AJMALINE CHALLENGE TO UNMASK ATRIOVENTRICULAR CONDUCTION DEFECTS IN PATIENTS WITH UNEXPLAINED SYNCOPE, NO STRUCTURAL HEART DISEASES AND A NORMAL ECG

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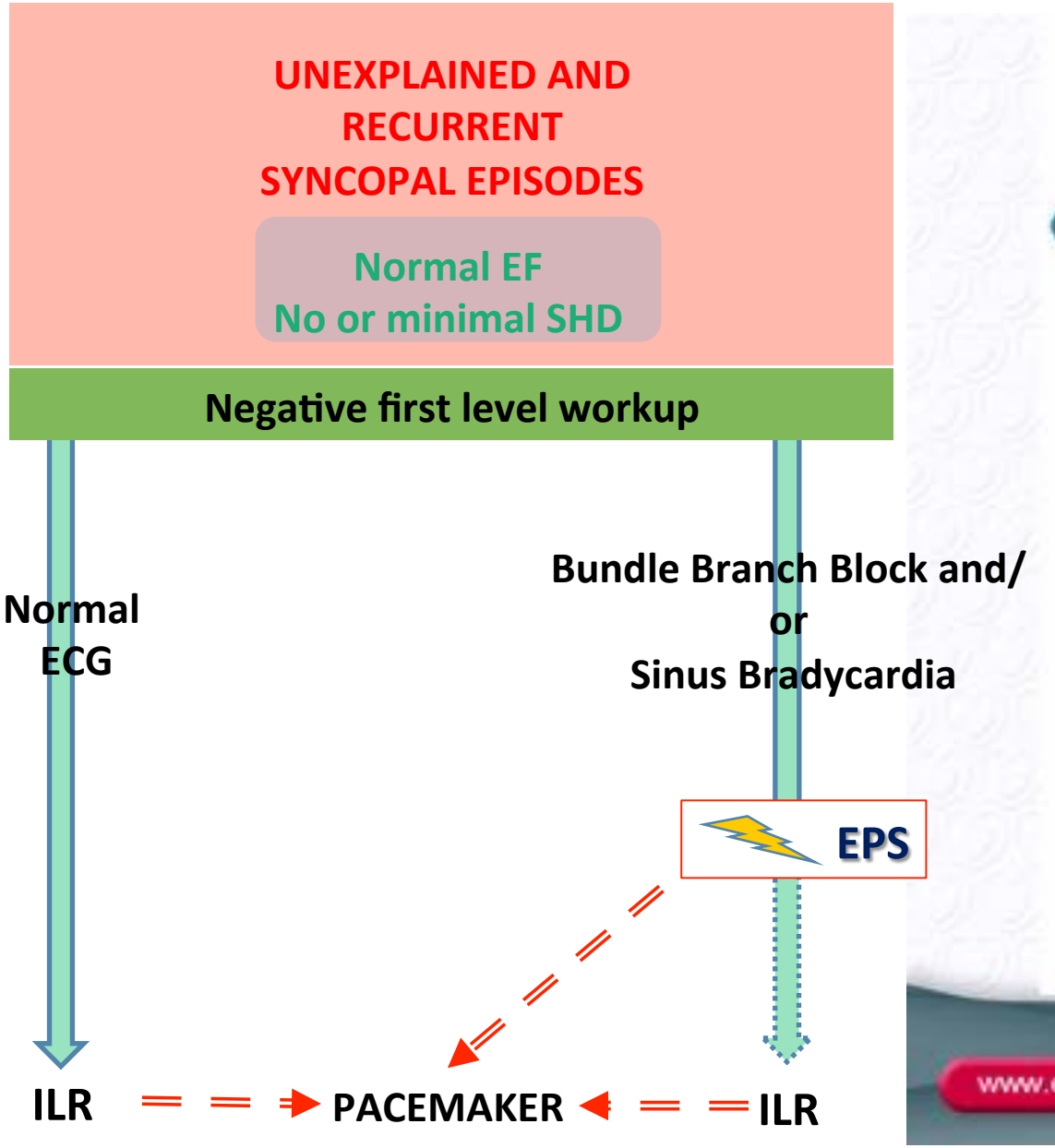
AZIENDA SANITARIA LOCALE N. 2 SAVONESE

BACKGROUND



European Heart Journal (2009) 30, 2631–2671
doi:10.1093/eurheartj/ehp298

ESC GUIDELINES

Guidelines for the diagnosis and management of syncope (version 2009)

The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)

Developed in collaboration with, European Heart Rhythm Association (EHRA)[1], Heart Failure Association (HFA)[2], and Heart Rhythm Society (HRS)[3]

Endorsed by the following societies, European Society of Emergency Medicine (EuSEM)[4], European Federation of Internal Medicine (EFIM)[5], European Union Geriatric Medicine Society (EUGMS)[6], American Geriatrics Society (AGS), European Neurological Society (ENS)[7], European Federation of Autonomic Societies (EFAS)[8], American Autonomic Society (AAS)[9]

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www.escardio.org/guidelines

European Heart Journal 2009;30:2631-2671

BACKGROUND

Sensitivity of basal EPS:

37.5% in pts with paroxysmal sinus pauses

15.4% in pts with paroxysmal AV block

Fujimura O et al, N Engl J Med 1989;321: 1703-7

BACKGROUND

Pharmacological stress testing of the His-Purkinje system

Ajmaline Procainamide Disopyramide	IA
Flecanide	IC

Sensitivity of stress EPS:

50 - 80%

Englund A et al. Pacing Clin Electrophysiol 1998; 21: 1979-87

BACKGROUND

ISSUE

Diagnostic yield of insertable loop recorder in patients with recurrent syncope: International Study on Syncope of Uncertain Etiology.

