

Management of syncope in 2014

Role of tilt test

Antonio Raviele, MD, FESC, FHRS

THE LANCET, JUNE 14, 1986



HEAD-UP TILT: A USEFUL TEST FOR INVESTIGATING UNEXPLAINED SYNCOPÉ

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Protocols / Head-up tilt test



Unmedicated

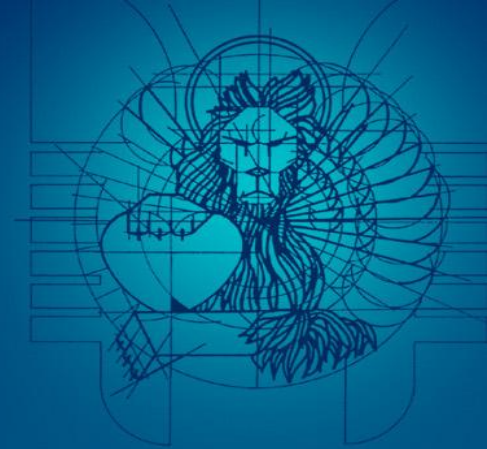
- Short-duration
- Long-duration

Pharmacologic

- Isoproterenol
- Nitroglycerin
- Edrophonium
- Adenosine
- Clomipramine

Head-up tilt test

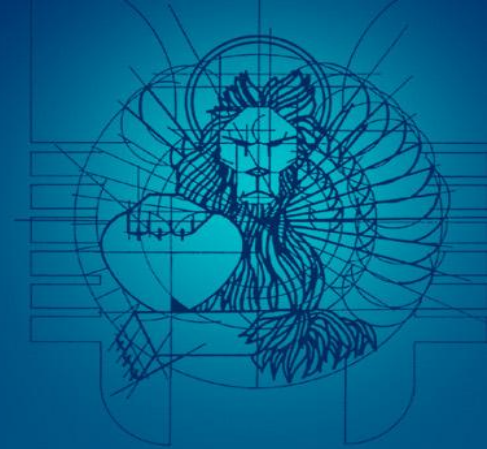
for the diagnosis of Vasovagal Syncope



Very popular

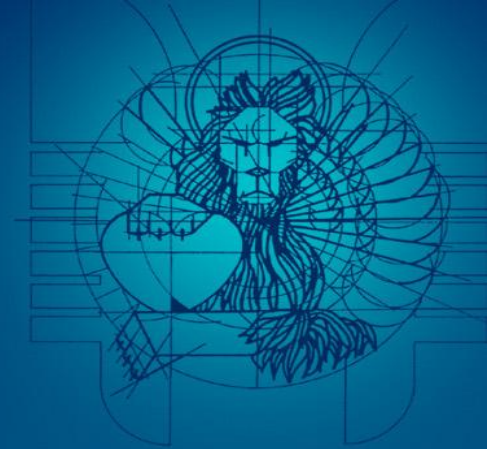
& widely accepted method

Uses / Head-up tilt test



- 1) To diagnose VVS
- 2) To diagnose OH, POTS, psychog. syncope
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Protocols / Head-up tilt test

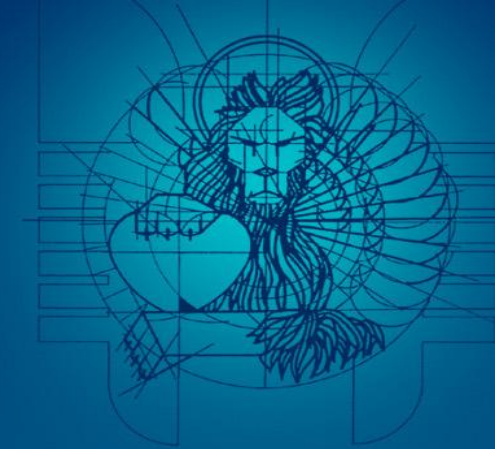


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Head-up tilt testing for diagnosing vasovagal syncope: A meta-analysis

Cinzia Forleo^{*,1}, Pietro Guida¹, Massimo Iacoviello, Manuela Resta, Francesco Monitillo, Sandro Sorrentino, Stefano Favale

Int J Cardiol 2013; 168: 27-35

This was the first meta-analysis providing data in a systematic fashion on sensitivity and specificity of head-up tilt testing for assessing

Table 2

Sensitivity, specificity and diagnostic odds ratios of head-up tilt testing protocols according to tilt phases and pharmacological agents used.

	Sensitivity (%)	Specificity (%)	Diagnostic odds ratio
Passive phase alone	25 (21–30)	99 (97–99)	10.08 (7.59–13.40)
Isoproterenol phase alone	48 (37–59)	88 (81–92)	5.94 (4.33–8.16)
Nitroglycerine phase alone	60 (53–66)	90 (84–93)	11.44 (8.97–14.59)
→ Overall passive protocols	37 (29–46)	96 (92–98)	10.14 (6.70–15.34)
→ Overall isoproterenol protocols	61 (52–69)	86 (79–91)	8.33 (6.38–10.86)
→ Overall nitroglycerine protocols	66 (60–72)	89 (84–92)	14.40 (11.50–18.05)
→ Overall protocols	59 (53–64)	91 (87–93)	11.28 (9.63–13.22)

Estimates with 95% confidence intervals.

