

Cardiovascular causes of falls

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Introduction

Cardiovascular disorders are responsible for as many as 77% of patients presenting to Accident and Emergency Departments with unexplained or recurrent falls and falls associated with unexplained loss of consciousness [1]. The importance of these disorders as a group is emphasized by the fact that fallers with an intrinsic cardiac cause have a greater mortality than those with non-cardiovascular or unknown causes [2]. Cardiovascular causes of falls can be divided into three main groups: i) neurally mediated disorders; ii) intrinsic cardiac abnormalities of structure and rhythm; and iii) miscellaneous causes (Table 1). This brief review highlights some of these disorders and discusses potential investigations and treatments.

Vasovagal syncope

Considerable overlap exists between the various neurally mediated disorders with two or more such diagnoses frequently coexisting [3]. Vasovagal syncope (VVS) is the commonest neurally mediated disorder, affecting all age groups with an equal sex incidence. A family history of the disorder is common and up to 30% of the population will suffer a vasovagal syncopal episode at least once in their lifetime, but VVS can be induced in anyone if enough physiological stress is applied! VVS may be precipitated by pain and emotional trauma and most commonly occurs in the standing position, but may also present whilst sitting or, most exceptionally, when supine. Pre-syncopal symptoms include dizziness, nausea, diaphoresis, palpitations and chest pain which may progress to loss of consciousness or a fall if evasive action is not taken. Premonitory symptoms may be attenuated in the elderly [4] and falls due to recurrent VVS, therefore, carry substantial risks in terms of morbidity and mortality in older people.

During pre-syncope, gradual declines in systemic blood pressure and peripheral vascular resistance are followed by more precipitous falls in both parameters with or without a fall in heart rate. The underlying pathophysiology of VVS is complex, but may involve abnormalities of intravascular volume, venous compliance, respiration, serotonin homeostasis and endothelial,

endogenous opioid, β adrenergic receptor and baroreceptor function. There is clear evidence, however, that hypotension results from an inappropriate withdrawal of peripheral sympathetic nerve activity resulting in a fall in vascular tone and that loss of consciousness is ultimately due to cerebral hypoperfusion as a consequence of deteriorating cerebral autoregulation [5]. More recently, it has been suggested that this impairment of cerebral autoregulation during pre-syncope may be due to a rise in cerebrovascular critical closing pressure precipitated by progressive hypocapnia [6].

Diagnosis of VVS relies on the clinical history and reproduction of symptoms in association with the characteristic haemodynamic profile during a 60–90° head-up tilt (HUT) test. VVS may be classified into three categories—vasodepressor, cardioinhibitory and mixed—according to the BP and heart rate changes during pre-syncope (Table 2) and this classification may be helpful in guiding treatment strategies [7]. Interpretation of the test is complicated, however, by the fact that a large number (13% in a recent study) of 'normal' subjects with no history of VVS have positive HUT tests [8].

Progressive amelioration of symptoms related to VVS occurs over time and, in our experience, the majority of patients need no intervention other than reassurance and education regarding avoidance of precipitating factors and evasive action should pre-syncopal symptoms occur. Discontinuation of medications with anti-hypertensive effects that may exacerbate vaso-depression may improve matters, but if episodes of VVS continue to affect quality of life, further intervention may be considered. In such instances, we find fludrocortisone to be most useful in younger patients and midodrine (an adrenergic agonist) to occasionally be helpful in older subjects who tend to be more intolerant of fludrocortisone [9], though adverse side effects are not uncommon. Where these measures prove inadequate, combinations of fludrocortisone and midodrine and other therapies such as elastic support stockings, increased dietary salt intake, β adrenergic blockers, serotonin reuptake inhibitors and moderate exercise and tilt training programmes may prove helpful in resistant cases. Permanent pacemakers with rate hysteresis have recently been shown to be useful in patients with the cardioinhibitory form of the syndrome [10] but,

