



STOP VASODEPRESSOR DRUGS IN REFLEX SYNCOPE (STOP-VD) A RANDOMIZED CONTROLLED TRIAL

Diana Solari, MD (1); Francesca Tesi, MD (2); Matthias Unterhuber, MD (3); Germano Gaggioli, MD (4); Andrea Ungar, MD (2); Marco Tomaino, MD (3); Michele Brignole, MD (1)

(1) Arrhythmologic Center, Department of Cardiology, Ospedali del Tigullio, Lavagna, Italy; (2) Cardiology and Geriatric Medicine, University of Florence, AOU Careggi, Florence, Italy; (3) Division of Cardiology, Ospedale Generale regionale, Bolzano, Italy; (4) Division of Cardiology, ospedale Villa Scassi, Genova, Italy (Gaggioli)

IMPORTANCE. Most elderly patients affected by reflex vasodepressor syncope take one or more hypotensive drugs. The role of these drugs in causing syncope has not yet been established.

OBJECTIVE. To investigate the clinical effects of discontinuing vasoactive drugs in patients affected by vasodepressor reflex syncope.

DESIGN, SETTING AND PARTICIPANTS. Randomized, parallel, prospective, safety/efficacy study conducted from January 2014 to December 2015 in 4 general hospitals. Of 328 initially screened participants, 58 patients (mean [SD] age 74 ± 11 years) affected by vasodepressor reflex syncope, which was reproduced by tilt testing (#54) or carotid sinus massage (#4), were enrolled (247 were excluded by inclusion/exclusion criteria; 23 declined to participate).

INTERVENTIONS. Discontinuation or reduction of any vasoactive therapy as much as possible, according to clinical judgment.

MAIN OUTCOMES AND MEASURES. Time to recurrence of syncope, pre-syncope and adverse events.

RESULTS. Of the 58 patients enrolled, 32 were randomized to stop/reduce and 26 to continue vasoactive drugs therapy. Of these, 55 participants completed the trial. After 1 month, systolic blood pressure was significantly higher in the “stop/reduce” group than in the “continue” group, in both supine (141 ± 13 mmHg vs 128 ± 14 mmHg; $p=0.004$) and standing (133 ± 13 mmHg vs 122 ± 15 mmHg; $p=0.02$) positions. During a mean follow-up of 9 ± 7 months, the primary combined end-point occurred in 6 “stop/reduce” patients (19%): 2 had syncope, 3 pre-syncope and 1 heart failure. Conversely, it occurred in 12 “continue” patients (50%): 9 had syncope, 2 pre-syncope and 1 cerebral transient ischemic attack. The hazard ratio was 0.37 (95% CI 0.14 – 0.95).

CONCLUSIONS AND RELEVANCE. Recurrence of syncope and pre-syncope can be safely prevented by discontinuing/reducing vasoactive therapy in most elderly patients affected by reflex vasodepressor syncope.



Table 1. Results

<i>Outcome</i>	Stop/reduce therapy (n=31)	Continue therapy (n=24)	Hazard ratio (95% CI)	p value
Primary combined end-point (syncope and/or pre-syncope and/or adverse event)	6 (19%)	12 (50%)	0.37 (0.14-0.95)	0.03
Recurrence of syncope and/or pre-syncope	6 (19%)*	11 (46%)	0.41 (0.15-1.05)	0.05
Recurrence of syncope	2 (6%)	9 (37%)	0.17 (0.05-0.55)	0.007
Assessment at 1 month:				
- Office supine SBP, mmHg	141±13	128±14		0.001
- Office standing SBP, mmHg	133±13	122±15		0.006
- Home daily SBP (average of 30-day measurements)	141±15	133±16		0.06
- SSS-OI Questionnaire: total score (score 0-70)	7.2±8.8	13.1±10.6		0.04

SBP = systolic blood pressure

SSS-OI = Specific Symptom Score - Orthostatic Intolerance

Adverse events: 1 patient in the stop/reduce therapy group had an episode of acute heart failure; 1 patient in the Continue therapy group had a cerebral transient ischemic attack