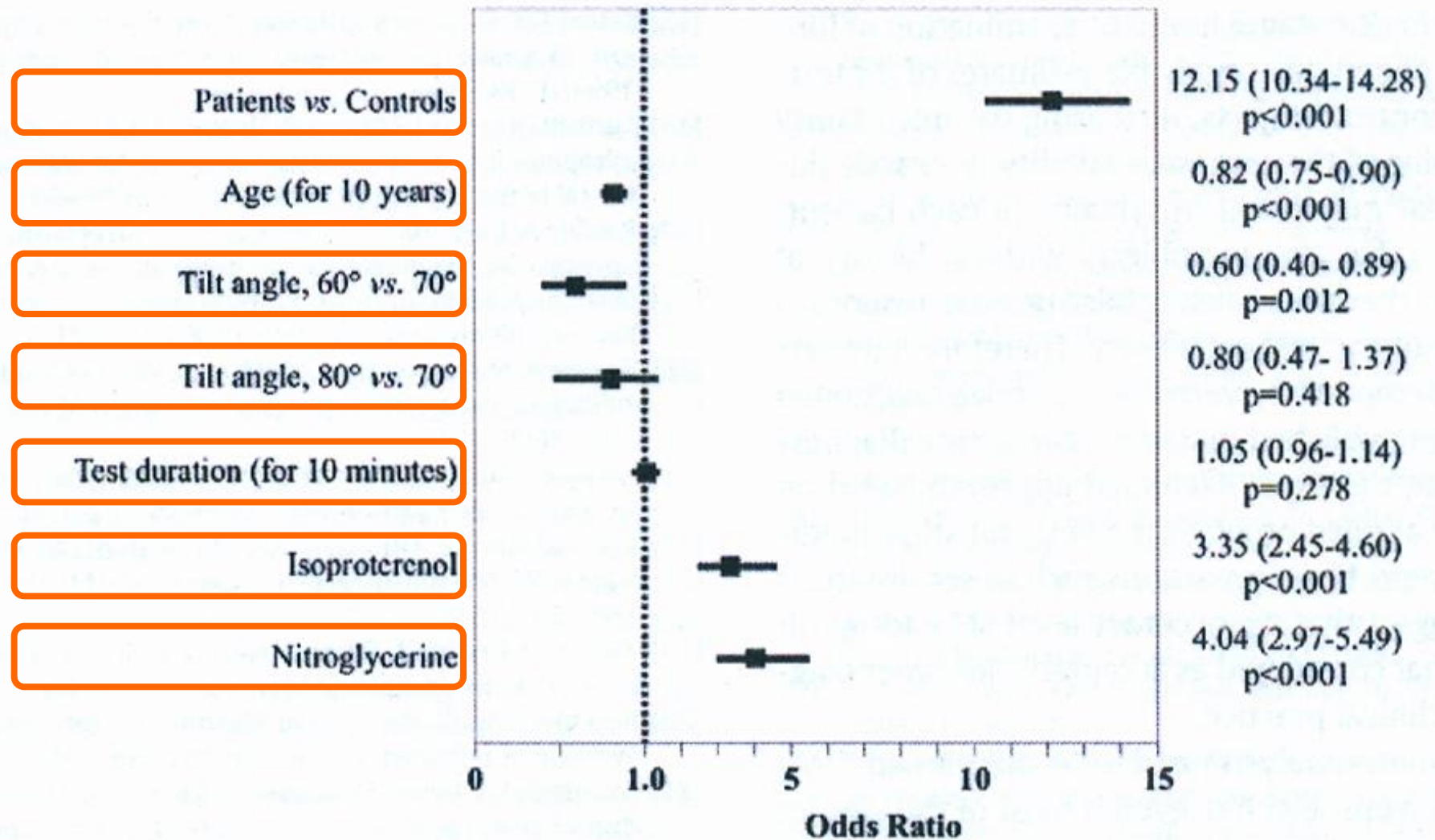
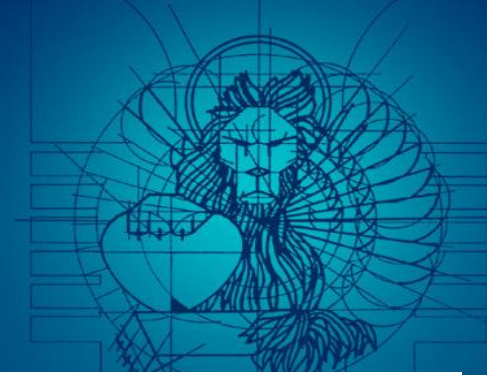


Fig. 4. Odds ratios at multivariate analysis and 95% confidence intervals for positive outcomes to head-up tilt testing.

HUTT / Diagnosis of VVS



- Head-up tilt testing is characterized by **high overall yield for diagnosing VVS**, enabling to support the test as a first choice investigation in the assessment of individual susceptibility to neurally mediated syncope
- Tilt testing protocols potentiated with nitroglycerin have **the highest diagnostic accuracy** (greatest sensitivity with acceptable specificity) and should be preferred



Twenty-eight years of research permit reinterpretation of tilt-testing: hypotensive susceptibility rather than diagnosis

