The different clinical presentations of vasovagal syncope

Paolo Alboni

ABSTRACT

For some decades, after the introduction of the head-up tilt test into clinical practice, the clinical presentation of vasovagal syncope (VVS) has been classified as typical (or classical) and atypical (or non-classical). Some clinical features and recent data suggest that even unexplained falls and syncope during sleeping hours may be possible clinical presentations of VVS. In recent studies, tilt testing and carotid sinus massage by means of the ‘method of symptoms’ were performed in one group of patients with unexplained falls and in another group with unexplained syncope (presence of prodromal symptoms). Overall, tilt testing and carotid sinus massage displayed a high positivity rate in the group of patients with unexplained falls (about 60%), which was similar to that of the unexplained syncope group. These new data seem to indicate that some unexplained falls could be cases of atypical VVS/carotid sinus syncope with retrograde amnesia. Some clinical features suggest that syncope during sleeping hours is a form of VVS with a different clinical presentation: high prevalence of autonomic prodromes, of diurnal episodes of typical VVS and specific phobias, and of positive tilt testing with severe cardioinhibition.

Vasovagal syncope (VVS) is a reflex (neurally mediated) syncope and appears to be the most common cause of transient loss of consciousness (TLoC). Since the description of VVS by Cotton and Lewis in 1918, our knowledge of this type of syncope has markedly improved, especially since the advent of the tilt table test in the clinical setting, and we have learned that VVS can have atypical clinical presentations. This review is an attempt to detail and classify the different clinical presentations of VVS in the light of very recent knowledge, though we are aware that any classification has its limits, especially when it deals with clinical features. To this end, an extensive bibliographical research on Medline and on the references to the most important contributions on neurally mediated syncope was conducted. The diagnostic aspects of the different clinical presentations are discussed, without systematically dealing with differential diagnoses.

For some decades, the clinical presentation of VVS has been classified as typical (or classical) and atypical (or non-classical). Some clinical features and recent data suggest that unexplained falls and syncope during sleeping hours may also be possible clinical presentations of VVS. The possible clinical presentations of VVS are summarised in table 1.

TYPICAL VVS

Typical VVS is a TLoC characterised by: (1) precipitating triggers such as emotional distress (emotions, fear, severe pain, disgust, medical setting) or orthostatic stress (prolonged standing) and (2) prodromal symptoms due to activation of the autonomic system, such as nausea, vomiting, abdominal discomfort, pallor and sweating. Other autonomic prodromes, such as feeling cold or feeling warm, palpitations, yawning, sighing, salivation, pupillary dilatation and urinary incontinence, may be present. In addition to autonomic symptoms, prodromes due to cerebral and retinal hypoperfusion, such as dizziness, light-headedness and blurred vision, are commonly reported. Among subjects with spontaneous typical VVS, symptoms were present even during the recovery phase in 95% of cases (mainly pallor, sweating, weakness, feeling cold, nausea). In some subjects, syncope cluster is observed and the syncopeal episodes are concentrated within some days, weeks or months, interspersed with very long asymptomatic periods (sometimes years). The mechanism of syncope cluster has not yet been elucidated.

Typical VVS is mainly observed in young subjects and rarely in the elderly. It is more frequent in women than in men, particularly when the attack is triggered by emotional distress. The most common age at which VVS first presents is 13–15 years. There is a consensus that when a TLoC is precipitated by an emotional or orthostatic trigger and is associated with autonomic symptoms, the diagnosis of VVS can be made after the initial evaluation, without further investigation. When the emotion is very strong or standing is very prolonged (e.g., standing in a long queue) the diagnosis of VVS is generally easy. However, there is a grey area characterised by uncertain triggers. Prolonged standing is not standardised; it mainly depends on the habits of the individual. Some individuals are accustomed to standing upright for long periods and others only for very short periods. Therefore, standing can only be defined as prolonged by the patient, not by the physician; an accurate medical history should be taken. TLoC is sometimes preceded by pain which is not severe, and the role of pain as a trigger is uncertain. TLoC has also been reported to occur in some potentially emotional circumstances, such as religious services, weddings, funerals (not involving close persons), visits to the cemetery and rock concerts. In such cases, the physician should investigate whether the individual was emotionally involved or not; in other words, whether a trigger played a real role. If the role of a trigger (emotional or orthostatic) remains uncertain, tilt testing may be indicated, and the...
diagnosis of VVS can be made if this test is positive in the absence of any competing diagnosis.

