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Rhythm Control with Amiodarone versus Rate Control Strategy Effect on Direct Current Cardioversion Outcomes for Atrial Fibrillation: A Retrospective Cohort Analysis in a Tertiary Referral Centre

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Abstract

Aim

There is ongoing debate over the most effective therapy for atrial fibrillation (AF) with the varied use of rhythm control (RyC) or rate control (RaC) therapy. To assess whether RyC therapy with amiodarone prior to direct current electrical cardioversion (DCCV) prevents AF recurrence compared to RaC therapy. To assess whether left atrial (LA) size is an effective predictor of early recurrence of AF after DCCV.

Methods

A retrospective cohort study of 136 patients with AF who attended a tertiary referral centre for DCCV from January 2019 to June 2020. The cohort was divided into two groups (RyC and RaC therapy) to compare DCCV outcomes and LA size.

Results

A total of 55% (n=39) of patients on amiodarone therapy successfully maintained sinus rhythm (SR) after DCCV as shown in figure 1. In comparison only 31% (n=20) of patients on RaC therapy successfully maintained SR after DCCV (χ^2 =8.06, p= 0.005). A significant difference was observed in mean LA size between successful (41.49mm±7) and unsuccessful (43.7mm ± 5.29) DCCV cohorts (t=2.135; p= 0.035).

Discussion

This study indicates a trend towards RyC therapy with amiodarone as a preferred choice over RaC therapy to maintain SR after DCCV. Mean LA size may be a predictor of early recurrence of AF after DCCV.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in aging populations worldwide. It has a direct correlation with an increased risk and severity of stroke, heart failure and mortality if left untreated.[1] A recent analysis of 50-year trends in AF from the Framingham heart study showed both an increase in prevalence and incidence of AF. This highlights the importance of further research to identify the most effective therapeutic intervention for AF in order to prevent its adverse consequences.[2] Strong evidence suggests the use of early rhythm control (RyC) therapy is associated with less cardiovascular adverse outcomes in AF.[3] Amiodarone is an anti-arrhythmic drug which has shown to be an effective agent at preventing reoccurrence of AF after direct current electrical cardioversion (DCCV).[4] In one comparative study, 69% of patients on amiodarone maintained SR when compared to 39% of patients on propafenone or sotalol therapy.[5] Similar results were also seen at one year in the AFFIRM study, where SR was maintained in 60% of patients on amiodarone compared to 38% of patients taking sotalol.[6] Similarly, a study by Channer et al. showed that at 8 weeks following DCCV, 51% patients on amiodarone remained in SR and at 1 year, 49% patients on long-term amiodarone were in SR.[7]

There is debate over enlarged atria as to whether they are both a cause and consequence of AF. One such study hypothesizes that individuals genetically susceptible to AF results in increased LA size.[8] It has been suggested that LA size plays a role in the maintenance of SR after DCCV. A study by Wang et al showed that atrial size is a strong parameter associated with successful cardioversion.[9] Similarly, a study by Mattioli et al. showed that a LA size of less than 40 mm is significantly associated with the recovery of LA mechanical function after DCCV.[10] More recently, systematic review and meta-analysis data has also shown that an increase in LA volume index correlates with an increased risk of AF recurrence following DCCV.[11]

Thus, the objective of this retrospective review is to examine the impact of amiodarone therapy versus rate control (RaC) therapy on success rates after DCCV, and also to assess the role played by LA size in recurrence of AF after DCCV.

Methods

This is a retrospective cohort study of patients with a diagnosis of AF who presented to St. James Hospital for DCCV during an 18-month period, from January 2019 to June 2020, sample size n=136. In order to minimise selection bias the inclusion criteria was clearly defined from the onset, to include patients with AF undergoing DCCV who were concordant with both anticoagulation therapy and rhythm or rate control therapy. Anticoagulation therapy consisted of direct acting oral anticoagulants (DOAC) or Warfarin. The cohort was divided into two groups to compare DCCV outcomes; RyC therapy with amiodarone and RaC therapy with bisoprolol. The duration of amiodarone therapy was a minimum of 1 week prior to DCCV. A number of patients in the RaC therapy group taking verapamil (n=5) were excluded from the study due to its anti-arrhythmic

effect. As per hospital protocol, patient follow up occurred at 6 months after DCCV with a 48-hour Holter monitor and echocardiogram. The primary outcome was successful DCCV, characterised by maintenance of SR upon follow up at 6 months confirmed with a 48-hour Holter monitor.