Richard Sutton^{1*} and Michele Brignole²

Eur Heart J 2014; 35: 2211-2

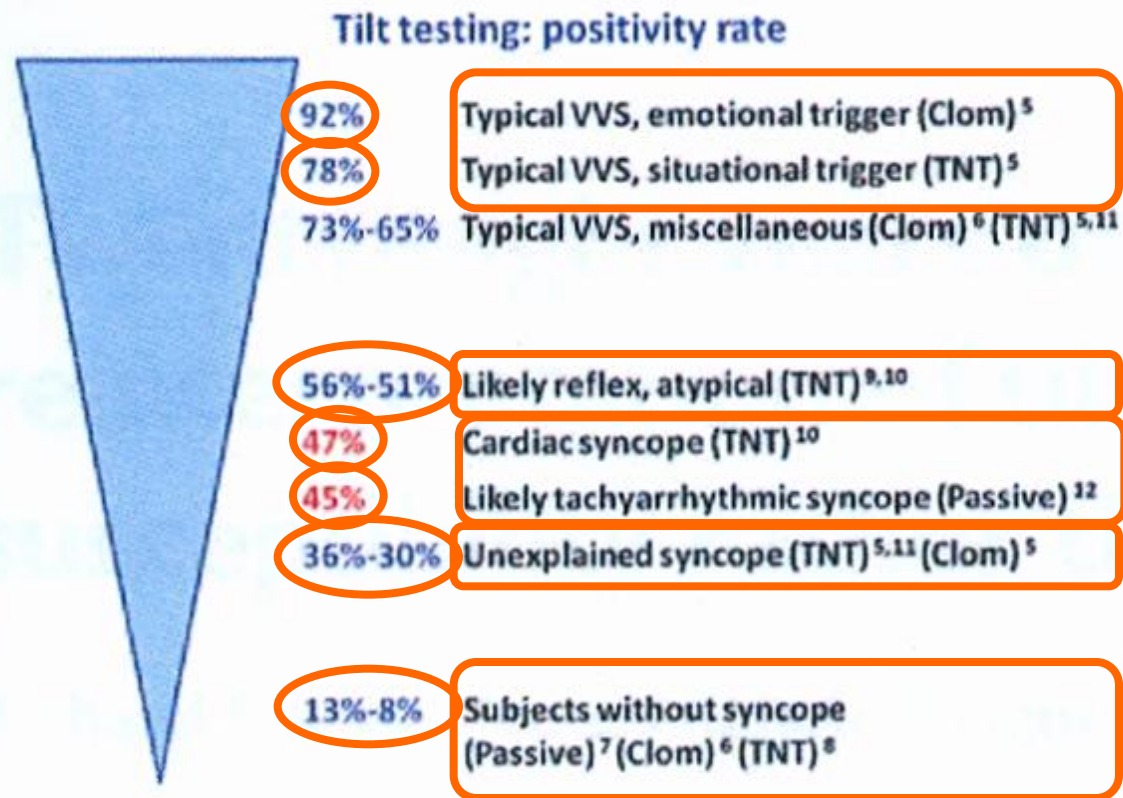



Figure 1 Tilt-testing positivity rate in different clinical conditions. The studies reported in the figure used the Westminster protocol for passive tilt,⁷ the Italian protocol for glyceryltrinitrate tilt,⁸ and the clomipramine protocol⁶ for a total of 1453 syncope patients and 407 control subjects without syncope. Studies using other tilt protocols, e.g. isoproterenol challenge, were not included. VVS, vasovagal syncope; clom, clomipramine; TNT, glyceryltrinitrate.



Diagnosis of neurally mediated syncope at initial evaluation and with tilt table testing compared with that revealed by prolonged ECG monitoring. An analysis from the Third International Study on Syncope of Uncertain Etiology (ISSUE-3)

Andrea Ungar,¹ Paolo Sgobino,² Vitantonio Russo,³ Elena Vitale,⁴ Richard Sutton,⁵ Donato Melissano,⁶ Xulio Beiras,⁷ Nicola Bottoni,⁸ Hans H Ebert,⁹ Michele Gulizia,¹⁰ Marcella Jorfida,¹¹ Angel Moya,¹² Dietrich Andresen,¹³ Nicoletta Grovale,¹⁴ Michele Brignole,¹⁵ on behalf of the International Study on Syncope of Uncertain Etiology 3 (ISSUE-3) Investigators

Heart 2013; 99: 1825-31



Table 3 Responses to tilt TT in patients with presumed NMS (ILR-documented and ILR-undocumented) and in patients in whom NMS was not confirmed by ILR findings

TT protocol/response	No ILR diagnosis n=282	NMS n=136	Non-NMS n=21	p Value (NMS likely vs non-NMS)
Passive+drug challenge (%):				
Any positive response	119 (42)	76 (56)	9 (43)	0.35
Negative response	163 (58)	60 (44)	12 (57)	
Passive+drug challenge (%):				
Asystolic response (VASIS 2B)	24 (9)	28 (21)	0 (0)	0.03
Any non-asystolic response	258 (91)	108 (79)	21 (100)	
Passive only (%):				
Any positive response	27 (10)	22 (16)	2 (10)	0.74
Negative response	255 (90)	114 (84)	19 (90)	

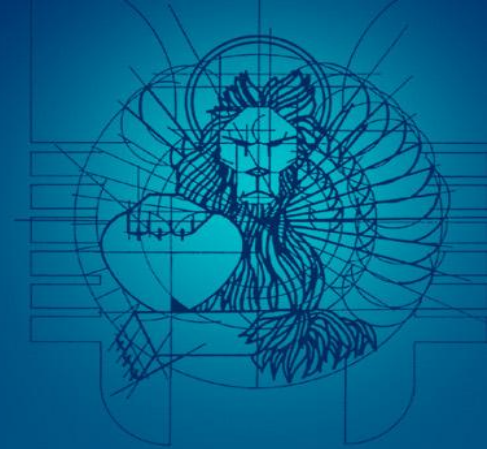
ILR, implantable loop recorder; NMS, neurally mediated syncope; TT, table testing.

HUTT / Diagnosis of VVS



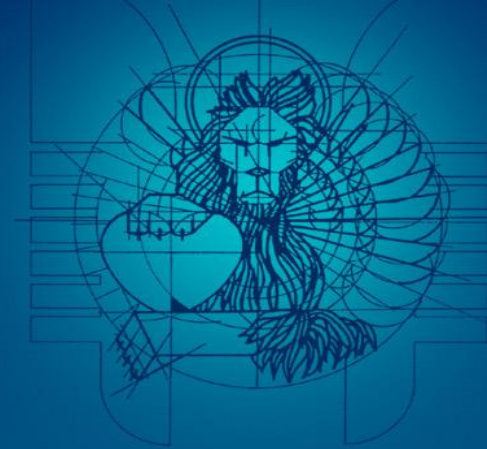
- Tilt testing offers **no diagnostic value in those for whom it is most needed** providing the basis for its critical appraisal.
- A possible explanation for this is that a positive tilt test suggests only **the presence of a hypotensive/vasodepressor susceptibility**, which may exist not only in reflex syncope but also in coincidence with other causes of syncope.

HUTT / Diagnosis of VVS



- However, despite these considerations, I believe that tilt testing **will continue to have in the future an important role in the diagnosis of VVS** that are difficult to make for nonexperts and in some cases also for experts in syncope

Uses / Head-up tilt test



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HUTT / Diagnosis of other conditions



- These conditions can have similar presentations and can be very difficult for most physicians to separate from VVS on clinical grounds alone.

