

ARRHYTHMIAS IN WILLIAMS SYNDROME

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Objectives: Patients with Williams syndrome (WS) are at increased risk of sudden cardiac death (SCD). The prevalence and types of primary arrhythmias is unknown in WS. We sought to establish the prevalence of primary arrhythmias and determine what role known repolarization abnormalities (QTc) might have on risk of arrhythmia and SCD in WS.

Methods: We retrospectively reviewed all patients with WS with ambulatory ECG monitoring at our institution between 10/2017 and 1/2022. Primary outcome was presence of arrhythmia (excluding isolated atrial or ventricular ectopy). Monitors were assessed for premature ventricular and atrial complex burden (%), arrhythmias, and QTc interval, which was manually calculated (Bazett correction) on rhythm strips at minimum, mean, and maximum heart rates. Degree of QTc change with varying heart rates was recorded to maintain internal validation. These findings were correlated with QTc and rhythm by 12-lead ECG and findings of electrophysiology study, when applicable.

Results: A total of 74 patients (55% female, median age 8 years [25th and 75th quartiles 3, 13]) underwent 108 ambulatory monitors. Arrhythmias were present in 9 (12%) patients. Of these, 3 (33%) had >1 arrhythmia, and 16/24 serial monitors on these patients were abnormal. Older age and symptoms (palpitations or syncope) were associated with arrhythmias. Arrhythmia was not associated with the degree of structural heart disease (Table 1). Atrial tachycardia was the most commonly identified arrhythmia (n=6). Two patients had typical atrioventricular node reentrant tachycardia and underwent cryoablation of the slow pathway. Ventricular arrhythmias were present in 3 patients (non-sustained ventricular tachycardia, n = 2; idioventricular rhythm, n = 1). One patient had 2:1 atrioventricular block with intermittent competing junctional escape rhythm versus 3rd degree heart block. The QTc increased with higher heart rates in all groups. There was a higher number of premature ventricular and atrial complexes per hour in patients with arrhythmias (Table 2).

Conclusions: There was a high prevalence of arrhythmia in WS. Higher percentage of atrial and ventricular complexes per hour may be predictive of increased risk of clinically significant arrhythmias. Abnormally, the QTc also increased with increasing heart rate. These data indicate routine ambulatory ECG monitoring is indicated in WS, particularly given increased risk of SCD in this population that may be related to primary arrhythmias, sequelae of myocardial ischemia, and/or intrinsic repolarization abnormalities.

Table 1: Demographics

Characteristic	Total population (N=74)	No arrhythmia (n=66)	Arrhythmia (n=8)	p Value
Age (years), median (Q1, Q3)	8.0 (3.0, 13.0)	6.5 (3.0,13.0)	13.0 (10.0, 24.0)	0.003
History of QTc > 460 ms, n(%)	25 (34.3)	19 (30.2)	6 (60.0)	0.08
Maximum degree of left ventricular hypertrophy, n(%)	70 (94.6)	60 (93.8)	10 (100)	0.8
No	33 (44.6)	28 (43.8)	5 (5.0)	
Mild	8 (10.8)	8 (12.5)	0 (0)	
Moderate	0 (0)	0 (0)	0 (0)	
Severe				
Right ventricular outflow tract obstruction, n(%)	14 (18.9)	13 (20.3)	1 (10.0)	0.7
Left ventricular outflow tract obstruction, n(%)	46 (62.2)	40 (62.5)	6 (60.0)	>0.99
Known coronary abnormality, n(%)	19 (25.7)	17 (26.6)	2 (20.0)	>0.99
History of palpitations, n(%)	10 (13.5)	6 (9.4)	4 (40.0)	0.025
History of syncope, n(%)	4 (5.4)	1 (1.6)	3 (30.0)	0.007
History of major cardiac event (peri-anesthesia), n(%)	6 (8.1)	4 (6.3)	2 (20.0)	0.2

Table 2: Ambulatory Rhythm Monitoring*

Characteristic	Total encounters (N=108)	No Arrhythmia (n=92)	Arrhythmia (n=16)	p Value
ECG QTc	438 (418, 451)	438 (421, 448)	422 (396, 455)	0.3
Monitor min heart rate	58 (49, 66)	60 (55, 67)	45 (39, 54)	<0.001
Monitor average heart rate	95 (85, 111)	100 (87, 114)	80 (76, 87)	<0.001
Monitor maximum heart rate	183 (161, 193)	183 (161, 192)	179 (162, 194)	0.9
Bazett QTc, min heart rate	398 (377, 429)	394 (374, 429)	407 (384, 429)	0.3
Bazett QTc, max heart rate	470 (439, 491)	465 (436, 489)	474 (459, 500)	0.2
QTc difference with max vs min HR	60 (38, 98)	62 (38, 95)	53 (38, 104)	0.99
PAC per hour worn	0.22 (0.03, 0.97)	0.17 (0.03, 0.91)	0.86 (0.05, 26.11)	0.03
PVC per hour worn	0.12 (0.01, 0.42)	0.10 (0.01, 0.23)	1.28 (0.26, 4.6)	0.0002

Data presented with median (IQR 25,75);

*ZioXT, iRhythm, CA, USA, n=104; BioTel ePatch, Philips, PA, USA, n = 4.