FOUR GROUPS

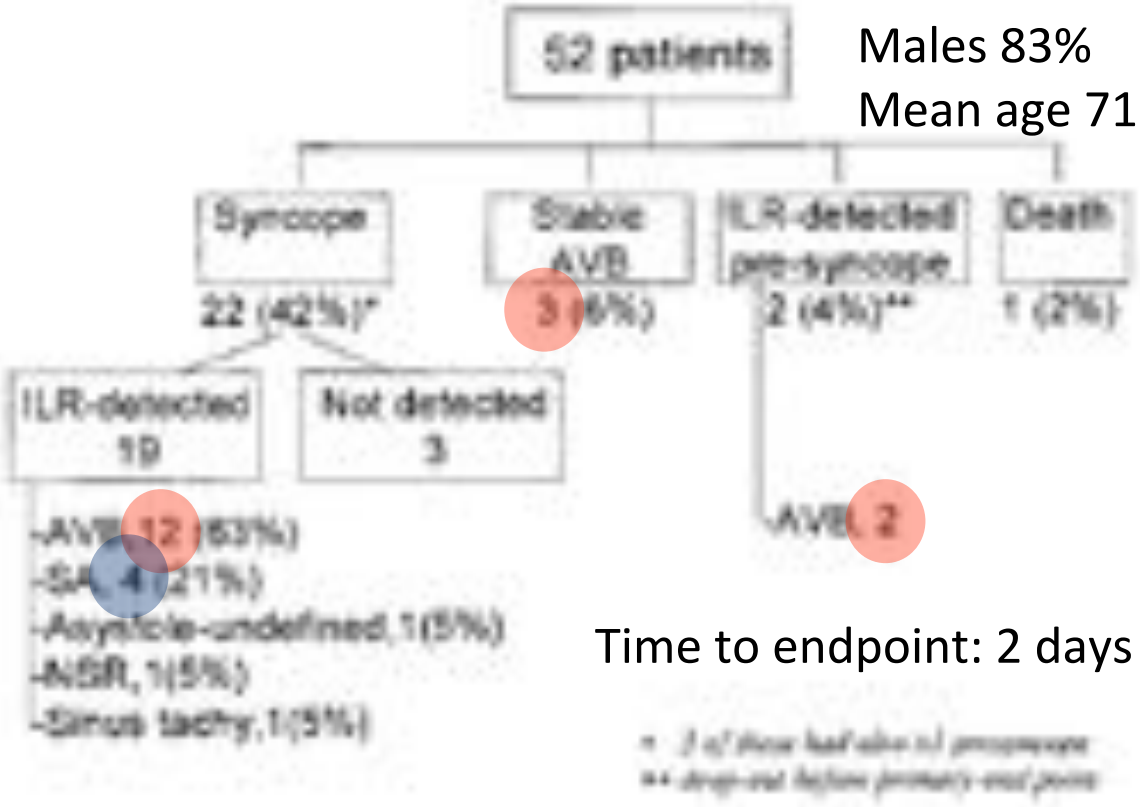
1 – syncope alone
2 – syncope alone and positive tilt test
3 – syncope + BBB and negative EPS (group brady)
4 – structural heart disease and negative EPS (group tachy)

Moya A et al. [abstract]. Eur Heart J 1999; 20: 442

BACKGROUND

Mechanism of Syncope in Patients With Bundle Branch Block and Negative Electrophysiological Test

Michele Brignole, MD; Carlo Menozzi, MD; Angel Moya, MD; Roberto Garcia-Civera, MD; Luis Mont, MD; Miguel Alvarez, MD; Francisco Errazquin, MD; Julio Beiras, MD; Nicola Bottoni, MD; Paolo Donateo, MD; on behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators*



Males 83%
Mean age 71 ± 8 y

Time to endpoint: 2 days to 1 year

21 asystolic pauses

4 pts (7.7%): Sinus pauses

17 pts (32.7%): AV block

1/3 not detected by EPS!!!
Criteria to consider + the EPS:
BASAL HV ≥ 70 msec
AFTER AJMALINE: 2nd or 3rd degree infrahisian block

Brignole M et al, Circulation 2001; 104: 2045-50

BACKGROUND

Mechanism of Syncope in Patients With Isolated Syncope and in Patients With Tilt-Positive Syncope

