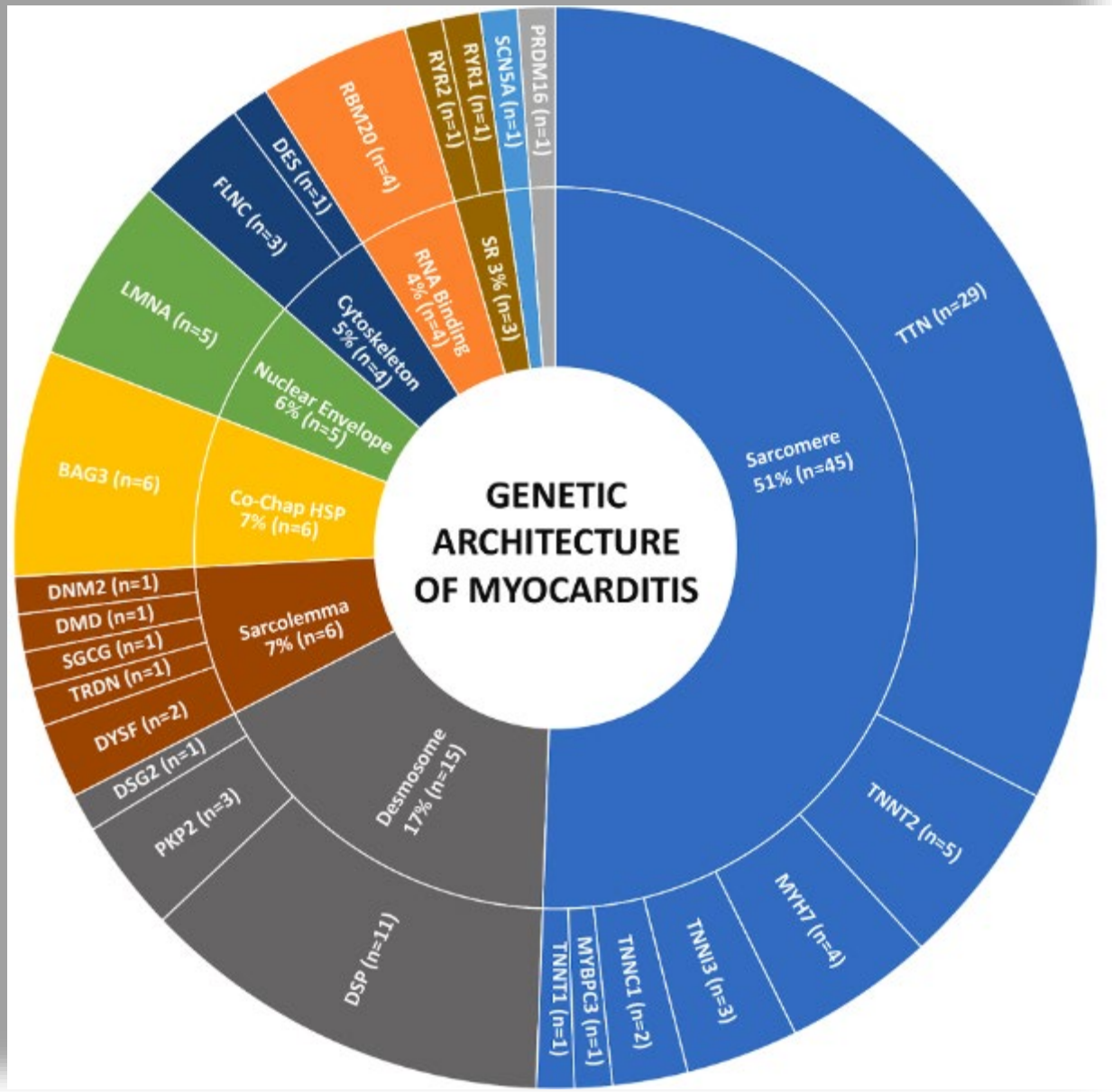
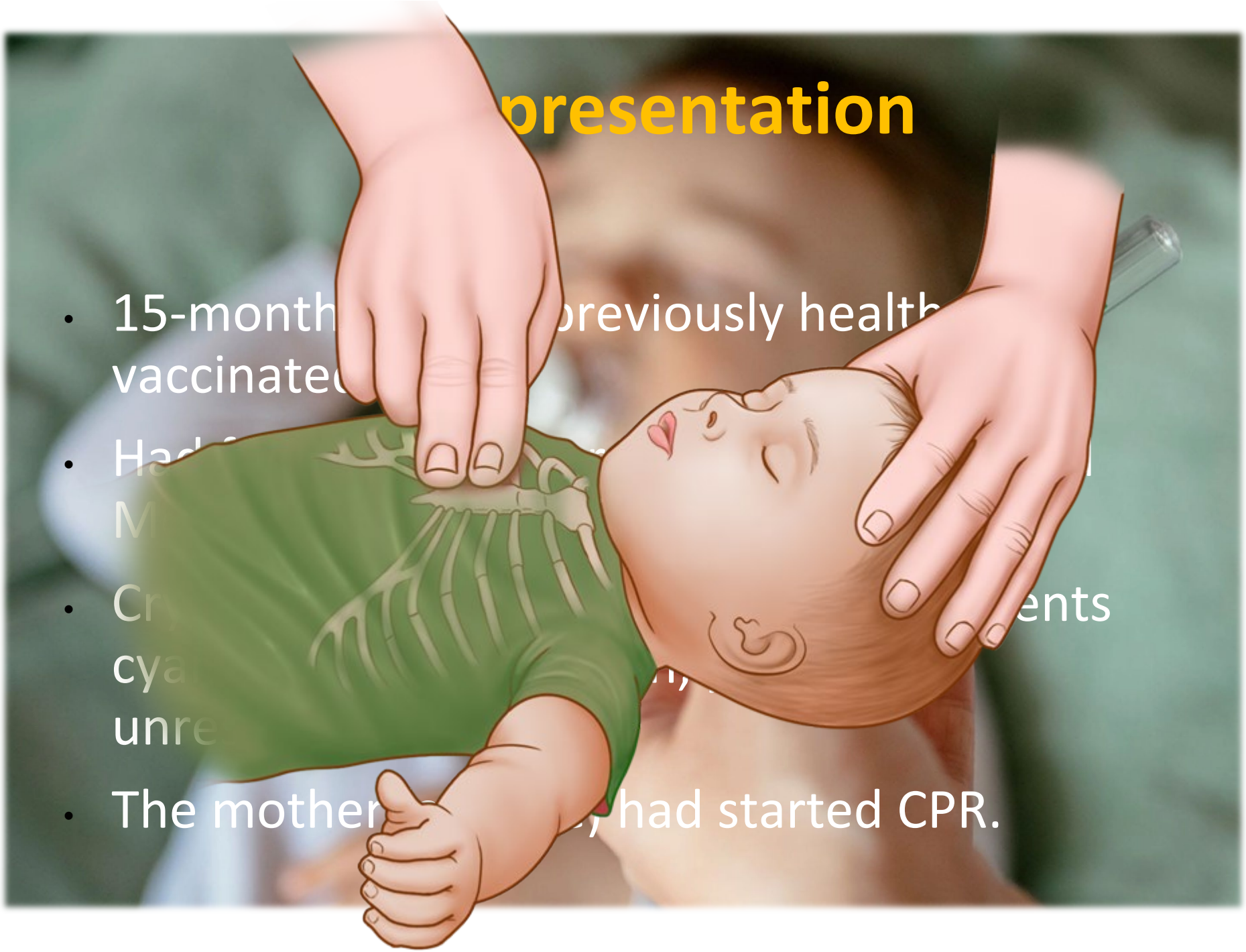
מעבר למיוקרדיטיס: גילוי גנטי מציל חיים באריתמיה בפעוטות

אילת שאואר, סמדר הורוביץ-צדרבויים, ברנרד בלאסן,
הפרעות קצב תורשתיות
מערך הלב הדסה
28.6.2024



JACC: Heart Failure, 2024-06-01, Volume 12, Issue 6,

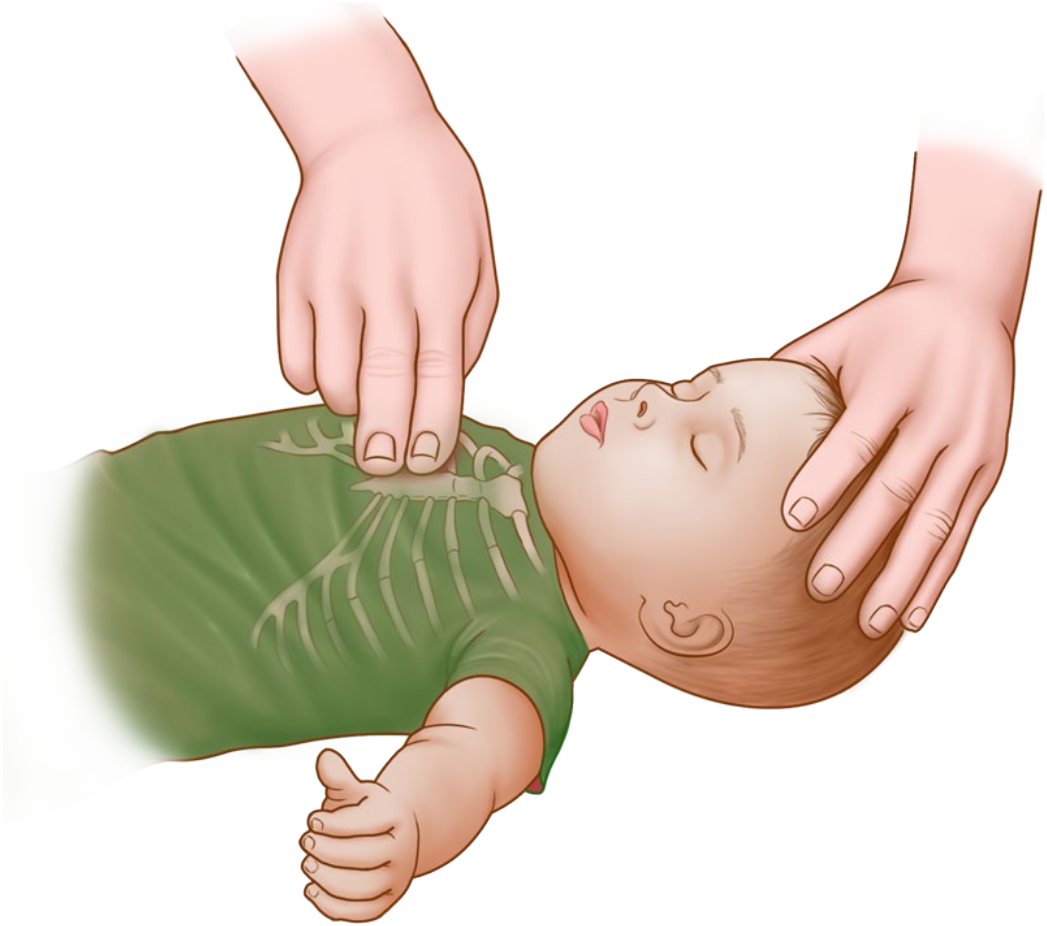


presentation

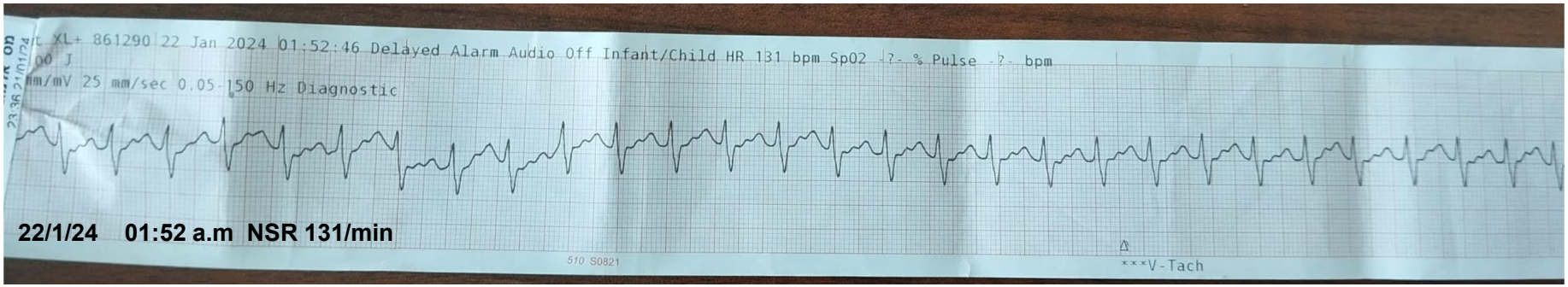
- 15-month … previously health… vaccinate…
- Had … M…
- Cr… …ents cya… …, unre…
- The mother … had started CPR.

