2012; White et al., 2015).

A pharmacologic cardioversion strategy may play a significant role in reducing hospital admissions and health care costs when integrated into a comprehensive recent-onset AF protocol that includes rate control and electrical cardioversion. The primary goal of this analysis was to characterize the experience and outcomes of a U.S. academic hospital ED with a procainamide-based cardioversion strategy for patients presenting with recent-onset AF.

METHODS

Study Design

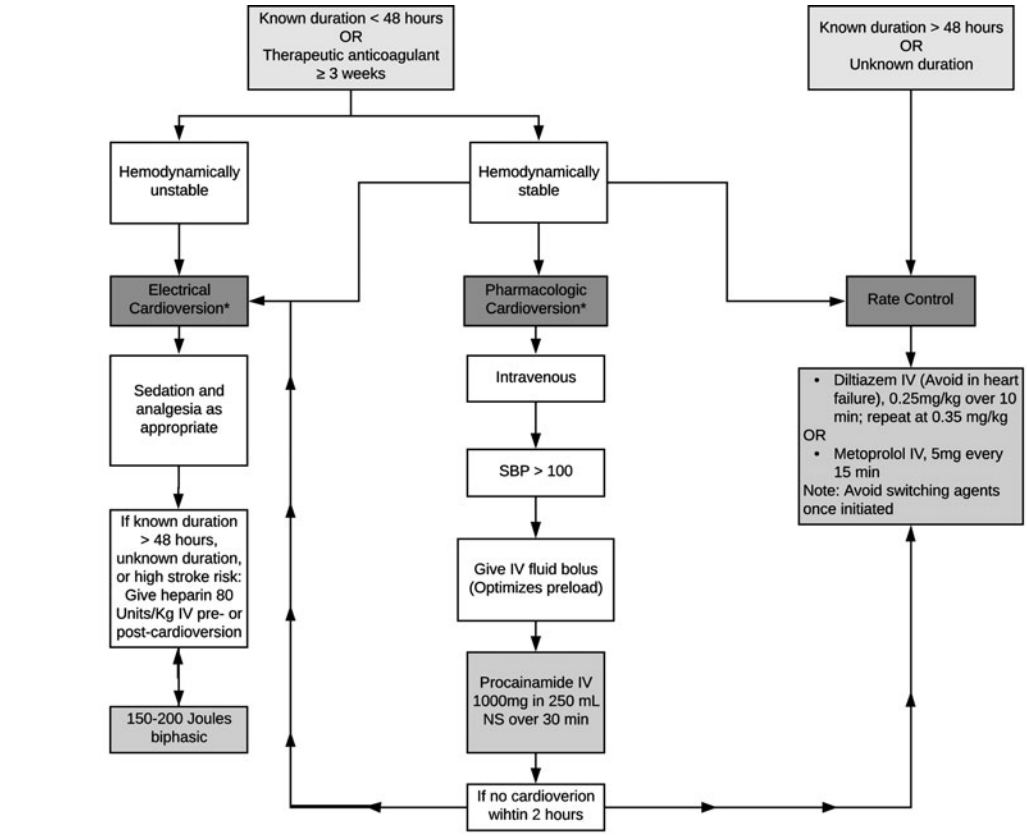
This was a retrospective chart review of ED visits in patients presenting with AF who were treated with procainamide intravenously (IV) between September 1, 2017, and January 31, 2019. The AF protocol is shown in Figure 1. The institutional review board (IRB) approved the study protocol as IRB exempt.

Study Setting and Population

The study site was a 700-bed academic teaching hospital ED with approximately 62,000 annual ED visits. The electronic medical record was queried to identify patients who had received procainamide IV during the ED visit. Patients younger than 18 years or those who were not being treated for AF or flutter were excluded.