Angel Moya, MD; Michele Brignole, MD; Carlo Menozzi, MD; Roberto Garcia-Civera, MD; Stefano Tognarini, MD; Luis Mont, MD; Gianluca Botto, MD; Franco Giada, MD; Daniele Cornacchia, MD; on behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators*

Moya A et al, Circulation 2001; 104: 1261-7

BACKGROUND

TABLE 1. Patient Characteristics

	Isolated (n = 82)	Tilt-Positive (n = 29)
Age, y	63 ± 17	64 ± 15
Male sex, n (%)	45 (55)	11 (38)
History of syncope		
Duration, y (range)	4 (2–6)	3 (2–10)
No. (range) of episodes during last 2 years	4 (3–6)	3 (2–10)
Patients with presyncopal episodes during the last 2 years, n (%)	45 (55)	18 (62)
Severe trauma (wounds, fractures), n (%)	23 (28)	6 (21)
No warnings, n (%)	57 (76)	19 (66)
Vasoactive therapy at the time of the index syncope, n (%)	34 (41)	17 (59)
Standard electrocardiogram		
Any abnormality, n (%)	21 (26)	7 (24)
Echocardiogram		
Any abnormality, n (%)	21 (26)	7 (24)
Associated structural heart disease		
Any abnormality, n (%)	26 (32)	9 (31)
Ischemic	7	4
Valvular	5	1
Hypertensive	12	4
Other	2	0
Associated arrhythmias, n (%)		
Nonsustained ventricular tachycardia on Holter recording	3 (4)	3 (10)
Paroxysmal atrial fibrillation	2 (2)	3 (3)
Electrophysiological study performed, n (%)	61 (74)*	12 (41)*
Tilt-testing response		
Positive during the passive phase, n (%)	0	6 (21)
Positive during the drug phase, n (%)	0	23 (79)†
Asystolic response, n (%)	0	6 (21)
Maximum pause duration, s	0	10 ± 5
Mixed type, n (%)	0	14 (48)
Vasodepressor type, n (%)	0	9 (31)

N = 111 patients

73 pts (66%): EPS

1/3 not performed EPS!!!

Moya A et al, Circulation 2001; 104: 1261-7

BACKGROUND

TABLE 2. Results: Primary End Point

	Isolated (n=82)	Tilt-Positive (n=29)
Mean follow-up duration	9±5	10±5
Documented syncope, n (%)	24 (29)	8 (28)
Median time to first syncope, d (range)	105 (47–226)	59 (22–98)
Findings at the time of syncope		
Asystolic pause(s)	11 (46)	5 (62)
Maximum pause duration, s (range)	15±6 (6–24)	17±9 (3–21)
Asystole type: sinus arrest/AV block, n	9/2	5/0
Bradycardia <40 bpm, n (%)	2 (8)	1 (12)
Normal sinus rhythm, n (%)	9 (37)*	2 (25)
Sinus tachycardia, n (%)	1 (4)	0
Atrial tachycardia, n (%)	1 (4)	0

Values are mean±SD, median (range), or number of patients (%). AV indicates atrioventricular.

*Ischemia followed by ventricular fibrillation in 1 case.

16 asystolic pauses

14 pts (12.6%): Sinus pauses

2 pts (1.8%): AV blocks

2 over 111 not detected by EPS (performed in 66 % of pts)

Moya A et al, Circulation 2001; 104: 1261-7

AIM

To evaluate the role of ajmaline challenge in patients with recurrent and unexplained syncope,
normal ECG and negative first level work-up

METHODS

STUDY POPULATION: includes consecutive patients referred to our institution between Sept. 2014 and March 2015

Inclusion criteria

- History of recurrent syncope (2 or more episodes/year) or

  1 episode (high risk setting or episode with severe trauma)
- Normal EF
- No or minimal SHD
- Negative first level work up

ECG CONDUCTION ABNORMALITIES: NOT AN EXCLUSION CRITERIA

METHODS

STUDY PROTOCOL:

METHODS

BASAL EPS

AH interval

HV interval

SNRTc (if sinus rhythm)

Anterograde and retrograde conduction

Arrhythmias induction

HV interval diagnostic only if › 70 msec *

* Boulè S et al. Can J Cardiol 2014; 30: 606-11

METHODS

AJMALINE CHALLENGE

If HV interval ≤ 70 ms. Dose: 1 mg/Kg over 2'

AH interval

HV interval

ST interval in right precordial leads

HV interval diagnostic only if ≥ 100 msec *

*** Conte G et al. Int J Cardiol 2014; 172: 423-7**

RESULTS

STUDY POPULATION

Baseline characteristics	N = 16
Age (years), mean ± SD	76 ± 5
Males	7 (44)
Associated structural heart diseases:	
Any abnormality	10 (62.5)
Ischemic	1 (6.25)
Valvular	5 (31)
Hypertensive	2 (12.5)
Other	2 (12.5)
LV ejection fraction (%), mean ± SD	57 ± 5
ECG conduction disturbances	9 (56)
Sinus Rhythm at EPS	16 (100)
History of paroxysmal/persistent AF	1 (6.25)

