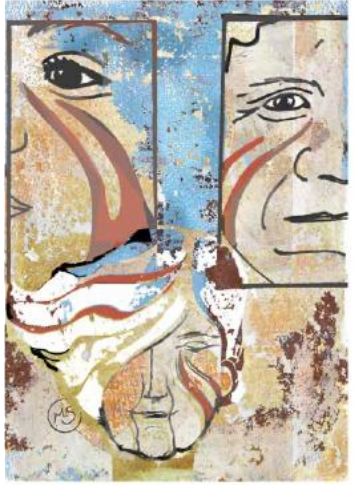


17·20 Dicembre 2025 Napoli

70° CONGRESSO NAZIONALE SIGG

LIBERI E LONGEVI

Università degli Studi di Napoli Federico II
Polo Didattico di **SCAMPIA**

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

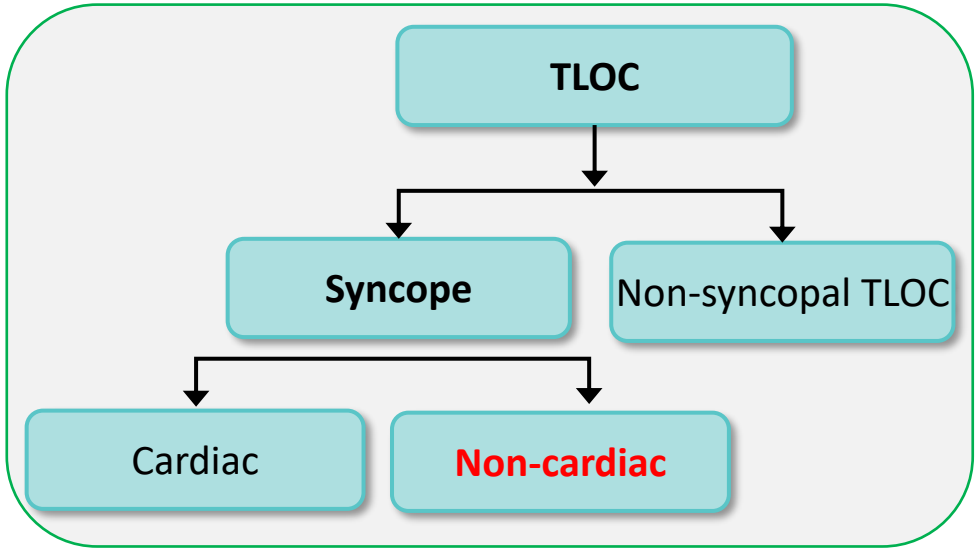
La terapia del fenotipo ipotensivo nel paziente ipoteso

Martina Rafanelli

Syncope Unit , Geriatria per l'Alta intensità e Cardiologia Geriatrica,
Università degli Studi di Firenze,
AOU Careggi, Firenze

Non-cardiac syncope

By etiology and clinical forms	By mechanism (ECG/BP documentation)
Reflex (neurally-mediated) Vasovagal Situational Carotid sinus Non-classical forms (including low-adenosine syncope)	**Intermittent bradycardia** Asystole: Sinus arrest Sinus bradycardia plus AVB Progressive (sinus) bradycardia
Orthostatic hypotension Primary autonomic failure Secondary autonomic failure Drug-induced Volume depletion	**Intermittent tachycardia** Progressive sinus tachycardia
	Intermittent hypotension Supine hypotension Orthostatic hypotension (early/classical or delayed)



The efficacy of therapy is largely determined by the mechanism of syncope rather than its aetiology or clinical presentation