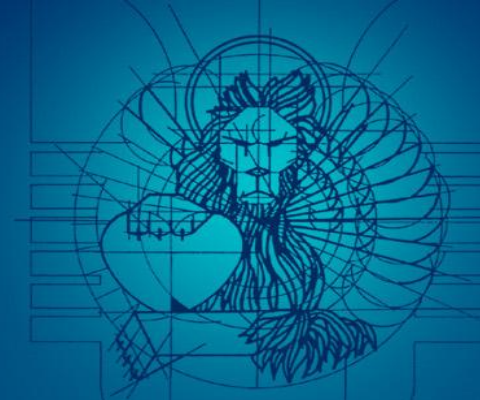
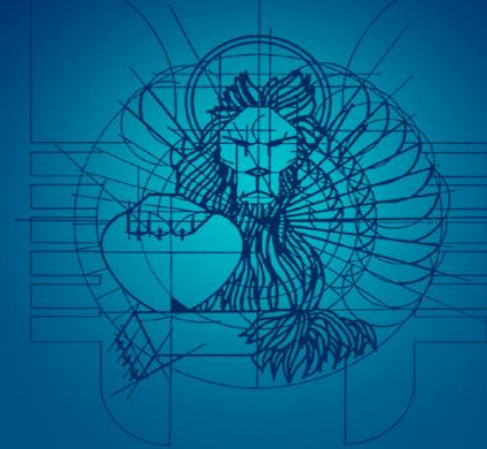


Table 1
Conditions in which tilt testing is valuable

Condition	Physiologic Changes	Value
Vasovagal syncope	Delayed BP fall, brady	Diagnostic if usual symptoms
Orthostatic hypotension	Immediate BP fall, No brady	Diagnostic
POTS	Modest prog BP fall, tachy	Diagnostic if usual symptoms
Psychogenic pseudosyncope	No physiol change (tachy)	Apparent LOC is diagnostic

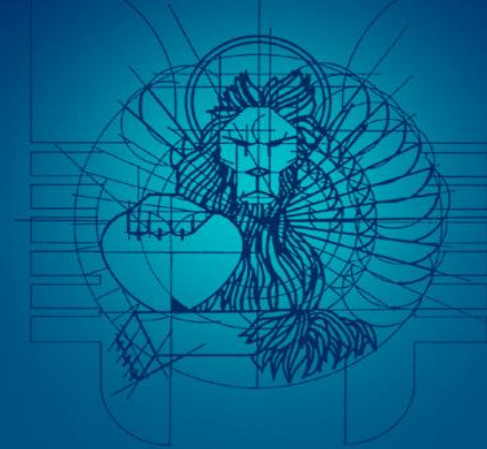
Abbreviations: BP, blood pressure; brady, bradycardia; LOC, loss of consciousness; prog, progressive; tachy, tachycardia.

Uses / Head-up tilt test

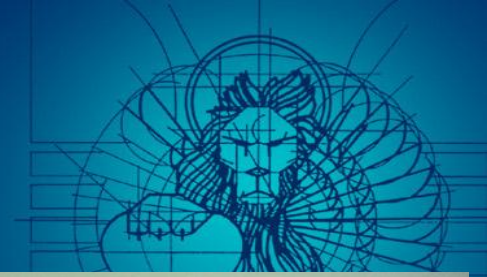


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**Leg Crossing &
Muscle Tensing**

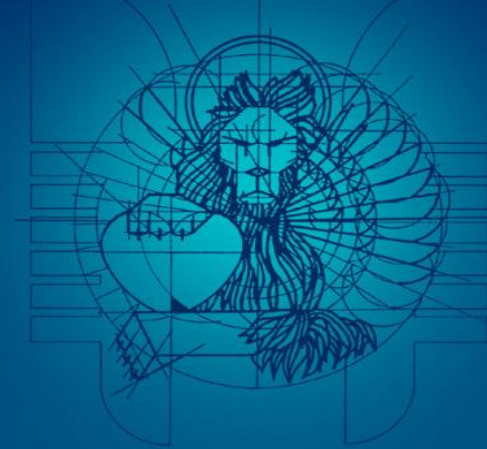


Handgrip

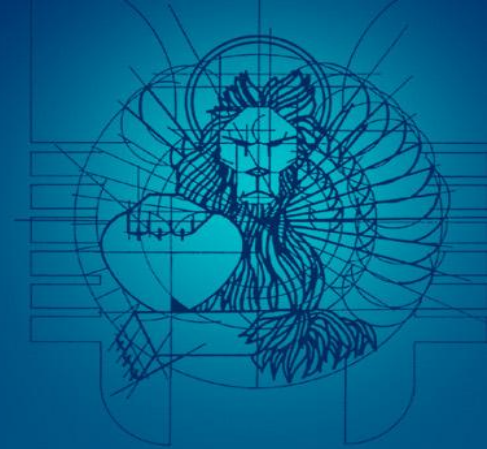


Arm muscle tensing

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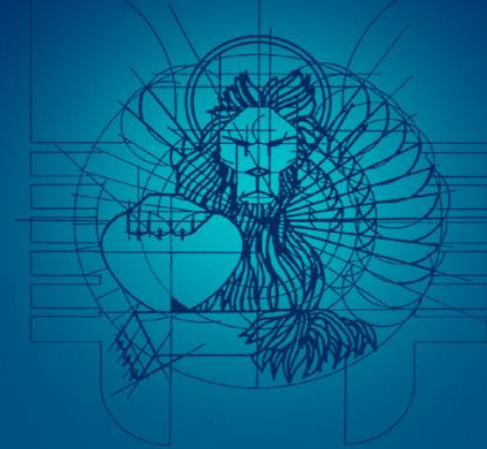


Tilt Training: A New Treatment for Recurrent Neurocardiogenic Syncope and Severe Orthostatic Intolerance