Data collection was performed by 2 independent reviewers using electronic patient records. Data recorded included patient age, sex, the presence of valvular heart disease, medical co-morbidities including hypertension and type 2 diabetes mellitus, LA size in millimetres and drug therapy. Patient data was anonymised throughout. Nominal parameters were analysed by cross tabulation and using the Chi-squared test. Continuous descriptive data was subject to T-testing after confirming the basic assumptions such as normality were met. LA size data obtained was subject to Two-Way ANOVA analysis for comparison between RaC and RyC with respect to cardioversion outcomes, alongside assessment of the assumptions for this test. Odds ratios were used to ascertain the factors which would increase the likelihood of successful cardioversion. All data analysis was performed using IBM SPSS 28. Patients were not involved in the design and conduct of this research. A research proposal form was approved by the hospital research and ethics committee prior to commencing the study.

Results

The patient data is separated to compare RyC therapy and RaC therapy, seen in Table 1. Patients (n=136) received treatment with amiodarone (n=71) and Bisoprolol (n=65) prior to DCCV. The RaC therapy group consisted of bisoprolol (n=65). Valvular heart disease was prevalent (n=80; 59%) of which mitral regurgitation was most predominant (n=58; 73%). Co-morbidities including hypertension (n=57; 42%) and type II diabetes mellitus (n=12; 9%) were observed. Notably, 47% of patients had moderate-to-severe dilatation (45-60mm) (n=63). It was shown that gender, hypertension, type II diabetes mellitus and valvular heart disease did not affect DCCV outcomes in the RaC, RyC or overall groups (Table 2). There was no loss to follow up.

A total of 55% (n=39) of patients on amiodarone therapy successfully maintained SR after DCCV as shown in table 1. In comparison only 31% (n=20) of patients on RaC therapy successfully maintained SR after DCCV (χ^2 =8.06, p= 0.005). The LA mean size distributions across treatment groups are shown in figure 1. The data is divided based on outcome, successful or unsuccessful maintenance of SR after DCCV. The mean LA size for the successful DCCV cohort was 41.49mm ± 7. The mean LA size for the unsuccessful DCCV cohort was 43.7mm ± 5.29. Successful DCCV outcomes were associated with a lower mean LA size (t=2.135; p= 0.035). However, based on two-way ANOVA analysis, the difference in LA size was insignificant when the interaction between DCCV outcome and drug therapy (RyC vs RaC) were taken into account (F = 2.563, p=0.112, partial eta^2 0.019) (Figure 1).

Table 1: Demographics. RyC – rhythm control, RaC – rate control, MR – mitral regurgitation, TR – tricuspid regurgitation, AS – aortic stenosis, AR – aortic regurgitation, DM – diabetes mellitus, LA – left atrium.

		RaC (N=65)	RyC (N=71)	Total (N=136)	p value
	Successful DCCV	20	39	59	0.005
	N Male	52	51	103	0.267
	Age (mean +-SD)	64.9 +- 9.9	65 +- 11.7	64.9 +- 10.8	0.176
Valvular Disease	**MR**	30	28	58	0.429
	TR	18	15	33	0.372
	AS	2	4	6	0.468
	MS	3	1	4	0.269
	AR	11	2	13	0.005
	MR & TR	16	12	28	0.266
	MR, TR & AR	4	1	5	0.142
	Hypertension	27	30	57	0.82
	Type II Diabetes Mellitus	5	7	12	0.677
	LA size (mean +- SD)	42.9 +- 5.8	42.63 +-6.6	42.8+-6.2	0.151

Table 2: Comparison of DCCV outcomes with relation to clinical characteristics using odds ratios (OR). Successful DCCV was characterised by maintenance of sinus rhythm upon follow up at 6 months. RyC – rhythm control, RaC – rate control, MR – mitral regurgitation, TR – tricuspid regurgitation, AS – aortic stenosis, AR – aortic regurgitation, DM – diabetes mellitus, LA – left atrium. 95% confidence intervals.

