

Isoproterenol for Risk Stratification in WPW

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מרכז הלב
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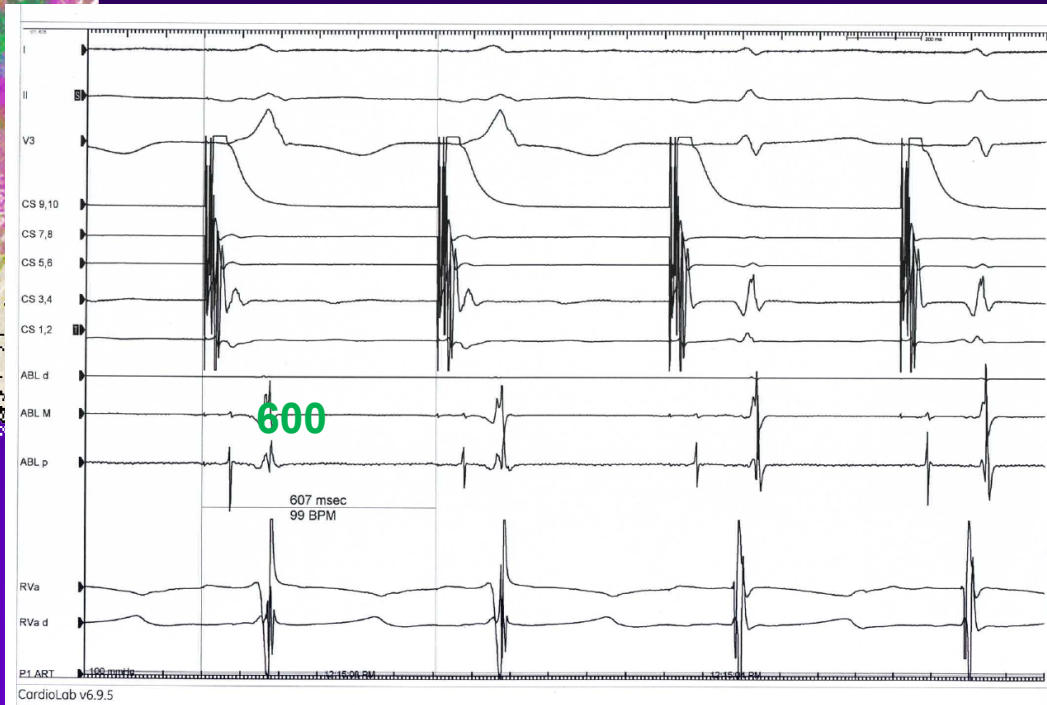
Introduction

- Pre excitation is known to cause sudden death
- The risk for SCD is dependent on the effective refractory period of the pathway
- Isoproterenol is a potent beta agonist in routinely used in the lab for diagnostic purposes
 - Beta-agonist → cAMP↑ → Ca↑ → ERP ↓

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- **The effect of isoproterenol on the ERP of pathways may vary**
 - **Recently we encountered several AP cases in which isoproterenol markedly changed the properties of the AP**