Brignole M, Heart 2021

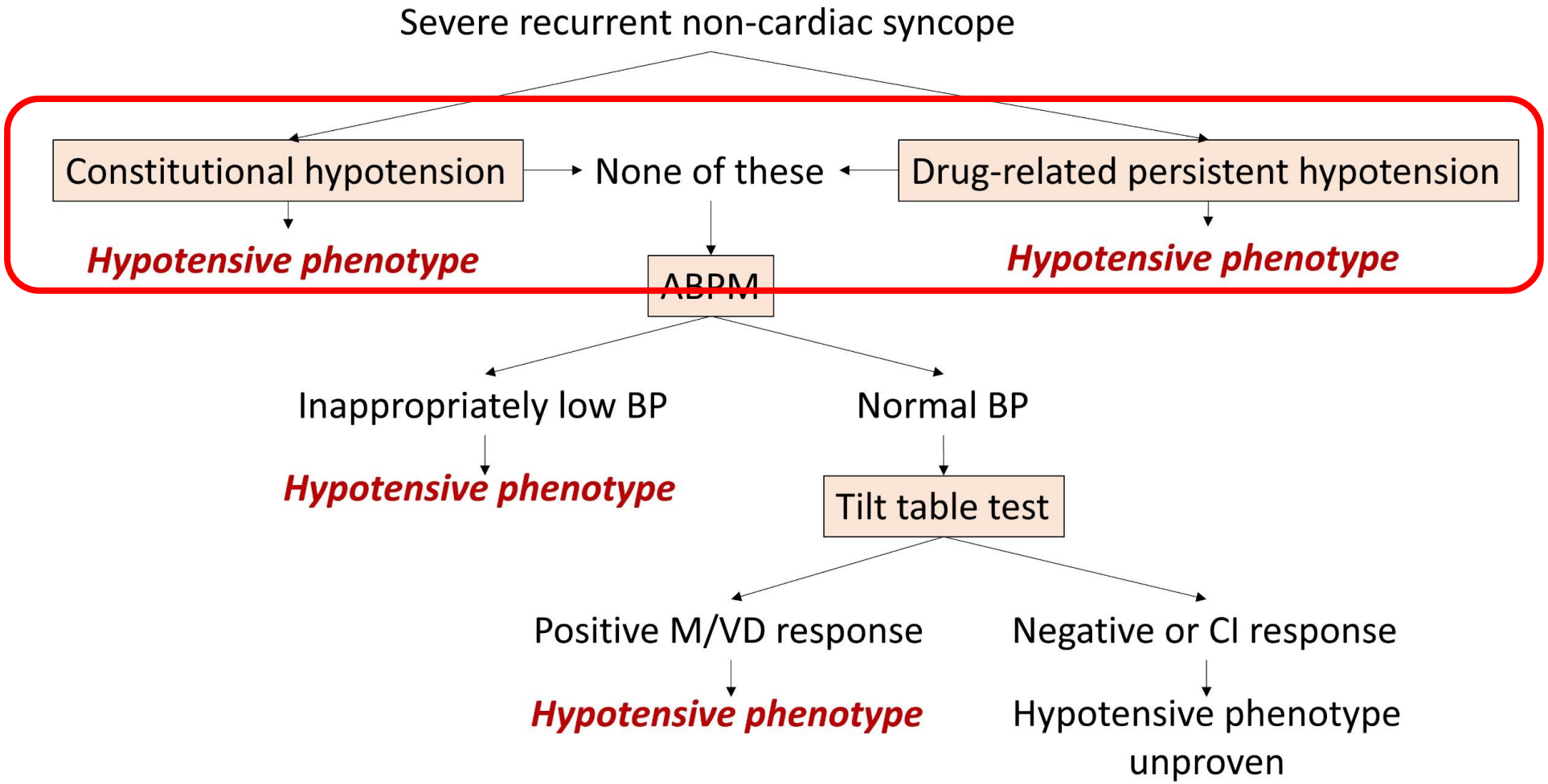
Mechanisms of non-cardiac syncope

Non-cardiac syncope	
Hypotensive phenotype	**Bradycardic phenotype**
Vasodepressor or mixed reflex syncope during TT	Cardioinhibitory response to TT
Vasodepressor or mixed carotid sinus syndrome	Cardioinhibitory carotid sinus syndrome
Blood pressure falls detected on 24h-ambulatory blood pressure monitoring	Syncopal reflex asystole (>3 sec) or non-syncopal reflex asystole (>6 sec) detected by ILR
	Low adenosine syncope

Abbreviations: ILR, implantable loop recorder; TT, Tilt Testing

Rivasi G et al., Kardiol Pol 2021

New insights in diagnostics and therapies in syncope: a novel approach to non-cardiac syncope



Brignole M. Heart 2021

Increasing Prevalence of Orthostatic Hypotension as a Cause of Syncope With Advancing Age and Multimorbidity

Alice Ceccofiglio MD [a], Chiara Mussi MD, PhD [b], Martina Rafanelli MD, PhD [a], Giulia Rivasi MD [a], Mario Bo MD, PhD [c], Enrico Mossello MD, PhD [a], Anna Maria Martone MD [d], Pasquale Abete MD, PhD [e], Andrea Ungar MD, PhD [a,*]

