

Orthostatic Hypotension in Elderly

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Chairman: Dr CY Yung

M&G UCH

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Overview

- Case history
- Physiology of blood pressure control
 - Failure to maintain blood pressure
- Aetiology of orthostatic hypotension
- Presentation and diagnosis
- Management of orthostatic hypotension
 - Non-pharmacological
 - pharmacological

Case History

- 90M. Lives alone. ADL independent. Walks with stick
- Dizziness/ diarrhoea/ vomiting
 - On and off dizziness for 2 years, worse on standing
 - Diarrhoea and vomiting for 1-2 days
 - Poor drug compliance
- PMH: hypertension/ hyperlipidaemia/ chronic kidney disease/ benign prostatic hypertrophy

Case History – Drug History

- Amlodipine 5mg daily
- Furosemide 40mg daily
- Losartan 100mg noon
- Methyldopa 500mg BD
- Terazosin HCL 6mg nocte
- Simvastatin 5mg nocte
- Hypromellose eye drops 1 drop QID/PRN

Case History – P/E

- Temp 37.8; BP 212/100; P 97
- Mildly dehydrated
- Otherwise examination unremarkable
- Bloods: WBC $10.6 \times 10^9/\text{L}$ (H); HGB 13.1g/dL(L); MCV 90.3fL; Plat $160 \times 10^9/\text{L}$; Na 144mmol/L; K 4.5mmol/L; Urea 14.5(H)mmol/L; Creat 184umol/L(H) (baseline Creat ~220); ALP 112IU/L; albumin 30g/L(L); ALT 40IU/L
- ECG/CXR/AXR: unremarkable

Why is he feeling dizzy?

- Multiple medications?
- Dehydration/ viral illness?
- Visual impairment?
- Cerebrovascular disease?
- Neck disorder?
- Autonomic dysfunction?
- Psychiatric disorder?
- Others?

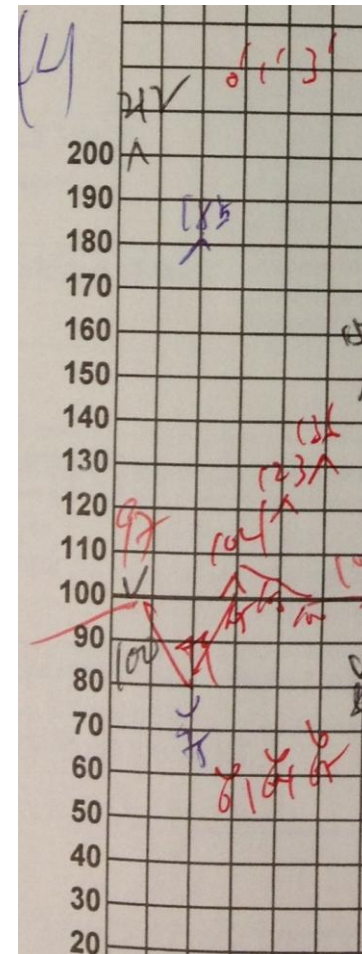
Case History

BP 185/75 (supine)

102/61 (standing 0 min)

123/64 (1 min)

136/65 (3 min)



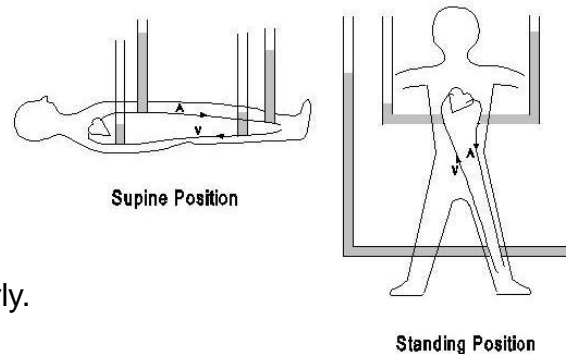
Orthostatic Hypotension – Prevalence

- Orthostatic hypotension is reported to be a common finding in elderly patients with a prevalence rate from 10% to 30%. In a study that looked at Chinese population the prevalence was noted to be 23%.
- Miu DKY, Chan MH. A study of postural hypotension in a Chinese elderly outpatient population: are there really associated risk factors. HKMJ 1997;3:8-14

Normal Response to Standing

- When we stand up, approximately 500-1000mL blood goes down from the chest to the distensible venous capacitance system below the diaphragm. This fluid shift produces a decrease in venous return, ventricular filling, cardiac output, and blood pressure.