Many patients seeking assistance for syncope mention external circumstances which, in their opinion, have been important in triggering the syncopal attack, such as hot weather, crowded places, overtiredness, lack of food, menstruation and saunas.4 In the personal opinion of some clinicians, these circumstances strongly suggest a VVS. Even internal factors such as hypotension, hyperventilation and straining could be responsible for syncope. This is an important issue, as the use of restricted criteria might cause VVS to be underdiagnosed, whereas broad criteria including many other stressors and circumstances that affect blood pressure would increase sensitivity but reduce specificity, that is, the number of patients incorrectly labelled as having VVS.13 In a study by Alboni et al.,3 some of the predisposing and precipitating factors showed a similar prevalence in patients with typical VVS and those with tilt-induced syncope; this seems to suggest that these factors could be very useful in diagnosing VVS. However, they were present even in patients with cardiac syncope, albeit with a lower prevalence. In order to define the diagnostic role of the predisposing and precipitating factors, further studies should be carried out in patients with various types of TLoC.

**ATYPICAL VVS**

An atypical VVS can be diagnosed in subjects with TLoC that is not preceded by any evident trigger, but who have a positive response to tilt testing, and have no evidence of any competing diagnosis. We can define this form of syncope as vasovagal, as it is triggered by orthostatic stress, even if not spontaneous (tilt testing). The term ‘atypical VVS’ is the most used in the literature and it appears to be the most appropriate, but other terms such as atypical reflex syncope, neurocardiogenic syncope, etc, are used (table 1) and that could be the cause of misunderstanding. Before the introduction of the head-up tilt test into clinical practice, we were unable to make a diagnosis in these subjects. However, since the positivity rate of tilt testing is about 50% and the reproducibility of a positive response is 31–92%,15 VVS is very probably underdiagnosed. In patients with an atypical presentation of syncope, without either overt heart disease or other competing diagnoses and with negative tests, syncope is generally classified as likely reflex (neurally mediated) or unexplained.

While typical VVS is mainly observed in young subjects, atypical VVS is observed in middle-aged and older subjects and only rarely in the young. However, some young subjects with recurrent VVS report typical and atypical episodes; in such cases, the presence of typical vasovagal attacks in the individual’s history allows atypical attacks to be accepted as vasovagal.

The clinical features of atypical VVS (tilt-induced syncope) were specifically investigated in a UK12 and an Italian study.3 Prodromal symptoms were absent in 24–39% of subjects. When prodromes were present, the most common were blurred vision (27–68%), fatigue (23–68%), pallor (48–82%), sweating (32–66%), nausea (13–60%), palpitations (10–37%), feeling cold (12–29%) and feeling warm (6–18%). During the syncopal phase, myoclonic jerks, investigated in the Italian study in the presence of witnesses, were observed in 13% of subjects, incontinence in 3–12%, minor trauma in 35–40% and fractures in 3–13%. During the recovery phase, symptoms were present in 74–76% of subjects.

**Influence of age on the clinical presentation.** The influence of age on the clinical presentation of VVS has been widely investigated.4–7 In older subjects, prodromal symptoms have been found to be of short duration. Moreover, the frequency of prodromes due to global cerebral hypoperfusion or to autonomic activation is lower in subjects >60–65 years.8 Only pallor is reported to display a similar prevalence in the young and the elderly.5 During the syncopal phase, myoclonic movements have rarely been observed in older subjects and in none aged >74 years.5 This could be explained by the less frequent occurrence of asystolic response in the elderly. Even during the recovery phase, the frequency of autonomic symptoms is reported to be lower in older subjects.5 Thus, in the elderly, the clinical features of VVS are very similar to those of cardiac syncope. The different clinical pattern of VVS observed in older subjects could be the result of several mechanisms, including an age-related decrease in parasympathetic activity, a diminished β-adrenergic response16 and a smaller increase in circulating adrenaline in the upright position.17 The results of some studies dealing with implantable loop recorders (ILRs)1 have shown that about half of spontaneous reflex synapses are asystolic.1 ILRs could be useful in patients with syncope of unknown origin in order to differentiate neurally mediated syncope from cardiac syncope and in selected patients with VVS in order to define the therapeutic strategy.1

**PRESENTATION OF VVS AS A FALL**

The clinical presentation of VVS could be a fall. A fall is defined as an event which results in a person coming to rest inadvertently on the ground or at another level. Falls may be accidental or unexplained. An accidental fall is defined as a simple slip, trip, accidental collision or environmental hazard resulting in a fall, whereas an unexplained fall is defined as a fall for which there is no apparent cause.

If syncope occurs when the patient is in the upright position, he/she will fall and, therefore, the clinical findings of syncope and falls could be very similar.18 19 In this regard, retrograde amnesia has been demonstrated in patients with syncope induced in the laboratory; about 25% of patients have been found not to remember their prodromal symptoms and TLoC during tilt-induced or carotid sinus massage (CSM)-induced syncope.20 21 In the international guidelines, syncope and falls are analysed separately. Indeed, the European guidelines on syncope1 make mention of falling only as a non-syncopal event without discussing the differential diagnosis. Similarly, the international guidelines on falls22 only mention that unexplained