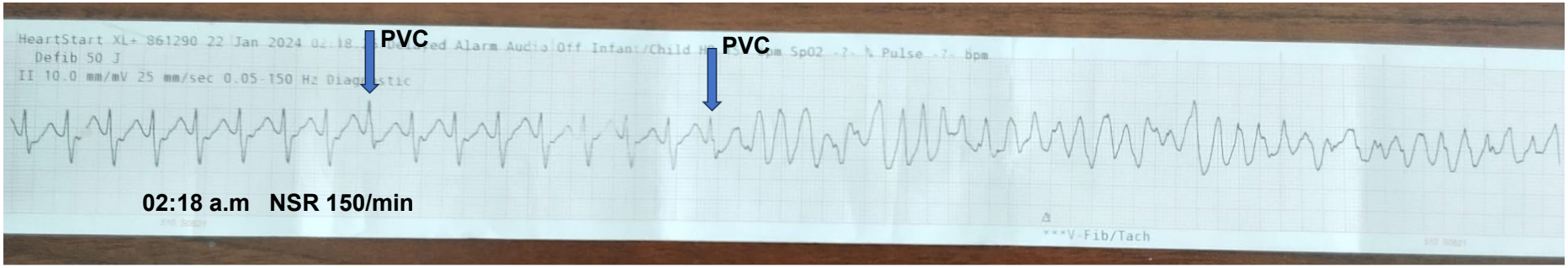
In Emergency Room..

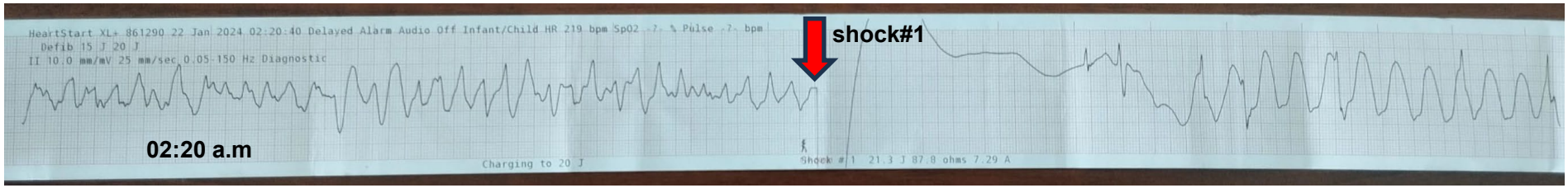
- Conscious, crying, then went unresponsive again



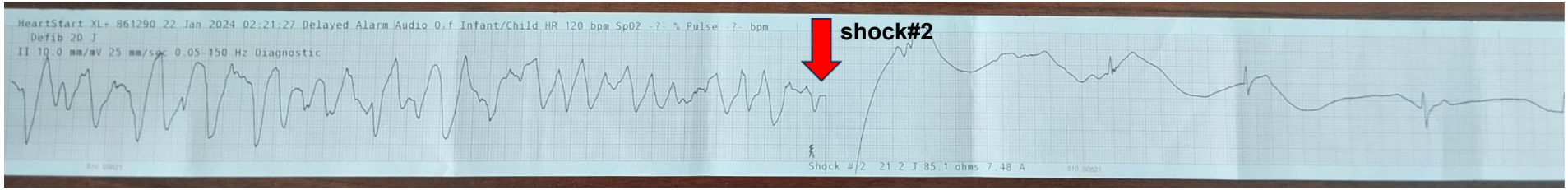
Initiation of VF and shock #1

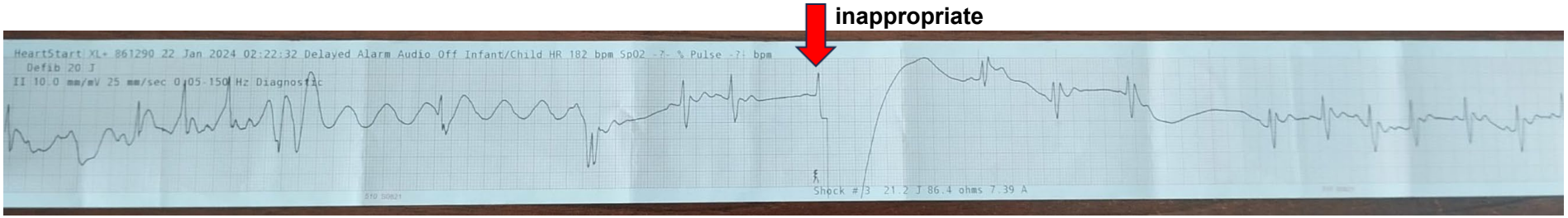


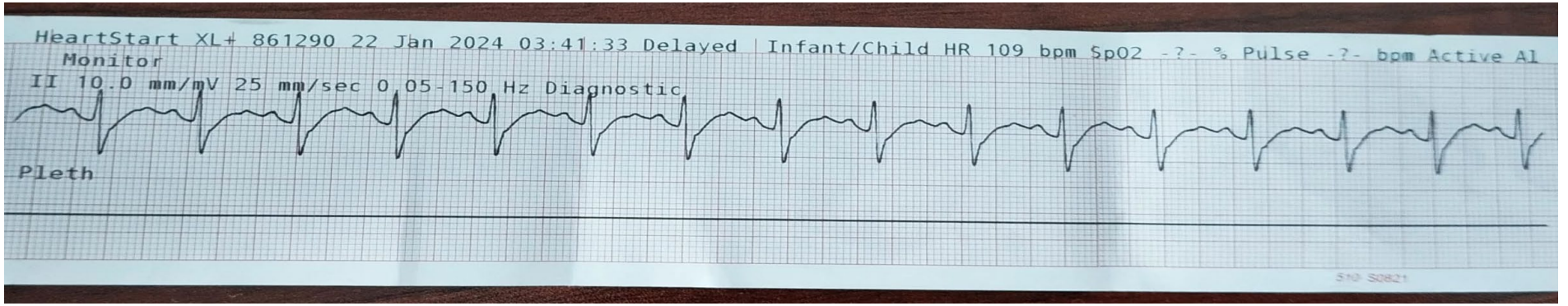




Shock #2

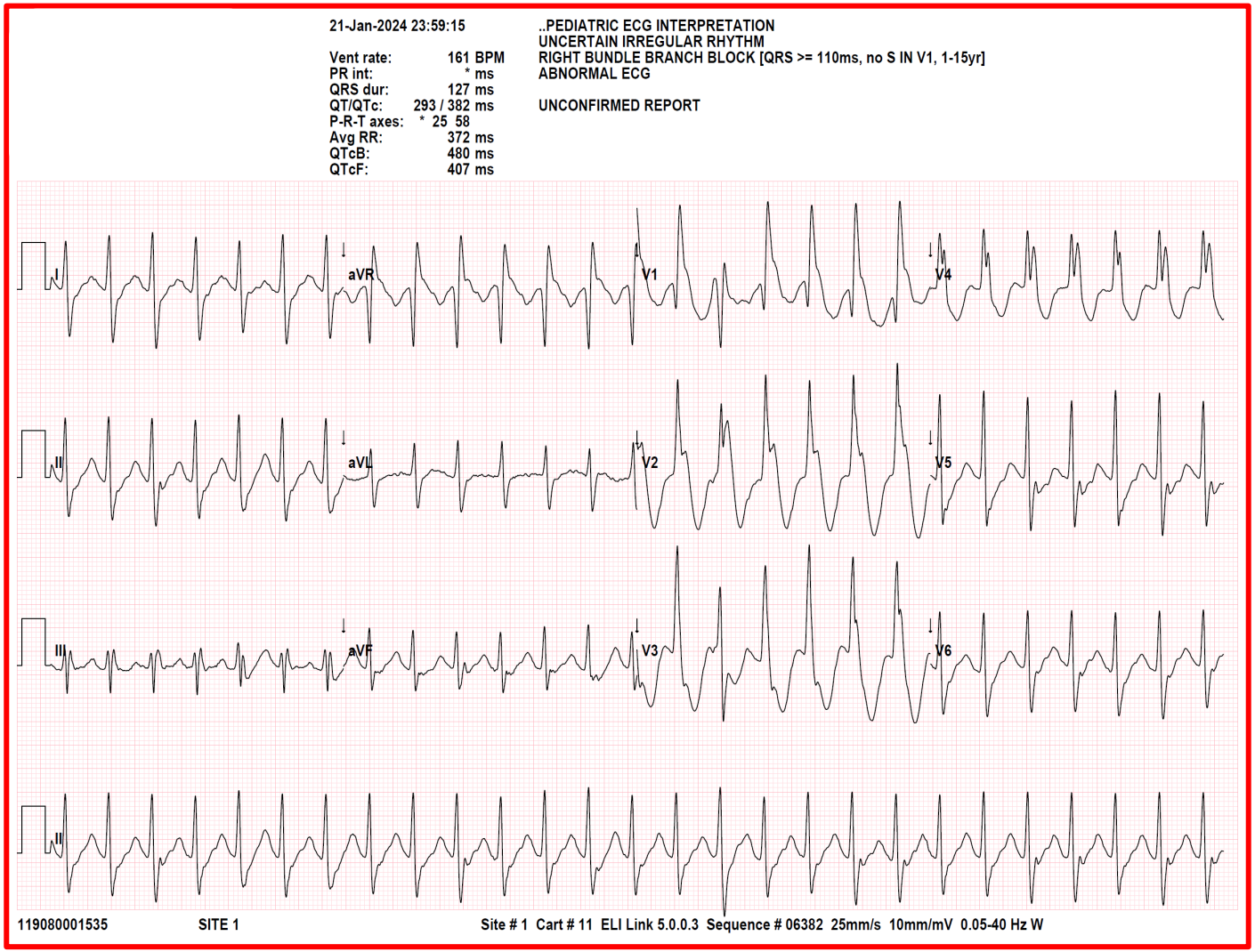

HeartStart XL+ 861290 22 Jan 2024 02:21:27 Delayed Alarm Audio Off Infant/Child HR 120 bpm SpO2 -?- % Pulse -?- bpm
Defib 20 J
II 10.0 mm/mV 25 mm/sec 0.05-150 Hz Diagnostic
shock#2
Shock # 2 21.2 J 85.1 ohms 7.48 A


inappropriate
HeartStart XL+ 861290 22 Jan 2024 02:22:32 Delayed Alarm Audio Off Infant/Child HR 182 bpm SpO2 -?- % Pulse -?- bpm
Defib 20 J
II 10.0 mm/mV 25 mm/sec 0.05-150 Hz Diagnostic
Shock # 3 21.2 J 86.4 ohms 7.39 A


HeartStart XL+ 861290 22 Jan 2024 03:41:33 Delayed Infant/Child HR 109 bpm SpO2 -?- % Pulse -?- bpm Active Al
Monitor
II 10.0 mm/mV 25 mm/sec 0.05-150 Hz Diagnostic
Pleth

ECG on Admission

Sinus Tachycardia 161bpm and RBBB



Admission Course

- Intubated and ventilated
- WBC=2300 Trop T=150
- Echo=normal LV and RV function and no structural abnormality
- Adenovirus positive