Study Protocol and Measurements

Data were extracted from the medical record by all study authors following training with selected patients. Data collected included baseline demographic information, procainamide dosing, and administration details, as well as hemodynamic and outcome data. Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the study center. Patients were subdivided into



Disposition

1. All patients with symptomatic AF:
- Increase home rate control agent or start new agent
- Assess CHA2DS2-VASc score
- ED referral to cardiology

2. Safe for discharge home if:
- Conversion to sinus rhythm with stable vitals

OR
- A-fib/flutter with HR < 100 at rest or < 110 after ambulation PLUS symptomatic improvement

3. For *new onset* AF:
- Order outpatient transthoracic echocardiogram

Note: If emergently electrocardioverted in ED and known duration > 48 hours, unknown duration, or high risk for stroke:
- Prescribe 4 weeks of anticoagulation

Factors Favoring Rate Control	Factors Favoring Rhythm Control
-Older -Many comorbidities -Onset > 48 hr or unknown duration -Longstanding/persistent A-fib -Recent TIA/stroke -Rheumatic heart disease -Mechanical heart valve	-Younger -Few comorbidities -Onset < 48 hr -Paroxysmal A-fib -Anticoagulated ≥ 3 weeks or therapeutic INR

***Exclusions to electrical or chemical cardioversion:**
- Permanent A-fib (chronic, persistent, or longstanding)
- Symptoms > 48 hours or unknown duration of time (unless therapeutically anticoagulated with warfarin for ≥ 3 weeks)
- Mechanical heart valve
- Rheumatic heart disease
- Recent TIA/stroke
- Additional primary diagnosis necessitating admission
- Avoid rhythm control agents in cardiac ischemia, severe CHF, hypotension

Figure 1. Atrial fibrillation protocol. *Note.* AF = atrial fibrillation; CHF = congestive heart failure; ED = emergency department; HR = heart rate; INR = international normalized ratio; IV = intravenous; NS = normal saline; SBP = systolic blood pressure; TIA = transient ischemic attack.

those who achieved cardioversion versus those who did not. Our primary outcome was the incidence of successful cardioversion with this therapy. Our secondary outcomes included incidence of hospital admission, incidence of stroke within 30 days, adverse events associated with procainamide infusion, and 30-day return visits for arrhythmia or serious adverse events.

Data Analysis

Descriptive statistics were used to describe demographic data. Nominal and continuous data were analyzed using χ^2 or Fisher's exact test and Student's t test, respectively. Significance was defined as an $\alpha = 0.05$ and a $\beta = 0.2$. All data analysis was conducted using GraphPad Prism Version 8.0.0 for Windows (GraphPad Software, San Diego, California).

RESULTS

The baseline characteristics and procainamide therapy details of the 64 AF patients are depicted in Table 1. The primary outcome of successful cardioversion was achieved in 39 (60.9%) patients. Regarding secondary outcomes of interest, 23 (35.9%)

Table 1. Characteristics of ED patients with recent-onset atrial fibrillation treated with intravenous procainamide with successful versus unsuccessful cardioversion to sinus rhythm

Characteristic	All patients ($n = 64$)	Cardioversion ($n = 39$)	No cardioversion ($n = 25$)	p value
Age, *M* (*SD*), year	58.0 (18.3)	60.0 (19.3)	54.9 (16.7)	0.284
Actual body weight, *M* (*SD*), kg	92.4 (21.2)	90.4 (23.2)	95.7 (17.5)	0.338
Height, *M* (*SD*), cm	174.6 (10.8)	174.4 (10.1)	174.8 (12.0)	0.906
Body mass index, *M* (*SD*), kg/m^2	30.3 (6.4)	29.5 (6.4)	31.6 (6.3)	0.232
Female, *n* (%)	25 (39.1)	17 (43.6)	8 (32.0)	0.435
Race, *n* (%)				
Black or African American	14 (21.9)	6 (15.4)	8 (32.0)	0.134
Caucasian	49 (76.6)	32 (82.1)	17 (68.0)	0.235
Other	1 (1.6)	1 (2.6)	0 (0)	>0.99
Onset <48 hr prior to presentation, *n* (%)	59 (92.2)	37 (94.9)	22 (88.0)	0.371
Received a second dose of procainamide, *n* (%)	5 (7.8)	2 (5.1)	3 (12.0)	0.371
Total procainamide dose, *M* (*SD*), mg	1062.4 (187.6)	1068.0 (210.2)	1053.0 (149.4)	0.751
Lowest systolic blood pressure within the first hour following procainamide, *M* (*SD*)	115.3 (14.9)	113.8 (15.2)	117.4 (14.7)	0.367
Lowest diastolic blood pressure within the first hour following procainamide, *M* (*SD*)	75.2 (14.1)	70.4 (11.6)	82.3 (14.7)	0.001
Lowest systolic blood pressure within the second hour following procainamide, *M* (*SD*)	119.4 (16.8)	120.2 (17.4)	118.3 (16.2)	0.709
Lowest diastolic blood pressure within the second hour following procainamide, *M* (*SD*)	77.0 (14.3)	73.2 (13.0)	82.4 (14.6)	0.033
Heart rate at disposition, *M* (*SD*)	82.3 (14.7)	79.1 (13.6)	87.2 (16.2)	0.031