HUGO ECTOR¹, TONY REYBROUCK^{2,3}, HEIN HEIDBÜCHEL¹, MARC GEWILLIG²,
FRANS VAN DE WERF¹

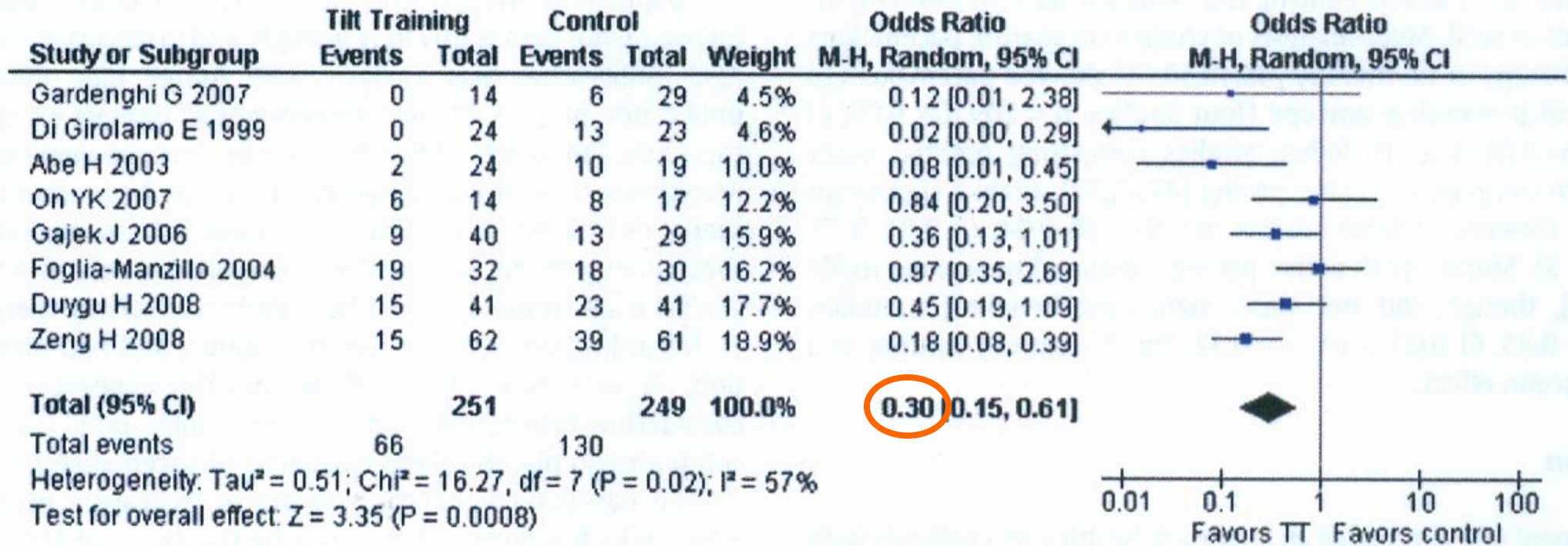
PACE 1998;21:193-196

HUTT / Tilt Training



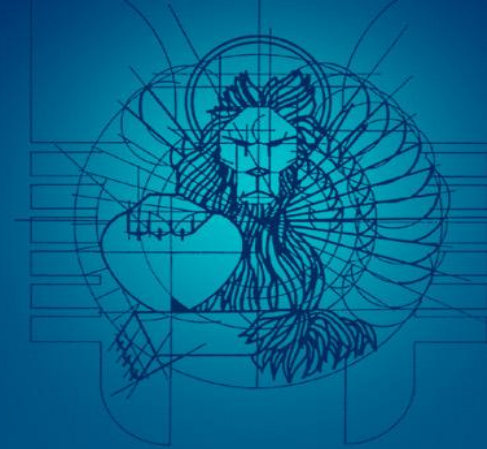
- 5 in-hospital head-up tilt sessions for a planned duration of 10-50 minutes at 60° (once a day for 5 days)
- daily tilt training at home by standing against a wall for a planned duration of up to 40 minutes (twice a day)

A recent metanalysis of all studies performed with tilt training has shown that this therapy is effective in preventing recurrences of VVS with 70% decrease



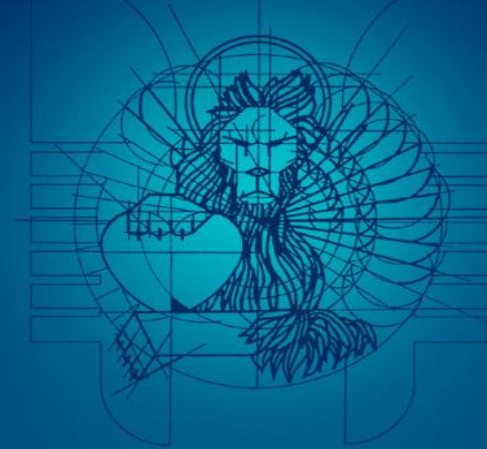
- However, the effect is lost if only randomized studies are included.
- Moreover, tilt training is hampered by the low compliance of the patients to continue the treatment for a long period of time.

HUTT / Tilt Training



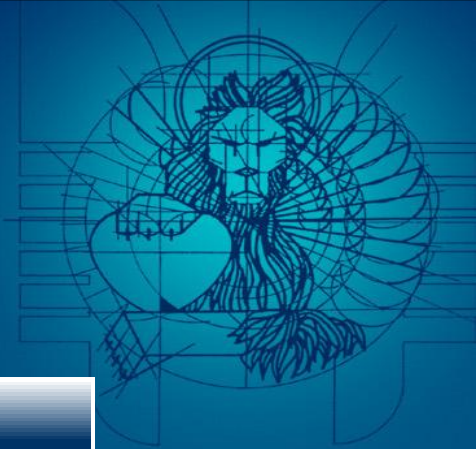
- Tilt training, at best, and if really effective, may be recommended only in a very selected group of highly motivated patients.