Data are expressed as No. (%) unless otherwise specified

RESULTS

Patients with ECG conduction disturbances

Baseline characteristics	N = 9
Age (years), mean ± SD	75 ± 6
Males	6 (67)
Associated structural heart diseases:	
Any abnormality	5 (56)
Ischemic	0 (0)
Valvular	3 (33)
Hypertensive	1 (11)
Other	1 (11)
LV ejection fraction (%), mean ± SD	57 ± 4
ECG conduction disturbances	9 (100)
QRS duration (msec), mean ± SD	133 ± 30
PR interval (msec), mean ± SD	234 ± 79

Data are expressed as No. (%) unless otherwise specified

Type of conduction disturbances (PR ≥ 200 msec and/or QRS duration > 100 msec)	
First degree AV Block	1 (11.1)
RBBB	2 (22.2)
LBBB	1 (11.1)
First degree AV block + LAFB	1 (11.1)
RBBB + LAFB	1 (11.1)
First degree AV block + LBBB	3 (33.3)

Data are expressed as No. (%)
RBBB = Right Bundle Branch Block
LBBB = Left Bundle Branch Block
LAFB = Left anterior fascicular block

RESULTS

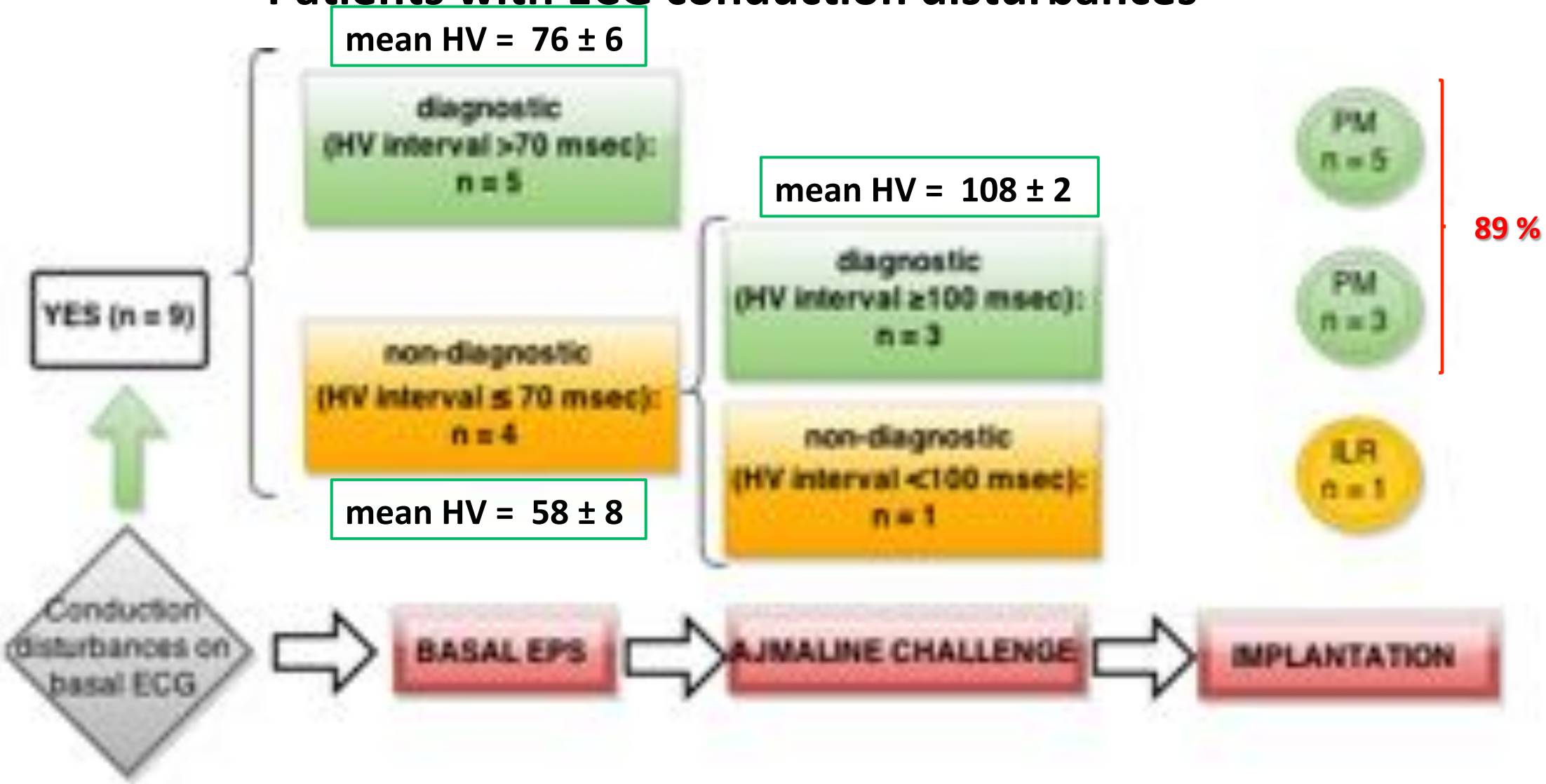
Patients without ECG conduction disturbances