Note. ED = emergency department.

Table 2. Outcomes of ED patients with recent-onset atrial fibrillation treated with intravenous procainamide with successful versus unsuccessful cardioversion to sinus rhythm

Characteristic	All patients ($n = 64$)	Cardioversion ($n = 39$)	No cardioversion ($n = 25$)	p value
Admitted to the hospital, *n* (%)	23 (35.9)	10 (25.6)	13 (52.0)	0.040
Underwent electrical cardioversion, *n* (%)	5 (7.8)	0 (0)	5 (20.0)	0.007
Rate control used, *n* (%)	23 (36.9)	7 (17.9)	16 (64.0)	0.001
Diltiazem, *n* (%)	12 (18.8)	4 (10.3)	8 (32.0)	0.048
Metoprolol, *n* (%)	11 (17.2)	3 (7.7)	8 (32.0)	0.018
Return to the ED for arrhythmia within 30 days, *n* (%)	13 (20.3)	10 (25.6)	3 (12.0)	0.220
Return to the ED within 30 days for a serious adverse event, *n* (%)	2 (3.1)	1 (2.6)	1 (4.0)	>0.99
Documented complications, *n* (%)	6 (9.4)	3 (7.7)	3 (12.0)	0.671
Hypotension	4 (6.3)	2 (5.1)	2 (8.0)	0.640
Bradycardia	1 (1.6)	0 (0)	1 (4.0)	0.391
QRS widening	0 (0)	0 (0)	0 (0)	NS
Tachyarrhythmia	1 (1.6)	1 (2.6)	0 (0)	>0.99
Shortness of breath	0 (0)	0 (0)	0 (0)	NS
Hypertension	1 (1.6)	0 (0)	1 (4.0)	0.391

Note. ED = emergency department; NS = not significant.

of all patients were admitted to the hospital and no patients returned to the ED within 30 days with a stroke (see Table 2). Adverse effects of procainamide occurred in 6 (9.4%) patients, the most common of which was hypotension in 4 (6.3%) that resolved with IV fluids. One patient had self-limiting bradycardia, one had nonsustained ventricular tachycardia prior to the administration of procainamide and subsequent cardioversion, and another became hypertensive without a change in subjective symptoms. Thirteen (20.3%) patients returned to the ED within 30 days for a presentation of AF. Only two (3.1%) patients returned to the ED within 30 days for a serious adverse event. In one instance, the patient had signs of acute heart failure during the initial visit and returned with flash pulmonary edema following ED discharge several hours later. The other returned for nausea and vision changes but was not hospitalized.

Overall, the mean age was 58 years and 49 (76.6%) were Caucasian. The average dose of procainamide was 1062.4 mg (12.1 mg/kg). It was noted that 7.8% of patients received a second dose of procainamide, deviating from the protocol. The 39 patients who achieved cardioversion following procainamide therapy were compared with the 25 patients who did not (see Table 1). No significant differences were noted in baseline characteristics between the two populations. However, patients who were successfully cardioverted were about half as likely to be admitted to the hospital (25.6% vs. 52.0%; $p = 0.04$), less likely to undergo electrical cardioversion (0% vs. 20.0%; $p = 0.007$), less likely to receive a rate control agent (17.9% vs. 64.0%; $p = 0.001$), and had significantly lower diastolic blood pressures and heart rates following procainamide therapy (see Table 2). There were no significant differences in 30-day ED return visits for serious adverse events

or arrhythmias between those who achieved cardioversion and those who did not.