Table 1. Cardiovascular causes of falls

Neurally mediated syndromes	
Vasovagal (neurocardiogenic) syncope	
Carotid sinus syndrome	
Orthostatic hypotension	
Postprandial hypotension	
Situational syncopes (Cough, sneeze, micturition, deglutition, defecation, gastrointestinal stimulation, Valsalva, diving reflex)	
Cardiac abnormalities	
Arrhythmias	– Supraventricular
	– Sinus node disease
	– 2 nd /3 rd degree heart block
	– Atrial fibrillation/flutter
	– Atrial tachycardia
	– Junctional (Wolff–Parkinson–White, Lown–Ganong–Levine)
– Ventricular	– Ventricular fibrillation/tachycardia
	– Torsades de pointes
Structural	– Valvular stenosis/incompetence
	– Hypertrophic obstructive cardiomyopathy
	– Atrial myxoma
	– Myocardial ischaemia/infarction
	– Aortic dissection
	– Tamponade
Miscellaneous	
Pulmonary embolism	
Subclavian steal syndrome	
‘Cerebral’ syncope	
Transient ischaemic attacks	
Migraine	

Table 2. Diagnostic criteria for neurally mediated causes of falls

Neurocardiogenic syncope	
Type 1 (mixed)*	
Systolic BP < 80 mmHg and heart rate > 40 bpm or < 40 bpm for < 10 seconds or asystole < 3 seconds	
Type 2 (cardioinhibitory)*	
Heart rate 40 bpm for > 10 seconds) or asystole > 3 seconds	
2A	BP falls prior to fall in heart rate
2B	BP falls at or after onset of fall in heart rate
Type 3 (vasodepressor)	
Systolic BP < 80 mmHg and heart rate > 90% of its peak value at syncope	
Carotid sinus syndrome	
Cardioinhibitory	Asystole > 3 seconds*
Vasodepressor	Systolic BP fall > 50 mmHg
Mixed	Systolic BP fall > 50 mmHg and asystole > 3 seconds*
Orthostatic hypotension	
Systolic BP fall of > 20 mmHg or diastolic BP fall of > 10 mmHg on standing or after HUT to at least 60°	
Postprandial hypotension	
Systolic BP fall of > 20 mmHg or absolute systolic BP < 90 mmHg when pre-prandial systolic BP > 100 mmHg within two hours of the start of a meal	

*Pacemaker insertion may be beneficial.

in our experience, such invasive treatments are rarely necessary.

Carotid sinus syndrome

Carotid sinus syndrome (CSS) is a disease of older people, being rare under the age of 50 years. The exact prevalence in elderly community dwellers is unknown, but it is probably commoner than previously thought, proving the commonest cause of ‘drop attacks’ [11] and

accounting for unexplained non-accidental falls in up to one-third of older people [12]. Symptoms are classically precipitated by manoeuvres that mechanically stimulate the carotid sinus, such as head turning, and may also result from straining, prolonged standing and pain but, in our experience, however, clear precipitating factors are often lacking. Amnesia for loss of consciousness is common, emphasising the importance of collateral histories from witnesses to unexplained falls. Males are more commonly affected and the majority have existing cardiovascular co-morbidity in the form of

ischaemic heart disease, cerebrovascular disease or hypertension [13].

The pathophysiology of CSS is unclear, but it may result from a central abnormality of baroreflex gain, possibly caused by atherosclerosis-induced ischaemia at myocardial or brainstem level. A strong association with other hypotensive disorders such as orthostatic hypotension and VVS suggests at least some common pathophysiology.

The diagnostic investigation is carotid sinus massage which is generally performed for 5 seconds longitudinally over the point of maximum carotid impulse, with 1 minute between stimuli. Massage is performed bilaterally in the supine position, but, if negative, must be repeated in the HUT position as up to one-third of patients with the syndrome exhibit hypersensitivity in the head-up position only [14]. Cardioinhibitory, vaso-depressor and mixed subtypes of the syndrome occur with almost equal frequency (Table 2) with the heart rate response occurring almost immediately on stimulation and the maximum blood pressure fall after ~18 seconds. As long as an abnormal response is reproducible, most protocols do not regard symptom reproduction as essential to make diagnosis, though this is controversial. In our opinion, if other investigations are normal, the finding of significant BP and/or heart rate changes with carotid sinus massage (Table 2) in a patient with recurrent unexplained falls is enough to make the diagnosis and warrant intervention even if symptoms have not been reproduced. We and others have found carotid sinus massage to be a safe procedure with a very low risk of complications (<1%) if patients with carotid bruits, recent myocardial infarction, recent cerebral ischaemia and previous ventricular tachyarrhythmias are excluded.