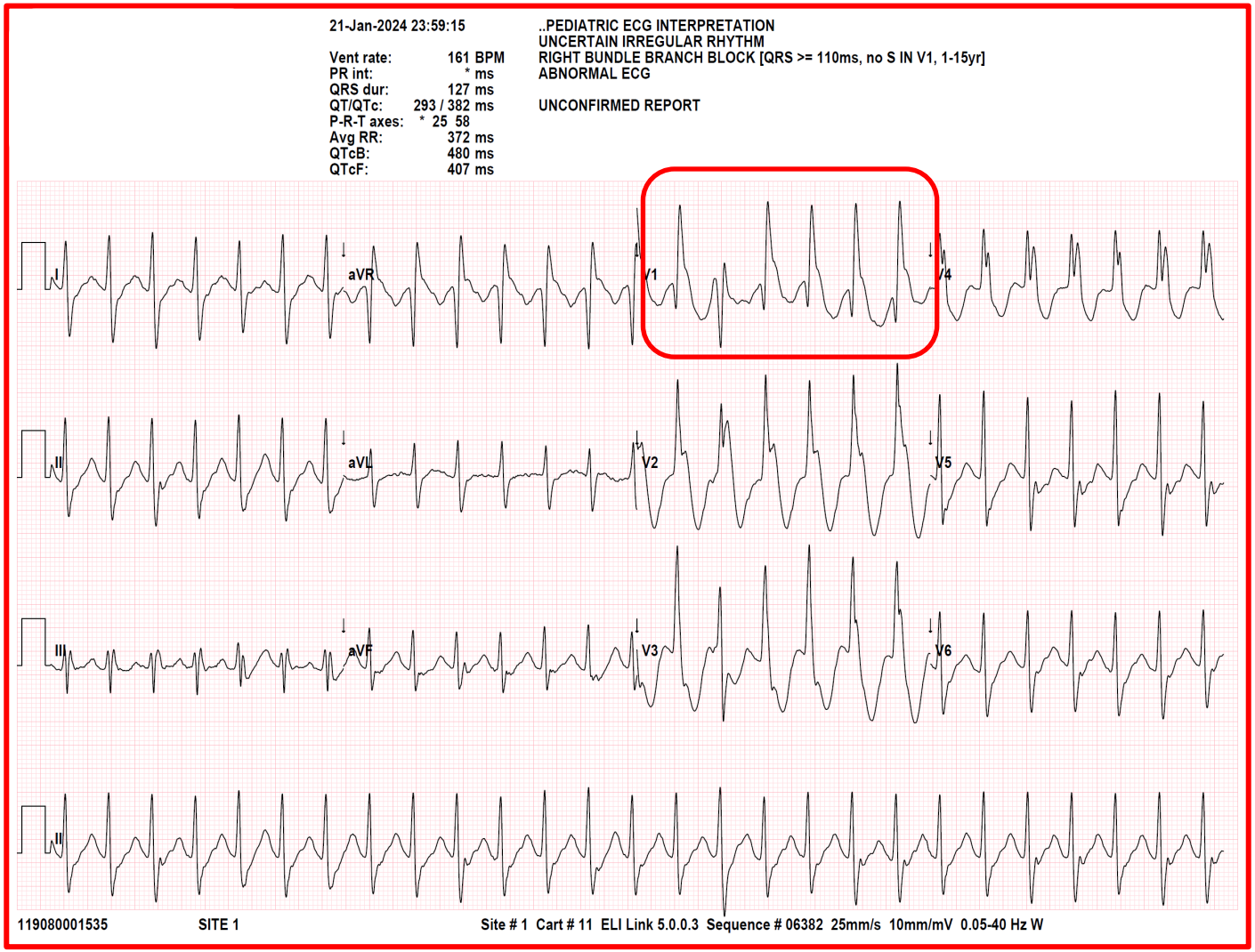
Diagnosis: Myocarditis

- Mild neurologic deficit
- Seizures – Started levetiracetam (Keppra) - resloved

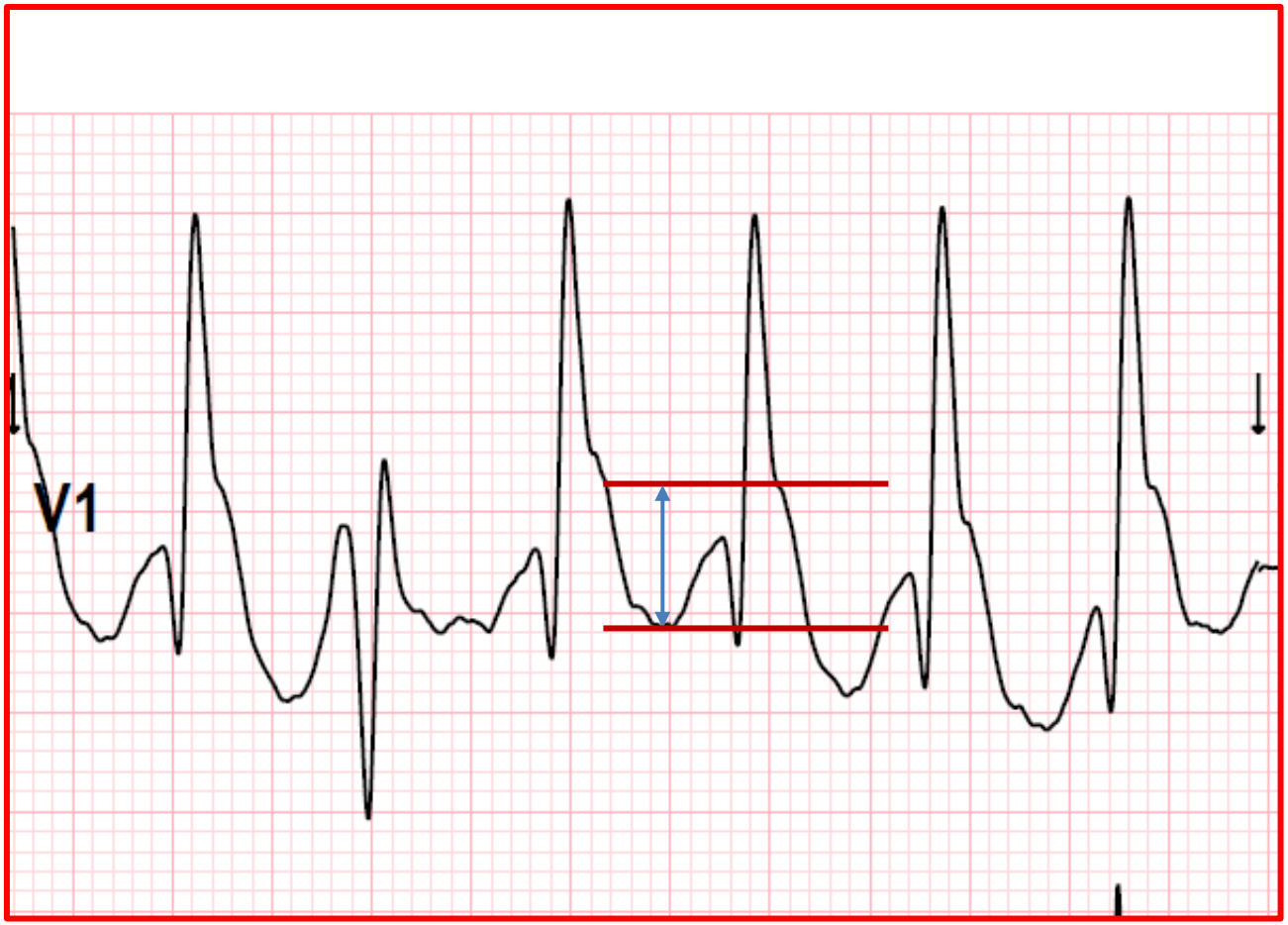
ECG on Admission

Sinus tachycardia 161bpm

RBBB with Coved ST elevation in V1

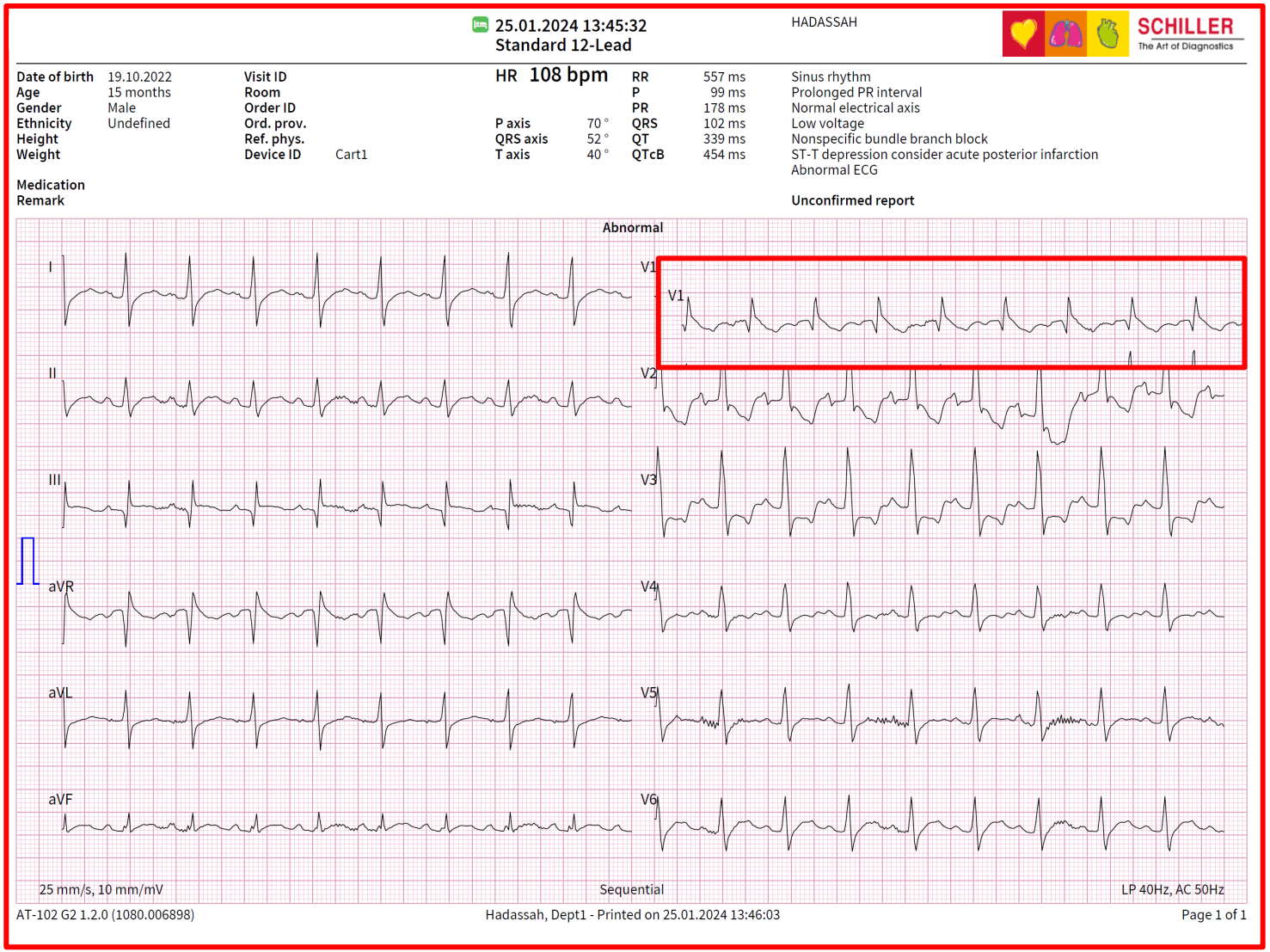


RBBB and 4-5mm coved ST elevation

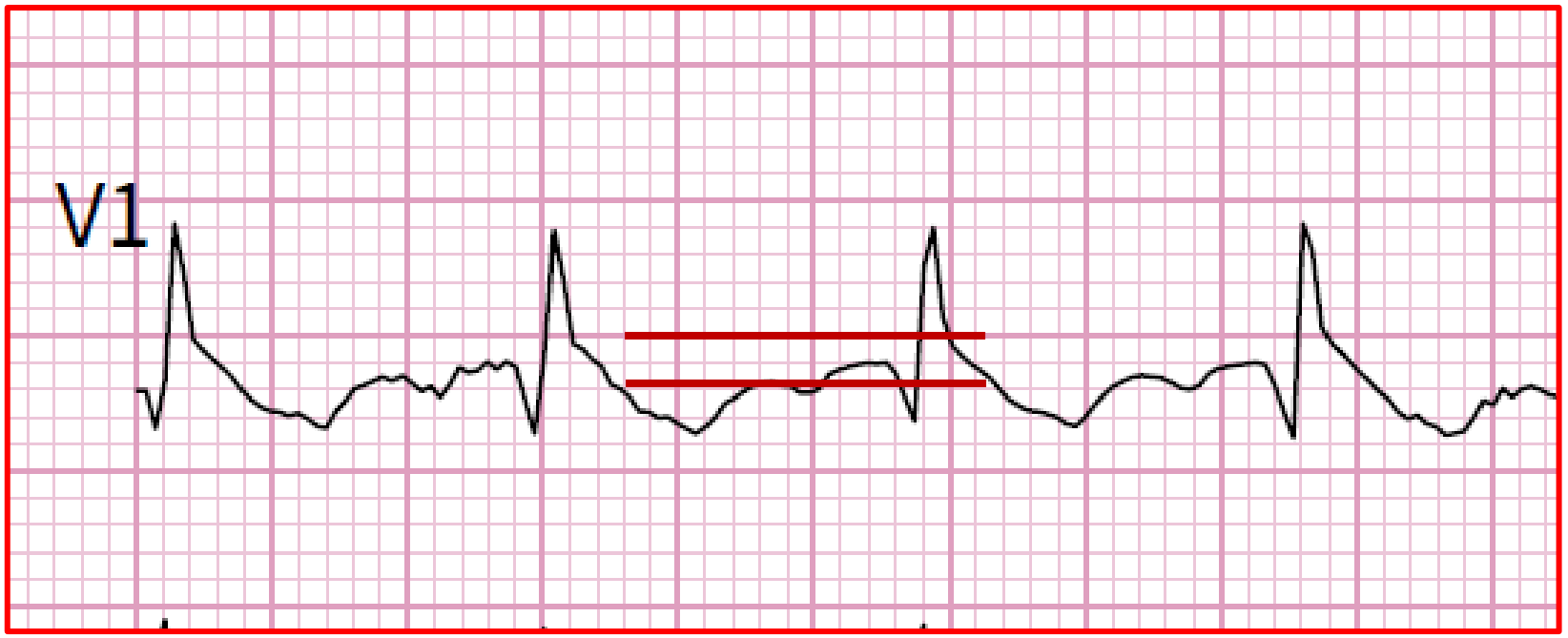


ECG 4 Days Later