Baseline characteristics	N = 7
Age (years), mean ± SD	76 ± 5
Males	1 (14)
Associated structural heart diseases:	
Any abnormality	5 (71)
Ischemic	1 (14)
Valvular	2 (29)
Hypertensive	1 (14)
Other	1 (14)
LV ejection fraction (%), mean ± SD	59 ± 2
ECG conduction disturbances	0 (0)
QRS duration (msec), mean ± SD	90 ± 7
PR interval (msec), mean ± SD	174 ± 22

Data are expressed as No. (%) unless otherwise specified

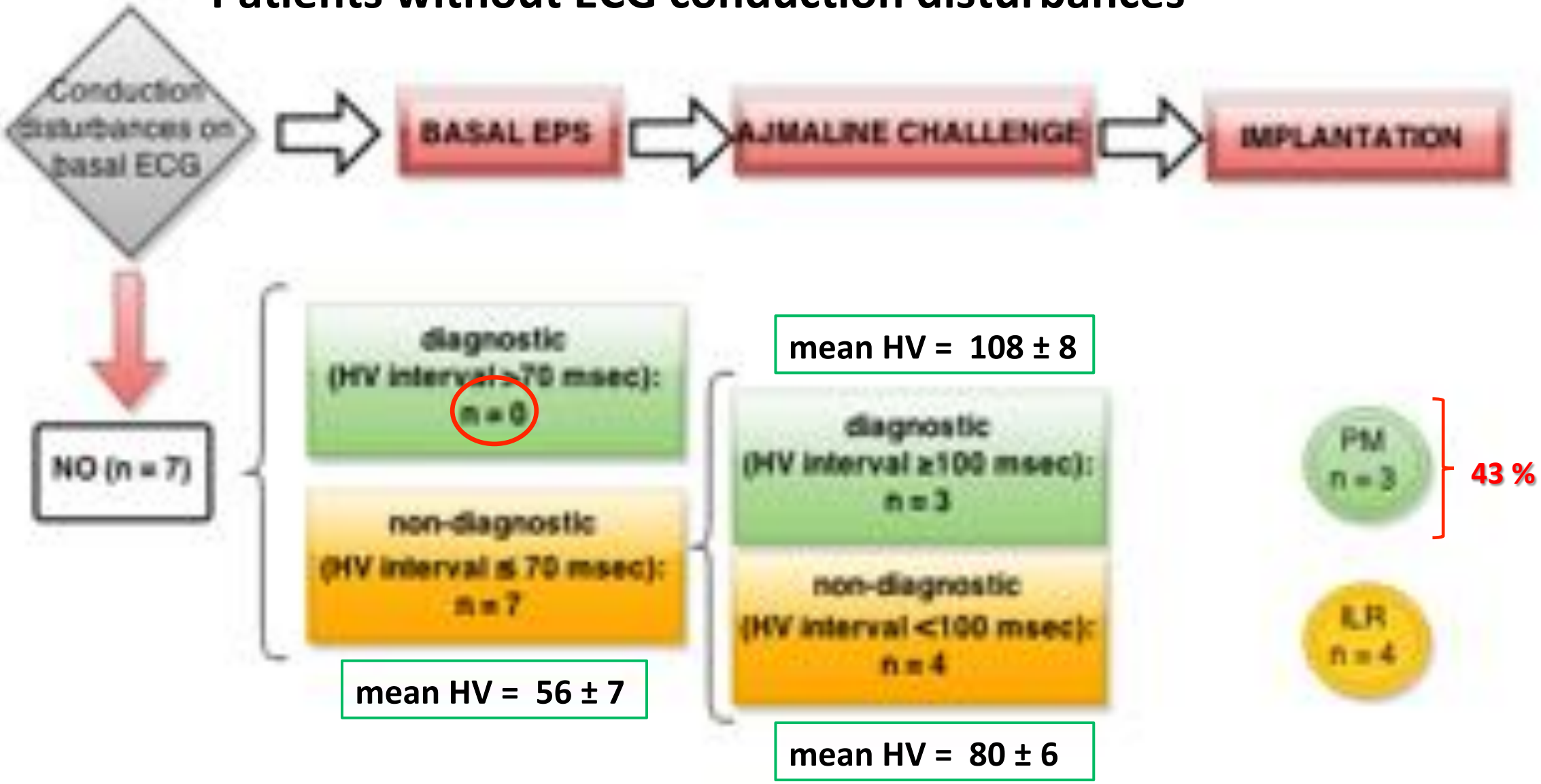
RESULTS

Patients with ECG conduction disturbances



RESULTS

Patients without ECG conduction disturbances



RESULTS

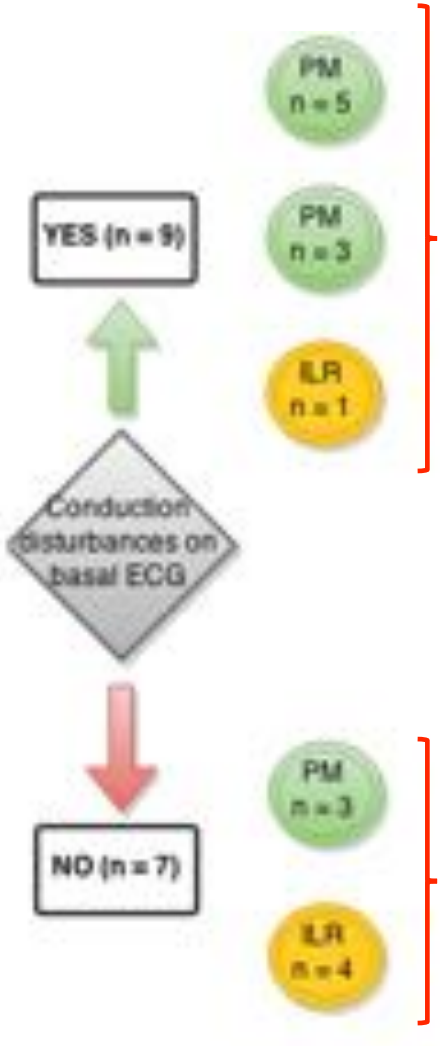
Comparison of HV interval values between patients with or without ECG conduction abnormalities

	BASAL EPS HV (ms)	AJMALINE CHALLENGE + HV (ms)
ECG ABNORMALITIES	68 ± 12	108 ± 2
NO ECG ABNORMALITIES	56 ± 7	108 ± 8
P Values	P = 0.036	P = 0.89

Data are expressed as mean ± SD unless otherwise specified

RESULTS

FOLLOW-UP: recurrence of syncope



After a mean of 9 ± 3 months:

No recurrence of syncope

1 death in PM group (cerebral neoplasya)