28y F Recurrent SVT

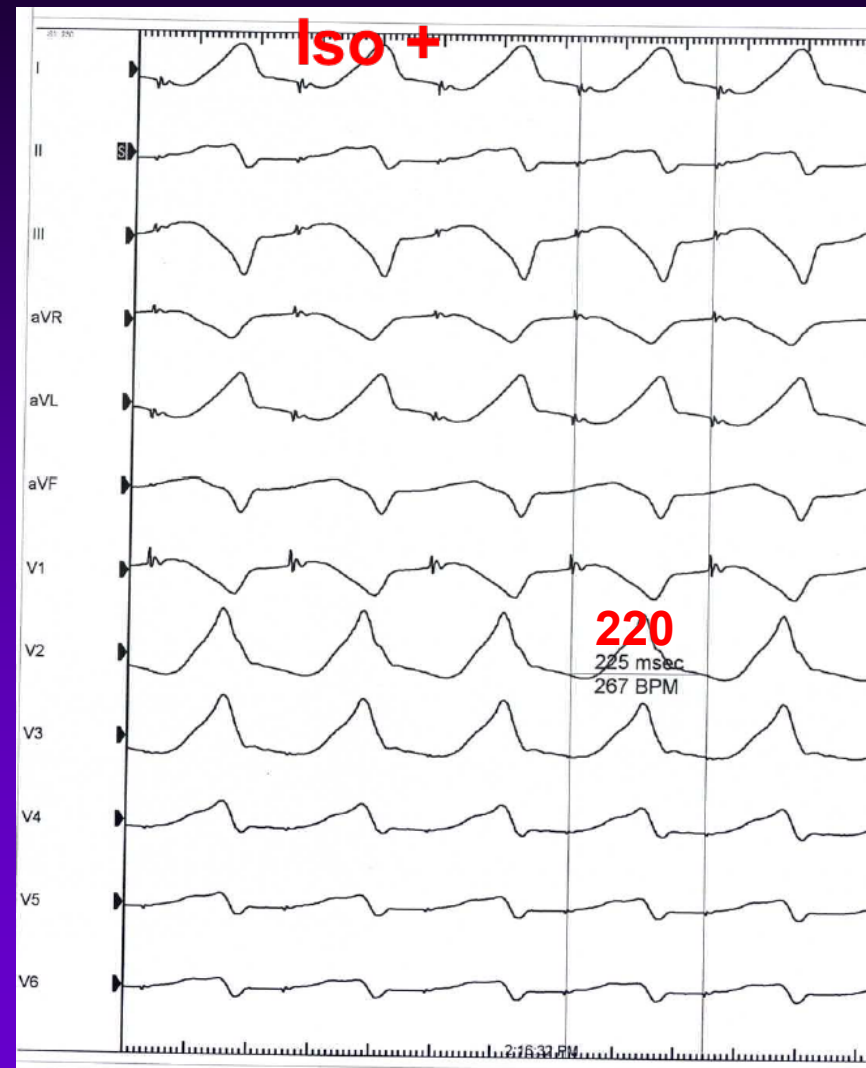
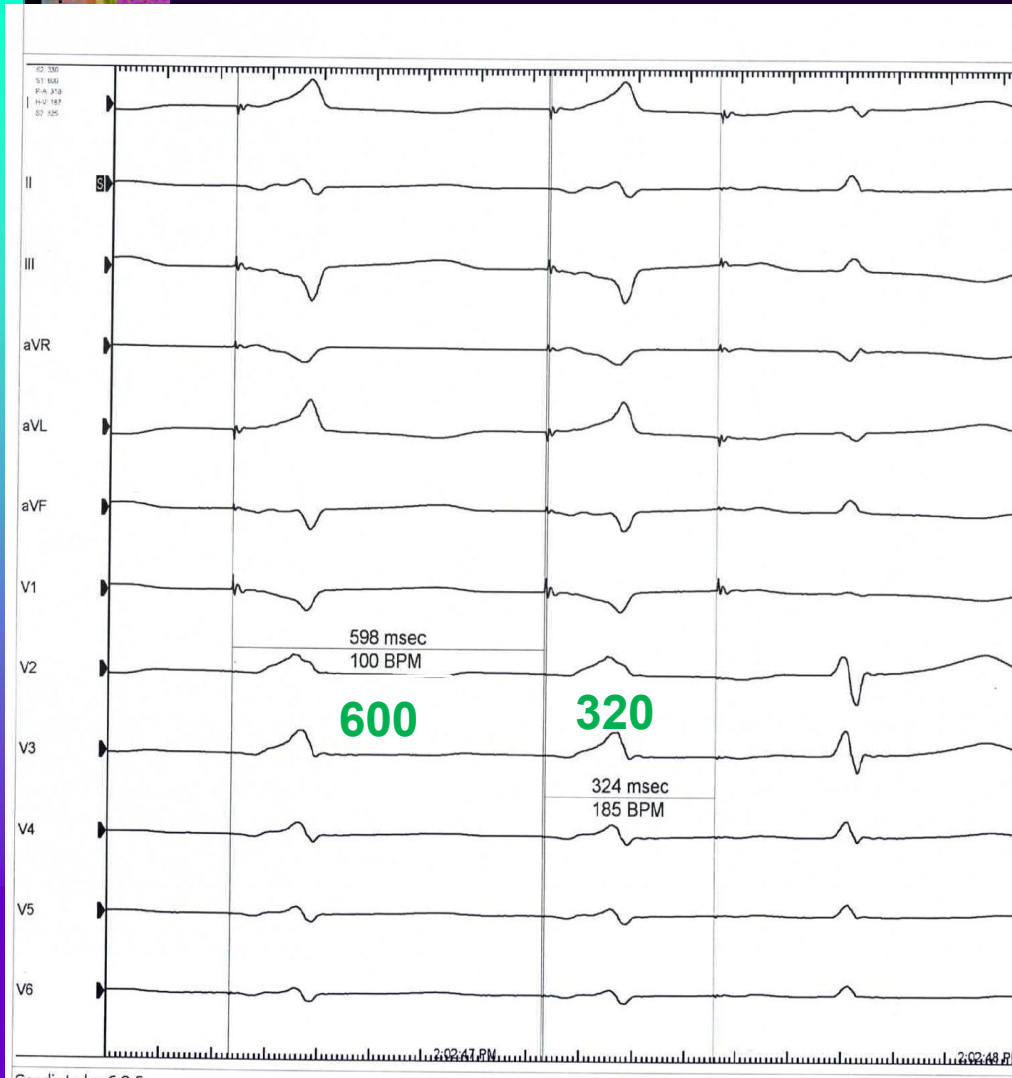
Iso +