Effect of Gravity on Cardiovascular Pressures



Lipsitz LA. Orthostatic hypotension in the elderly.
N Engl J Med. 1989;321:952-957

Normal Response to Standing

- In healthy individuals, compensatory reflex initiated by baroreflex, causing an increase in sympathetic activation, increases heart rate, contractility, venoconstriction, arteriolar constriction, thus increasing blood pressure
- Normal response: decrease SBP (5-10mmHg), increase DBP (5-10mmHg) and increase in pulse rate (10-25bpm)

Failure to Maintain Blood Pressure

- In many individuals especially in older and frail individuals the adjustments may be inadequate

Table 1 Age-Related Changes that Can Affect Normal Blood Pressure Regulation

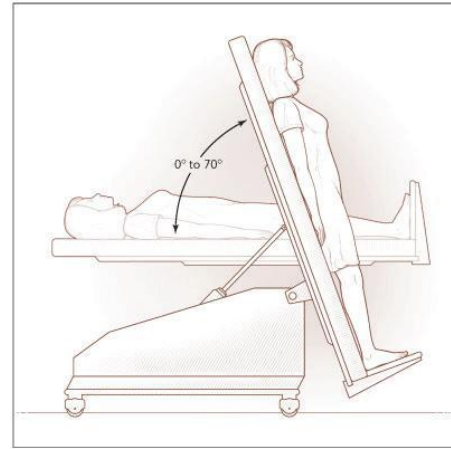
Decreased baroreflex sensitivity
Decreased α -1-adrenergic vasoconstrictor response to sympathetic stimuli
Decreased parasympathetic activity
Decreased renal salt and water conservation
Increased vascular stiffness
Reduced left ventricular diastolic filling

Orthostatic Hypotension – Definition

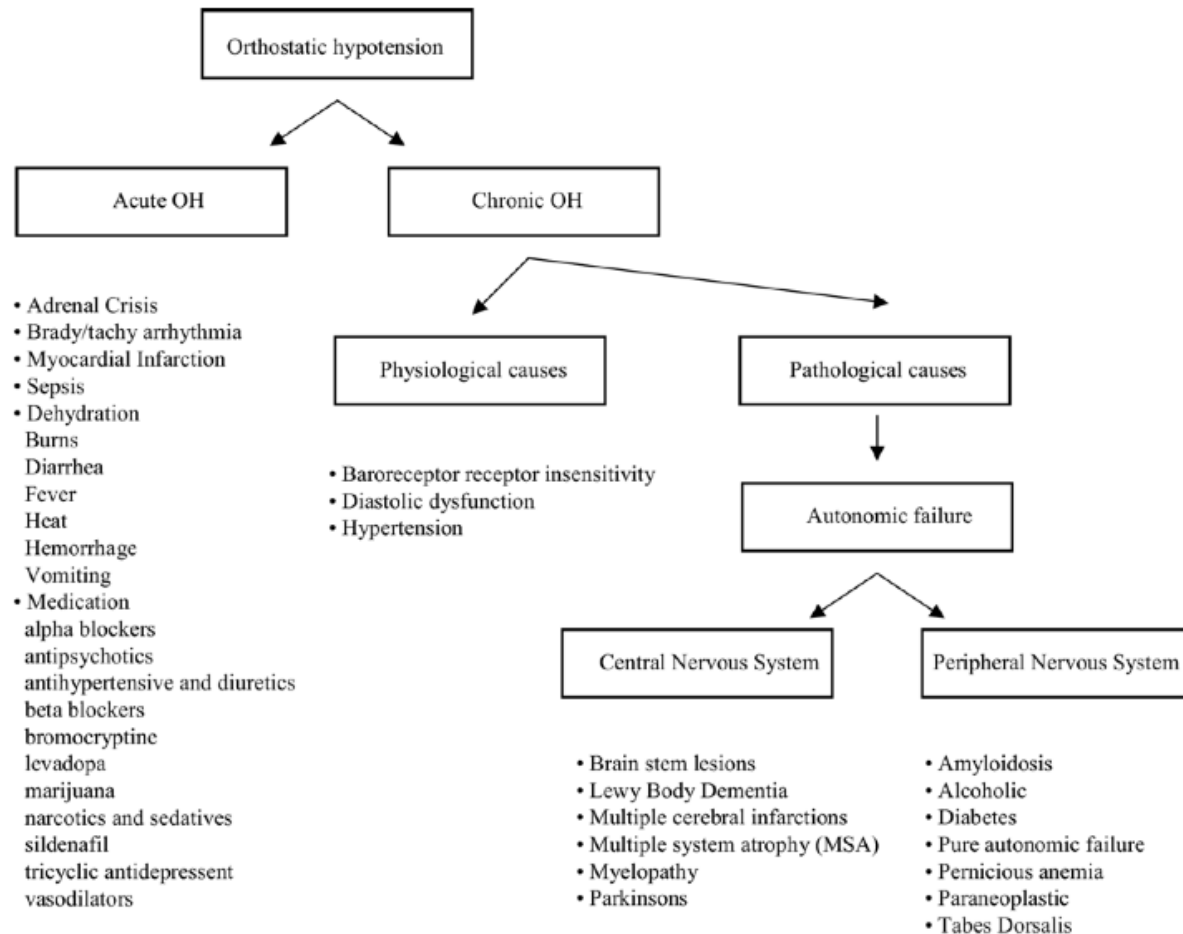
- Consensus committee of the American Autonomic Society & the American Academy of Neurology
 - A drop of systolic BP $>20\text{mmHg}$
 - A drop of diastolic BP $>10\text{mmHg}$
 - Within 3 minutes of assuming upright posture
- Kaufmann H, Schatz IJ, et al. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. *Neurology*. 46:1470 and *Clin Auton Res* 1996;6:125–6.
- Wieling W, Schatz IJ. The consensus statement on the definition of orthostatic hypotension: a revisit after 13 years. *J Hypertens*. 2009;27:935-938