*one patient had both an adverse event and pre-syncope

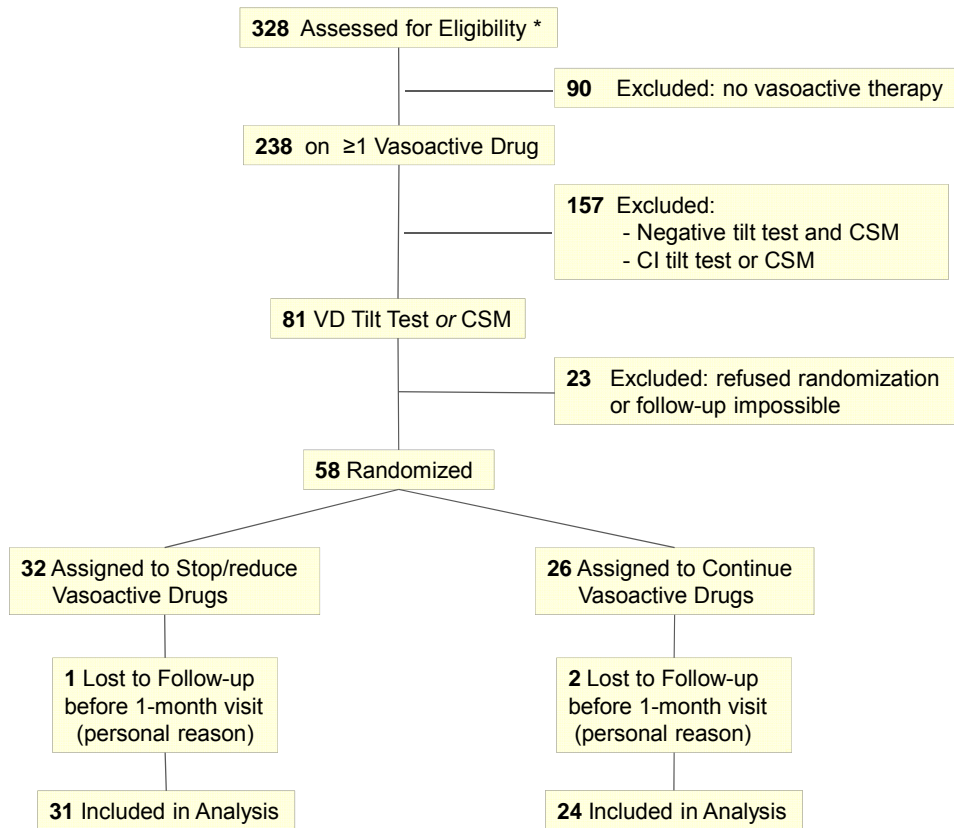
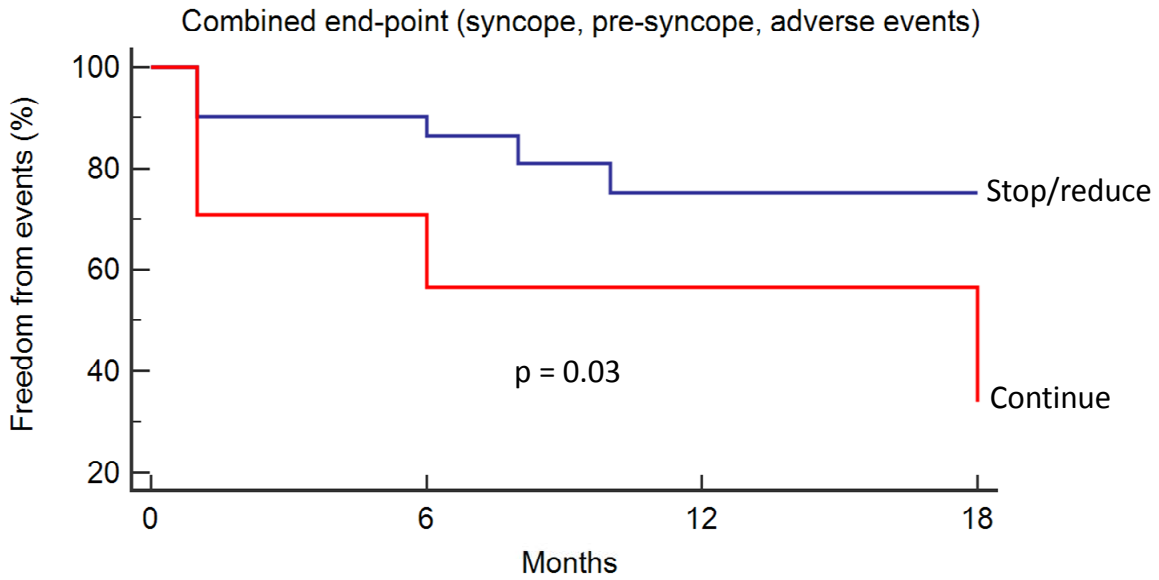