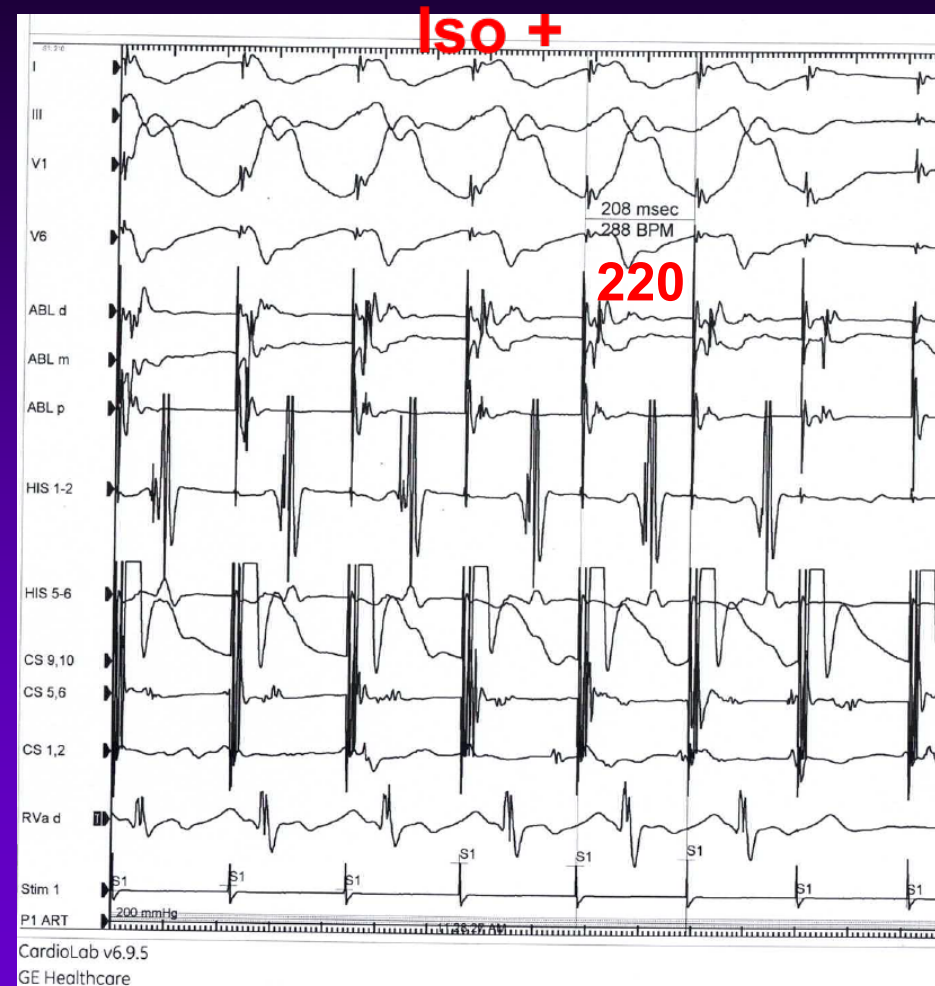
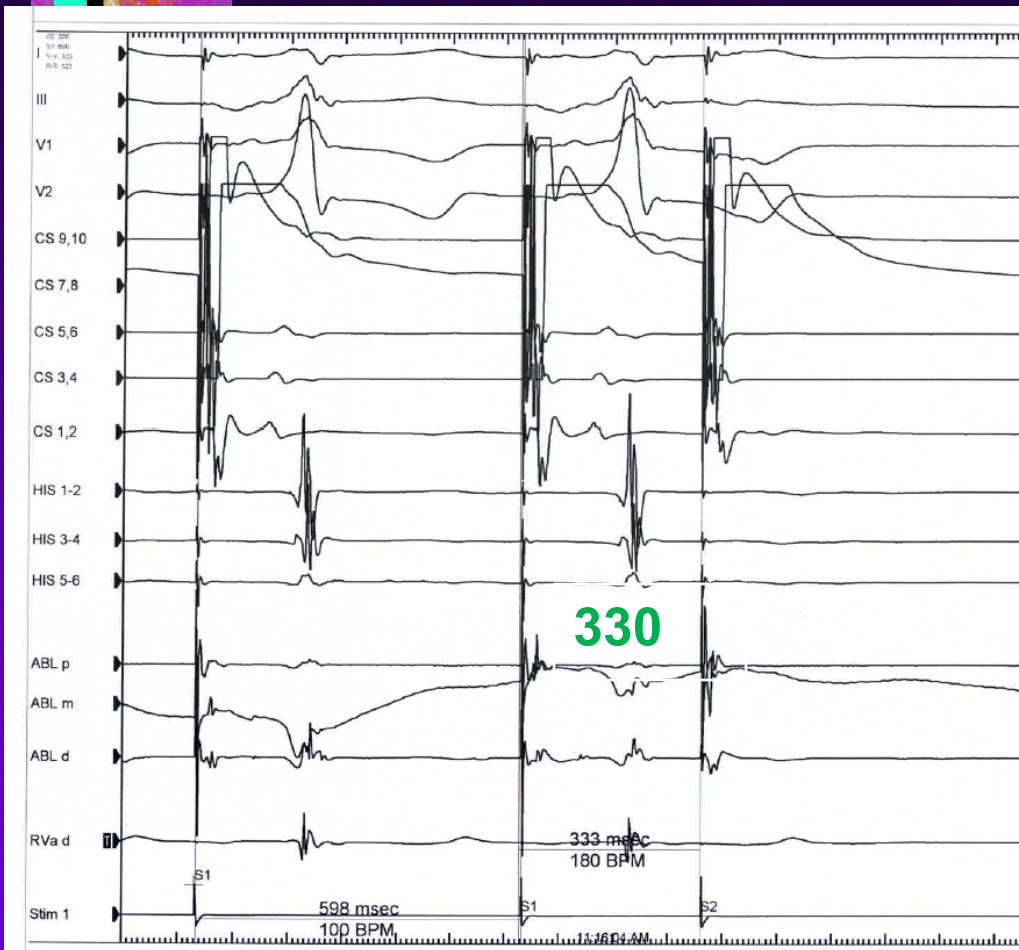
Intermittent
conduction at 600ms