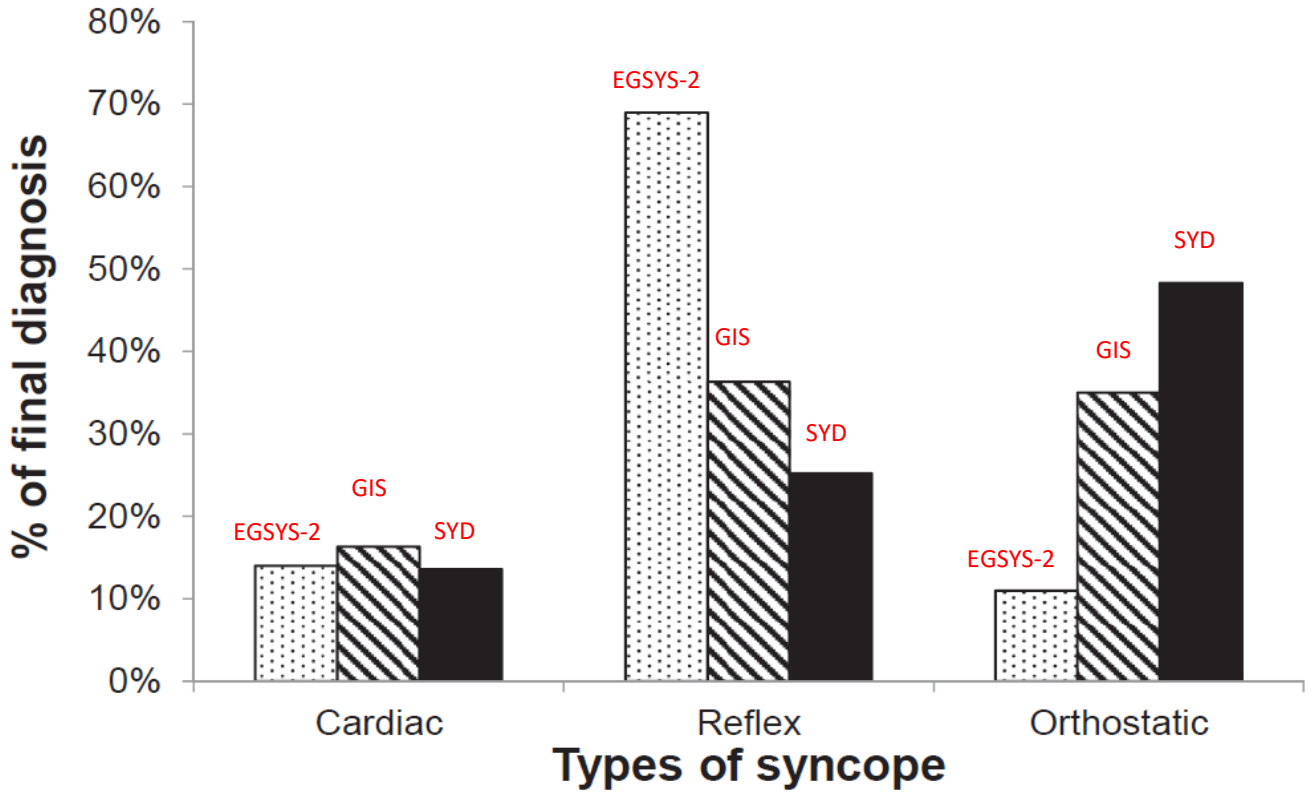


Fig. 1. Prevalence of cardiac, reflex, and orthostatic syncope in Evaluation of Guidelines in Syncope Study 2 (EGSYS-2) study, Italian Group for the Study of Syncope (GIS) study, and Syncope and Dementia (SYD) registry.
▪ = Evaluation of Guidelines in Syncope Study 2 (EGSYS-2) study
▨ = Italian Group for the Study of Syncope (GIS) study
■ = Syncope and Dementia (SYD) registry.

orthostatic syncope was more common in older subjects and was the leading cause of syncope in older patients with dementia.

JAMDA 20 (2019) 586–588

Syncope: new solutions for an old problem

Table 2. Diagnostic role of 24-hour ambulatory blood pressure monitoring in patients with syncope.

Diagnosis	Definition	BP cut-offs	
Constitutional hypotension	Blood pressure values <5th percentile of blood pressure appropriate for sex and time of day [30, 93]	Male 24-hour SBP <105 mm Hg Daytime SBP <115 mm Hg Nighttime SBP <97 mm Hg	Female 24-hour SBP <98 mm Hg Daytime SBP <105 mm Hg Nighttime SBP <92 mm Hg
Drug-related persistent hypotension	Blood pressure values persistently below the recommended target [37]	Customized blood pressure cut-off based on hypotensive and cardiovascular risks [37]	
Hypotensive drops	Episodic hypotension	≥1 episodes of daytime SBP <90 mm Hg [48]	
Orthostatic hypotension	Blood pressure drops during standing	Hypotensive episodes <90 mm Hg while standing (on patient's daily diary) may suggest OH A reverse dipping profile frequently coexists in patients with autonomic failure [46]	
Post-prandial hypotension	Blood pressure falls during or immediately after meals	Drop in SBP of 20 mm Hg within 75 min of eating meals, compared to the mean of the last three blood pressure measurements before the meal [45, 47, 94]	