CSS of any subtype is associated with a substantial increase in morbidity but not mortality while syncope recurs within 36 months in 57% of untreated CSS patients [15]. Simple advice to avoid precipitating factors is standard in patients with CSS, but further intervention is generally reserved for patients with a history of two or more symptomatic episodes. In view of the high injury rate associated with symptomatic episodes, however, we believe that intervention should also be considered in individuals with a solitary severe event. Cardioinhibitory and mixed subtypes of CSS may be treated with permanent cardiac pacing which abolishes syncope in up to 90% of patients [15]. Dual chamber demand pacing is best tolerated and results in less hypotension during pacing and is, therefore, the mode of choice. We find, however, that a substantial number of paced patients have residual presyncopal symptoms, possibly caused by an untreated vasodepressor component, the development of pacemaker syndrome or the adverse effect of atrioventricular asynchrony on cardiac haemodynamics. We have found treatment of the vasodepressor component of CSS to be even less rewarding and, as most pharmacological therapies

work by elevating BP, concomitant hypertension often limits their use. Fludrocortisone significantly reduces symptoms and the vasodepressor response to carotid sinus massage [16], but may be poorly tolerated by elderly patients [9]. Midodrine may prove an effective alternative but, as there are few data with this or other therapies such as ephedrine and dihydroergotamine, no firm recommendations can be given.

Orthostatic hypotension

Blood pressure criteria for diagnosing orthostatic (or postural) hypotension (OH) are arbitrary (Table 2) and correlate poorly with symptoms [17]. The issue is complicated by the fact that, using these criteria, OH can be diagnosed in up to 30% of asymptomatic healthy elderly people living at home [17]. What predicts why some patients develop symptoms with OH and others do not is unclear but co-existing impaired cerebral autoregulation may play a role [18]. OH is poorly reproducible [19] and the length of time after standing needed to detect OH is a matter of debate, with measurements most commonly made at 1, 3 and 5 minutes. OH is probably under-diagnosed in both community and hospital settings and the lack of a BP fall in the presence of suggestive symptoms, therefore, warrants further investigation in view of the numerous factors that may influence OH (e.g. drug use, speed of posture change, prolonged recumbency, warm environment, food/alcohol ingestion) [20].

The prevalence of OH increases with age and is associated with increased morbidity and mortality, due in part to the increased incidence of falls and vascular death, especially stroke. However, OH is not a diagnosis in itself and should lead to a search for a possible underlying cause (Table 3). Explanation of the cause of symptoms and education regarding avoidance or circumvention of precipitating factors are fundamental for successful treatment [20]. Older hypertensive patients frequently have OH and whether reducing BP levels in such patients improves postural BP control is not clear [21] but withdrawal of medications with hypotensive effects may ameliorate symptoms [20]. Various non-pharmacological measures have been used with varying degrees of success and tolerability (Table 4) but if these measures prove inadequate, pharmacological intervention may be necessary (Table 4). Very similar to our experience with the vasodepressor component of CSS, we find that fludrocortisone and midodrine prove the most useful medications but that co-existing hypertension often limits their usefulness.

