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Efficacy Of Radiofrequency Catheter Ablation Versus Antiarrhythmic Drugs In Treating High Burden Premature Ventricular Contractions In Children With Structurally Normal Heart

Salaheldin Hefny Alahwany [1], Wagdy Abdelhamid Galal [2], Mazen Tawfik Ghaniem [3], Maha Mohamed Khalifa [4], Lamyaa Elsayed Allam [5]

[12345]Department of Cardiology, Ain Shams University - Faculty of Medicine, Egypt

[*]**Corresponding author: Salaheldin Hefny Alahwany**
Tel: +201019406524,
Email: dr.alahwany.md@med.asu.edu.eg

ABSTRACT

Background: Scarce literature on whether antiarrhythmic drugs (AADs) or radiofrequency catheter ablation (RFCA) is more efficacious when treating children suffering from a high load idiopathic premature ventricular contractions (PVCs) with many questions remain unanswered in this age group.

Objectives: The purpose of this study was to compare the efficacy of RFCA and AADs on high burden idiopathic PVCs in children.

Methods: A total of 60 eligible child ≤18 years with High burden PVCs (≥10% of total beats per day) that were treated by either AADs (group A) or RFCA (group B). Both the baseline and follow-up measurements were taken. After gathering clinical complaints, a physical examination, a repeat standard ECG, a standard or 12-lead Holter recording, and echocardiography were all conducted.

Results: Among RFCA (n=30) and AADs (n=30) groups, treatment success was 80.0% and 20.0% respectively, while AADs medications cessation was 73.3% and 26.7% respectively, the differences were statistically significant.

Conclusion: In terms of PVC reduction and, as a result, AADs medication cessation post-ablation, RFCA appears to be more effective than AADs. It was a safe and extremely successful therapeutic option performing RFCA in children to use traditional mapping.

Keywords: Premature ventricular contractions; radiofrequency catheter ablation; antiarrhythmic drugs; children; radiofrequency catheter ablation.

Abbreviations: AADs = antiarrhythmic drugs; RFCA = radiofrequency catheter ablation; PVC = premature ventricular contraction.

INTRODUCTION

In the pediatric population, premature ventricular complexes (PVCs) are regularly seen in Hearts that are structurally normal as well as those that are structurally abnormal. Idiopathic PVCs are PVCs that occur in children with hearts that are anatomically normal. A lot of PVCs emanating from various places in both ventricles, right and left are considered normal and do not indicate a malignant prognosis. PVCs that are idiopathic or benign have a typical QRS morphology, are monomorphic, and most commonly originate in the right ventricular outflow tract/left ventricular outflow tract or left ventricular fascicles, but they can also occur in less common places like around the mitral or tricuspid annulus [(1)].

PVCs can be discovered in up to 40% of healthy children using 24-hour Holter monitoring. [(2)]. In children without obvious structural heart disease, the prevalence of idiopathic PVCs ranges from 10% to30%, depending on the duration and type of screening. [(3)].

People who have been exposed to PVCs have experienced a diverse set of clinical signs and symptoms, ranging from asymptomatic syncope to death. [(4, 5)], or ventricular tachycardia or ventricular fibrillation, which can be life-threatening [(6, 7)]. The prognosis of PVCs is correlated with its site of origin [(8)].

OBJECTIVES

The purpose of this study was to compare the efficacy of RFCA and AADs on high burden idiopathic PVCs in children.

Patients and methods

This was a prospective, observational study at Electrophysiology Unit-Ain Shams University from October 2018 to September 2020. the study was conducted on 60 child ≤18 years referred to

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Electrophysiology Unit-Ain Shams University with High burden PVCs (≥10% of total beats per day) that were divided into two groups, each composed of children and of both sexes, referred for possible Electrophysiology study and radiofrequency catheter ablation.