Technique for Measuring Orthostatic Hypotension

- Supine for >5 minutes, measure BP and HR
- On standing up, measure BP, HR at intervals of 1min, 2min, 3min
- If symptomatic, immediately measure the BP and HR and terminate procedure



Aetiology of Orthostatic Hypotension



Management of Orthostatic Hypotension

- General measures
 - Patient education: shift from supine to an erect position in gradual stages
 - Minimise exposure to high environmental temperature
 - Ensure well hydrated (>2-2.5L/day)
 - Increase salt intake (>10g or 185mmol/day)
 - Review medications (discontinue hypotensive drugs)

Medication Review

- Amlodipine 5mg daily
- Furosemide 40mg daily
- Losartan 100mg noon
- Methyldopa 500mg BD
- Terazosin HCL 6mg nocte
- Simvastatin 5mg nocte
- Hypromellose eye drops 1 drop QID/PRN

Medication Review

- Amlodipine
 - Furosemide
 - Losartan
 - Methyldopa
 - Terazosin
 - Simvastatin
- Amlodipine is a long-acting calcium channel blocker that exerts its effect by blocking the transmembrane influx of calcium ions into cardiac and vascular smooth muscles. It also reduces peripheral vascular resistance and lowers BP by causing a direct vasodilatation in the peripheral arteries of the vascular smooth muscle

Medication Review

- Amlodipine
 - Furosemide
 - Losartan
 - Methyldopa
 - Terazosin
 - Simvastatin
- Furosemide is a potent diuretic that works by blocking the absorption of sodium and chloride in the kidney tubules causing a profound increase in urine output

Medication Review

- Amlodipine
 - Furosemide
 - Losartan
 - Methyldopa
 - Terazosin
 - Simvastatin
- Losartan is a reversible, non-competitive, angiotensin II receptor antagonist. It deters vasoconstriction and aldosterone-secreting effects by specifically intercepting the binding of angiotensin II to the AT(1) receptor

Medication Review

- Amlodipine
 - Furosemide
 - Losartan
 - Methyldopa
 - Terazosin
 - Simvastatin
- Methyldopa is a prodrug which is metabolised to the active agent alpha-methylnorepinephrine, a potent alpha-2 adrenergic agonist. It acts centrally to stimulate alpha receptors. This results in a decrease in sympathetic outflow and decrease blood pressure.