RBBB and minimal ST elevation



RBBB and 2mm ST elevation in lead V1

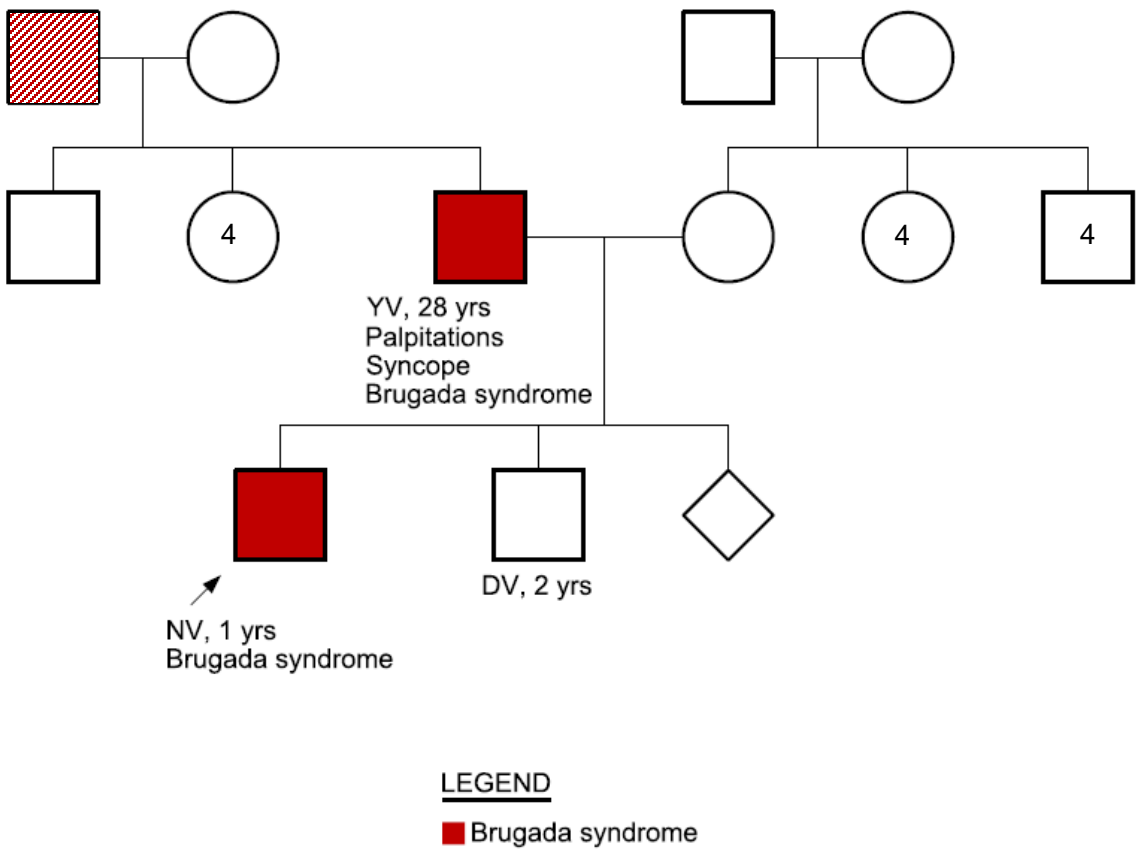


Genetic test results

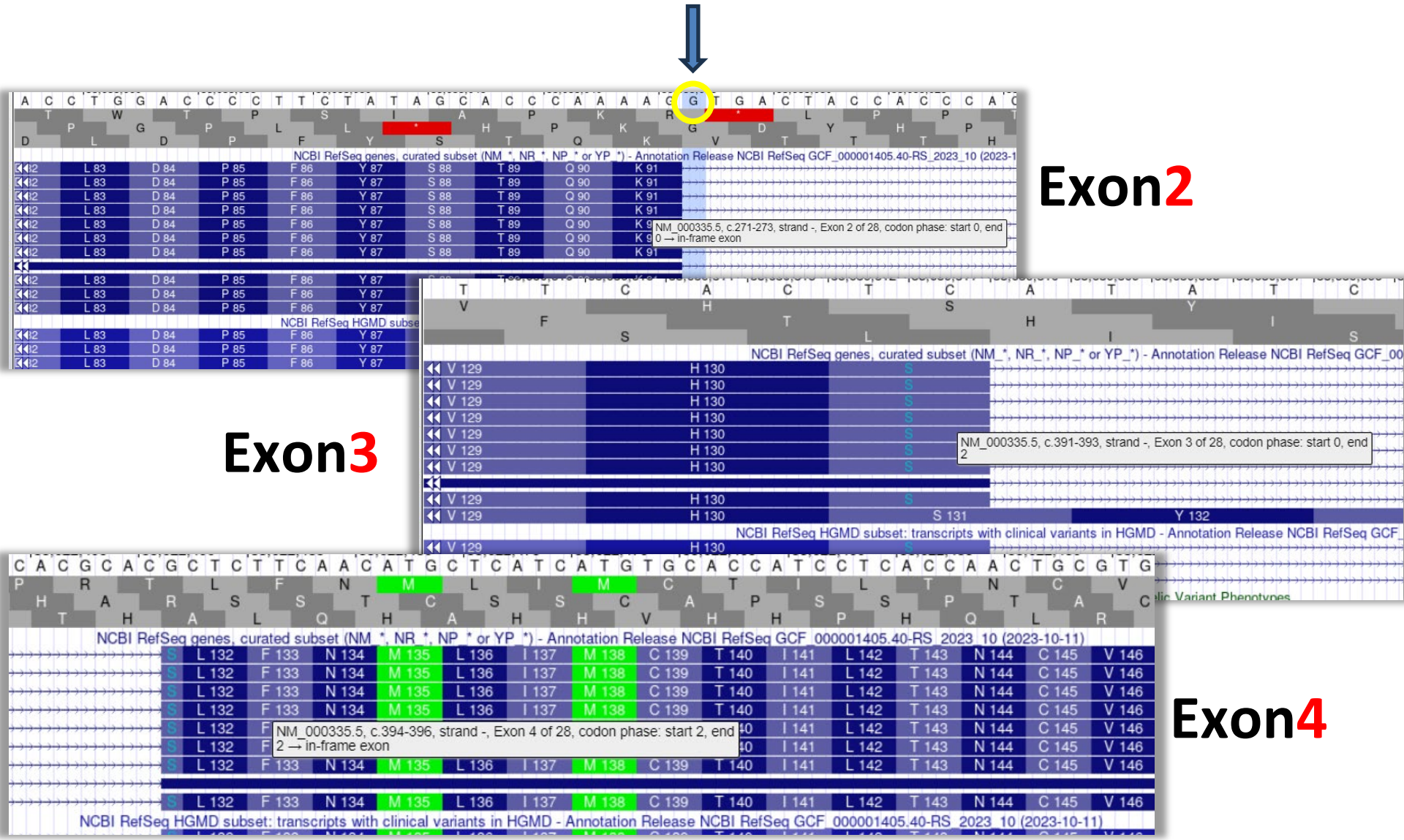
LIKELY PATHOGENIC	סיווג
SCN5A: c.273+1G>T chr3-38674525 C>A NM_000335.5	

SCN5A

Family Tree

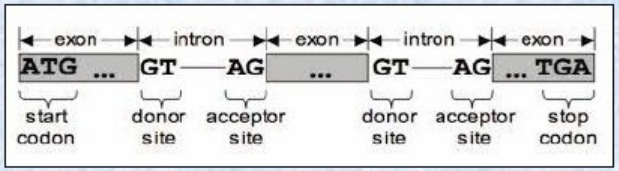

4
4
4
YV, 28 yrs
Palpitations
Syncope
Brugada syndrome
DV, 2 yrs
NV, 1 yrs
Brugada syndrome
LEGEND
Brugada syndrome