Abbreviations: OH, orthostatic hypotension; SBP, systolic blood pressure

Rivasi G et al., Kardiol Pol 2021

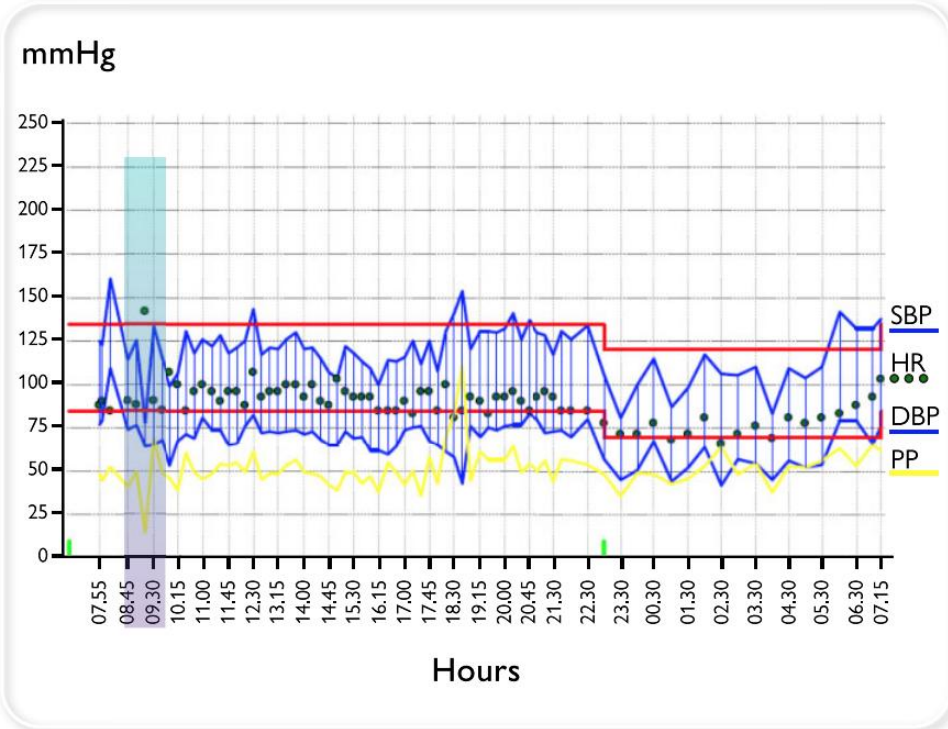
Association between hypotension during 24 h ambulatory blood pressure monitoring and reflex syncope: the SynABPM 1 study

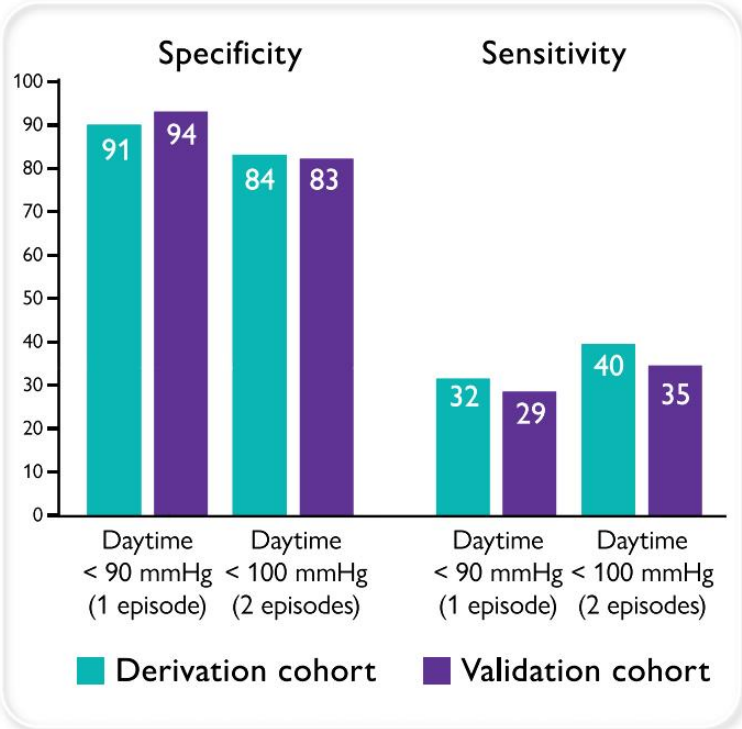
Giulia Rivasi [1]*, Antonella Groppelli[2], Michele Brignole [2], Davide Soranna[3], Antonella Zambon[3,4], Grzegorz Bilo [2], Martino Pengo [2], Bashaaer Sharad[5], Viktor Hamrefors [5], Martina Rafanelli[1], Giuseppe Dario Testa [1], Ciara Rice[6], Rose Anne Kenny[6,7], Richard Sutton [5,8], Andrea Ungar[1], Artur Fedorowski [5,9†], and Gianfranco Parati [2†]

In the derivation sample, daytime SBP drops were significantly more common in 158 syncope patients than 329 controls.