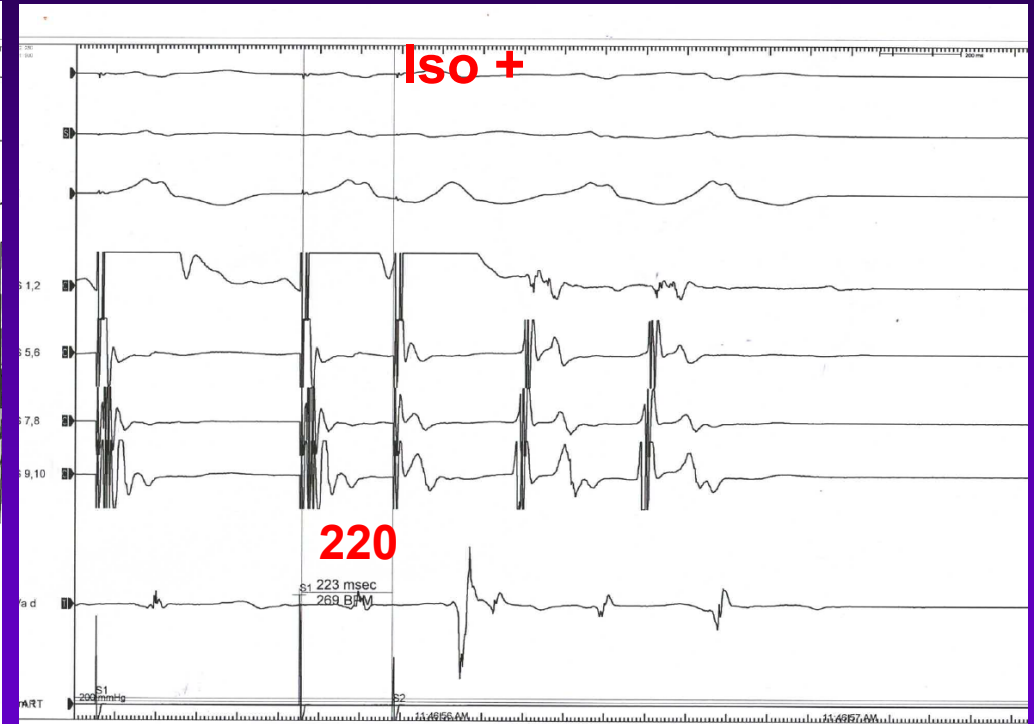
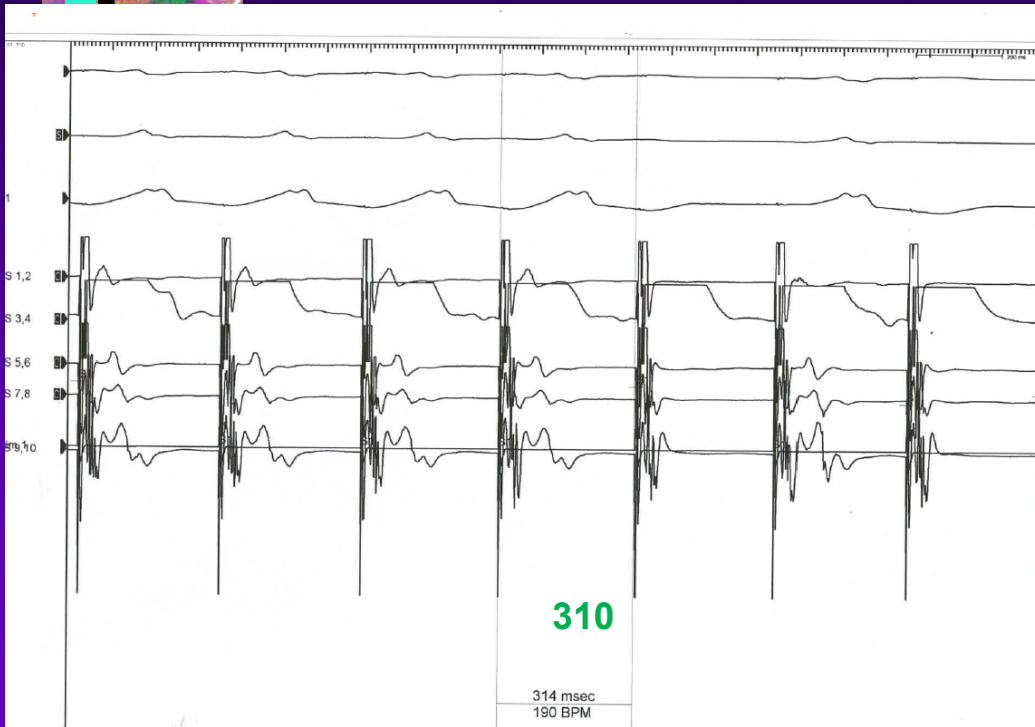
17yo f refugee



