

## Supplementary material

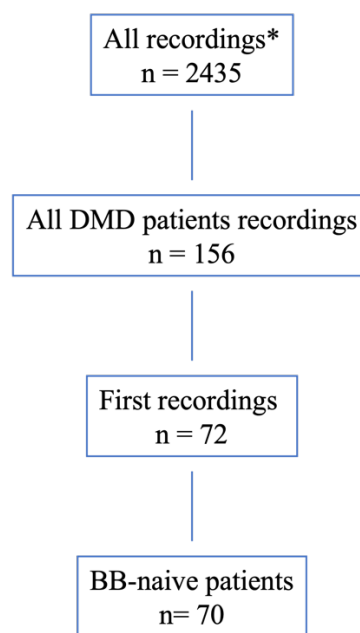
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*Bazgier M, Meyer-Szary J, Tarnowska R, et al. Prevalence and severity of sinus tachycardia and arrhythmias by Holter monitoring in children with Duchenne muscular dystrophy. Kardiol Pol. 2023.*

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## METHODS

### Data acquisition



**Figure S1.** Data acquisition flowchart

\*All Holter ECG recordings stored in the repository in the years 2017–2019

### Genetic diagnostics

Multiplex Ligation-dependent Probe Amplification and Sanger sequencing techniques had been performed in all the patients confirming mutation in the dystrophin gene.

### SD values calculation

Based on the analysis of the published regression equations we concluded the models assumed homoscedasticity and appropriate SD values were calculated for those parameters, separately for both sexes. This was further used for calculations of the standardized values (z-scores) of the analyzed parameters. The t-test was used to compare the means of the standardized values between the study and the reference populations. Also, z-score values above  $-1.65$  or below  $+1.65$  (corresponding to 5<sup>th</sup> percentile and 95<sup>th</sup> percentile) were classified as abnormal and interpreted as follows: “Tachycardia” for Mean HR, “Elevated” for Minimal HR and “Shortened” for Maximal RR. Additionally, four age subgroups divided arbitrarily at evenly spaced thresholds at ages 4.5, 9, 13.5 were selected for a frequency analysis.

**Table S1.** Inclusion and exclusion criteria

Inclusion criteria	<ul style="list-style-type: none"> <li>• presence of mutation within dystrophin gene with a clinical course typical for DMD</li> <li>• age &lt;18 years old</li> </ul>
Exclusion criteria	<ul style="list-style-type: none"> <li>• taking beta-blockers (BB) during or within a month prior to the recording</li> <li>• sub-standard recording quality (less than 18 hours of good quality recording for the analysis).</li> </ul>

As of our knowledge there is no widely accepted sinus tachycardia severity scale (STSS). We propose STSS based on 24-hour Holter Mean HR normalised as z-score based on the reference population data published by Salameh et al. and categorization as presented in the Table S2.

**Table S2.** Sinus tachycardia severity scale (STSS)

Category name	Mean HR z-score	Corresponding percentile
Normal HR	-1.65–1.65	5–95
Mild ST	1.65–2.00	95–97
Moderate ST	2.00–3.00	97–99
Severe ST	>3.00	>99

## RESULTS

**Table S3.** Baseline and pharmacotherapy characteristics

Total recordings (n)	n = 70
Number of patients (n)	n = 70
Sex – M n (%)	68 (97.1%)
Age [years], Mean (SD)	9.9 (4.0)
ACEi treatment as n (%)	26 (31.9%)
perindopril	14 (20.0%)
enalapril	7 (10.0%)
captopril	1 (1.4%)
cilazapril	2 (2.9%)
ramipril	1 (1.4%)
lisinopril	1 (1.4%)
Steroid treatment as n (%)	47 (67.1%)
deflazacort	22 (31.4%)
prednisone	25 (35.7%)