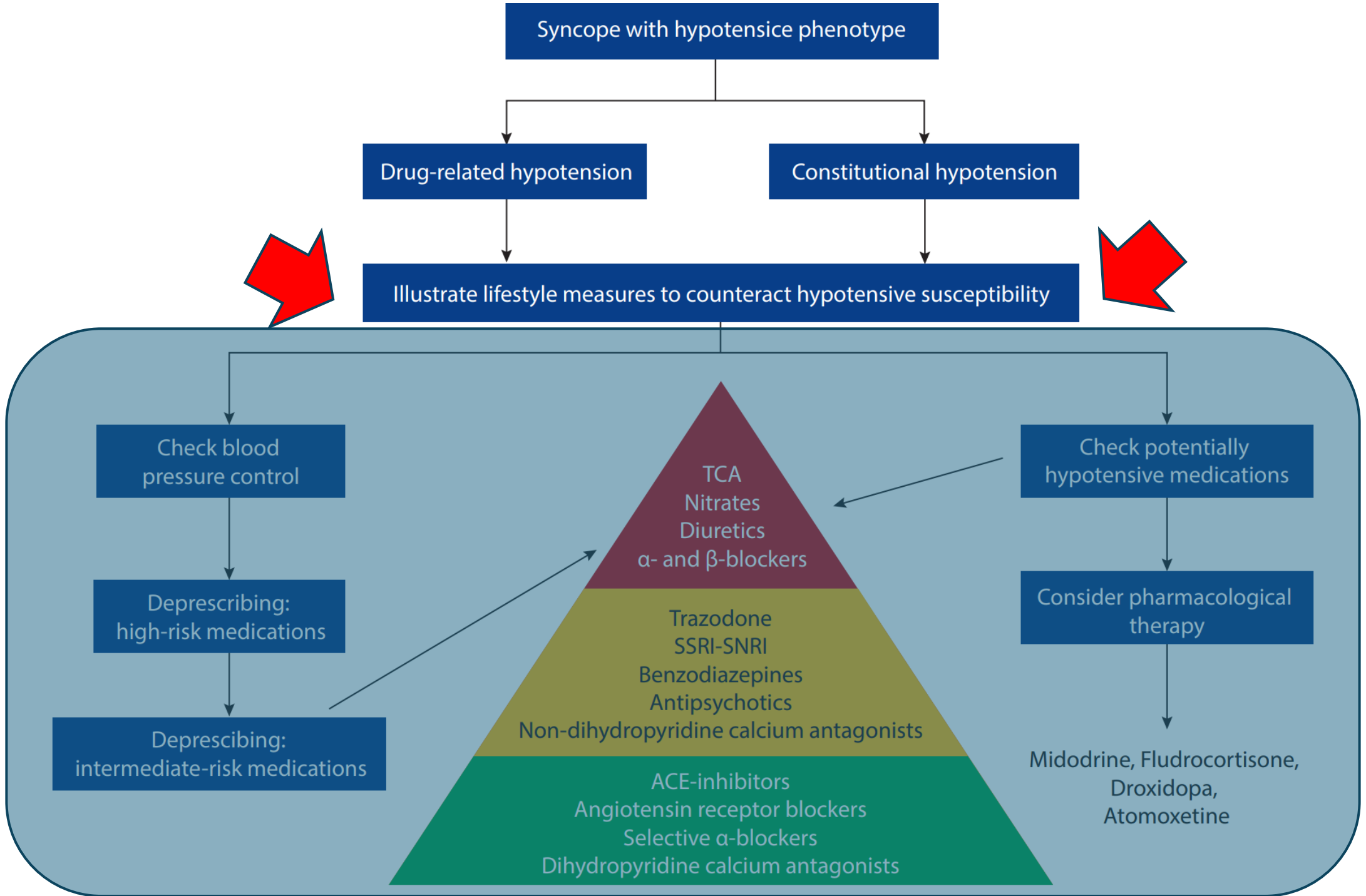
One or more daytime drops <90 mmHg achieved 91% specificity and 32% sensitivity [odds ratio (OR) 4.6, P< 0.001]. Two or more daytime drops <100 mmHg achieved 84% specificity and 40% sensitivity (OR 3.5, P=0.001).

Systolic blood pressure drops on ABPM may help to identify hypotensive susceptibility in reflex syncope patients