Medication Review

- Amlodipine
 - Furosemide
 - Losartan
 - Methyldopa
 - Terazosin
 - Simvastatin
- Terazosin (hytrin) is an alpha-1-selective adrenoceptor blocker that blocks the alpha-1-adrenoceptor in the neck of the urinary bladder and prostate gland, thereby producing relaxation of smooth muscles in these sites. It also causes vasodilatation resulting in orthostatic hypotension by inhibiting alpha-1-adrenoceptors in peripheral blood vessels

Medication Review

- Uncontrolled hypertension, use of three or more antihypertensives and multiple comorbidities are predictors of orthostatic hypotension in older women

Kamaruzzaman S, Watt H, Carson C, et al. The association between orthostatic hypotension and medication use in the British Women's Heart and Health Study. *Age and Ageing* 2010;39:51-56.

Management of Orthostatic Hypotension

- Non-pharmacological
 - Withdrawing offending medications
 - Increase salt and water intake; ensure well hydrated
 - Sleeping head-up
 - Physical counter-maneuvers
 - Standing training
 - Isometric exercise
 - Compression bandages (abdominal binders/ graded compression stockings)

Management of Orthostatic Hypotension

- Sleeping head-up
 - Raise head of bed to 10-20 degrees
 - May diminish renal filtration and increase angiotensin II production thus reducing risk of volume depletion in the morning
 - Transfer of fluid to the dependent extravascular space in the lower extremities may increase tissue pressure and prevent further losses when the individual arises

Management of Orthostatic Hypotension

- Physical counter-maneuvers
 - Gradual staged movements with postural changes
 - Stay active: avoid prolonged recumbence
 - Acute measures
 - Leg crossing/ muscle tensing/ squatting/ bending forward
 - Long-term prevention
 - Standing training/ isometric exercise/ support hose and abdominal binders/ graded compression stockings

Management of Orthostatic Hypotension

- Pharmacological
 - Fludrocortisone
 - Midodrine
 - Supplementary agents
 - Pyridostigmine (acetylcholinesterase inhibitor)
 - Nonsteroidal antiinflammatory drugs (limiting the vasodilating effects of circulating PG and arachidonic acid derivatives)
 - Caffeine (blocking of vasodilating adenosine receptors)
 - Erythropoietin (improves orthostatic tolerance in patients with anaemia)

Management of Orthostatic Hypotension

- Third line and experimental agents
 - Yohimbine (centrally active vasoconstrictor)
 - Somatostatin e.g. Octreotide (may benefit patients with post-prandial hypotension)
 - Dihydroergotamine (selective venoconstrictor effect)
 - Vasopressin analogues e.g. DDAVP (prevents nocturia and reduces morning postural fall in BP)
 - Dihydroxyphenylserine
 - Dopamine antagonists
 - B-blockers e.g. pindolol (improves postural baroreflex)

Management of Orthostatic Hypotension

- Fludrocortisone
 - Synthetic mineralocorticoid with minimal glucocorticoid effect which minimise salt loss and expand blood volume
 - Offers the potential to expand intravascular and extravascular body fluid, sensitise vascular receptors to pressor amines, and increase fluid content of vessel walls that makes them more resistant to stretching

Management of Orthostatic Hypotension

- Midodrine
 - Pro-drug that is converted to its active metabolite desglymidodrine after absorption
 - Acts on alpha-adrenoreceptors to cause constriction of both arterial resistance and venous capacitance vessels, with the predominant effect being on the venous side
 - Little central stimulant effects