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HUTT/ Selection of drug therapy



1st HUTT positive



Acute Drug Test

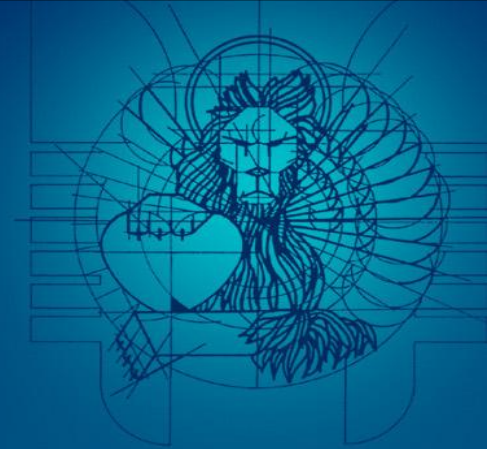


2nd HUTT negative



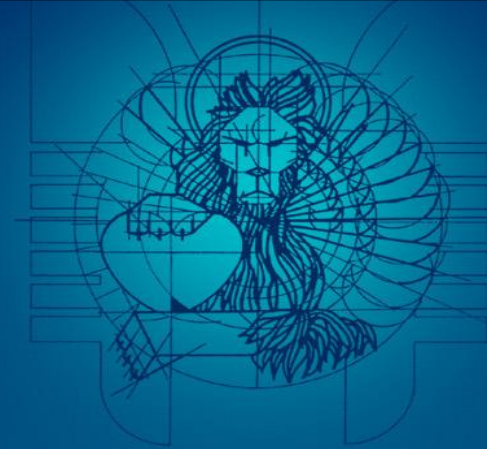
The drug is effective and is administered chronically

Assumptions



- High reproducibility of a positive response to baseline HUTT
- Existence of drugs really effective in preventing vasovagal syncope

HUTT/ Reproducibility



Negative Response

85% - 94%

Positive Response

31% - 92%

Sheldon AJC 1992, Grubb PACE 1992, De Buitler AJC 1993,
Brooks AJC 1993, Blanc AJC 1993

VVS/ Placebo-controlled trials



**No Difference in the Recurrence Rate
of Syncope during Follow-up**

**Pts Treated
With Drugs**

**Pts treated
With placebo**

**raising serious doubts about the real effectiveness of any drug
therapy for VVS**

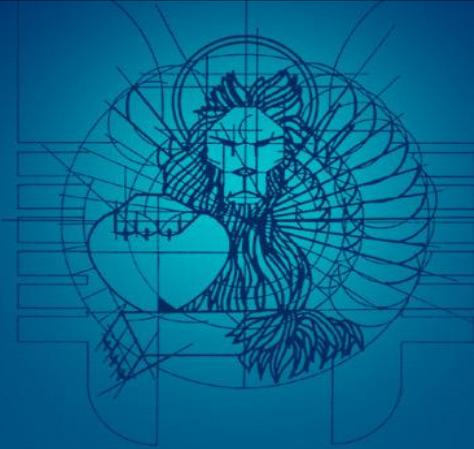
HUTT/ Selection of drug therapy



How can tilt test predict the efficacy of drug therapy

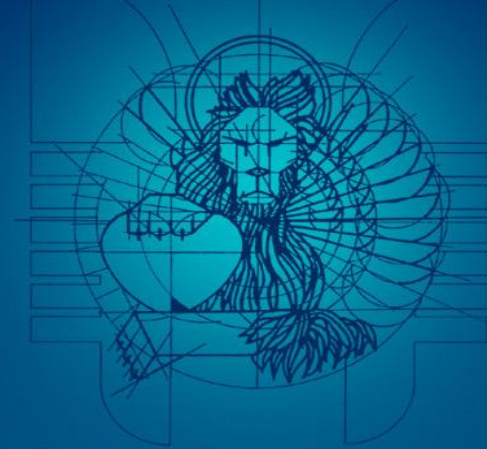
- If the **reproducibility** of positive responses to baseline head-up tilt testing is **low**
- If there is **no effective drug** to test

HUTT/ Selection of drug therapy



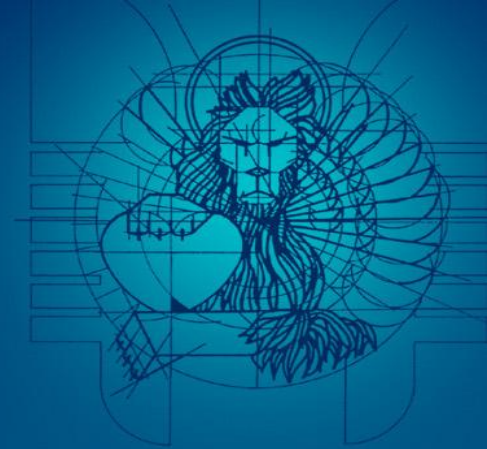
- Serial HUTT is **not a reliable method to select chronic drug therapy** in patients with VVS and should not be used to this purpose

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HUTT / PM implantation



- Based on the documentation of a **tilt-induced ventricular asystole > 3 sec** at the time of occurrence of vaso-vagal reaction

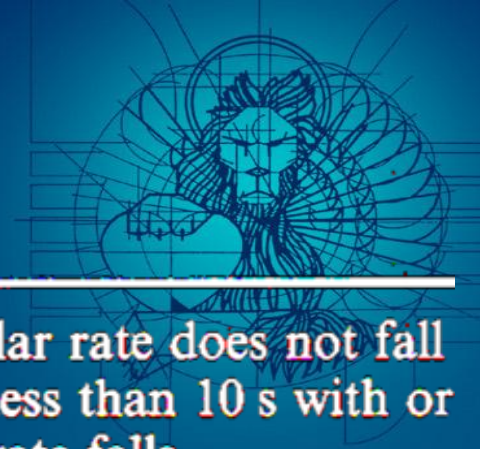


Table 2.4 *Classification of positive responses to tilt testing*

- Type 1 Mixed. Heart rate falls at the time of syncope but the ventricular rate does not fall to less than 40 beats $\cdot \text{min}^{-1}$ or falls to less than 40 beats $\cdot \text{min}^{-1}$ for less than 10 s with or without asystole of less than 3 s. Blood pressure falls before the heart rate falls.
- Type 2A Cardioinhibition without asystole. Heart rate falls to a ventricular rate less than 40 beats $\cdot \text{min}^{-1}$ for more than 10 s but asystole of more than 3 s does not occur. Blood pressure falls before the heart rate falls.
- Type 2B Cardioinhibition with asystole. Asystole occurs for more than 3 s. Blood pressure fall coincides with or occurs before the heart rate fall.
- Type 3 Vasodepressor. Heart rate does not fall more than 10% from its peak at the time of syncope
- Exception 1. Chronotropic Incompetence. No heart rate rise during the tilt testing (i.e. less than 10% from the pre-tilt rate).
- Exception 2. Excessive heart rate rise. An excessive heart rate rise both at the onset of the upright position and throughout its duration before syncope (i.e. greater than 130 beats $\cdot \text{min}^{-1}$).