After a mean of 9 ± 2 months:

No recurrence of syncope

In 1 patient after 3 months ILR memory showed a non syncopal 2:1 AV block

CONCLUSIONS

Ajmaline challenge is a useful tool to unmask the presence of an infrahisian disease in patients with conduction disturbances on surface ECG.

It could be a useful tool to unmask the presence of a infrahisian disease also in patients without any conduction disturbances on surface ECG.

Due to the very little number of patients in this cohort, larger population is required to validate this hypothesis.

Nowadays, a prolonged monitoring strategy remains the cornerstone for the diagnosis of unexplained syncope.

Thanks for your attention

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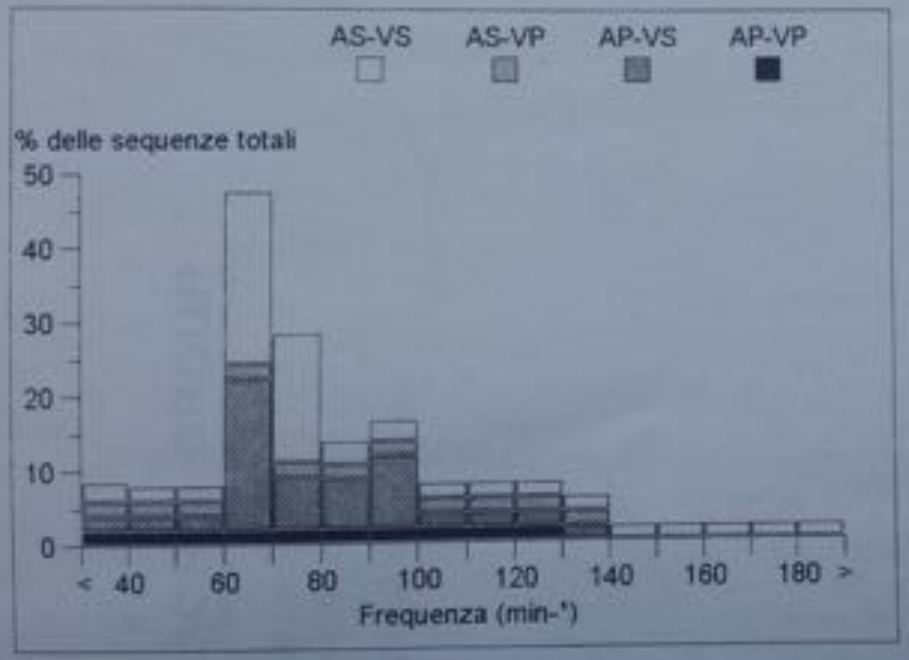
https://plus.google.com/102151338689111143346/posts

Modello pacemaker: Medtronic Adapta ADDR01
Numero di serie: NWB043868

12.10.15 14:55:29
Software SW003 7.3
Copyright (c) Medtronic, Inc. 2005

Scheda istogr. conduzione A-V a lungo term.