Management of Orthostatic Hypotension – Systematic Review

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SYSTEMATIC REVIEW

Efficacy of treatments for orthostatic hypotension: a systematic review

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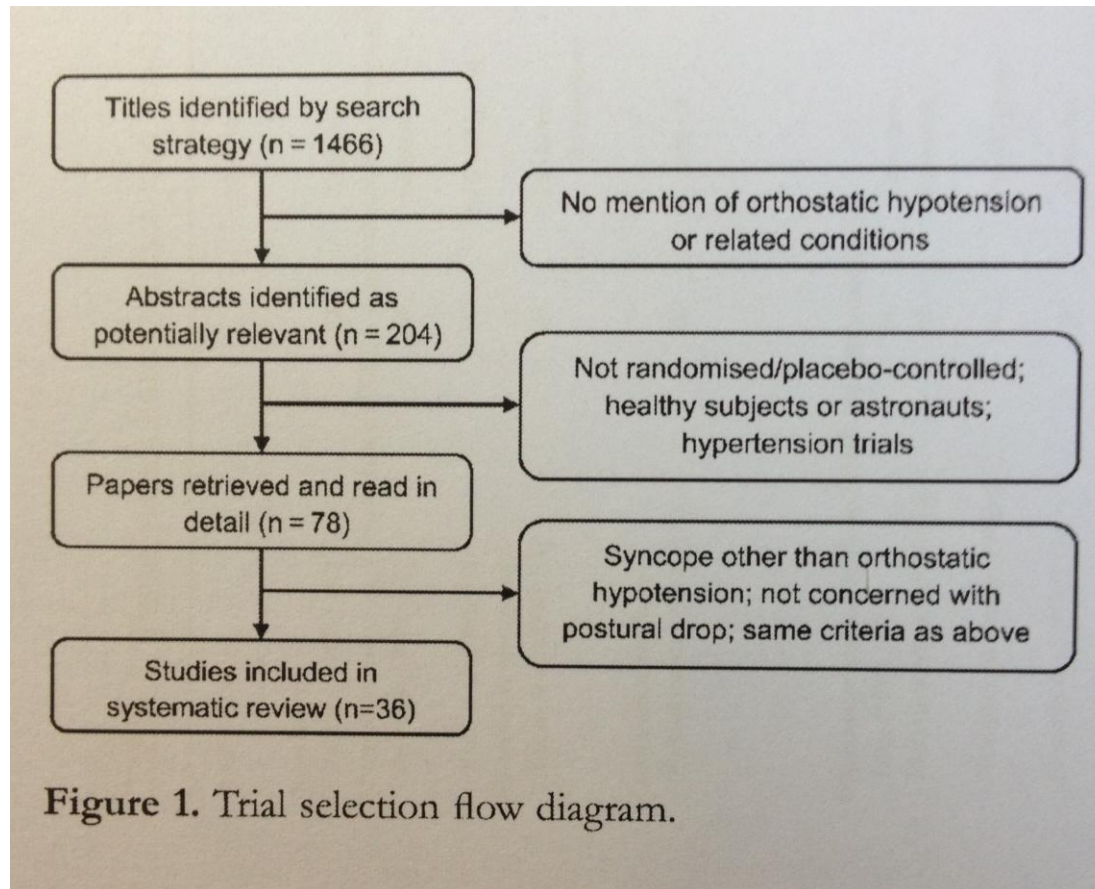
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Management of Orthostatic Hypotension – Systematic Review

Study quality:



Management of Orthostatic Hypotension – Systematic Review

- Effect on postural drop
 - Minor improvements
 - Clonidine
 - Sleeping head-up
 - Improvement in postural drop
 - Compression bandages
 - Indomethacin
 - Oxilofrine
 - Potassium chloride
 - yohimbine
- Inconsistent trend towards worsening of the postural drop
 - Midodrine
 - Pyridostigmine
- Worsening of the postural drop
 - Amezinium, glypressin, octreotide, xamoterol

Management of Orthostatic Hypotension – Systematic Review

- Effect on symptoms
 - Insufficient information to comment on their effect on symptoms
 - Fludrocortisone, indomethacin, glypressin, clonidine, nitroglycerine, amezinium, xamoterol, octreotide
 - Inconsistent trend
 - Midodrine, dihydroxyphenylserine, dihydrergotamine, pindolol, oxilofrine
 - No impact on symptoms
 - Pacing, sleeping head-up
 - Minor improvement in symptoms
 - Yohimbine
 - Significant improvement in symptoms
 - Compression bandages and potassium chloride
 - Worsening of symptoms
 - pyridostigmine