	RaC			RyC			Overall		
	OR	**Lower CI**	**Upper CI**	**OR**	**Lower CI**	**Upper CI**	**OR**	**Lower CI**	**Upper CI**
Gender	1.542	0.434	5.48	0.759	0.269	2.14	1.117	0.508	2.459
Hypertension	1.647	0.569	4.772	0.773	0.297	2.009	1.099	0.55	2.195
T2DM	3.706	0.568	24.185	0.583	0.121	2.822	1.321	0.403	4.326
MR	1.25	0.435	3.592	0.72	0.277	1.875	0.867	0.436	1.724
TR	1.179	0.369	3.769	0.922	0.294	2.891	0.95	0.43	2.098
AS	2.316	0.138	38.99	2.583	0.256	26.118	2.727	0.482	15.425
AR	0.816	0.192	3.465	0.816	0.049	13.579	0.549	0.161	1.88
MR & TR	1.03	0.304	3.487	0.788	0.227	2.73	0.809	0.346	1.889

Table 3: Comparison of DCCV outcomes with LA size (mm) in both treatment groups. Successful DCCV was characterised by maintenance of sinus rhythm upon follow up at 6 months. RyC – rhythm control, RaC – rate control, MR – mitral regurgitation, TR – tricuspid regurgitation, AS – aortic stenosis, AR – aortic regurgitation, DM – diabetes mellitus, LA – left atrium.

	RaC			RyC			Total		
DCCV outcome	**Mean**	**Std. Deviation**	**N**	**Mean**	**Std. Deviation**	**N**	**Mean**	**Std. Deviation**	**N**
Unsuccessful	44.24	5.028	45	43.06	5.656	32	43.75	5.294	77
Successful	39.95	6.468	20	42.28	7.302	39	41.49	7.062	59
Total	42.92	5.813	65	42.63	6.578	71	42.77	6.203	136

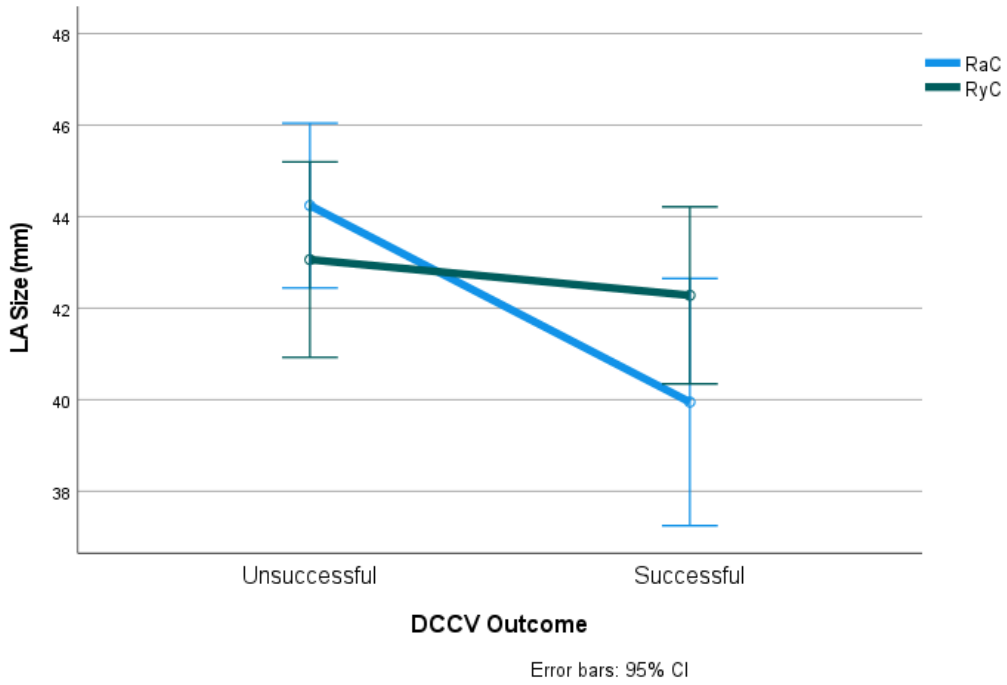

Figure 1: Distribution of LA size(mm) relative to successful and unsuccessful outcomes after DCCV. Error bars represent the 95% confidence interval. RyC therapy (amiodarone) versus RaC therapy (Bisoprolol) with respect to successful and unsuccessful maintenance of sinus rhythm. RyC – rhythm control, RaC – rate control.

Discussion

The results of this retrospective cohort analysis demonstrate that a greater percentage of patients on amiodarone therapy successfully maintained SR after DCCV compared to RaC therapy. This echoes results seen in the literature to date, where amiodarone has shown to be an effective therapy at preventing AF recurrence following DCCV.[5,6,7]

Larger LA size has been associated with reduced success rates after DCCV in other studies, [9,10,11] and similar effects were observed in the mean LA size between the successful DCCV cohort (41.49mm ± 7) and unsuccessful DCCV cohort (43.7mm ± 5.29) in our study. This suggests that there is a relationship between LA size and DCCV outcomes.