DISCUSSION

We conducted an analysis of the outcomes of using a standardized protocol for recent-onset AF in an academic ED with a procainamide-based cardioversion strategy. Although not frequently used in the United States, pharmacologic cardioversion is supported by clinical practice guidelines and has been widely accepted abroad (Camm, Camm, & Savelieva, 2012; January et al., 2014, 2019; Stiell et al., 2010; Stiell, Macle, & CCS Atrial Fibrillation Guidelines Committee, 2011). Previous investigations using procainamide have documented cardioversion rates of 52%–67% and hospital admission rates of 3%–15% (Scheuermeyer et al., 2012; Stiell et al., 2007, 2010, 2017; Vinson, 2012; White et al., 2015). These reported cardioversion rates following procainamide use are similar to the results of this analysis (60%). However, the admission rates in these studies were substantially lower than ours (35.9%). Unlike the other protocols, ours did not explicitly recommend an aggressive electrical cardioversion strategy when procainamide failed to cardiovert, which may have contributed to fewer discharges. Nevertheless, our hospital admission rate of 35.9% was notably lower than admission rates in U.S. studies (60%–64%) in which a rate control strategy was used (McDonald et al., 2008; White et al., 2015). These data suggest that the addition of antiarrhythmic agents to a more comprehensive AF protocol may safely increase overall discharge rates for recent-onset AF.

In this study, 9.4% of patients experienced an adverse event and none presented with a stroke within 30 days. These findings are consistent with previous studies demonstrating a low incidence of stroke (<1%) and non-life-threatening adverse events (3%–10%) associated with procainamide use (Scheuermeyer et al., 2012; Stiell et al., 2007, 2010, 2017; Vinson, 2012; White et al., 2015). Although all patients who received procainamide for recent-onset AF were included in the analysis, it should be noted that four patients had characteristics that should have precluded the use of procainamide according to the institution's protocol: two patients with clear signs of heart failure, one patient with sepsis, and one patient with dehydration and hypotension. Of these, one patient had no adverse events and two patients had transient hypotension that improved with fluids. One patient with signs of heart failure was successfully cardioverted but returned to the ED several hours later with flash pulmonary edema and hypertensive emergency. These protocol deviations underscore the importance of appropriate risk stratification prior to administering an antiarrhythmic agent. Hypotension, bradycardia, and tachyarrhythmias are known side effects of procainamide (Stiell et al., 2017). As such, antiarrhythmic agents like procainamide should only be used in lower risk populations, and ED-based clinical pathways need to clearly identify higher risk populations. Finally, although ED literature demonstrates that procainamide use in lower risk recent-onset AF is safe and effective, this literature is not widely known or practiced in all stakeholder circles. Early collaboration with cardiology practitioners to garner support for cardioversion-based protocols is highly recommended.

LIMITATIONS

This was a retrospective chart review that relied on accurate documentation by practitioners. Because it excluded recent-onset AF patients for whom procainamide was not used—including patients who underwent a rate control strategy only—the admission rate for all recent-onset AF patients may have been higher. Selection bias also prevents assessment of clinical characteristics and other outcomes of patients excluded from the protocol. Further, it is possible that patients could have visited other EDs in the area, hence limiting the analysis of ED return visits. Additionally, the absence of a control

group limits comparisons as well as a more comprehensive analysis. Hence, these results primarily support previous findings that pharmacologic cardioversion is safe and effective and secondarily are hypothesis-generating to serve as a foundation for future investigations.

CONCLUSION

The implementation of a procainamide-based cardioversion strategy for patients presenting to the ED with recent-onset AF resulted in a 60.9% cardioversion rate and a higher discharge rate than previous AF studies that predominantly used a rate control strategy. No patients returned to the ED within 30 days secondary to a stroke or bleeding complication. Fewer than 10% of patients had non-life-threatening complications associated with procainamide use, the most common of which was transient hypotension (6.3%). Further prospective investigation is necessary to assess the generalizability of a pharmacologic-based cardioversion strategy at other institutions.

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