Postprandial hypotension

Postprandial hypotension (PPH), diagnosed according to the criteria in Table 2, may be exacerbated by posture

Table 3. Causes of orthostatic hypotension

Hypovolaemia	Addison's disease Dehydration Haemorrhage	
Neurogenic failure	Primary	Shy-Drager syndrome
		Parkinson's Disease
		Pure autonomic failure
	Secondary	Pandysautonomia
		Diabetic neuropathy
		Systemic amyloidosis
		Chronic renal failure
		Surgical sympathectomy
		Spinal cord transection/myelitis
		Guillain-Barre syndrome
		Paraneoplastic syndrome
		Clostridium tetani infection
		HIV infection
Nerve growth factor deficiency		
Dopamine β -hydroxylase deficiency		
Prolonged bed rest		
Medications	antihypertensives, anti-anginals, antidepressants, phenothiazines, anticholinergics, antimuscarinics, dopamine agonists, benzodiazepines, opiates, alcohol, marijuana	
Idiopathic		

Table 4. Treatment of orthostatic hypotension

Non-pharmacological measures	
	Head-up tilt during sleep
	Increase salt intake
	Exercise
	Physical manoeuvres (e.g. leg crossing, bending forward)
	Thigh-length elastic stockings
	Abdominal binders
	Avoid – Sudden head-up postural change
	– Prolonged recumbency
	– Warm environments
	– Drugs with hypotensive side effects
Pharmacological interventions	
	Fludrocortisone
	Midodrine
	Ephedrine
	Potassium supplements
	Dihydroergotamine
	Indomethacin
	Fluriprofen
	Desmopressin
	Metoclopramide, domperidone
	Erythropoietin

change, but is a distinct entity that differs from OH. The prevalence of PPH is unknown but it may be more common than OH [22], being present in up to one-half of patients with unexplained syncope [23] but the effects on morbidity and mortality are not known [22]. The situation is, once again, complicated by the fact that mild, meal-induced decreases in BP are common in healthy older persons. PPH occurs in both sitting and supine positions [24], can be found at all meal times and is associated with symptoms similar to those produced by OH [22]. The BP nadir varies but generally occurs within 30–90 minutes post-meal [25]. The causes

of PPH are unclear but the size and nutrient content [25] of meals affect the magnitude of the decrease in postprandial BP, with carbohydrates and, more specifically, simple carbohydrates such as glucose being particularly implicated [25]. Underlying mechanisms for PPH remain unclear, but adenosine-induced splanchnic vasodilatation may play a role.

Non-pharmacological measures that we find helpful include smaller, more frequent meals with reduced simple carbohydrate content and withdrawal of medications with hypotensive effects. A variety of pharmacological options have been tried with varying degrees of success. Despite evidence of the development of tolerance, caffeine may have some therapeutic value [26] and as its usual mode of delivery is inexpensive, relatively safe and pleasant to many, there is little to lose in recommending a post-prandial caffeinated beverage. Octreotide has been shown to be beneficial in elderly hypertensives [27] and in patients with autonomic dysfunction [28] but cost, side effects and its inconvenient mode of administration severely limit its usefulness.

Other causes

A variety of situational syncopes (Table 1), which may cause falls through neurally mediated cardioinhibition and/or vasodepression, can occur in isolation but more often co-exist with other neurally mediated syndromes. Treatment usually involves a combination of education, avoidance of precipitating factors and, occasionally, the insertion of permanent pacemakers in patients with cardioinhibition.

Falls may also result from intrinsic cardiac structural abnormalities and arrhythmias. Supraventricular

and ventricular arrhythmias can be diagnosed using standard electrocardiography which has the advantages of being easy, risk-free and inexpensive but the yield may be low (~5%) [29]. Holter monitoring over 24 hours yields a diagnosis in up to 18% of patients with unexplained syncope or pre-syncope and excludes the diagnosis in a further 15% [29]. Extending the period of monitoring to 72 hours does not, however, increase the yield for arrhythmias associated with symptoms [30]. External ambulatory loop electrocardiography may be performed for 30 days or more and is most useful in patients with palpitations, but a high degree of patient compliance and cooperation is essential [29]. Formal intracardiac electrophysiological testing is safe but expensive and invasive, probably only being useful in fallers with known organic heart disease [29]. Exercise stress testing is generally unhelpful for diagnostic purposes with a yield likely to be <1% [29]. Where all these investigations are normal and a high index of suspicion is maintained for arrhythmia-induced falls in the face of uncertainty regarding the presence of organic heart disease, implantable loop recorders may reveal treatable arrhythmias, usually bradycardias, in as many as 20% of patients [31]. Treatment is tailored to particular arrhythmias and may include anti-arrhythmic medications, pacemakers, cardioversion, implantable defibrillators or the withdrawal of offending medications.