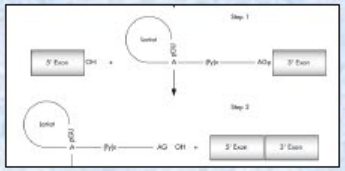
SCN5A:c.273+1G>T

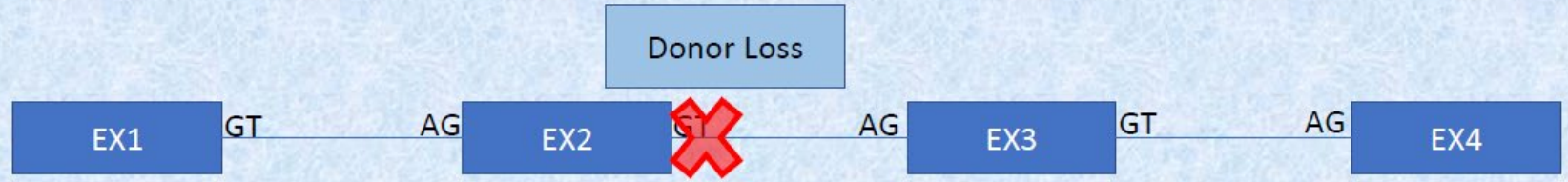


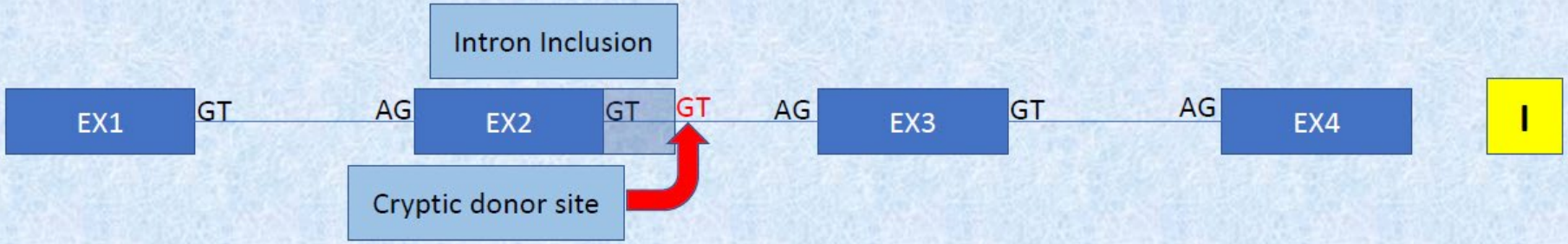
Splice Site Mutations

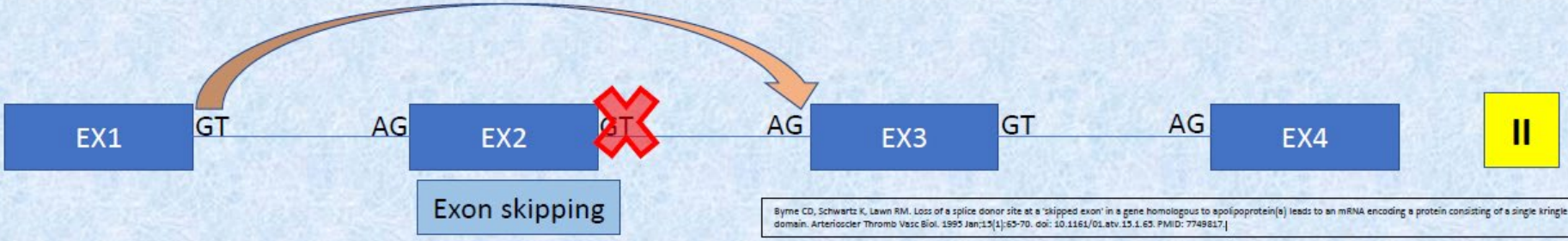
Alternative Splicing - Types







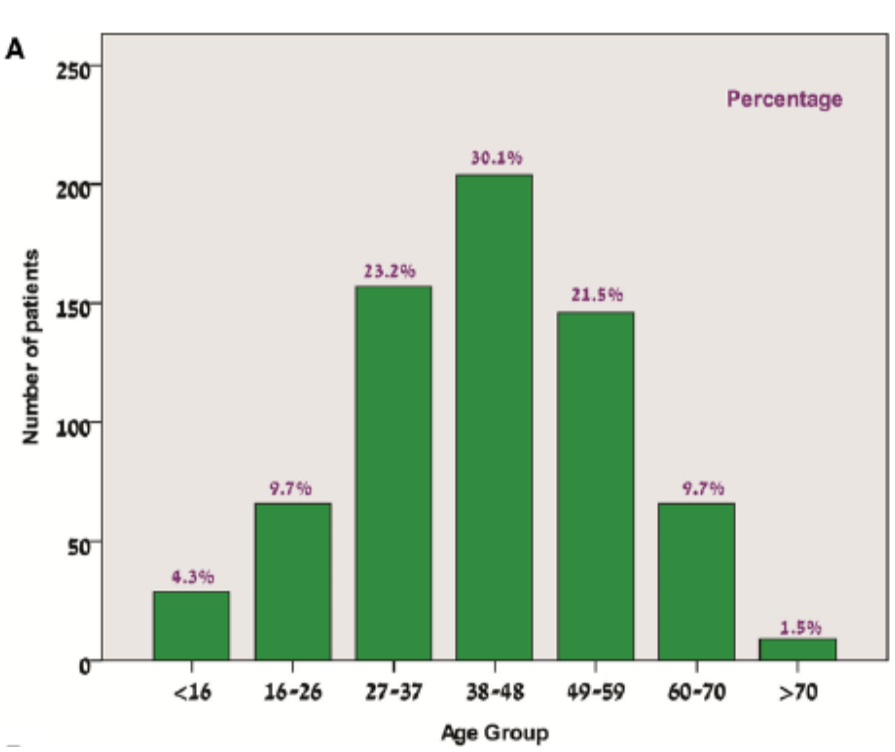




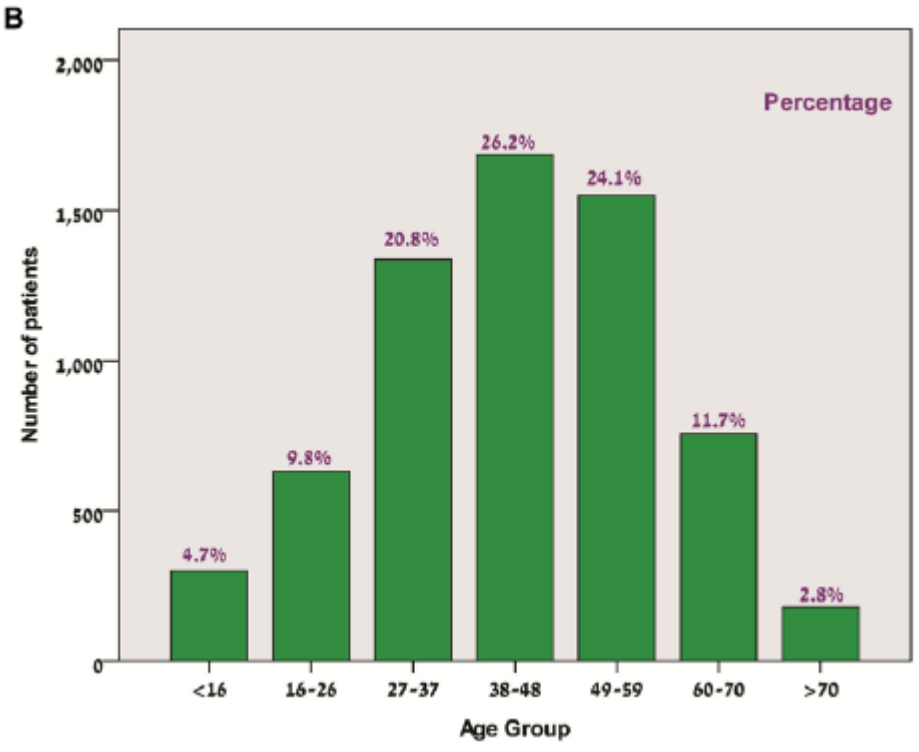
Byrne CD, Schwartz K, Lawn RM. Loss of a splice donor site at a 'skipped exon' in a gene homologous to apolipoprotein(a) leads to an mRNA encoding a protein consisting of a single kringle domain. Arterioscler Thromb Vasc Biol. 1995 Jan;15(1):65-70. doi: 10.1161/01.atv.15.1.65. PMID: 7749817.

Brugada Syndrome in the Pediatric Population

Arrhythmic Event in Brugada Pediatric Population is Rare!



SABRUS patients

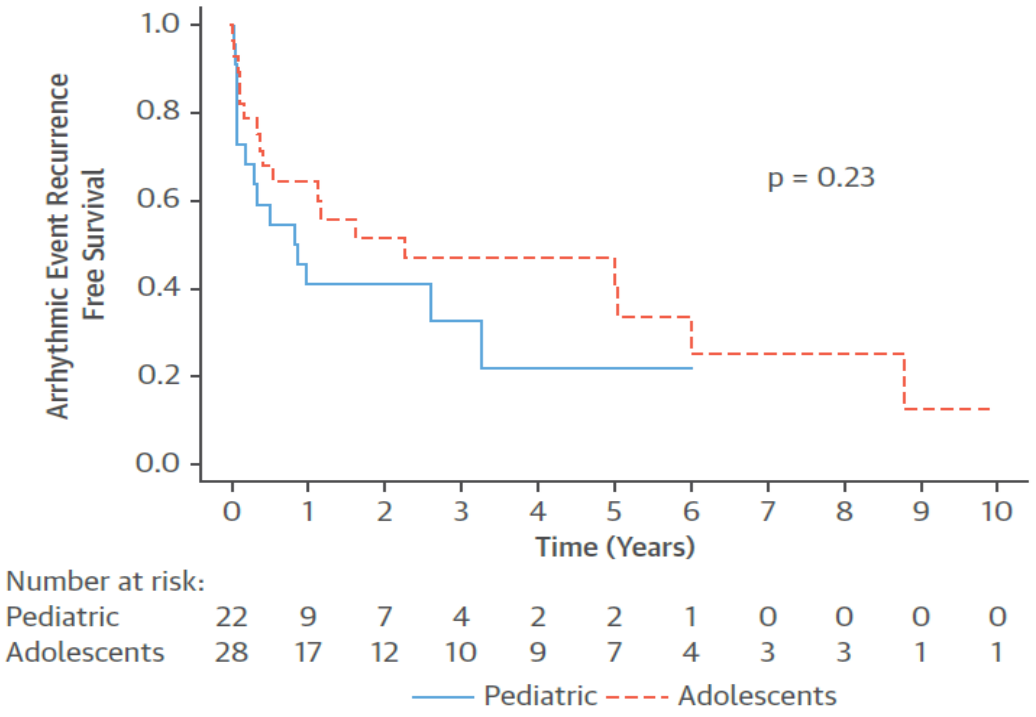


All patients

Milman et al; Age of First Arrhythmic Event in Brugada Syndrome
Circ Arrhythm Electrophysiol. 2017;10:e005222. DOI: 10.1161/CIRCEP.117.005222

The Rate of Recurrent Arrhythmic Event is Higher at age<12yo than 13-20yo

FIGURE 1 Kaplan-Meier Curve for Recurrent Arrhythmic Events Among Pediatric and Adolescent Patients



In both age groups, a high recurrence arrhythmic event rate (59.1% and 35.7% at 12 months, respectively; p = 0.27) was observed with median time to recurrence of 9.9 months and 27.2 months, respectively.

Risk Factors for Recurrent AE

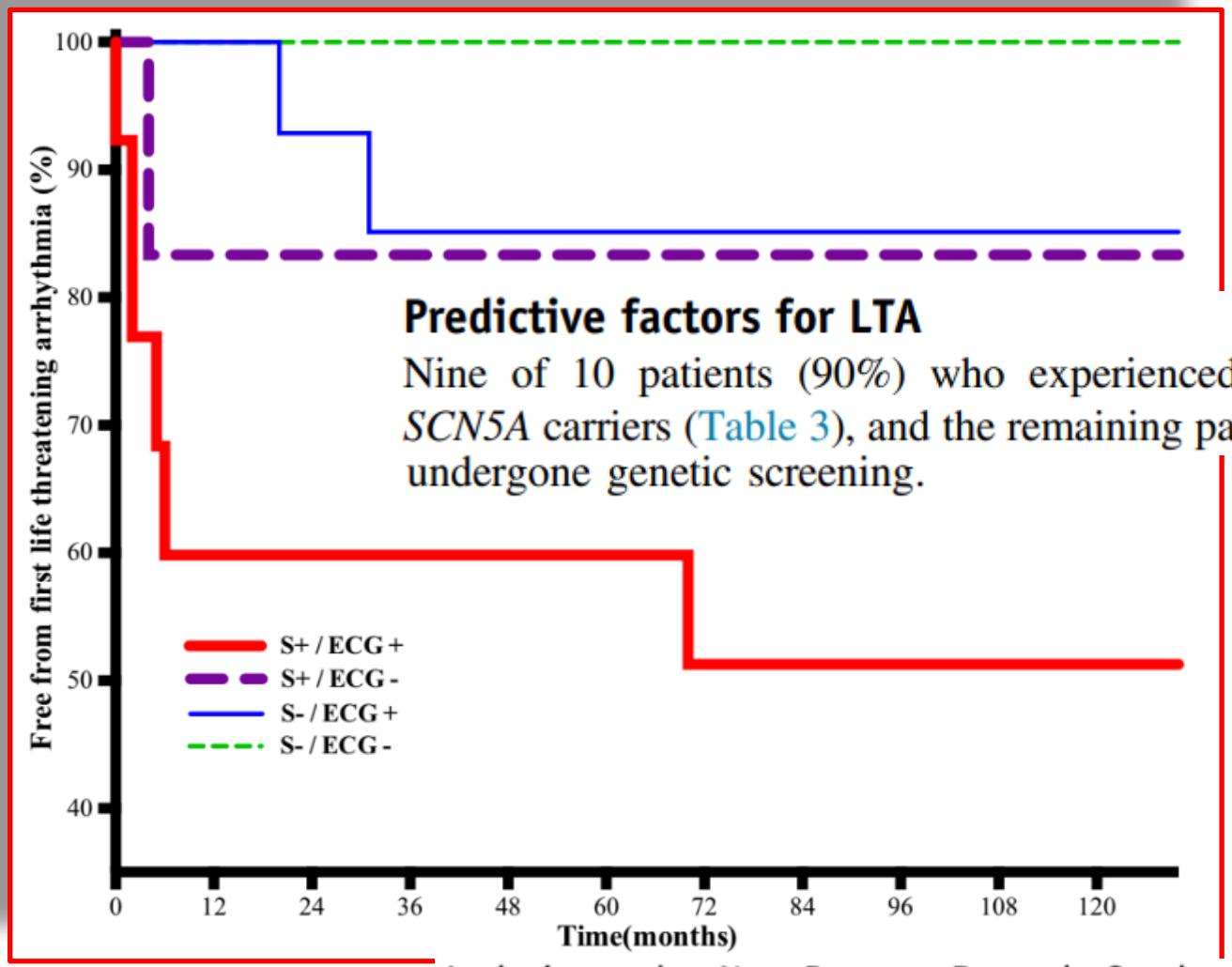
TABLE 3 Risk Factors for Recurrent AE

	Event Rate With Variable*	Event Rate Without Variable†	HR	95% CI	p Value
Age ≤12 yrs					
SND	7/7 (100)	7/14 (50)	3.3	1.1-9.7	0.03
Atrial arrhythmias	9/9 (100)	6/13 (46)	3.0	1.07-8.70	0.04
IVCD	9/9 (100)	6/13 (46)	3.4	1.2-9.8	0.02
Large S in ECG lead I	6/6 (100)	8/14 (57)	3.1	1.04-9.30	0.04
Either vs. none of the above	12/12 (100)	3/10 (30)	6.9	1.9-25.2	0.004
Age 13-20 yrs					
SCN5A mutation	8/9 (89)	3/8 (38)	5.0	1.03-23.80	0.045

*Number of patients with the variable and recurrent AE/total number of patients with the variable (%). †Number of patients without the variable and recurrent AE/total number of patients without the variable (%).

CI = confidence interval; HR = hazard ratio; IVCD = intraventricular conduction delay (QRS ≥110 ms); SND = sinus node dysfunction.