Abbreviation: ACEi, angiotensin-converting-enzyme inhibitors

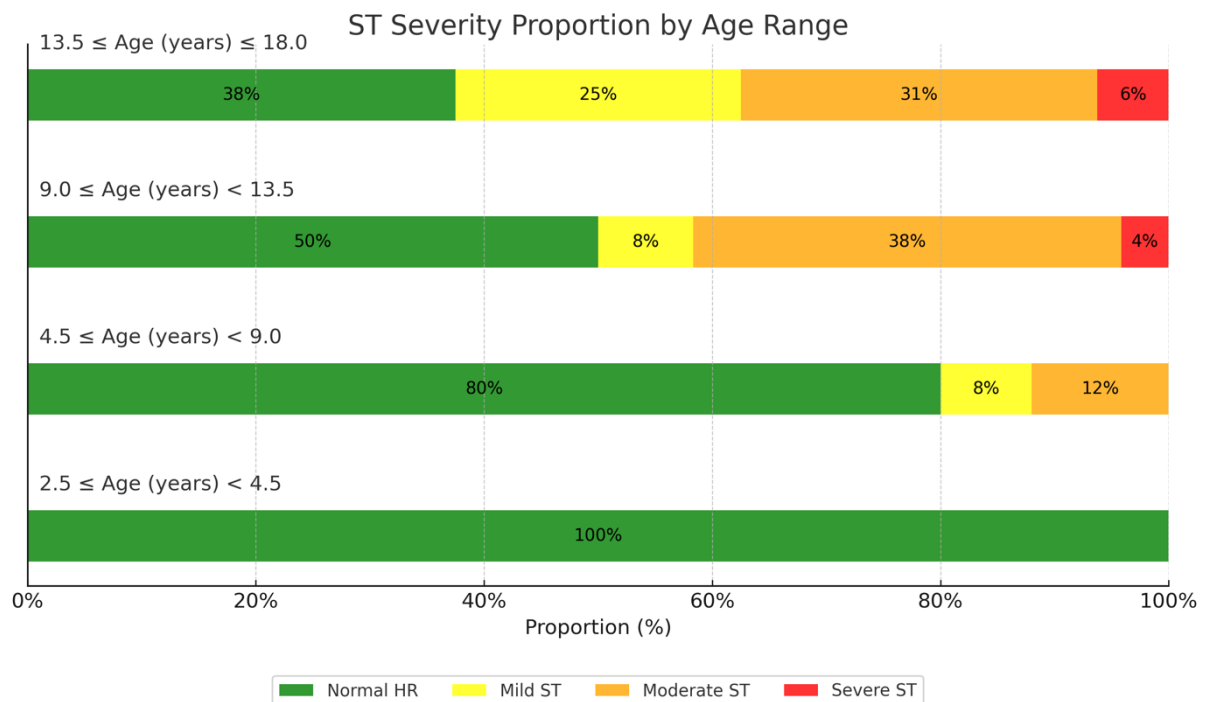
**Table S4.** ST severity based on Mean HR [z], all values are significantly ( $P < 0.001$ ) different from the expected mean for normal population (zero) using one-sample t-test

<i>ST severity</i>	<b>count</b>	<b>MeanHR [z]</b>	<b>MaxRR [z]</b>	<b>MinHR [z]</b>
Normal HR	43 (61%)	0.76 (0.55)	-0.51 (0.69)	0.95 (0.64)

ST overall	27 (39%)	2.39 (0.53)	-1.29 (0.70)	2.35 (0.85)
Mild ST	8 (11%)	1.80 (0.13)	-0.90 (0.76)	1.56 (0.81)
Moderate ST	17 (24%)	2.53 (0.27)	-1.43 (0.60)	2.64 (0.62)
Severe ST	2 (3%)	3.53 (0.47)	-1.68 (0.98)	3.05 (0.80)

The Table S4 shows the count and mean values of Mean HR [z], Max RR [z], Min HR [z], in different subgroups based on the presence of ST and severity of ST. Normal HR group counting 43 (61%) patients had Mean HR [z] of 0.76 (0.55). ST overall: This group consists of 27 (39%) patients with Mean HR at 2.39 (0.53) significantly higher than the Normal HR group ( $P < 0.001$ ). Similarly, Max RR [z] and Min HR [z] were significantly different (both  $P < 0.001$ ). ST severity subgroup characteristics is also shown in Table S2.