Cardiac structural abnormalities, e.g. aortic stenosis or hypertrophic obstructive cardiomyopathy, may be uncovered by echocardiography in up to 5–10% of unselected patients with unexplained syncope [32] but other imaging techniques, such as cardiac catheterization and magnetic resonance imaging, may need to be employed where the diagnosis is unclear or where more specific diagnostic information is required. Management is best decided by experienced cardiologists and cardiothoracic surgeons in consultation.

In summary, cardiovascular disorders are increasingly being recognized as common causes of falls, possibly due to an improvement in diagnostic techniques and understanding of the pathophysiology involved. In view of the high morbidity and mortality associated with many of these disorders, and the fact that successful treatments are available, careful consideration should be given to these disorders when assessing patients with unexplained or recurrent falls.

References

1. Davies AJ, Kenny RA. Falls presenting to the Accident and Emergency Department: types of presentation and risk factor profile. *Age Ageing* 1996; 25: 362–6.
2. Kapoor WN, Karpf M, Wieand S, Peterson JR, Levey GS. A prospective evaluation and follow-up of patients with syncope. *New Engl J Med* 1983; 309: 197–204.

3. McIntosh SJ, Lawson J, Kenny RA. Clinical characteristics of vasodepressor, cardioinhibitory and mixed carotid sinus syndrome in the elderly. *Am J Med* 1993; 95: 203–8.
4. Grubb BP, Samoil D. Neurocardiogenic Syncope. In Kenny RA ed. *Syncope in the Older Patient*. London: Chapman & Hall, 1996; 91–106.
5. Carey BJ, Manktelow BN, Panerai RB, Potter JF. Dynamic cerebral autoregulatory responses to head-up tilt in normal subjects and patients with recurrent vasovagal syncope. *Circulation* 2001; 104: 898–902.
6. Carey BJ, Eames PJ, Panerai RB, Potter JF. Carbon dioxide, critical closing pressure and cerebral haemodynamics prior to vasovagal syncope in humans. *Clinical Sci* 2001; 101: 351–8.
7. Sutton R, Petersen M, Brignole M, Raviele A, Menozzi C, Giani P. Proposed classification for tilt induced vasovagal syncope. *Eur J Cardiac Pacing Electrophysiol* 1992; 3: 180–3.
8. Petersen MEV, Williams TR, Gordon C, Chamberlain-Webber R, Sutton R. The normal response to prolonged passive head up tilt testing. *Heart* 2000; 84: 509–14.
9. Hussain RM, McIntosh SJ, Lawson J, Kenny RA. Fludrocortisone in the treatment of hypotensive disorders in the elderly. *Heart* 1996; 76: 507–9.
10. Connolly SJ, Sheldon R, Roberts RS, Gent M. The North American vasovagal pacemaker study (VPS). A randomised trial of permanent cardiac pacing for the prevention of vasovagal syncope. *J Am Coll Cardiol* 1999; 33: 16–20.
11. Dey AB, Stout NR, Kenny RA. Cardiovascular syncope is the most common cause of drop attacks in the elderly. *Pacing Clin Electrophysiol* 1997; 20: 818–9.
12. Richardson DA, Bexton RS, Shaw FE, Kenny RA. Prevalence of cardioinhibitory carotid sinus hypersensitivity in patients 50 years or over presenting to the accident and emergency department with unexplained or recurrent falls. *Pacing Clin Electrophysiol* 1997; 20: 820–3.
13. Draper AJ. The cardioinhibitory carotid sinus syndrome. *Annals of Internal Med* 1950; 32: 700–16.
14. Parry SW, Richardson DA, O’Shea D, Sen B, Kenny RA. Diagnosis of carotid sinus hypersensitivity in older adults: carotid sinus massage in the upright position is essential. *Heart* 2000; 83: 22–3.
15. Brignole M, Menozzi C, Lolli G, Bottoni N, Gaggioli G. Long term outcome of paced and non-paced patients with severe carotid sinus syndrome. *Am J Cardiol* 1992; 69: 1039–43.
16. da Costa D, McIntosh S, Kenny RA. Benefits of fludrocortisone in the treatment of symptomatic vasodepressor carotid sinus syndrome. *Br Heart J* 1993; 69: 308–10.
17. Caird FI, Andrews GR, Kennedy RD. Effect of posture on blood pressure in the elderly. *Br Heart J* 1973; 35: 527–30.
18. Wollner L, McCarthy ST, Soper NDW, Macy DJ. Failure of cerebral autoregulation as a cause of brain dysfunction in the elderly. *Br Med J* 1979; 1: 1117–8.
19. Youde JH, Manktelow B, Ward-Close S, Potter JF. Measuring postural changes in blood pressure in the healthy elderly. *Blood Press Monitoring* 1999; 4: 1–5.