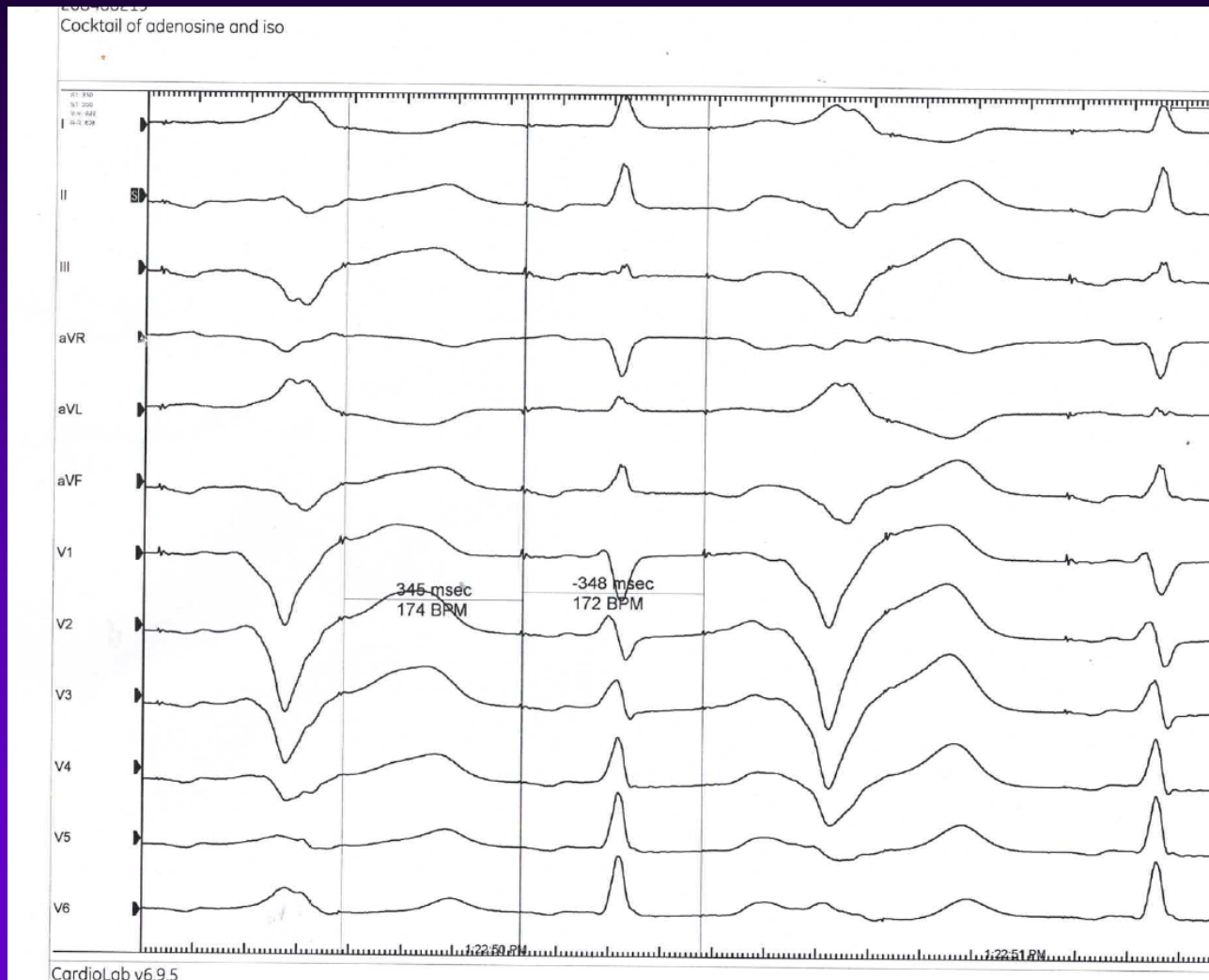
22 yo m volunteer



21 yo elite unit



28 yo m known VVS



A decorative vertical bar on the left side of the slide, featuring a gradient from purple at the top to blue at the bottom, with a central section of abstract, colorful patterns in shades of green, yellow, and red.

What does the literature say?

Who will live and who will die based on EP stratification?