European Heart Journal (2022) **43**, 3765–3776

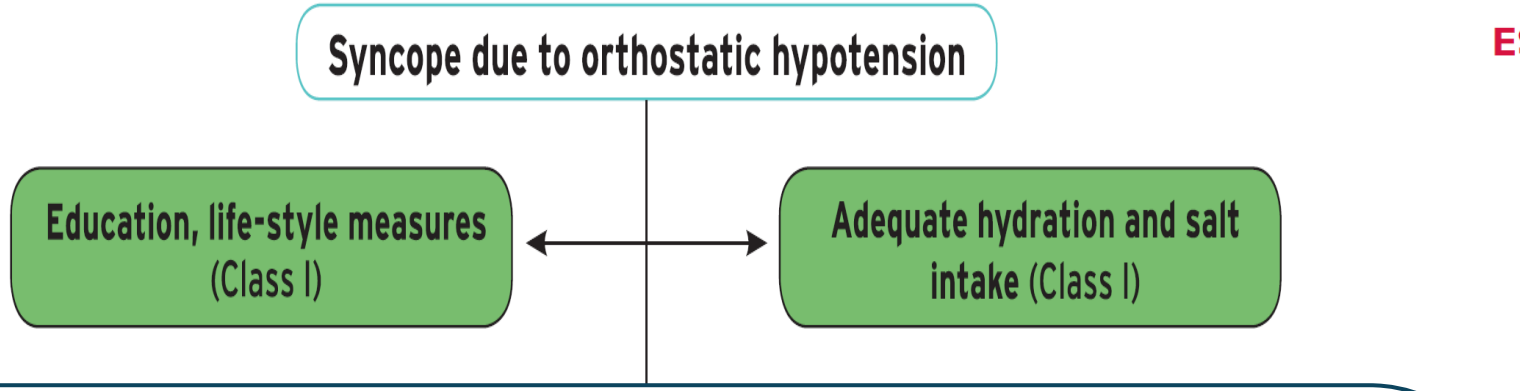

Syncope with hypotensice phenotype
Drug-related hypotension
Constitutional hypotension
Illustrate lifestyle measures to counteract hypotensive susceptibility
Check blood pressure control
Deprescribing: high-risk medications
Deprescibing: intermediate-risk medications
TCA
Nitrates
Diuretics
α- and β-blockers
Trazodone
SSRI-SNRI
Benzodiazepines
Antipsychotics
Non-dihydropyridine calcium antagonists
ACE-inhibitors
Angiotensin receptor blockers
Selective α-blockers
Dihydropyridine calcium antagonists
Check potentially hypotensive medications
Consider pharmacological therapy
Midodrine, Fludrocortisone, Droxidopa, Atomoxetine

2018 ESC Guidelines for the diagnosis and management of syncope

- Rassicurazione;
- Educazione ed evitamento di fattori favorenti e situazioni scatenanti;
- Precoce riconoscimento dei prodromi;
- Posizione di sicurezza.

Actions to take to avoid an impending attack of reflex syncope

European Heart Journal (2018) **39**, e43–e80



In assenza di HF/insufficienza renale, I pz. devono essere istruiti ad assumere 2-3 lt di acqua/die e fino a 10 g di NaCl nella dieta.

Nell'ipotensione post-prandiale o post-esercizio fisico, ingestione rapida di boli di acqua 500 cc.

Orthostatic hypotension: Review and expert position statement

Changes in the daily habits and environment of the patient can be a key element [78]. Such measures include standing up gradually, raising the bed by 10 ° (which, by reducing nocturnal natriuresis, prevents early morning OH), avoiding supine napping (by the use of a recliner), or installing a chair in the bathroom to enable seated showers. In very severe cases, a

Orthostatic hypotension: Review and expert position statement

6.1.3. Venous compression and physical maneuvers

Venous compression using elastic leg stockings reduces orthostatic systolic BP drop and is classically advised [74]. Compression therapy is more efficient when it extends to the waist, reducing venous pooling in the splanchnic and mesenteric circulations [82]. However, elastic stockings or

Guidance for the management of orthostatic hypotension

Persistence of symptoms and/or lack of blood-pressure response

- Education of the patient (exacerbating factors)
- Lifestyle modifications (non-pharmacologic treatment)

Cornerstone therapy is based on the use of midodrine and fludrocortisone. The initial drug should be started at low dose, and progressively increased. If there is no response to a single drug, combining midodrine and fludrocortisone has a strong pathophysiological rationale and appears to be more effective and better tolerated than increasing the dosage of a single

Progress in the pharmacological management of vasovagal syncope

Vincenzo Giosuè Giambusso[a], Martina Rafanelli[a] and Robert S. Sheldon[b]

Fludrocortisone

9.1. Rationale

The rationale for fludrocortisone is that as a mineralocorticoid it causes renal sodium retention and should expand intravascular volume. Most syncope occurs during upright positions, and head-up tilt alone can induce syncope [47,71]. Furthermore, fludrocortisone has been a cornerstone in the management of orthostatic hypotension attributed to autonomic failure [72]. Its mechanism of action may be similar to that of saline infusion, which prevents syncope in tilt test studies [73,74]. In turn, this might increase venous return and cardiac preload, thereby maintaining cardiac output and prevent hypotension.

Progress in the pharmacological management of vasovagal syncope

Vincenzo Giosuè Giambusso[a], Martina Rafanelli[a] and Robert S. Sheldon[b]

Fludrocortisone

Dosaggio 0.1-0.3 mg/die.

Lunga emivita, evitare come prima scelta in caso di ipertensione supina nota.

E. Coll: ipertensione supina, ipokaliemia, edema.

EXPERT REVIEW OF CLINICAL PHARMACOLOGY
https://doi.org/10.1080/17512433.2025.2596875

Progress in the pharmacological management of vasovagal syncope

Vincenzo Giosuè Giambusso[a], Martina Rafanelli[a] and Robert S. Sheldon[b]

Fludrocortisone

9.2. Evidence

The multicenter POST 2 was a randomized, placebo-controlled, double-blind trial [75] that assessed the effects of fludrocortisone in vasovagal syncope over a 1-year treatment period.

When restricted to patients who achieved a stabilized dose of 0.2 mg, there was a significant reduction in symptoms due to treatment with fludrocortisone (HR 0.51, $p = 0.019$).

Midodrine *Rationale*

Midodrine, a synthetic sympathomimetic amine, is a prodrug. It is rapidly hydrolyzed in the liver to desglymidodrine, an active metabolite that selectively stimulates peripheral α1-adrenergic receptors [80]. This induces vasoconstriction of arterial and venous capacitance vessels, increasing systemic vascular resistance and augmenting venous return, cardiac output, and blood pressure. Midodrine's application in VVS directly targets core

The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension

Midodrina

2.5-10 tid. Emivita breve.

Ore 08:00-12:00-16:00. Evitare somministrazione serale.