Periodo di raccolta dei dati: 26.03.15 13:16 - 12.10.15 14:49 (Ultimi 7 mesi)



Interrogazione iniziale

Modo	AAIR<=>DDDR
Freq. min.	60 min-¹
Freq. max. trasc.	130 min-¹
Freq. max. sens.	130 min-¹
AV stimolato	150 ms
AV rilevato	120 ms
AV adattato alla freq.	Off

Sequenze A-V

Sequenze totali	19,708,517
AS-VS	52.7%
AS-VP	0.2%
AP-VS	46.8%
AP-VP	0.4%

Reply DR W2.92 419ZK00D

dal 24/Ott/2014 a 14/Ott/2015

Statistiche

Data di reset (aa-mm-gg)	14-10-24
Modo	SafeR (AAI<=>DDD)
N° di Mode Switch	8
Tempo Fbk	06min 15s
Numero di TMS	3
ESA bloccate	994172 (2.4%)
Committed AV	0
N° di episodi in DDD	9
Percentuale di tempo in AAI	99.7%

Statistiche da (aa-mm-gg)	14-10-24 12:11:38
Cicli Cardiaci	40983345

Generale

Stimolazioni atriali	1259642
Stimolazioni ventricolari	1908
Stimolazione in finestra di committed	0
Cicli ventricolari associati	98%
Ap-Vp senza sensore	259 (<1%)
Ap-Vp con sensore	0 (0%)
Ap-Vs senza sensore	1259336 (3%)
Ap-Vs con sensore	0 (0%)
As-Vp	1373 (<1%)
As-Vs	38723419 (94%)
Cicli V in A.A.	2.4%
Detezione	992581 (2%)
Stimolazione	276 (<1%)

BACKGROUND


Contents lists available at ScienceDirect
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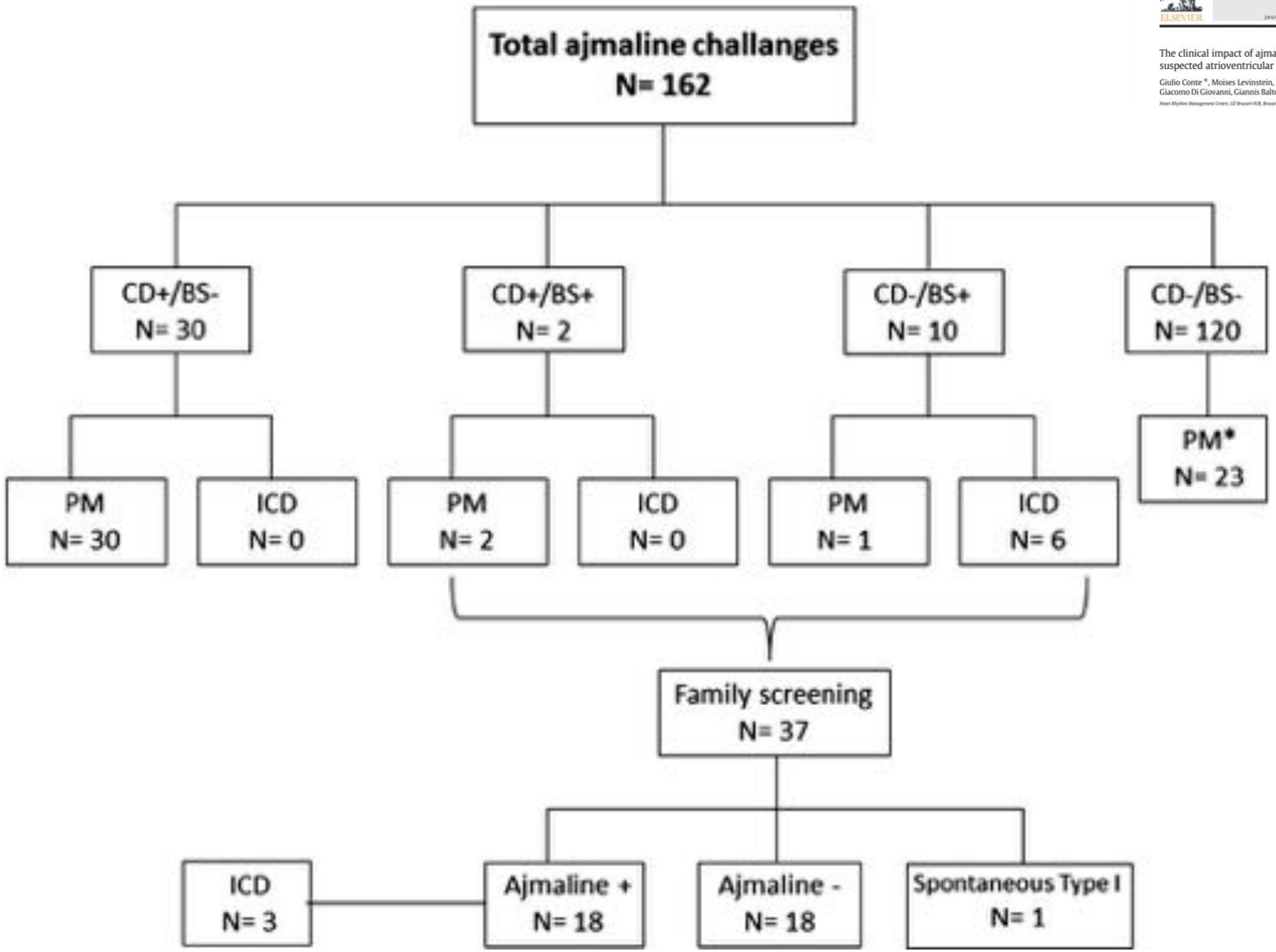
journal homepage: www.elsevier.com/locate/ijcard