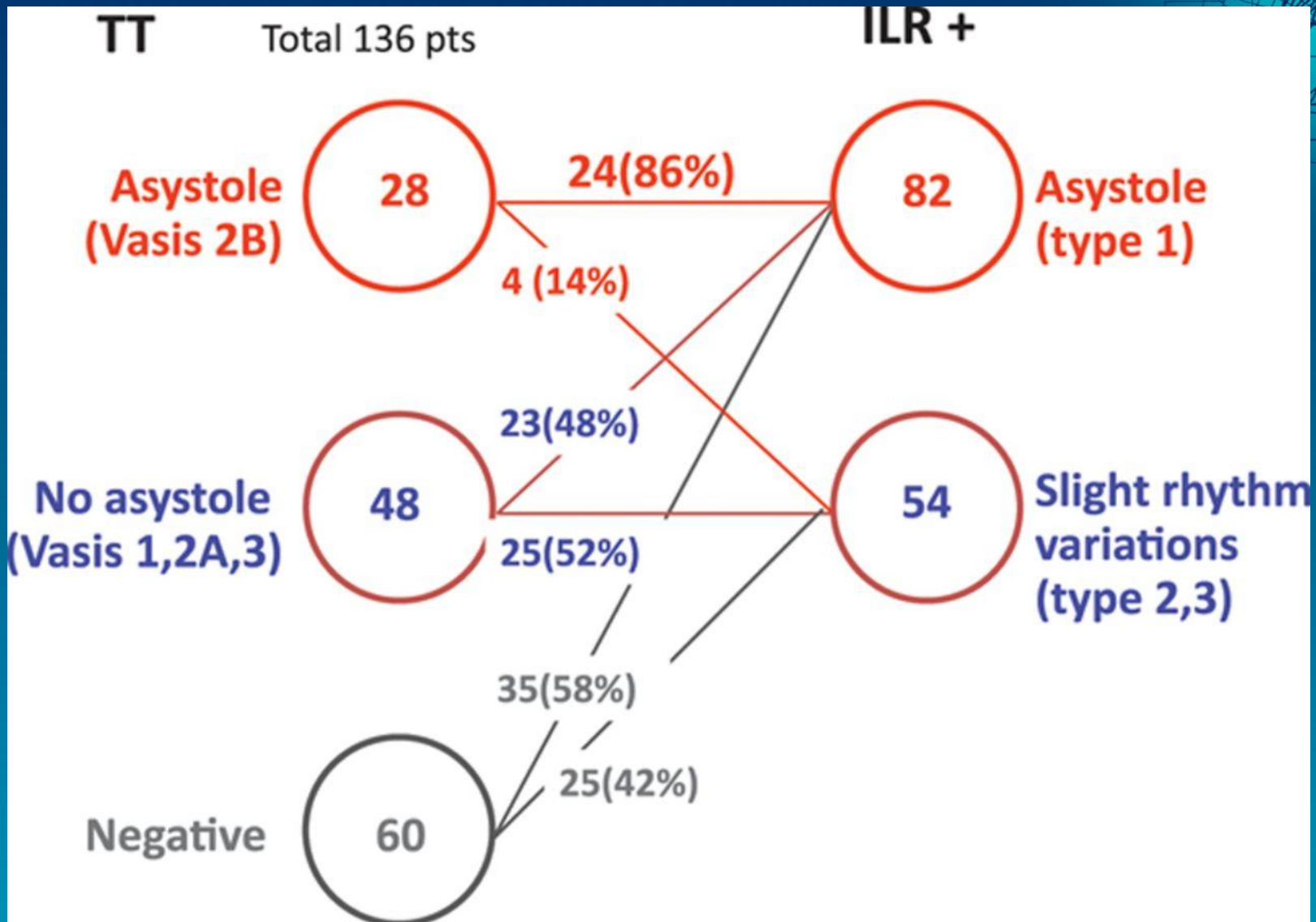
Benefit of Pacemaker Therapy in Patients With Presumed Neurally Mediated Syncope and Documented Asystole Is Greater When Tilt Test Is Negative

An Analysis From the Third International Study on Syncope of Uncertain Etiology (ISSUE-3)