Patients taking amiodarone were subject to regular liver and thyroid function testing. There were no adverse side effects associated with amiodarone seen in this patient cohort. Despite the benefit of amiodarone seen in this study, regular liver and thyroid function testing as well as baseline pulmonary function testing should be carried out to monitor for toxicity described in the literature.[12,13]

Limitations of the study include selection bias and unobserved confounding factors which pose a threat to internal validity. Selection bias was minimized by clearly stating the inclusion criteria for the study from the onset and using 2 independent reviewers to perform data collection. There was no loss to follow up preventing possible information bias.

In conclusion, this study indicates a trend towards amiodarone therapy as a preferred choice over RaC therapy to maintain SR after DCCV. Early RyC could be implemented throughout tertiary hospitals on a wider scale to improve DCCV outcomes highlighting the need for prospective research in this area. Additionally, based on the data collected in this retrospective review, mean LA size may be a predictor of early recurrence of AF after DCCV.

Declaration of Conflicts of Interest:
The authors report no conflict of interest.

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References

1. Morillo, C.A., Banerjee, A., Perel, P., Wood, D. and Jouven, X., 2017. Atrial fibrillation: the current epidemic. Journal of geriatric cardiology: JGC, 14(3), p.195.
2. Schnabel, R.B., Yin, X., Gona, P., Larson, M.G., Beiser, A.S., McManus et al., 2015. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study. The Lancet, 386(9989), pp.154-162.
3. Kirchhof, P., Camm, A.J., Goette, A., Brandes, A., Eckardt, L., Elvan, A. et al., 2020. Early rhythm-control therapy in patients with atrial fibrillation. New England Journal of Medicine, 383(14), pp.1305-1316.
4. Capucci, A., Villani, G.Q., Aschieri, D., Rosi, A. and Piepoli, M.F., 2000. Oral amiodarone increases the efficacy of direct-current cardioversion in restoration of sinus rhythm in patients with chronic atrial fibrillation. European heart journal, 21(1), pp.66-73.
5. Roy, D., Talajic, M., Dorian, P., Connolly, S., Eisenberg, M.J., Green, M. et al, 2000. Amiodarone to prevent recurrence of atrial fibrillation. New England Journal of Medicine, 342(13), pp.913-920.
6. Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators, 2002. A comparison of rate control and rhythm control in patients with atrial fibrillation. New England Journal of Medicine, 347(23), pp.1825-1833.
7. Channer, K.S., Birchall, A., Steeds, R.P., Walters, S.J., Yeo, W.W., West, J.N., et al., 2004. A randomized placebo-controlled trial of pre-treatment and short-or long-term maintenance therapy with amiodarone supporting DC cardioversion for persistent atrial fibrillation. European heart journal, 25(2), pp.144-150.
8. van de Vegte, Y.J., Siland, J.E., Rienstra, M. and van der Harst, P., 2021. Atrial fibrillation and left atrial size and function: a Mendelian randomization study. Scientific reports, 11(1), pp.1-9.
9. Wang, T., Wang, M., Fung, J.W., Yip, G.W., Zhang, Y., Ho, P.P. et al., 2007. Atrial strain rate echocardiography can predict success or failure of cardioversion for atrial fibrillation: a combined transthoracic tissue Doppler and transoesophageal imaging study. International journal of cardiology, 114(2), pp.202-209.
10. Mattioli, A.V., Castelli, A., Andria, A. and Mattioli, G., 1998. Clinical and echocardiographic features influencing recovery of atrial function after cardioversion of atrial fibrillation. The American journal of cardiology, 82(11), pp.1368-1371.
11. Thangjui, S., Yodsuwan, R., Kewcharoen, J. and Trongtorsak, A., 2021. Left atrial volume index associated with recurrent atrial fibrillation after electrical cardioversion: meta-analysis and systematic review. Journal of the American College of Cardiology, 77(18_Supplement_1), pp.273-273.
12. Zimetbaum, P., 2007. Amiodarone for atrial fibrillation. New England Journal of Medicine, 356(9), pp.935-941.
13. Tanayan, C., Janda, T., Ilkanich, C., Pastoral, M. and Silver, K., 2019. Amiodarone toxicity: sooner than you expect. Journal of the American College of Cardiology, 73(9S1), pp.2938-2938.