Patients with Symptoms + Spontaneous Type Brugada are at Higher Risk for Arrhythmic Events

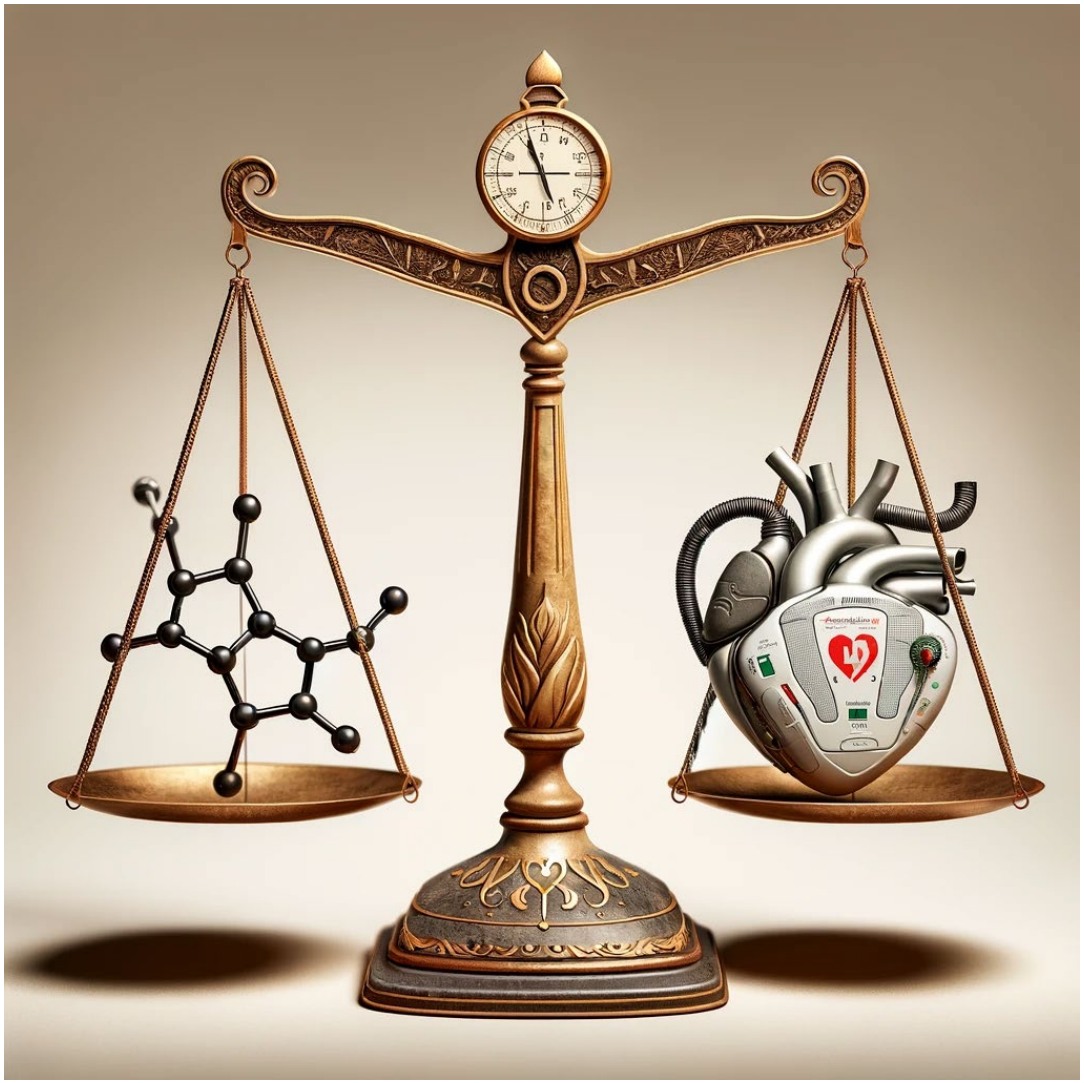


Predictive factors for LTA

Nine of 10 patients (90%) who experienced LTA were *SCN5A* carriers (Table 3), and the remaining patient had not undergone genetic screening.

Andorin et al New Data on Brugada Syndrome in the Young
Heart Rhythm, Vol 13, No 6, June 2016

Quinidine or ICD??



ICD complications

Serious ICD-related complications occurred in 9 of 22 patients (41%), including lead failures (n = 4), inappropriate shocks (n = 4), endocarditis with reimplantation (n = 2), and hemothorax (n = 1). Two (9%) patients had both lead failure and inappropriate shocks or endocarditis. All complications were related to endocardial devices except the hemothorax, which appeared in the early postoperative period after epicardial ventricular lead implantation.

Andorin et al New Data on Brugada Syndrome in the Young
Heart Rhythm, Vol 13, No 6, June 2016

ABSTRACT

BACKGROUND Young patients presenting with symptomatic Brugada syndrome have very high risks for ventricular arrhythmias and should be carefully considered for implantable cardioverter-defibrillator (ICD) placement. However, this therapy is associated with high rates of inappropriate shocks and device-related complications.

OBJECTIVES This study investigated clinical features, management, and long-term follow-up of young patients with Brugada syndrome and ICD.

METHODS Patients diagnosed with Brugada syndrome, who underwent implantation of an ICD at an age of ≤20 years, were studied.

RESULTS The study included 35 consecutive patients. The mean age at ICD placement was 13.9 ± 6.2 years. Ninety-two percent were symptomatic; 29% presented with aborted sudden cardiac death and 63% with syncope. During a mean follow-up period of 88 months, sustained ventricular arrhythmias were treated by the ICD in 9 patients (26%), including shocks in 8 patients (23%) and antitachycardia pacing in 1 patient (3%). Three patients (9%) died in an electrical storm. Seven patients (20%) experienced inappropriate shocks, and 5 patients (14%) had device-related complications. Aborted sudden cardiac death and spontaneous type I electrocardiogram were identified as independent predictors of appropriate shock occurrence.

CONCLUSIONS ICD therapy is an effective strategy in young patients with symptomatic Brugada syndrome, treating potentially lethal arrhythmias in >25% of patients during follow-up. Appropriate shocks were significantly associated with previously aborted sudden cardiac death and spontaneous type I electrocardiograms. However, ICDs are frequently associated with complications and inappropriate shocks, both of which remain high regardless of careful device implantation and programming. (J Am Coll Cardiol 2018;71:148–57) © 2018 by the American College of Cardiology Foundation.

Gonzalez Corcia, M.C. et al. J Am Coll Cardiol. 2018;71(2):148-57.

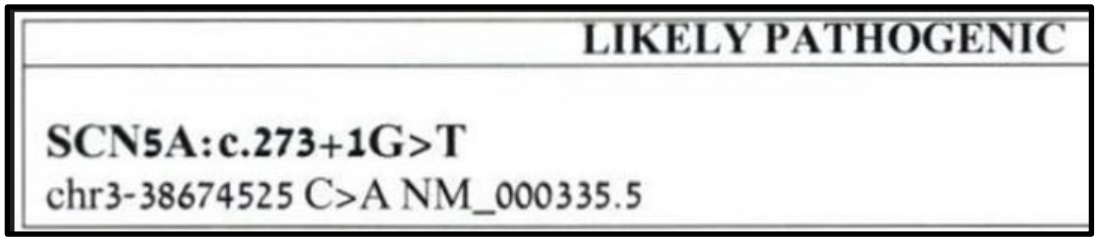
Conclusions

- Fever and ventricular fibrillation in a baby is NOT always myocarditis
- When seizures are present post ventricular fibrillation consider arrhythmia as the cause
- Consider in-hospital genetic testing and results on “emergency basis”
- Pediatric population with Brugada is at higher risk for recurrent arrhythmic events
- Quinidine may not prevent arrhythmia completely in the pediatric population, thus an ICD should be implanted.
-

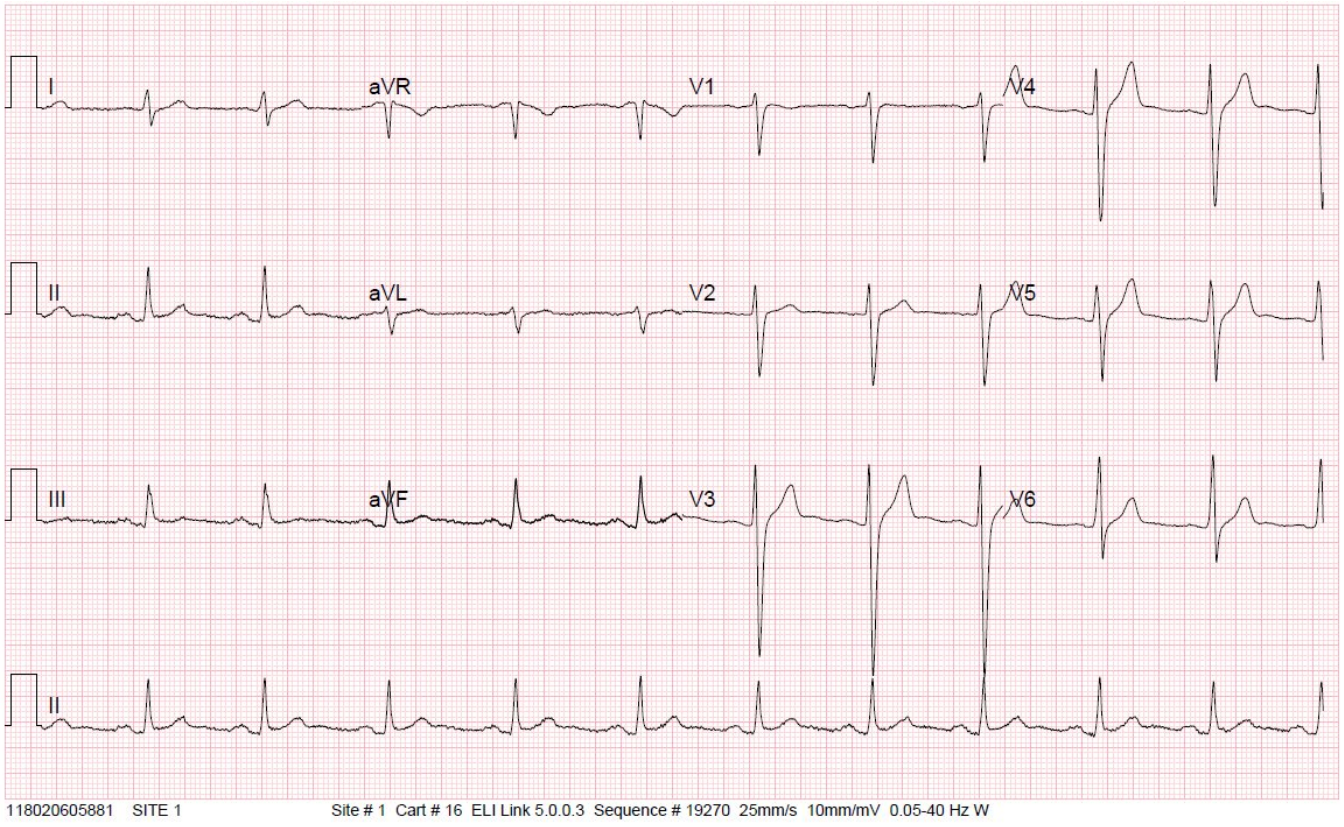

THINK
OUTSIDE
THE

Case

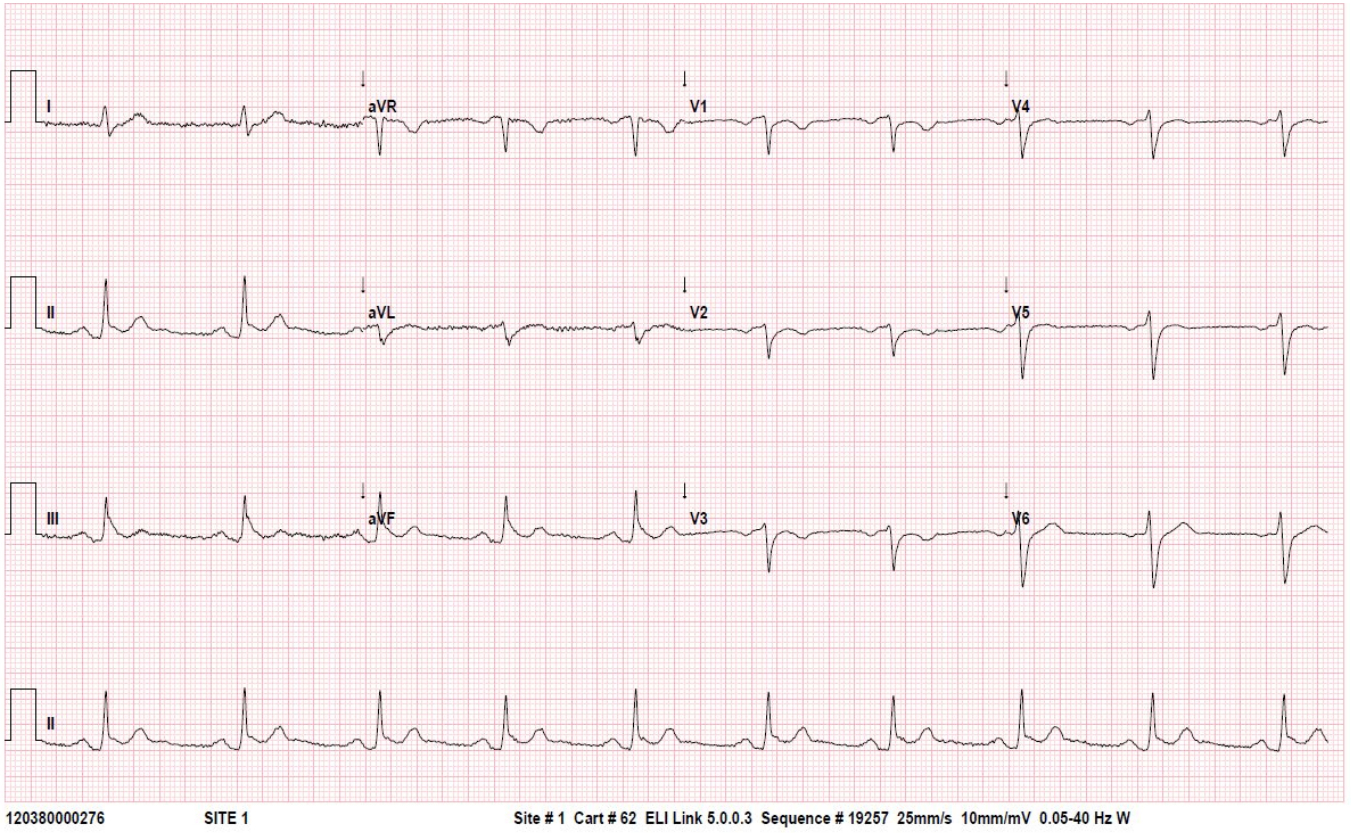
- 29yo, previously healthy
- Admitted for Ajmaline test due to family Hx of Brugada.
- A father of a boy who had CA at 15mo