- ***Inclusion Criteria:*** Children with two or less PVC morphologies and A 24-hour Holter monitor revealed at least 10% ventricular ectopy load and a structurally normal heart.
- ***Exclusion Criteria:*** Congenital heart disease, electrical heart disease, includes channelopathies such long QT syndrome and Brugada syndrome, as well as catecholaminergic polymorphic VT. All cases with hypertrophic or dilated cardiomyopathy. If cardiomyopathy is the initial diagnosis, came before the detection of PVCs, case was ruled out.
- **Then the study population was divided into two groups:**

- **Group A:** Antiarrhythmic medicines were prescribed with close monitoring, and RFCA was postponed.
- **Group B:** Electrophysiology study and RFCA in children under the age of four years old who met any of the following criteria:
  1. Still symptomatic despite at least 3 months duration of AADs or developed adverse effects from AADs.
  2. Started to develop PVCs induced cardiomyopathy manifestations, either clinically or via echocardiographic parameters.
- **Sampling Method:** In this prospective, observational study we enrolled 60 successive children referred to Electrophysiology Unit-Ain Shams University between October 2018 and September 2020**.**
- **Sample Size:** 60 child ≤ 18 years according to the recent definition by WHO organization.

Ethical Considerations: All parents of children <12 year provided us a written informed consent for the study and both children ≥ 12 years and their parents gave us a written informed consent The study was authorized by Ain Shams University's institutional review board.

Methods

- **Baseline evaluation**

Organic heart diseases were excluded by physical examination, chest radiography, and echocardiography.

Electrocardiographic measurements

Each 12-lead electrocardiogram (ECG) and Holter monitoring result was thoroughly checked. Both 12-lead Holter monitoring, as well as 12-lead ECG were used to pinpoint the source of the PVC provisionally.

Site of origins of PVCs were defined by the location of origin: [9]

1. RVOT: morphology like a left bundle branch block, with an inferior axis, towering R waves in inferior leads, and R transition in lead V3 or V4.
2. LVOT: morphology like a right bundle branch block, with an inferior axis, tall R waves in inferior leads, and an early R transition in lead V1 or V2.
3. LV non-OT: morphology of the right bundle branch block lacks the properties of the LVOT.
4. RV non-OT: Left bundle branch block morphology, lacking the RVOT's usual inferior axis features.

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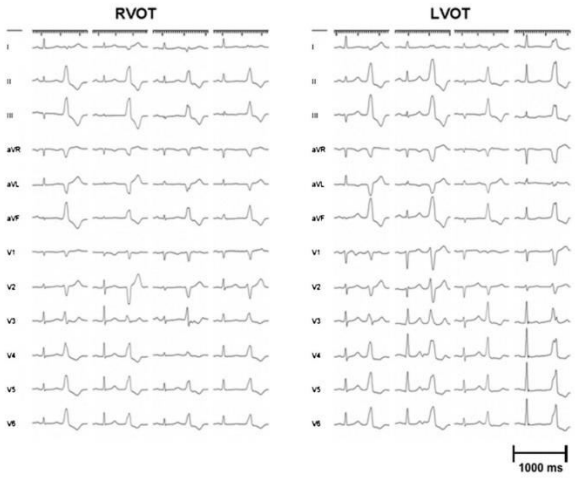

Figure (1): Representative Outflow Tract PVC Surface ECG Recordings [10].

Holter

Holter was used to determine PVC's Burden at the start of the study. PVCs made up what percentage of all beats? is known as the PVC load. At the start of the study, each case had 24 or 48 hours of Holter monitoring to determine the prevalence of PVC. The ratio of PVCs in relation to the overall the quantity of QRS complexes is known as the PVC burden. This study examined cases with a PVC burden of less than 10% [2, 11, & 10].

Drug therapy

Cases that were treated medically were a part of the AAD group (group A). β-blockers, CCBs, sotalol, and propafenone are examples of AADs [13]. Therapy with AADs had to last at least three months. Cases that were unable to take AADs were referred for RFCA, and those who stopped using AADs before completing three months of treatment were ruled out of the trial.

Electrophysiology procedure and ablation

Decapolar inside Coronary sinus, quadripolar catheter to make His region and 4 mm irrigated tip ablation catheter were navigated into various zones of mainly RVOT & LVOT regions after informed consent was acquired. Cases were observed without anesthesia while fasting. To test the inducibility of PVCs, we used burst pacing and single or double extra-stimuli at both atrium and ventricle under local anesthetic. Total eradication and failure to induce clinical PVCs or non-sustained VT were the procedure's endpoints [12, 13].