Management of Orthostatic Hypotension – Systematic Review

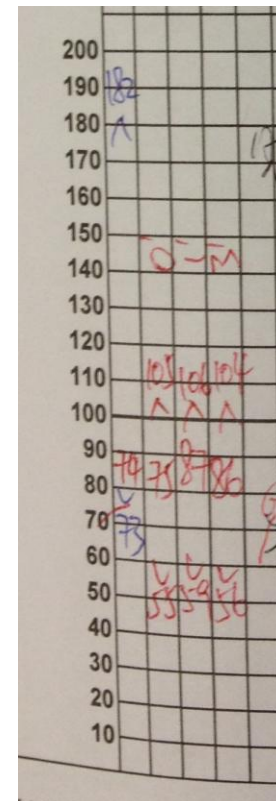
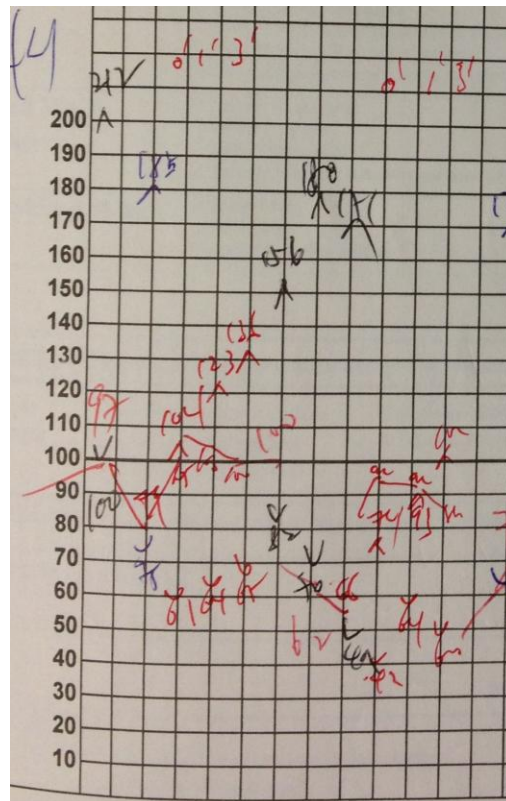
- This review highlighted that many of the commonly recommended therapeutic interventions for orthostatic hypotension do not have a large, high-quality evidence base to support their use
- Difficult for the authors to make any strong recommendations in light of the findings of the review

Management of Orthostatic Hypotension – Systematic Review

- Authors suggested high quality, randomised, controlled trials are needed to underpin clinical practice for this condition

Supine Hypertension with Orthostatic Hypotension

- What do we do if the patient has supine hypertension with orthostatic hypotension?



Supine Hypertension with Orthostatic Hypotension

- Maximise nonpharmacological measures
- Avoid lying down during the day
- Rest in a seated position/ sleeping head-up
- Treat supine hypertension at night with a transdermal nitroglycerin patch which is removed in the morning prior to the assumption of an upright position
- Treatment must be individually tailored

Shannon J, Jordan J, Costa F, et al. The hypertension of autonomic failure and its treatment. *Hypertension*. 1997;30(5):1062

Biaggioni I, Robertson RM. Hypertension in orthostatic hypotension and autonomic dysfunction. *Cardiol Clin* 2002;20:291-301

Target BP in Elderly Patients

- Target BP for uncomplicated hypertension: 140/90; Diabetes: 130/80
- Target BP for patients >80 years old: SBP generally 140-145
 - Limited data
 - Most trials excluded patients >80 years old
 - Not clear if the BP targets should be different in patients 65-79 years old than those >80 years old
- HYVET 2008: target BP 150/80

Conclusion

- Orthostatic hypotension is common and often very disabling
- It can be drug-induced, caused by dehydration, hypovolaemia, anaemia; or as a result of concomitant conditions such as Parkinsonism or other diseases associated with autonomic dysfunction.

Conclusion

- Treatment of orthostatic hypotension is imperfect and focuses on symptom relief rather than cure
- Important to pay attention to the patients with supine hypertension and orthostatic hypotension
- Target blood pressures are often difficult to accomplish and the treatment approach must be individualised

Thank You

References

- Brignole M, Benditt DG. Syncope. London: Springer-Verlag; 2011.
- Lanier JB, Mote MB, Clay EC. Evaluation and Management of Orthostatic Hypotension. American Family Physician. 2011;84(5):527-36.

Measuring Postural Blood Pressure

- Is sitting and standing blood pressure measurements accurate for diagnosing orthostatic hypotension?

Cooke J, Carew S, O'Conner M, et al. Sitting and standing blood pressure measurements are not accurate for the diagnosis of orthostatic hypotension. QJM May 2009;102(5):335-9.