Figure 1. Screening flow.

* Criteria for eligibility:

- suspected or certain reflex syncope, age >40 years
- ≥ 2 syncopes/last year
- absence of orthostatic hypotension
- no competitive diagnoses
- no severe heart failure requiring life-threatening vasoactive therapy
- no previous TIA/stroke

Abbreviations: M= mixed; VD= vasodepressor; CSS= carotid sinus syndrome;



Number at risk

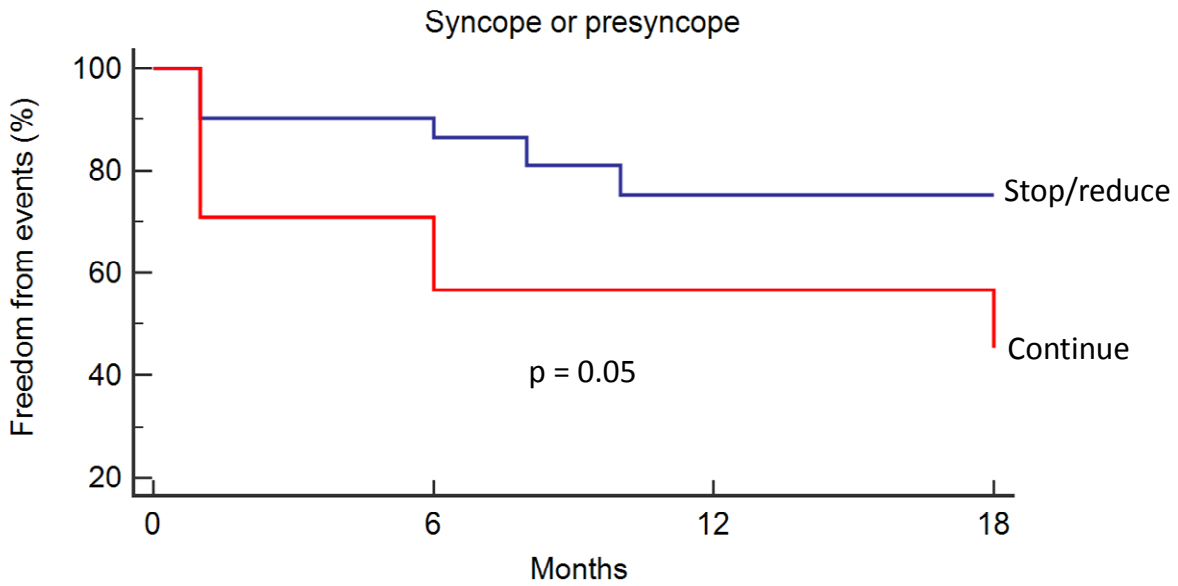
Stop/reduce vasoactive drugs

31 18 7 1

Continue vasoactive drugs

24 11 8 1

Figure 2. Combined end-point of syncope, pre-syncope and adverse events



Number at risk

Stop/reduce vasoactive drugs

31 18 7 1

Continue vasoactive drugs

24 11 8 1

Figure 3. Combined end-point of syncope and pre-syncope