- **Follow-up**

At 3, 6, and 12 months after performing RFCA or commencing AADs, cases were requested to return for frequent follow-up. Clinical signs and symptoms were gathered. Physical examination, as well as a repetition of the usual ECG, Holter recording (standard or 12-lead), and echocardiogram were all done.

Statistical methods

Statistical Package for Social Sciences software was used to code, tabulate, and statistically analyze the obtained data. If the P value was less than 0.050, it was statistically significant; otherwise, it was non-significant.

Results

Sixty consecutive children divided into two equal groups in number according to whether RFCA was performed or AADs was continued (mean age ± SD: 13.4±3.3 years, range: 6.0–18.0 in RFCA group and mean age ± SD: 12.7±4.3 years, range: 12.7±4.3) with high burden idiopathic PVCs were

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prospectively, evaluated for almost 1 year follow-up duration at both groups. The study consisted of 33 boy and 27 girls distributed on both groups.

Table (1) shows that There were no significant differences in age between the groups studied at intervention, age at follow up, follow up duration and gender.

During baseline 24-hour Holter monitoring, the average PVC burden (percentage) was 23.3±9.0 and 21.6±8.2 in RFCA group and AADs group, respectively.

The average period from therapy to follow-up Holter monitoring was 1.10.5 years. Both RFCA and AADs dramatically reduced the frequency and burden of PVC. However, There were no significant differences between the groups tested in terms of baseline PVC burden; PVC Burden significantly decreased in both groups. RFCA reduced PVCs more effectively than AADs (P<0.001). table (4) figure (3)

PVC reduction with AADs was 20% effective, while with RFCA, it was 80% effective. Table (3)

Table (3), figures (1) and figures (2) show that treatment success and AADs Cessation were significantly more frequent among RFCA group.

Most of the cases had conventional ablation, except for two cases who had RFCA that was guided by electroanatomic mapping. Table (2)

Table (1): Age and gender among the groups analyzed

Variables		RFCA (N=30)	AADs (N=30)	P-value
Age at enrollment (years)		13.4±3.3	12.7±4.3	^0.444
Age at follow up (years)		14.6±3.4	13.7±4.2	^0.326
Follow up duration (years)		1.2±0.6	1.0±0.5	^0.131
Gender	**Male**	16 (53.3%)	17 (56.7%)	#0.795
	Female	14 (46.7%)	13 (43.3%)	

^Independent t-test. #Chi square test

Table (2): RFCA details among RFCA group

Variables		N	%
Site	**RVOT**	17	56.6
	LVOT	11	36.7
	RVOT&LVOT	2	6.7
Technique	**Conventional**	28	93.3
	3D mapping	2	6.7
Catheter	**Irrigated tip**	30	100.0
Cuspogram		4	13.3
		Mean±SD	**Range**
RF watt (watt)		40.7±3.7	30.0–45.0
Duration (sec)		134.4±46.7	60.0–260.0
Temperature (celsius)		44.2±2.8	40.0–54.0
Procedural time (min.)		62.1±20.9	40.0–110.0
Fluoroscopy time (min.)		41.6±21.8	18.0–90.0

Total=30

Table (3): Treatment success and medications cessation among the groups analyzed

Variables	RFCA (N=30)	AADs (N=30)	P-value	Effect size Relative risk (95% CI)
Treatment success	24 (80.0%)	6 (20.0%)	**<0.001***	4.00 (1.91−8.37)
AADs Cessation	22 (73.3%)	8 (26.7%)	**<0.001***	4.00 (1.91−8.37)

#Chi square test. CI: Confidence interval. Effect size: value of RFCA relative to AADs