Table 2 Invasive electrophysiologic parameters in asymptomatic children and young adults with WPW pattern

Author	Pts	Age (y)	F/U (y)	APERP	APERP ≤240	SPERRI	SPERRI ≤250	Inducible SVT	PPV of SCD (SPERRI ≤250)	NPV of SCD (SPERRI ≤250)	VF arrest	Actual death
Pappone ³⁸	212	36	3	275 ± 34				47 (22%)			3*	
Santinelli ²⁹	184	10	4.7	270 (240–290)	48 (26%)			77 (42%)	3/48**	136/136**	3*	
Dubin ⁷⁵	23	12	2.5		2 (9%)			14 (61%)			0	0
Leitch ⁸⁰	72	34	4.3	293 (280–310)		274 (240–325)	23 (31%)	22 (29%)	0/23	49/49	0	0
Beckman ⁸²	15	33	7.5	356 ± 194		438 ± 106	2 (13%)	3 (20%)	0/2	13/13	0	0
Milstein ⁴⁸	42	36	2.4	333 ± 106 288 ± 29		277 ± 48	7 (17%)	16 (38%) 5 (15%)	0/7	35/35	0	0
Satoh ¹⁵⁷	34	36	1.3	252 ± 23 [^]	3 (9%)			12 (55%) [^]	0/3	31/31	0	0
Brembilla ⁷⁶	40	35	1.8		2 (5%)	341 (150–650)	7 (18%)	7 (18%)	0/7	33/33	0	0
Pappone ⁵⁰	27	10	1.6	240 (230–270)		230 (215–230) ^Δ		12 (44%)			3	
Pappone ¹⁵⁸	35	22	5	240 (230–260)		240 (225–250) [†]		14 (40%)			1*	
Bertaglia ^{84‡}	88	20	3.8				27 (30%)		0/27	61/61	0	0
Fazio ^{87‡}	8	7.8	4.2		2 (25%)		2 (25%)	0 (0%)	0/2	1	0	0
Sarubbi ⁵³	35	10	4	276 ± 39 [¶] 255 ± 27 ^f		238 ± 9	5 (14%)	17 (48%)	1/5	30/30	1	1

AF = atrial fibrillation; APERP = accessory pathway effective refractory period; EP = electrophysiologic; NPV = negative predictive value; PPV = positive predictive value; SPERRI = shortest pre-excited RR in atrial fibrillation; WPW = Wolff-Parkinson-White; Other abbreviations as in Table 1.

A portion of this table was previously published (Copyright Permission: Journal of Cardiovascular Medicine 2007;8:668–674).

*SPERRI ≤230.

**APERP ≤240.

Can Isoproterenol Improve Accuracy?

- After isoproterenol, 67% of patients had a shortest RR between preexcited complexes <250 ms (during AF), the traditional marker of risk for ventricular fibrillation, versus 33% in the control state. (Am J of Card 1989)
- Isoproterenol facilitates arrhythmia induction

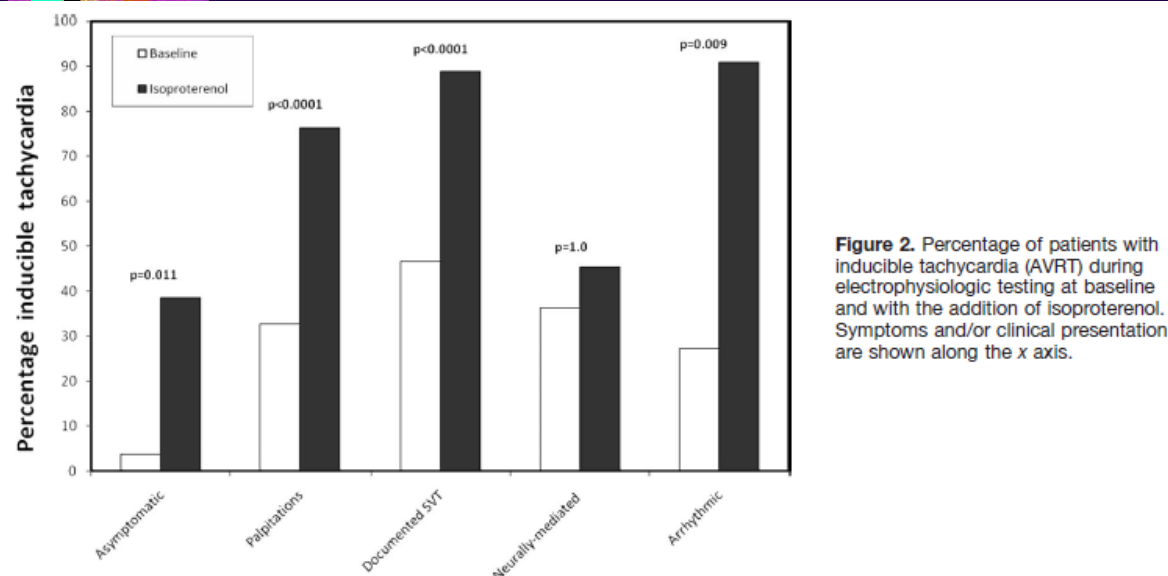


Figure 2. Percentage of patients with inducible tachycardia (AVRT) during electrophysiologic testing at baseline and with the addition of isoproterenol. Symptoms and/or clinical presentation are shown along the x axis.