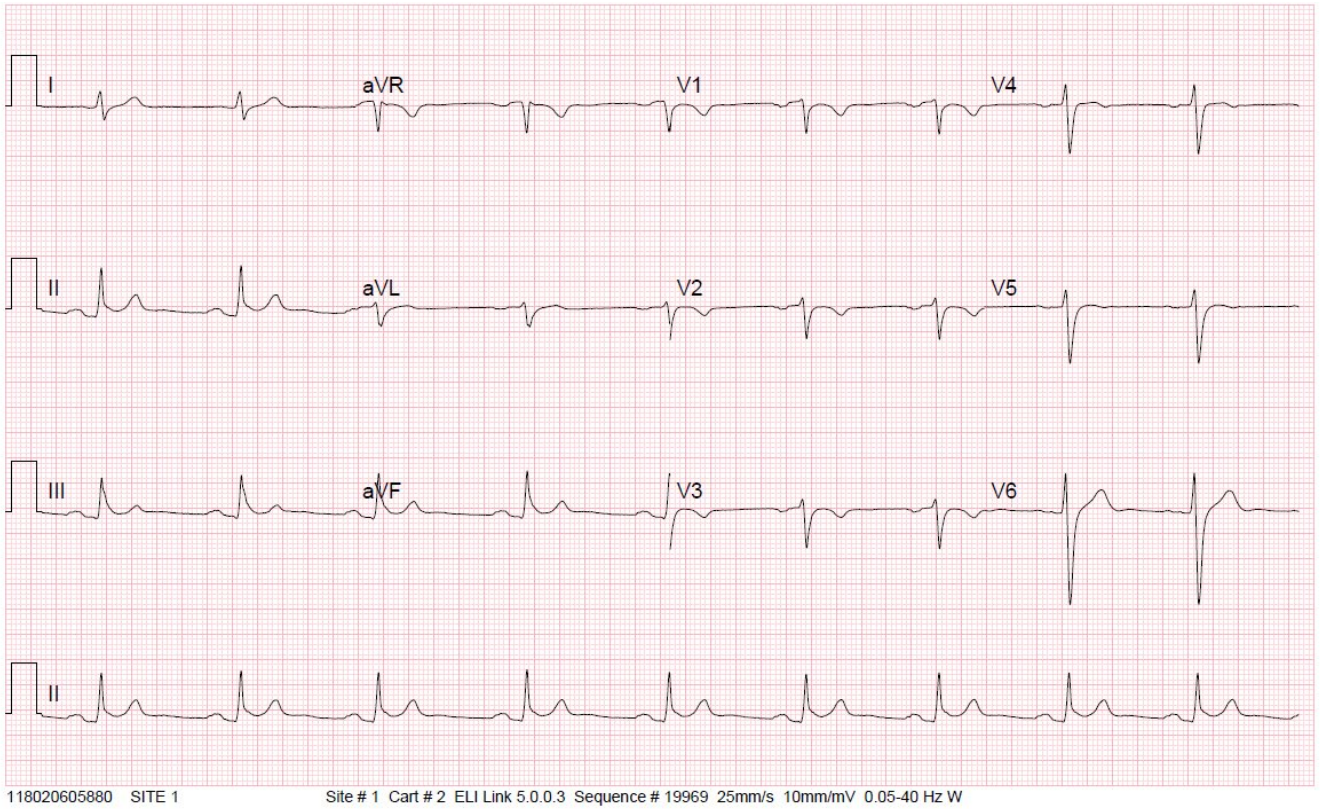
Baseline ECG 1



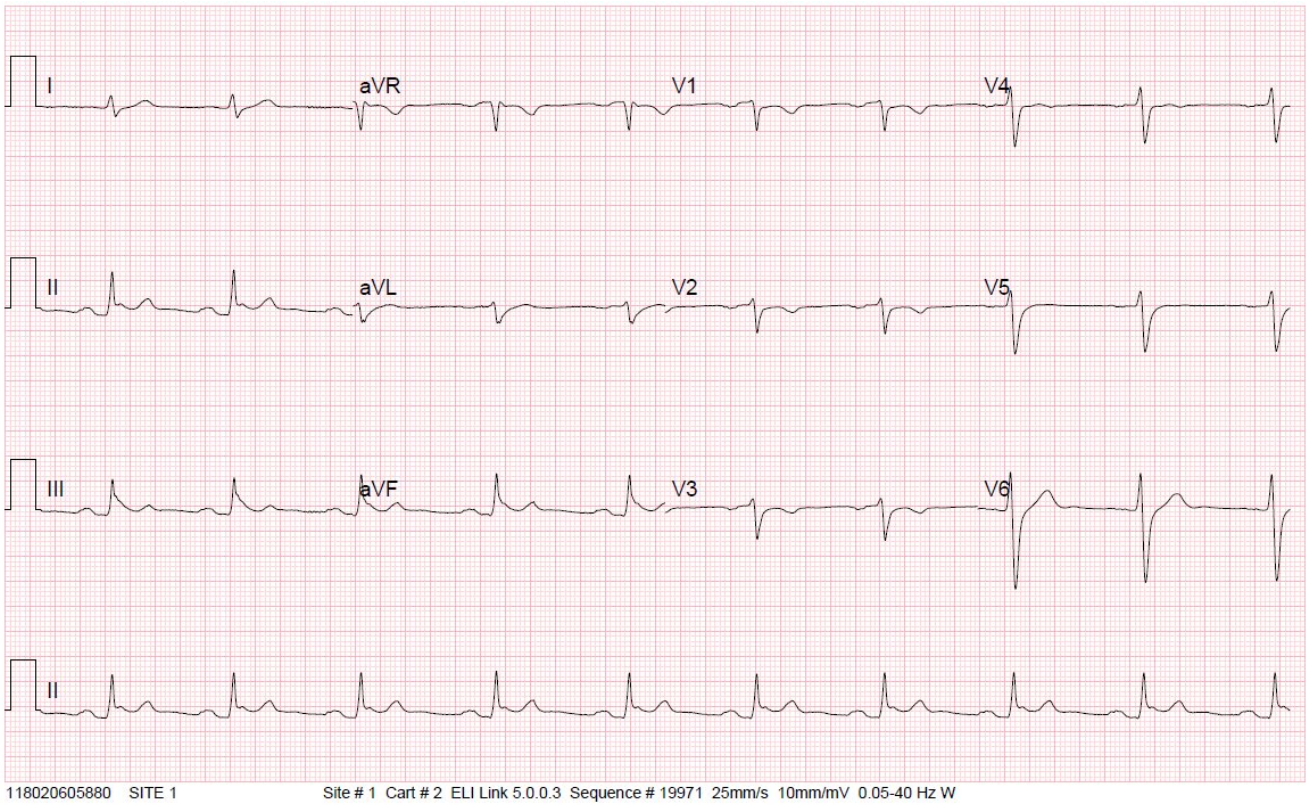
Baseline ECG 2 High leads



Ajmaline baseline ECG



Ajmaline 50mg



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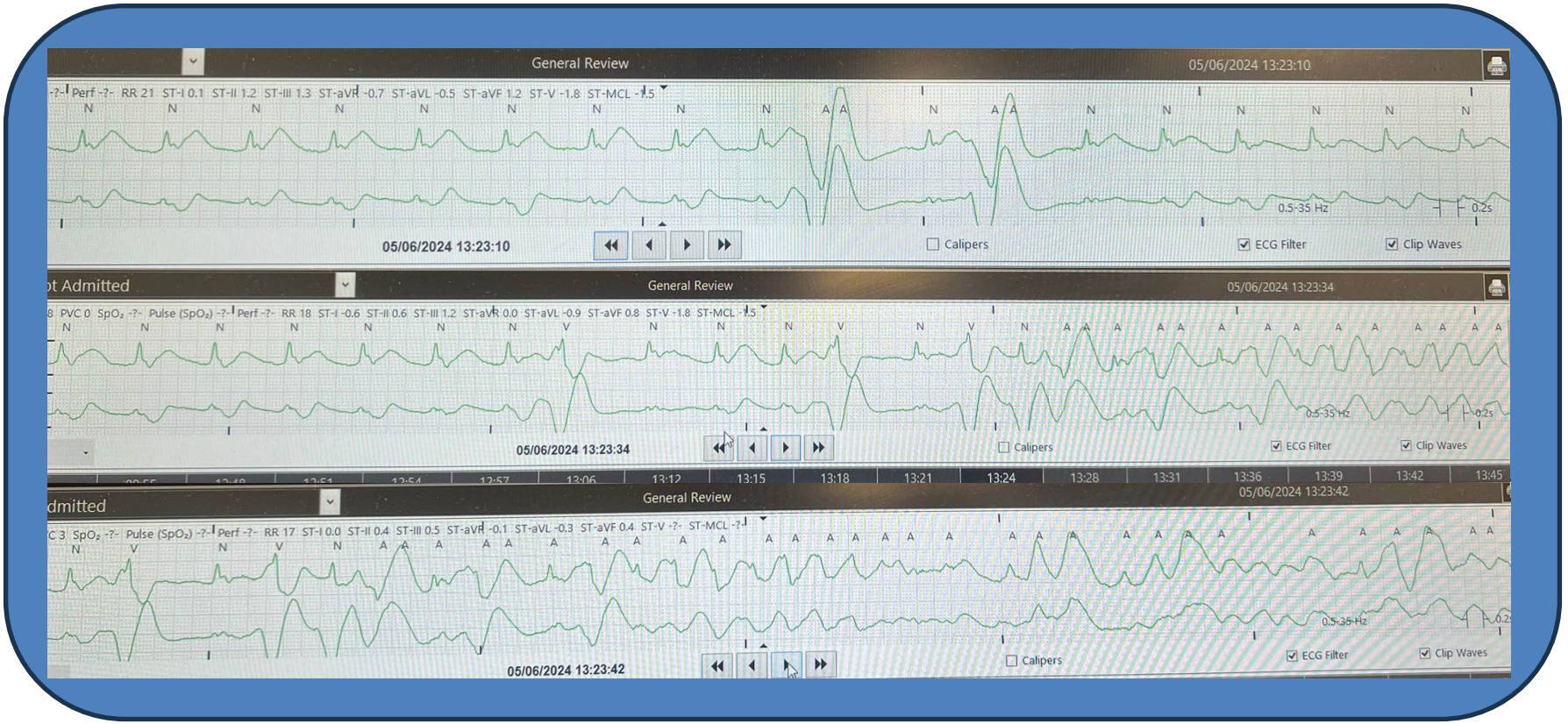
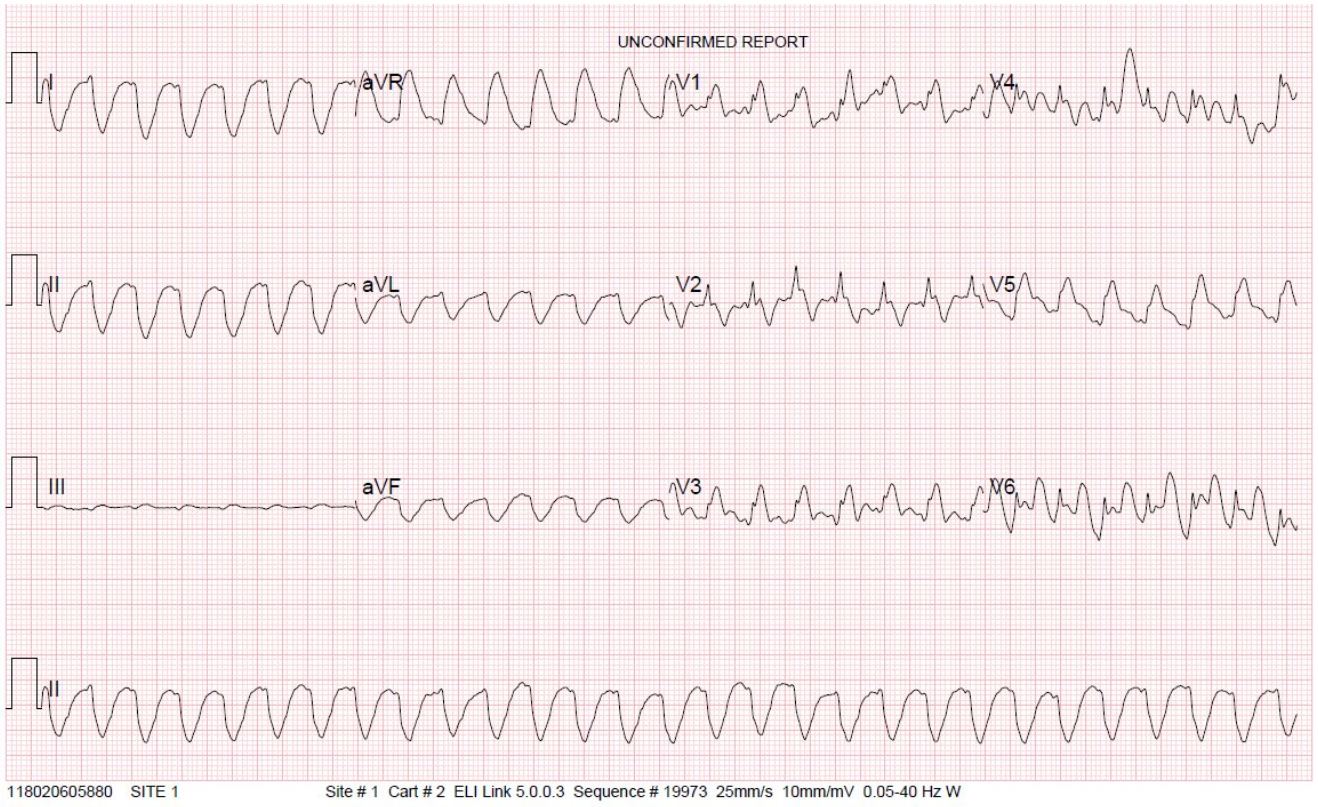