E. Coll: Piloerezione, parestesie cuoio capelluto, ritenzione urinaria.

Particolare attenzione in caso di coronaropatia, vasculopatia e IPB.

Gibbons C.H et al. J Neurol 2017

Droxidopa for neurogenic orthostatic hypotension

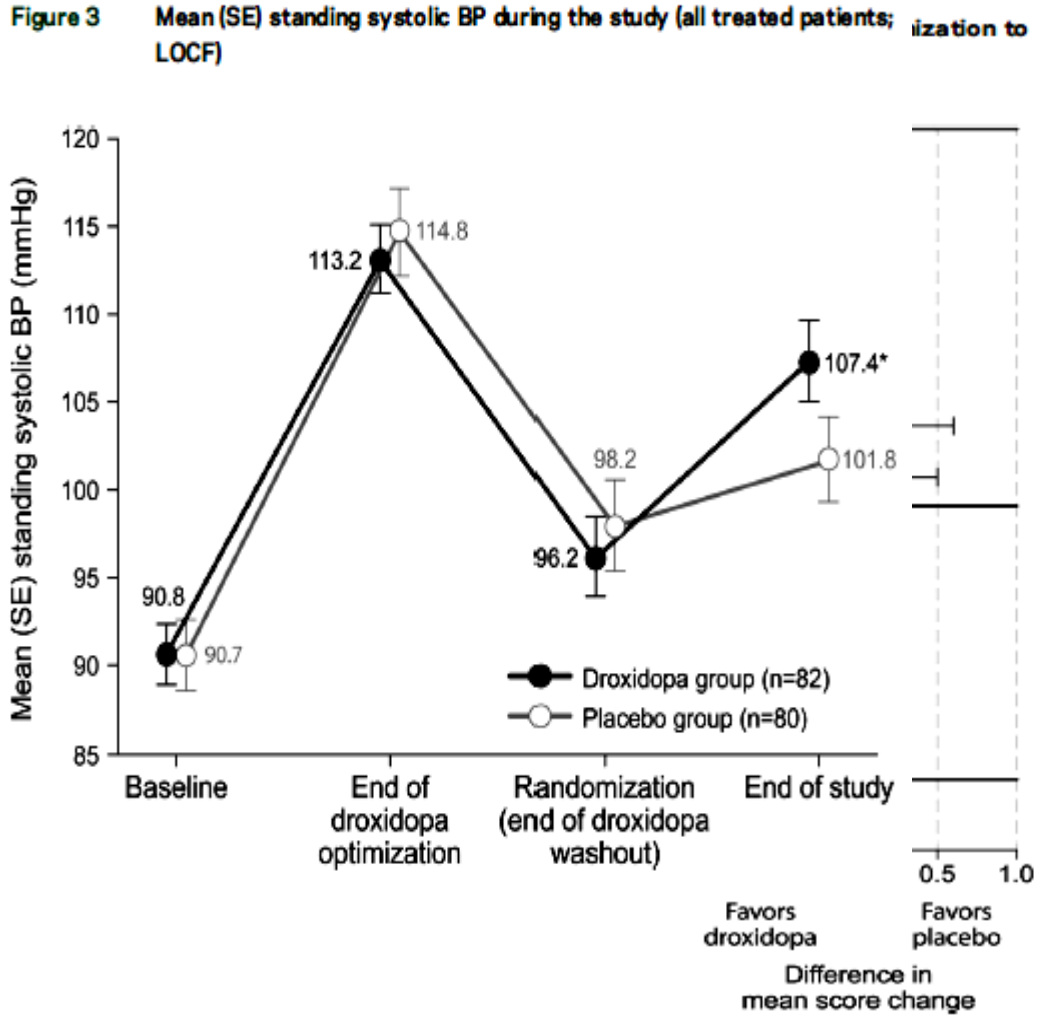
A randomized, placebo-controlled, phase 3 trial

Droxidopa (L-threo-3,4-dihydroxyphenylserine) is an orally administered artificial amino acid converted both peripherally and centrally into norepinephrine. Because the enzyme responsible for this conversion, aromatic amino acid decarboxylase, is widely expressed, administration of droxidopa increases norepinephrine even if postganglionic sympathetic neurons are not intact.

Horacio Kaufmann, MD Neurology® 2014;83:328-335

Droxidopa for neurogenic orthostatic hypotension

A randomized, placebo-controlled, phase 3 trial



Miglioramento dei sintomi

e dell'influenza degli stessi sulla qualità della vita

Dalla randomizzazione alla fine dello studio si osserva un aumento di PAS in ortostatismo nei soggetti trattati

Horacio Kaufmann, MD Neurology® 2014;83:328-335

The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension

Droxidopa 60-100 mg tid. Emivita breve

Ore 08:00-12:00-16:00. Evitare somministrazione serale.