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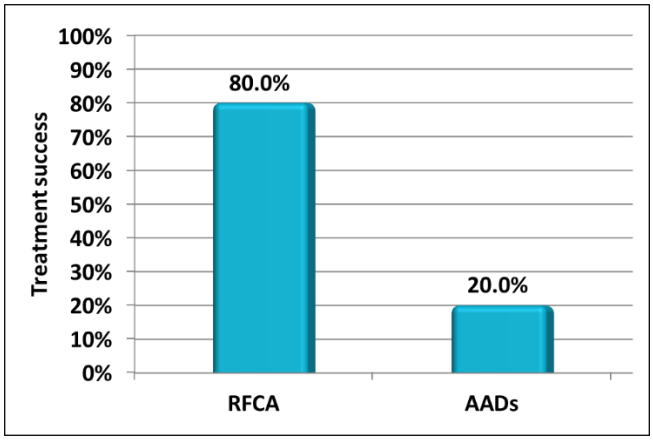

Figure (3): Treatment success among the studied groups

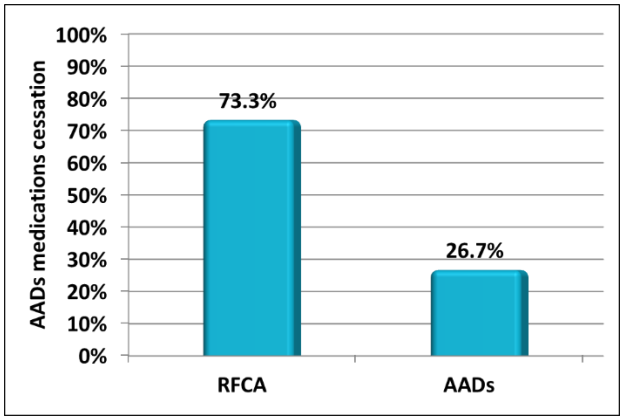

Figure (4): AADs medications cessation among the studied groups

Table (4): PVC burden among the groups analyzed

	Time	Measures	RFCA (N=30)	AADs (N=30)	^P-value (groups)	Effect size Mean±SE 95% CI
Burden (%)	Baseline	Mean±SD	23.3±9.0	21.6±8.2	0.442	1.7±2.2
		Range	10.0–45.0	14.0–46.6		-2.7–6.2
	FU	Mean±SD	1.5±2.0	11.8±8.2	**<0.001***	-10.4±1.5
		Range	0.0–7.0	4.0–33.0		-13.5–-7.3
	Change	Mean±SD	-21.8±9.1	-9.8±9.3	**<0.001***	-12.1±2.4
		Range	-45.0–-9.3	-42.6–8.0		-16.8–-7.3
	#P-value (times)		**<0.001***	**<0.001***		

Change= FU-baseline (negative values indicate reduction. ^Independent t-test (RFCA vs AADs). #Paired t-test (baseline vs. follow up). *Significant. Effect size: value of RFCA relative to AADs. SE: standard error. CI: Confidence interval

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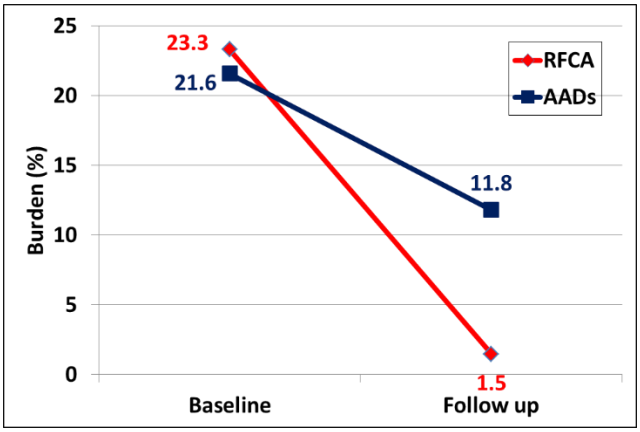

Figure (5): PVC Burden among the studied groups

DISCUSSION

The primary findings of our study were that, among 30 children performed RFCA and the corresponding 30 child kept on AADs groups, treatment success was 80.0% and 20.0% respectively, while AADs medications cessation was 73.3% and 26.7% respectively, the differences were statistically significant.