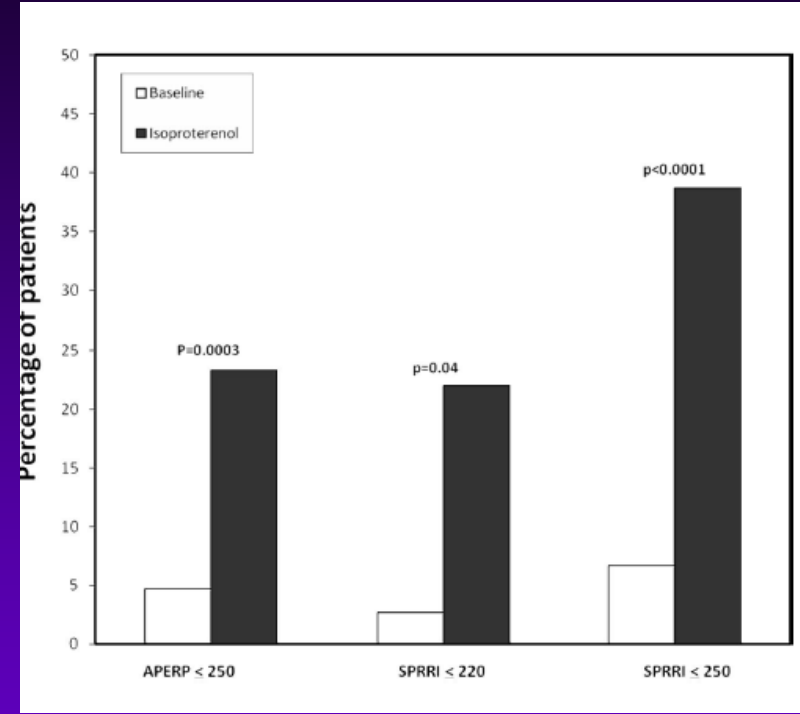


Figure 3. Percentage of patients with inducible tachycardia (AVRT) during electrophysiologic testing at baseline and with the addition of isoproterenol.

Life-Threatening Event Risk in Children With Wolff-Parkinson-White Syndrome

A Multicenter International Study

TABLE 5 EPS Data for Isoproterenol

	Cases	Subjects	p Value
Risk stratification on isoproterenol performed	18/96 (19%)	201/816 (25%)	NS
APERP, ms	249 ± 54	265 ± 40	NS
SPERRI, ms	237 ± 47	284 ± 44	0.009
SPPCL, ms	205 ± 74	259 ± 51	0.001
APERP ≤250 ms (%)	71 (10/14)	43 (63/148)	0.05
SPERRI ≤250 ms (%)	56 (5/9)	26 (9/35)	NS
SPPCL ≤250 ms (%)	91 (10/11)	58 (86/149)	0.05
≥1 functional measurement ≤250 ms (%)	78 (14/18)	59 (119/201)	NS

Values are n/N (%), mean ± SD, or % (n/N).

Abbreviations as in [Tables 1 and 4](#).

TABLE 6 Factors Associated With LTE: Univariate Analysis

	Odds Ratio (95% CI)	p Value
APERP, ≤250 ms	5.32 (3.14–9.01)	<0.0001
SPERRI, ≤250 ms	8.28 (3.89–17.62)	<0.0001
SPPCL, ≤250 ms	3.27 (1.83–5.83)	<0.0001
>1 AP	4.11 (2.19–7.69)	<0.0001
At least 1 functional characteristic ≤250 ms	5.10 (3.12–8.31)	<0.0001
Males	2.58 (1.56–4.26)	0.0002
CHD	2.39 (1.01–5.67)	0.0478
Ebstein malformation of the tricuspid valve	4.43 (1.48–13.24)	0.0077
Symptomatic status	0.29 (0.18–0.45)	<0.0001
Inducible ORT	0.63 (0.40–0.97)	0.0366
Inducible ART	5.47 (1.79–16.70)	0.0029
Inducible atrial flutter	3.88 (1.19–12.66)	0.0244
Inducible atrial fibrillation	2.96 (1.89–4.63)	<0.0001
Isoproterenol APERP ≤250 ms	3.37 (1.01–11.25)	0.0479
Isoproterenol SPERRI ≤250 ms	3.61 (0.79–16.47)	0.0973
Isoproterenol SPPCL ≤250 ms	7.33 (0.91–58.71)	0.0607
Isoproterenol at least 1 functional characteristic ≤250 ms	2.38 (0.76–7.50)	0.1378

CI = confidence interval; other abbreviations as in [Tables 1, 3, and 4](#).

AHA SVT 2006

Pre-excitation, asymptomatic	None	I	C	
	Catheter ablation	Ila	B	55,57,85,106– 111

The order in which treatment recommendations appear in this table within each class of recommendation

2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia

2015

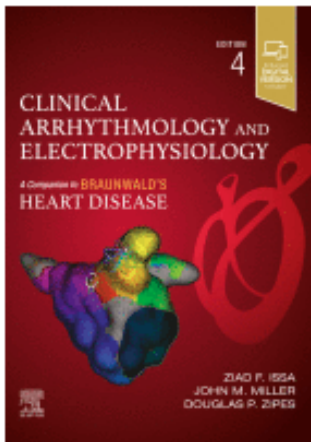
I	B-NR ^{SR}	1. In asymptomatic patients with pre-excitation, the findings of abrupt loss of conduction over a manifest pathway during exercise testing in sinus rhythm ^{294–297} (Level of Evidence: B-NR) ^{SR} or intermittent loss of pre-excitation during ECG or ambulatory monitoring ²⁹⁷ (Level of Evidence: C-LD) ^{SR} are useful to identify patients at low risk of rapid conduction over the pathway.
	C-LD ^{SR}	
Ia	B-NR ^{SR}	1. An EP study is reasonable in asymptomatic patients with pre-excitation to risk-stratify for arrhythmic events. ^{254,256,298–300}
Ia	B-NR ^{SR}	2. Catheter ablation of the accessory pathway is reasonable in asymptomatic patients with pre-excitation if an EP study identifies high risk of arrhythmic events, including rapidly conducting pre-excited AF. ^{254,302,303}

No mention of isoproterenol!