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20. Mathias CJ, Kimber JR. Treatment of postural hypotension. *J Neurol Neurosurg Psychiatry* 1998; 65: 285–9.
21. Luukinen H, Koski K, Laippala P, Kivela S-L. Prognosis of diastolic and systolic orthostatic hypotension in older persons. *Arch Intern Med* 1999; 159: 273–80.
22. Jansen RW, Lipsitz LA. Postprandial hypotension, epidemiology, pathophysiology and clinical management. *Annals of Internal Med* 1995; 122: 286–95.
23. Jansen RW, Connelly CM, Kelley-Gagnon MM, Parker JA, Lipsitz LA. Postprandial hypotension in elderly patients with unexplained syncope. *Arch Internal Med* 1995; 155: 945–52.
24. Haigh RA, Harper GD, Burton R, Macdonald IA, Potter JF. Possible impairment of the sympathetic nervous system response to postprandial hypotension in elderly hypertensive patients. *J Human Hyperten* 1991; 5: 83–9.
25. Potter JF, Heseltine D, Hartley G, Matthews J, MacDonald IA, James OF. Effects of meal composition on the postprandial blood pressure, catecholamine and insulin changes in elderly subjects. *Clin Sci* 1989; 77: 265–72.
26. Heseltine D, Dakkak M, Woodhouse K, Macdonald IA, Potter JF. The effect of caffeine on postprandial hypotension in the elderly. *J Am Geriatr Soc* 1991; 39: 160–4.
27. Jansen RW, Peeters TL, Lenders JW, van Lier HJ, v't Laar A, Hoefnagels WH. Somatostatin analog octreotide (SMS 201–995) prevents the decrease in blood pressure after oral glucose loading in the elderly. *J Clin Endocrin Metab* 1989; 68: 752–6.
28. Raimbach SJ, Cortelli P, Kooner JS, Bannister R, Bloom SR, Mathias CJ. Prevention of glucose-induced hypotension by the somatostatin analogue octreotide (SMS 201–995) in chronic autonomic failure: haemodynamic and hormonal changes. *Clin Sci* 1989; 77: 623–8.
29. Linzer M, Yang EH, Estes NAM, Wang P, Vorperian VR, Kapoor WN. Clinical guideline: Diagnosing syncope. Parts I & II. *Annals Internal Med* 1997; 126: 989–96 and 127: 76–86.
30. Bass EB, Curtiss EI, Arena VC *et al.* The duration of Holter monitoring in patients with syncope. Is 24 hours enough. *Arch Internal Med* 1990; 150: 1073–8.
31. Kenny RA, Krahn AD. Implantable loop recorder: evaluation of unexplained syncope. *Heart* 1999; 81: 431–3.
32. Krumholz HM, Douglas PS, Goldman L, Waksmonski C. Clinical utility of transthoracic two-dimensional and Doppler echocardiography. *J Am Coll Cardiol* 1994; 24: 125–31.