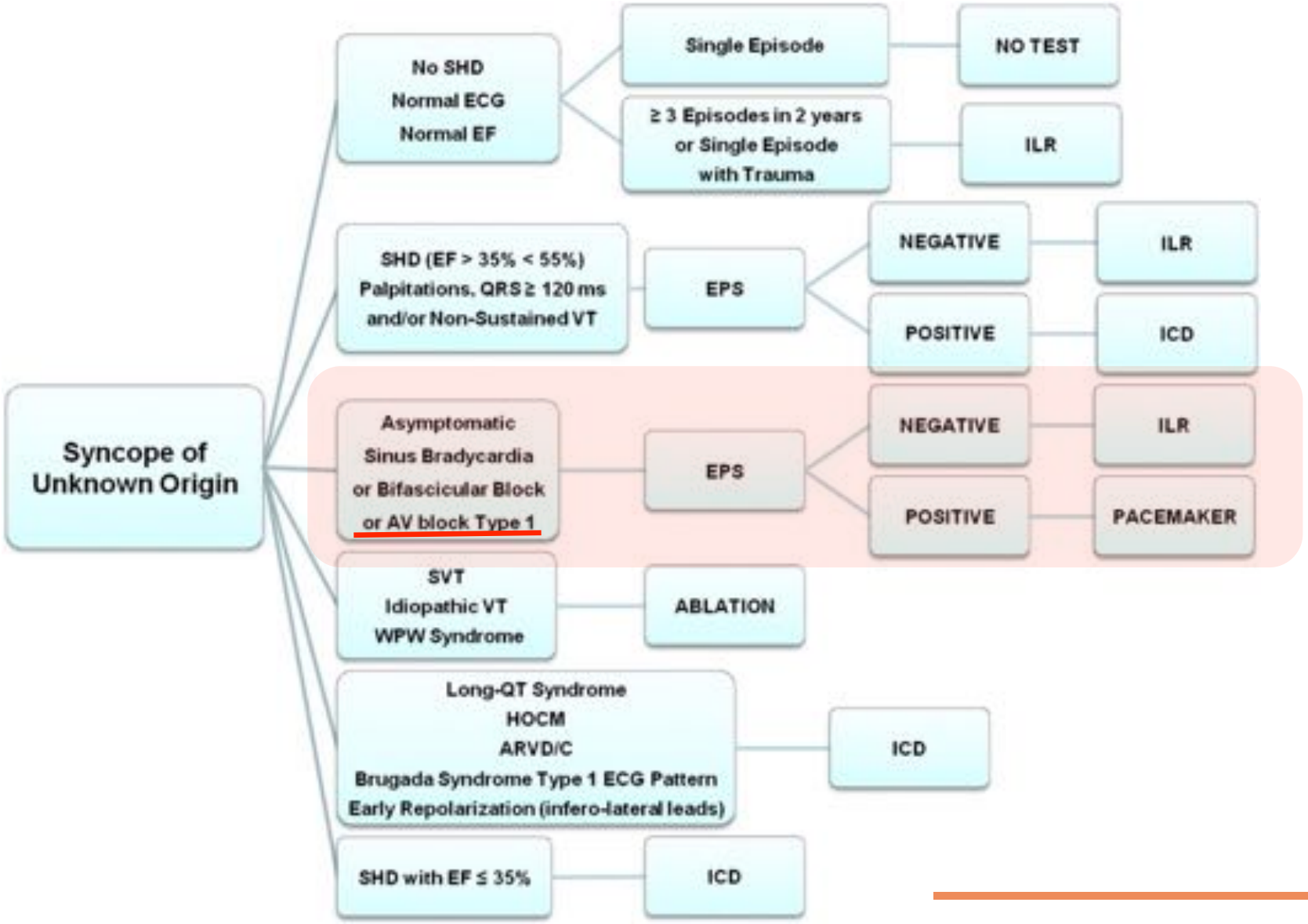
The clinical impact of ajmaline challenge in elderly patients with suspected atrioventricular conduction disease

Giulio Conte *, Moises Levinstein, Andrea Sarkozy, Juan Sieira, Carlo de Asmundis, Gian-Battista Chierchia, Giacomo Di Giovanni, Giannis Baltogiannis, Giuseppe Ciconte, Kristel Wauters, Gudrun Pappaert, Pedro Brugada
Heart Rhythm Management Centre, UZ Brussel-VUB, Brussels, Belgium



Conte G et al. Int J Cardiol 2014; 172: 423-7

BACKGROUND



Rosanio S et al. Int J Cardiol 2013; 162: 149-157

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