In the present study, all the children with high burden PVCs were kept on AADs primarily for at least 3 months and the RFCA was deferred as for cases with symptomatic PVCs, pharmacotherapy is a suitable first step [(14)]. And this was done in the hopes of reducing the incidence of ectopic beats using AADs [(15)].

Our findings are AADs had a statistically significant effect on frequent PVCs. (P-value <0.001), With a mean change of -9.8% in PVC load on Holter recording, it was nevertheless less effective than the RFCA group, which had a change of -21.8 percentage points.

On the contrary are the main findings by Bertels et al. that showed Anti-arrhythmic medications (AAD) had a relatively limited effect on frequent PVCs, with a mean change of 4.4 percentage points in PVC load on Holter recording, compared to a control group with a change of 4.2 percentage points. Furthermore, the fact that this illness is self-limiting may have influenced the outcomes [(16)].

Stec et al. reported that PVC reduction with AADs had varying degrees of success. Those highly responders to AADs with 90% regression of PVCs from mean 13,767 ± 9,423 to 251 ± 390, p<0.0001 and non-responders with only a minimal regression of PVCs count (13,767 ± 9,423 *vs* 7,850 ± 6,328, p < 0.003) [(17)].

As compared to our study, AADs medications cessation was significantly more frequent among RFCA group. In cases that continued medications baseline side effects were significantly more frequent in RFCA group. There were no significant differences between the groups tested in terms of follow-up adverse effects. AADs side effects significantly decreased in RFCA group.

Zhong et al. reported that RFCA's average PVC reduction rate (93%) was slightly greater than that of class I/III AADs (82%)[(9)].

In our study the effectiveness of AADs in reducing PVC was 20% and with RFCA was 80%. In comparison to 48% reduction with AADs and 93% with RFCA by Zhong et al retrospective study [(9)].

The 80% Treatment success of RFCA in the present study (24 out of 30 children) and 20% recurrence rate can be compared with successful RFCA in 68 out of 75 children with PVCs, with a success achieved, 90.67% [(13)].

Our results were consistent with literature for children of the 83–88 % RFCA success rate previously reported for children for RFCA of OTVAs with 2D guided mapping by *Smeets et al.*. [(18)] and the acute success rate of 87.5 percent for 2D guided mapping RFCA of OTVAs by *Li et al. (2016)* [(19)].

Our present study clearly showed that RCA was significantly capable to nearly abolish and reduce PVC frequency from mean baseline burden 23.3% to a mean 1.5% at follow-up after performing RFCA with a P-value < 0.001 which is about 95% reduction as compared to baseline burden while about 50% burden reduction in AADs group only from mean baseline burden 21.6% to a mean 9.8% at follow-up.

Those finding are similar with Zhong et al. who demonstrated that with a relative PVC quantity regression of more than 90% compared to 50% in the medication group, RFCA was more effective than

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AADs. In cases with an elevated PVC quantity, RFCA was even more beneficial. PVC decrease resulted in an increase in LVEF and reversed LV remodeling in cases with a high PVC frequency [(9)].

LIMITATIONS OF THE STUDY

Our findings could have been influenced by several factors. Furthermore, the study sample size and one-year follow-up duration may be insufficient to assess either therapy modality's long-term efficacy. The RFCA group had a higher mean PVC burden, indicating that RFCA therapy works better than AAD therapy.

Some early cases are included in the research. Despite having similar baseline features, the less favorable outcomes in these cases could be due to a lack of knowledge of OTVAs and less modern facilities and equipment at the time of treatment. We couldn't tell which treatment was better because the trial had a variable age range and a restricted sample size, and there was no randomization between AADs and RFCA.

CONCLUSION

RFCA showed to be more efficacious than AADs in decreasing PVCs quantity and consequently AADs medications cessation post-ablation. RFCA was found to be a safe and effective therapy alternative in children with traditional mapping. Given the limitations of our work, a larger, well-powered, multi-center randomized trial is needed to better describe this population and identify characteristics that predict the development of ventricular dilatation and dysfunction, as well as the resolution of high ectopy load.

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Conflict of Interest: None.

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