E. Coll: cefalea, vertigine, nausea, astenia, ipertensione supina.

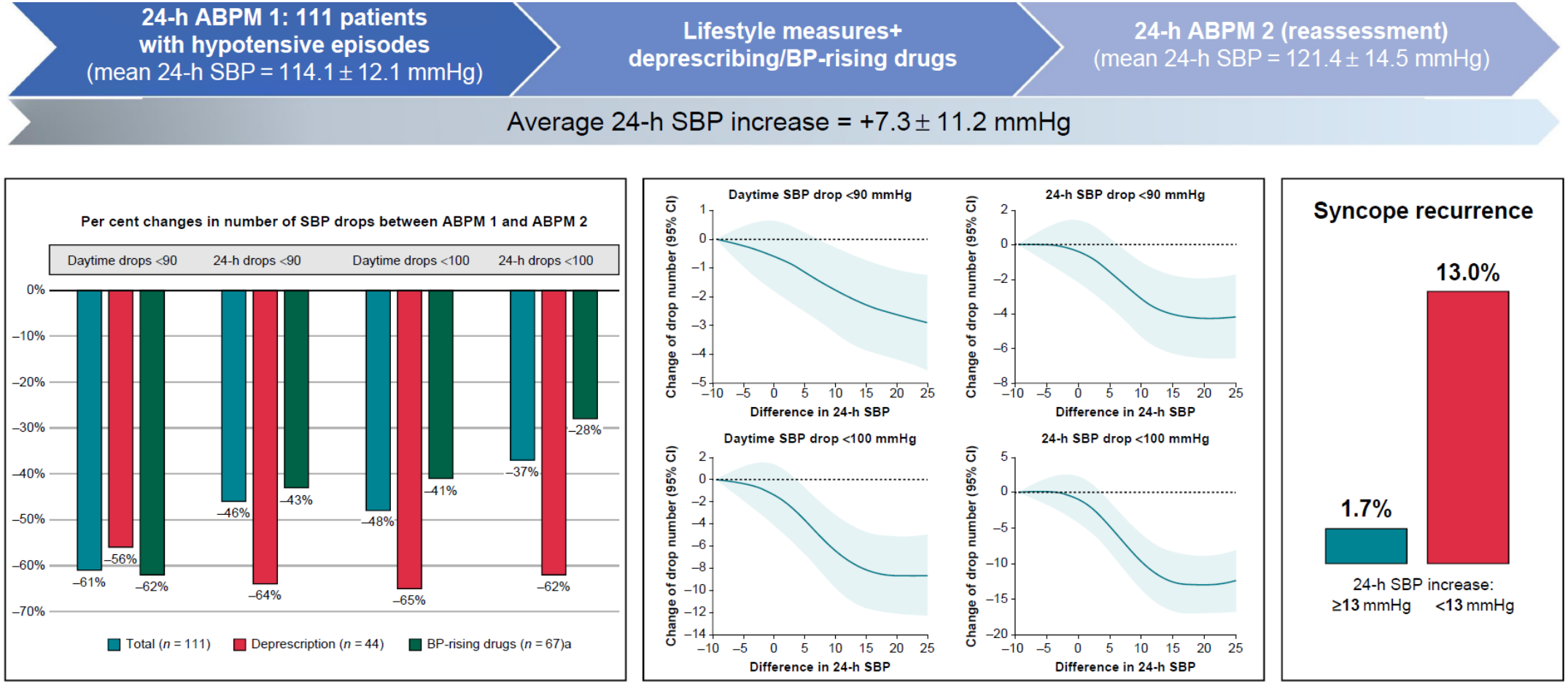
Gibbons C.H et al. J Neurol 2017

Table 3 – Summary of the drugs used for the treatment of orthostatic hypotension (OH).

Drug *Mechanism of action*	Recommended dose	Side effects[a]
Midodrine *Direct α_1-adrenergic receptor agonist*	2.5–15 mg 2 or 3 times and 3–4 h before going to bed or tailored to the patients' needs	Piloerection (goose bumps), itchy scalp, urine retention, bradycardia
Fludrocortisone *Synthetic mineralocorticoid agonist*	50 – 200 μg once a day	Hypokalemia, edema, hypertension related end-organ damage
Droxidopa *Synthetic norepinephrine precursor*	100–600 mg 3 times a day and 3–4 h before going to bed or tailored to the patient's needs	Headache, nausea, fatigue
Acarbose *Alpha-glycosidase inhibitor*	50–150 mg before meals (only recommended for post-prandial hypotension)	Abdominal gas, bloating
Atomoxetine *Norepinephrine reuptake inhibitor*	10–18 mg twice a day	Insomnia, irritability, decreased appetite
Pyridostigmine *Acetylcholinesterase inhibitor*	30–60 mg 2 or 3 times a day	Abdominal cramps, diarrhea, sialorrhea, excessive sweating, urinary incontinence

[a] All drugs induce supine hypertension except acarbose and pyridostigmine and should be used with caution in patients at risk for cardiac and renal failure.

Interventions aimed to increase average 24-h systolic blood pressure reduce blood pressure drops in patients with reflex syncope and orthostatic intolerance



Interventions aimed to increase average 24-h systolic blood pressure reduce blood pressure drops in patients with reflex syncope and orthostatic intolerance

Europace (2024) **26**, 1–9