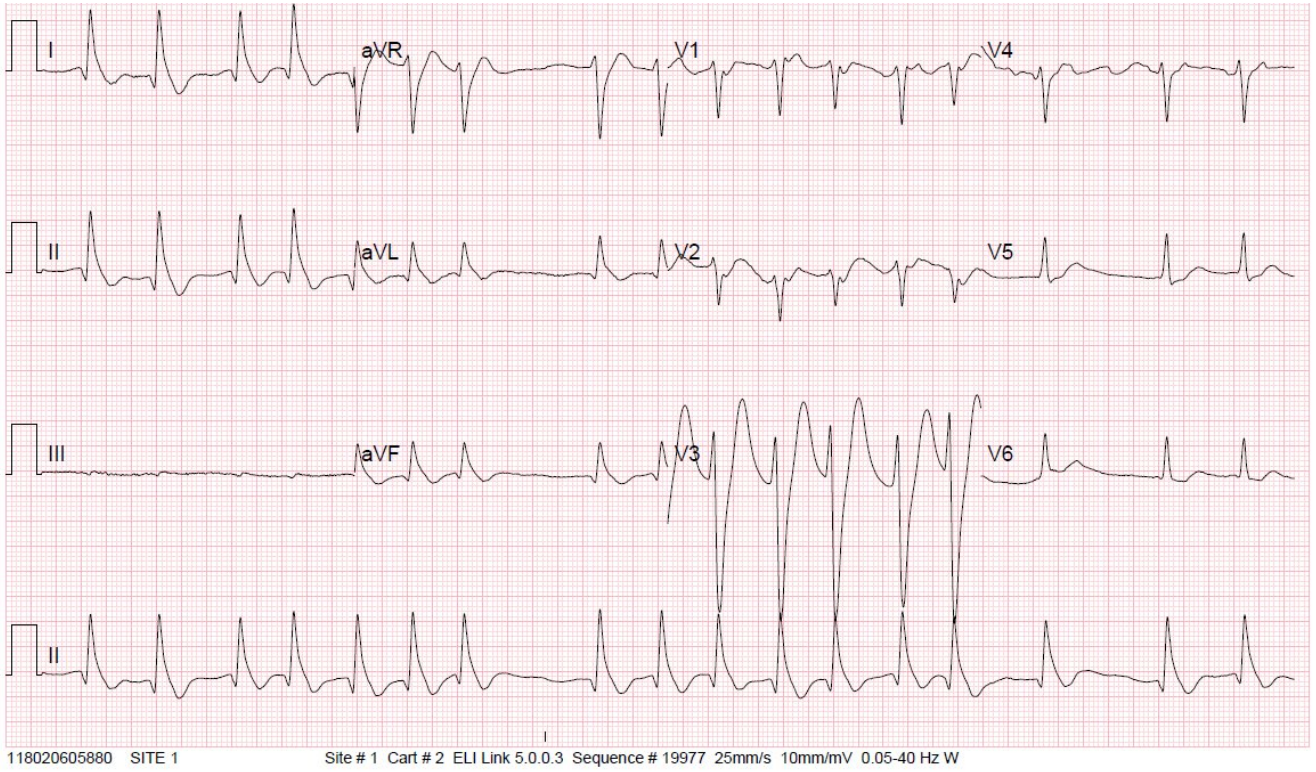


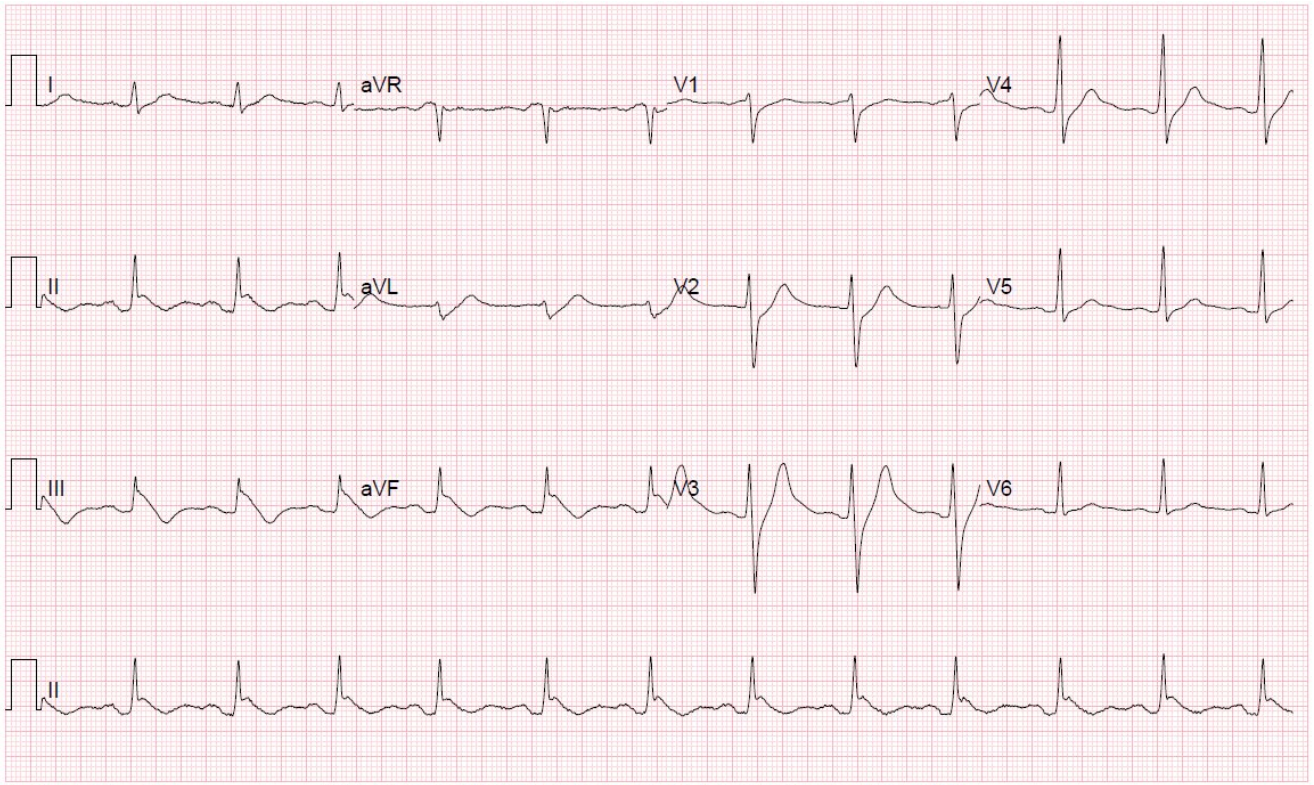
Monomorphic VT originating from LV inferior wall



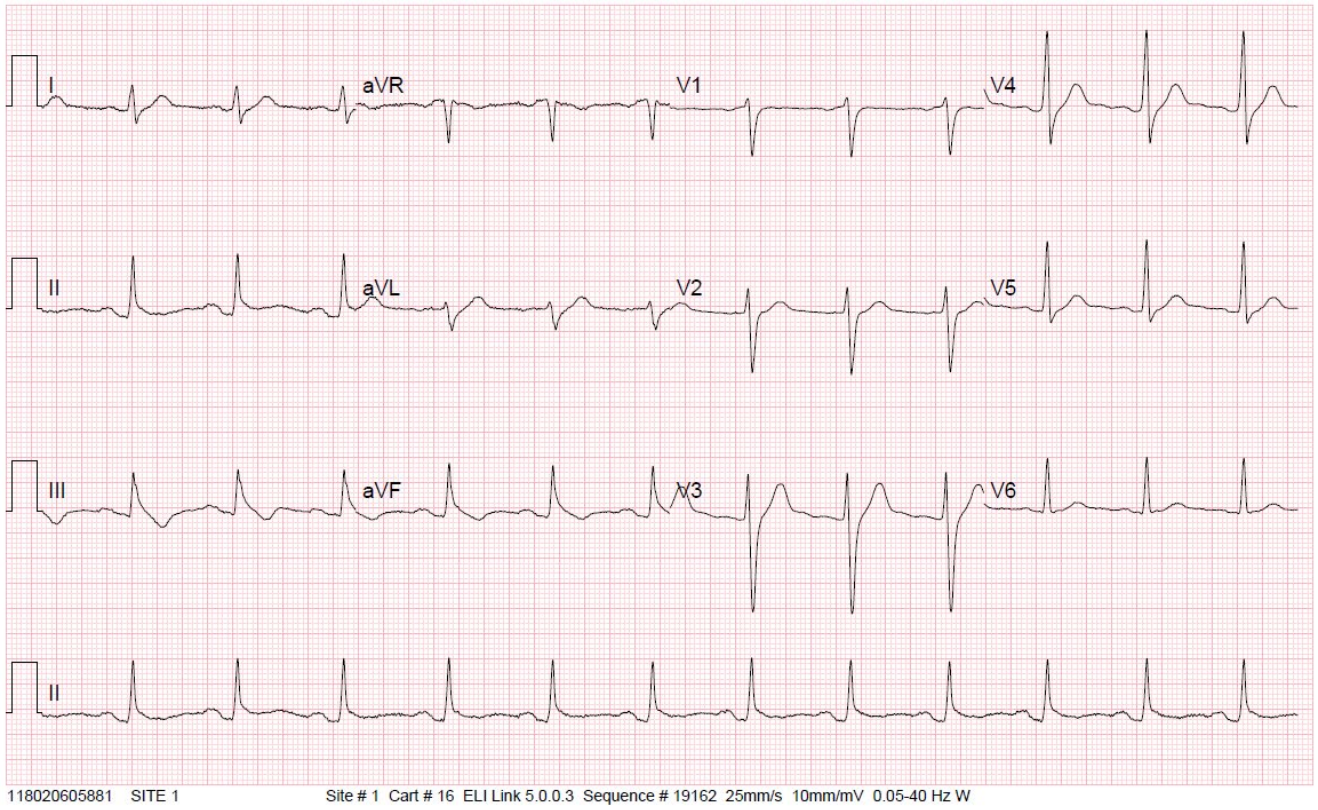
Atrial fibrillation post resuscitation



ECG 1 day post Ajmaline test



ECG 2 day post Ajmaline test



ECG 3 day post Ajmaline test