Interestingly, patients categorized as Normal HR (not fulfilling ST criteria) had significantly higher Mean HR and Min HR and lower Max RR as compared to reference population ( $P < 0.001$  for all three outcomes) suggesting that even this group (supposedly normal) is not entirely free from accelerated HR.



**Figure S2.** Sinus tachycardia severity by age groups;

Abbreviations: ST, sinus tachycardia; HR, heart rate

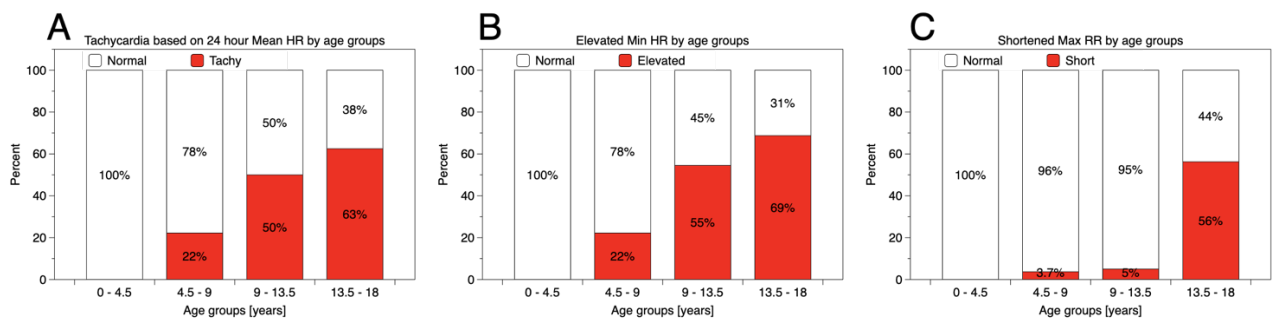
**Table S5.** Holter ECG recording results

Total recording time [h], median (IQR)	21.2 (20.3–22.4)
Total Beats Count, Mean (SD) [n]	125526 (15594)
Beats Analyzed [%], Median (IQR)	99.7 (99.3–99.9)
Mean HR [bpm], Mean (SD)	100.8 (10.8)
Mean HR z-score, Mean (SD)	1.4 (0.9), $P < 0.001^*$
Tachycardia by Mean HR, N (%)	27 (38.6%)

Min HR [bpm], Mean (SD)	62.1 (7.9)
Min HR z-score, Mean (SD)	1.5 (0.97), $P < 0.001^*$
Min HR – Elevated, N (%)	29 (41.4%)
Max RR [s], Median (IQR)	1.2 (1.1–1.3)
Max RR z-score, Mean (SD)	-0.8 (0.8), $P < 0.001^*$
Max RR– Shortened, N (%)	11 (16.2%)
Max HR [bpm], Mean (SD)	157.8 (17.4)
Recordings with SVPC, N (%)	60 (85.7%)
SVPC [n] count**, Median (IQR)	15 (4–54)
Recordings with SVPC > 200, N (%)	16 (22.9%)
Recordings with VPC, N (%)	10 (14.3%)
VPC [n] count**, Median (IQR)	26 (5–200)
Recordings with VPC >10, N (%)	5 (7.1%)

\* $P$ -values for one-sample t-test with mean of zero expected for normal population; \*\*Based on recordings with at least one SVPC or VPC respectively

Abbreviations: HR, heart rate; SVPC, supraventricular premature contraction; VPC, ventricular premature contraction



**Figure S3.** Prevalence of abnormalities by age groups. **A.** Sinus tachycardia (by mean heart rate [HR]). **B.** Elevated minimum HR. **C.** Shortened maximal RR

### Highlights

In the studied population of children with DMD sinus tachycardia was the most common finding, its prevalence and severity age-dependent. SVPC and VPC were rare and no complex arrhythmias were observed.

To our best knowledge this is the first study describing not only the prevalence of sinus tachycardia but also its severity, using z-scores and a novel sinus tachycardia severity scale (STSS).

### Limitations

The limitations of the study are small population analyzed and the cross-sectional nature of the study. Further studies should be directed at determining the underlying cause of ST and its prognostic value.