2019 ESC Guidelines for the management of patients with supraventricular tachycardia

Recommendation	Class ^a	Level ^b
Performance of an EPS, with the use of isoprenaline, is recommended to risk stratify individuals with asymptomatic pre-excitation who have high-risk occupations/hobbies, ^c and those who participate in competitive athletics. ^{439,450–452,454–460}	I	B

athletics. ^{439,450–452,454–460}		
Catheter ablation is recommended in asymptomatic patients in whom electrophysiology testing (with the use of isoprenaline identifies high-risk properties, such as SPERRI ≤ 250 ms, AP ERP ≤ 250 ms, multiple APs, and an inducible AP-mediated tachycardia. ^{439,450,452,454–460}	I	B
Catheter ablation is recommended in high-risk patients with asymptomatic pre-excitation after discussing the risks, especially of heart block associated with ablation of anteroseptal or MS APs, and benefits of the procedure. ^{439,440,473–476}	I	C
Performance of an EPS to risk stratify individuals with asymptomatic pre-excitation should be considered. ^{439,450–452,454–460}	IIa	B
Non-invasive evaluation of the conducting properties of the AP in individuals with asymptomatic pre-excitation may be considered. ^{459,461–463,465–469}	IIb	B
Invasive risk stratification with an EPS is rec-		



Issa, Ziad F., MD, MMM

2023

“However, a strategy to perform an EP study for all asymptomatic patients with the WPW ECG pattern for the purpose of risk stratification is still controversial and not widely accepted.”

- **“Also, a shortest preexcited R-R interval less than 250 milliseconds during AF has been noted in 20% to 26% of asymptomatic adults with a WPW pattern, and in up to 67% when isoproterenol is administered. Thus, although isoproterenol raises the sensitivity of invasive EP testing, it markedly reduces the specificity”**

תודה!

Table 2. Characteristics of the 105 Asymptomatic Children with the Wolff–Parkinson–White Syndrome Who Were at Low Risk for Arrhythmias.

Variable	Value
Age (yr)	
Median	9
Interquartile range	7–11
Male sex (%)	61
Structural heart disease (%)	7
Anterograde refractory period of accessory pathways (msec)	
Before isoproterenol	
Median	280
Interquartile range	260–295
After isoproterenol (msec)	
Median	220
Interquartile range	210–230
Multiple accessory pathways (%)	7
Location of single accessory pathways (%)*	
Left free wall	58
Right free wall	19
Posteroseptal	21
Anteroseptal	2
Location of multiple accessory pathways (%)†	
Left free wall and posteroseptal	43
Left free wall and right free wall	43
Right free wall and posteroseptal	14
Induced arrhythmias(%)	
Nonsustained atrial fibrillation	17
Atrioventricular reciprocating tachycardia	0
Atrioventricular reciprocating tachycardia, triggering atrial fibrillation	0

Table 2. Characteristics of the 15 Untreated WPW Patients Experiencing VF During Follow-Up

Patient	Asymptomatic/Symptomatic	Age at Enrollment, y	Sex	SHD	Multiple	AP Location	AP-AERP, ms	AVRT-AF	Follow-up, mo
1	Asymptomatic	11	Male	–	–	PS	230	+	12
2	Asymptomatic	32	Male	–	–	PS	200	–	22
3	Asymptomatic	32	Female	–	–	LFW	200	+	15
4	Asymptomatic	10	Male	–	–	PS	220	+	25
5	Asymptomatic	10	Male	–	+	LFW+PS	220	+	31
6	Asymptomatic	12	Male	–	+	LFW+PS	210	+	15
7	Asymptomatic	8	Male	–	–	PS	220	+	22
8	Asymptomatic	10	Male	–	+	LFW+PS	220	–	41
9	Asymptomatic	10	Male	–	–	PS	210	+	15
10	Asymptomatic	14	Male	–	–	RFW	220	–	28
11	Asymptomatic	14	Male	–	+	LFW+PS	220	+	21
12	Asymptomatic	10	Male	–	–	PS	240	+	55
13	Asymptomatic	11	Male	–	–	PS	230	–	53
14	Symptomatic	9	Female	–	–	PS	230	+	12
15	Symptomatic	11	Male	–	+	LFW+PS	230	+	65

AP-AERP indicates baseline accessory pathway antegrade effective refractory period; AVRT-AF, atrioventricular reentrant tachycardia triggering atrial fibrillation; LFW, left free wall; PS, posteroseptal; RFW, right free wall; VF, ventricular fibrillation; and WPW, Wolff-Parkinson-White.