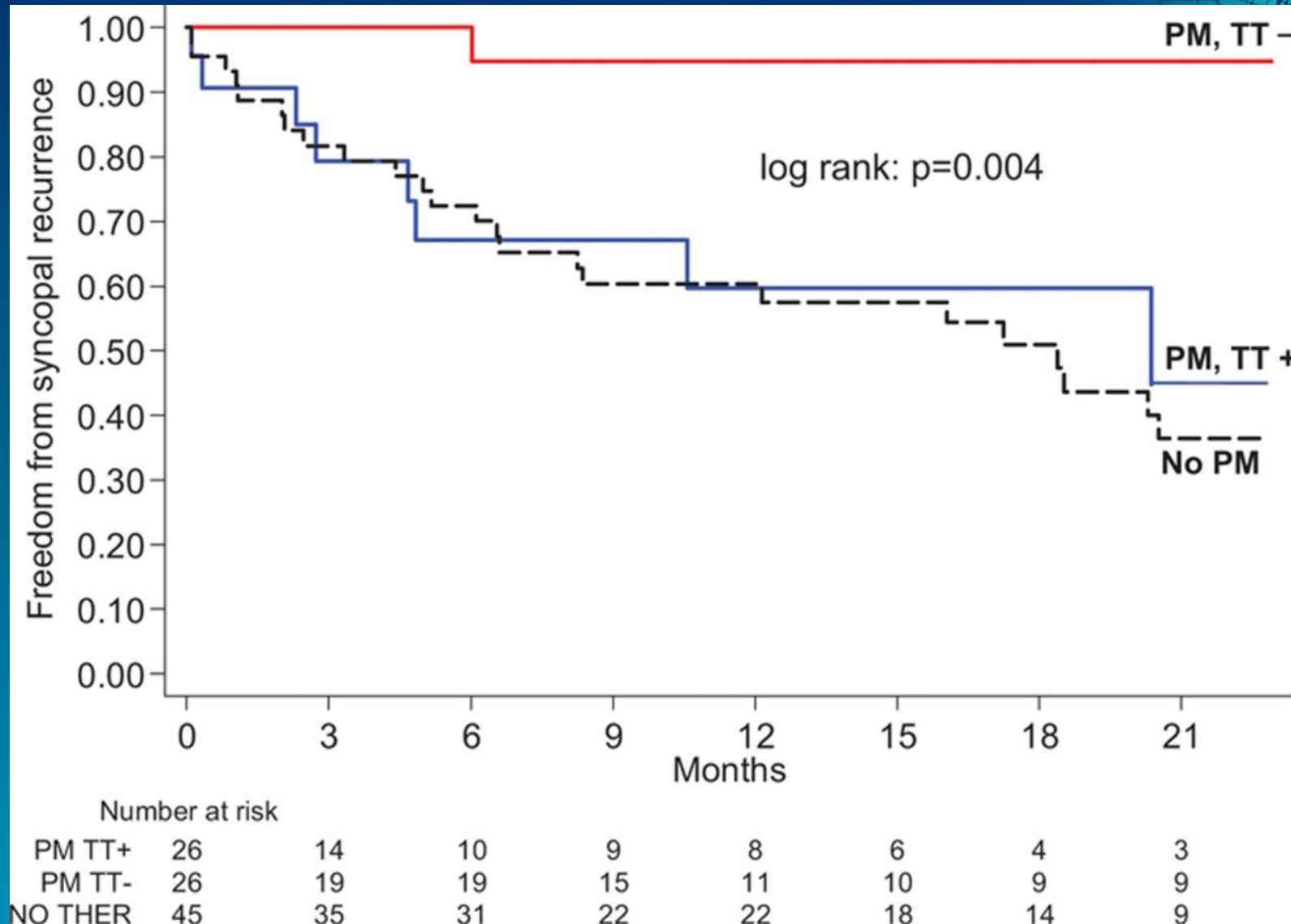
Michele **Brignole** MD; Paolo Donateo, MD; Marco Tomaino, MD; Riccardo Massa, MD; Matteo Iori, MD; Xulio Beiras, MD; Angel Moya, MD; Teresa Kus, MD, PhD; Jean Claude Deharo, MD; Silvia Giuli, MSc; Alessandra Gentili, MSc; Richard Sutton, DSc; on behalf of the International Study on Syncope of Uncertain Etiology 3 (ISSUE-3) Investigators

Circ Arrhythm Electrophysiol 2014; 7: 10-16

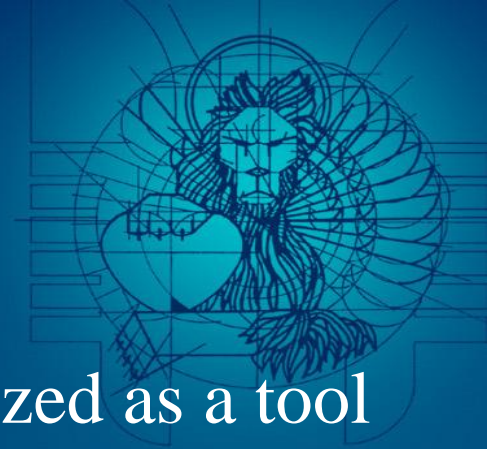
Correlation between tilt test (TT) responses and the mechanism of syncope, as documented by implantable loop recorder (ILR).



Kaplan–Meier freedom from syncope recurrence after pacemaker therapy in tilt-negative asystolic neurally mediated syncope (NMS) and in tilt-positive asystolic NMS patients.

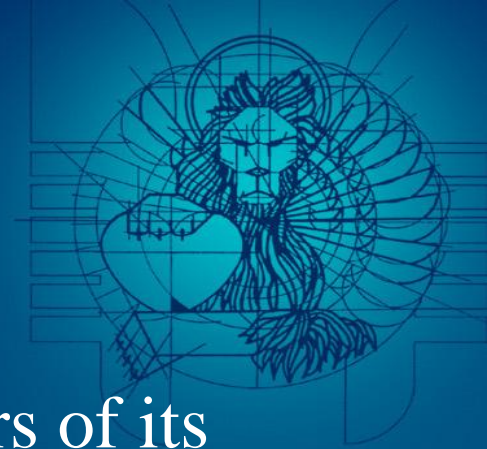


HUTT / PM implantation



- These results suggest that HUTT may be utilized as a tool to decide pacemaker implantation in patients with presumed VVS but, paradoxally and differently from what believed in the past, only for **patients with negative response to HUTT** and with documented asystole during spontaneous syncopal recurrences in the follow-up.
- On the contrary, caution should be recommended over pacemaker implantation in **patients showing asystole during HUTT**.

Conclusions



- Head-up tilt testing, still remain, after 28 years of its introduction in clinical practice, **a valuable investigation** in the management of patients with syncope **but its role is changing from a test essentially aimed at the diagnosis of VVS to a useful tool** to diagnose other clinical conditions such as orthostatic hypotension, POTS and psychogenic pseudosyncope, to educate & reassure pts, to teach physical maneuvers, and **to decide PM implantation in patients with presumed VVS** and documented asystole during follow-up