Measuring postural blood pressure

Table 2 Summary of diagnostic accuracy of sit-stand testing for the identification of OH

Sensitivity	15.5%
Specificity	89.9%
PPV	61.7%
NPV	50.2%
LR	1.6

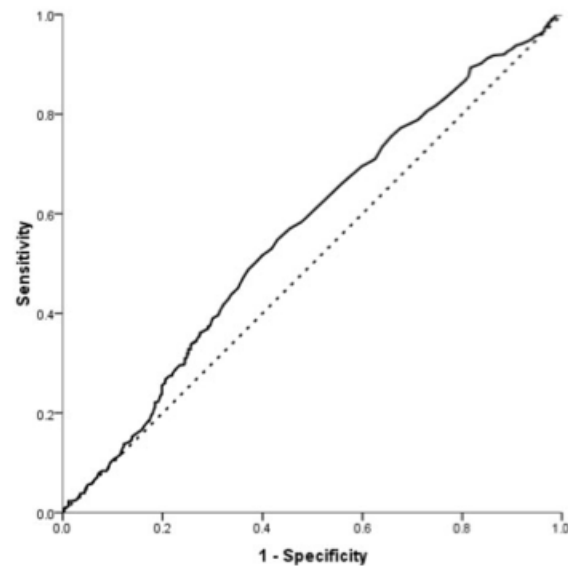
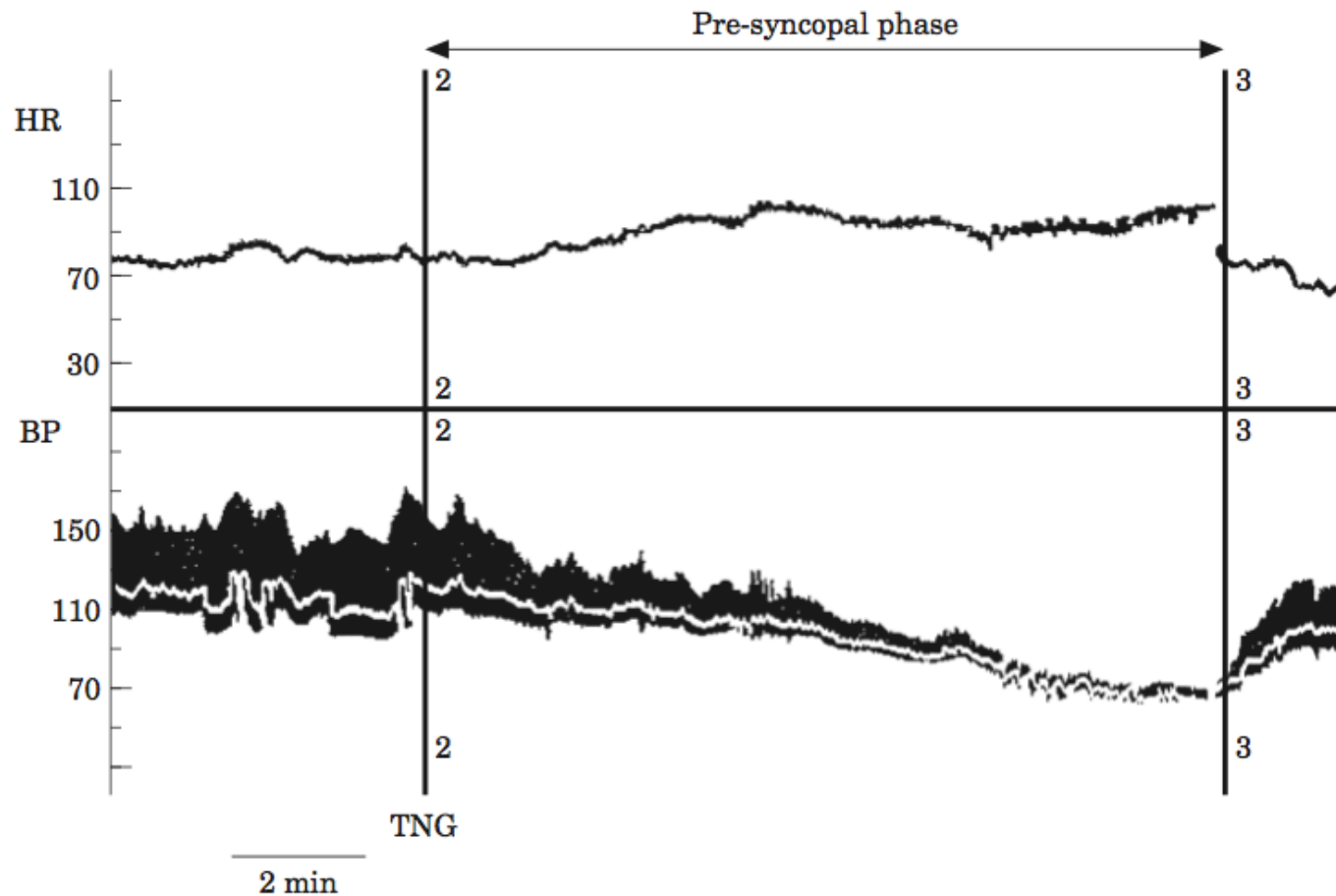


Figure 2. ROC for diagnostic accuracy of sit-stand testing for the diagnosis of OH.

Ambulatory Blood Pressure Monitoring

- What if the patient with syncope has a history suggestive of impaired orthostatic blood pressure control but in whom measurements in upright position may be normal?
 - 24 hour ambulatory blood pressure recording
 - Offers the potential to capture spontaneous events

Ambulatory Blood Pressure Monitoring



Systematic Review – Results

Table 2. Commentary on effect on postural drop and symptoms, comparing active arm to placebo arm [28–64]

Treatment	Studies (n)	Patients (n)	Effect on postural drop (active versus placebo)	Effect on symptoms (active versus placebo)	GRADE quality of evidence [27]
Amexinium [28]	1	12	Worsened	?	Moderate (§)
Camphor-crataegus berry compound (CCC) [29, 30]	2	86	No effect No effect	? Variable effect	Very low (**, ‡)
Clonidine [31]	1	23	Minor improvement	?	Very low (**, §)
Compression bandages [32]	1	21	Significant improvement	Significant improvement	Very low (**, §)
Dihydroergotamine (DHE/DHE Plus) [33–37]	5	178	Significant improvement Minor improvement Minor improvement Insufficient data No effect	Significant improvement Minor improvement No effect No effect ?	Very low (**, ‡, §)
Dihydroxyphenylserine (L-DOPS/DL-DOPS) [38–42]	5	270	No effect/minor improvement Minor improvement Insufficient data No effect No effect	? No effect Variable effect Minor improvement ?	Very low (*, ‡, §)
Fludrocortisone [43, 44]	2	19	Insufficient data Insufficient data	? ?	Very low (*, ‡, §)
Glypressin [45]	1	7	Worsened	?	Very low (**, §)
Indomethacin [46, 47]	2	34	Significant improvement Significant improvement	? ?	Low (*, §)
Midodrine [48–51]	4	292	Worsened No effect No effect Worsened	Variable effect Minor improvement No effect Variable effect	Very low (*, ‡, §)
Nitroglycerine [31]	1	23	No effect	?	Very low (**, §)
Norfenefrine [44]	1	13	Insufficient data	?	Low (*, §)
Octreotide [52]	1	9	Worsened	?	Moderate (§)
Oxlofine [53]	1	59	Significant improvement	Variable effect	Moderate (*)
Pacing [54]	1	6	Insufficient data	No effect	Very low (**, §)
Pindolol [55, 56]	2	18	Insufficient data No effect	Minor improvement No effect	Low (*, §)
Potassium chloride [57]	1	10	Significant improvement	Significant improvement	Low (*, §)
Pyridostigmine [58, 59]	2	89	Worsened No effect	? Worsened	Very low (**, ‡)
Sleeping head-up [60]	1	100	Minor improvement	No effect	Moderate (*)
Xamoterol [61]	1	11	Worsened	?	Moderate (§)
Yohimbine [59, 62–64]	3	55	Significant improvement Significant improvement Minor improvement (only diastolic BP given)	Minor improvement No effect (both worsened) Minor improvement	Very low (**, ‡, §)

Postprandial hypotension

- Situational
- Common disorder of BP regulation in elderly; commoner than orthostatic hypotension
- Within 2 hours of start of a meal
- Probably due to inadequate SANS compensation for meal-induced splanchnic blood pooling, impaired baroreflex function, inadequate peripheral vasoconstriction, inadequate postprandial increase in CO

Postprandial hypotension

- Avoid large carbohydrate meals and alcoholic drinks
- A brief walk or supine rest after a meal
- Caffeine intake help preserve blood pressure
- Consider midodrine preprandial
- Somatostatin both reduces splanchnic circulation and increase forearm vascular resistance