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Possible clinical presentations of VVS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diagnostic criteria</td>
</tr>
<tr>
<td>Typical VVS* (classical VVS)</td>
<td>TLoC triggered by emotional distress or orthostatic stress, associated with symptoms due to autonomic activation</td>
</tr>
<tr>
<td>Atypical VVS* (non-classical VVS, atypical reflex syncope, atypical neurally mediated syncope, neurocardiogenic syncope)</td>
<td>TLoC not preceded by any evident trigger, but triggered by a non-spontaneous orthostatic trigger (tilt testing), in the absence of any competing diagnosis</td>
</tr>
<tr>
<td>Unexplained fall</td>
<td>Unexplained fall with positive tilt testing, in the absence of any competing diagnosis</td>
</tr>
<tr>
<td>Syncope during sleeping hours* (sleep syncope)</td>
<td>TLoC in the absence of any trigger, preceded by autonomic prodromes occurring during the sleeping hours (supine position), after exclusion of a potential cause of cardiac syncope</td>
</tr>
</tbody>
</table>

*Other terms used in the literature are reported in brackets. TLoC, transient loss of consciousness; VVS, vasovagal syncope.
falls could be a clinical manifestation of syncope in patients without any prodromal symptoms. A patient with a fall of uncertain origin should be asked whether he/she had prodromal symptoms. If the patient remembers these symptoms, we can diagnose a syncopal attack. If prodromal symptoms are not present, a fall should be considered. The patient should be asked to describe every part of the entire incident (Figure 1). If the patient clearly remembers the cause of the fall (slip, trip, etc.), an accidental fall can be diagnosed. If a cause of fall does not emerge, the fall can be regarded as unexplained. In such cases, some patients are able to remember the mechanism of the fall, how they lost their balance, the moment when they hit the ground; in these cases, a fall can be diagnosed. Often, the description of the event is confused and a differential diagnosis between unexplained fall and syncopal fall cannot be made. This diagnostic problem mainly involves older persons, though young and middle-aged subjects are sometimes involved, too. Witnesses, when present, should be asked whether the patient was unresponsive to external stimuli, particularly acoustic stimuli, during part of the event. In the presence of reliable witnesses, the differential diagnosis between syncope and fall can be made. Unfortunately, in 40–60% of cases, falls are not witnessed.

The literature does not offer evidence-based data about what to do when the differential diagnosis between unexplained fall and syncopal fall has not been made after the patient’s history has been taken. As suggested by the guidelines on falls, the initial evaluation should be the same as in patients with syncope: patient’s history, physical examination, including supine and standing blood pressure measurement and an ECG. If structural heart disease and/or history of arrhythmias are present, cardiological investigation should be performed, as in patients with suspected cardiac syncope. If a cardiac cause does not emerge, tilt testing and CSM appear, on the basis of the results of very recent studies, to be the most useful examinations. Paling et al performed tilt testing and CSM by means of the ‘method of symptoms’ on 101 patients with unexplained falls and 179 patients with unexplained syncope (presence of prodromal symptoms). The tilt test/CSM protocol used by Paling et al was a modification of the commonly used one. CSM was performed in the supine position; if syncope/presyncope was induced, the investigation was interrupted. If there was no or insignificant response, subjects were tilted to 70° and kept in the head-up tilt position for 15 min. If there was no response to head-up tilting, they had CSM performed during tilt testing. If there was no response to CSM, a sublingual spray of glyceryl trinitrate was administered and the subject remained in the head-up tilt position for another 20 min. This means that not all the patients underwent CSM and tilt testing. However, the combination of CSM/tilt testing provided a positive response in 67/111 patients (60%) with unexplained falls and in 113/179 patients (63%) with unexplained syncope (difference not statistically significant). These results suggest that many patients with unexplained falls could have atypical VVS or carotid sinus syncope. Rafanelli et al performed tilt testing and CSM by means of the ‘method of symptoms’ on 298 patients with unexplained falls and 989 patients with unexplained syncope. These examinations were performed in the usual sequence. The prevalence of positive tilt testing was high (36%) in patients with unexplained fall, though lower than in those with unexplained syncope (51%). Carotid sinus syncope showed a similar prevalence in both groups (14% and 10%). Overall, tilt testing and CSM displayed a high positivity rate in the group of patients with unexplained falls (61%), which was similar to that

**Figure 1** Patients with fall of uncertain origin.
of the unexplained syncope group (64%). These results are very similar to those reported by Paling et al.\textsuperscript{24} In these two studies, a control group without a history of syncope or falls was not investigated. However, in all the studies carried out so far, the prevalence of a positive tilt test has been significantly higher in subjects with suspected VVS than in control subjects without a history of syncope. Although orthostatic hypotension is probably the most frequent cause of unexplained falls, these new data seem to indicate that some unexplained falls could be cases of atypical VVS/carotid sinus syncope with retrograde amnesia, and that the fall is a consequence of TLoC.

These results suggest that patients with falls of unexplained origin should undergo tilt testing and CSM, in addition to orthostatic testing, after the initial evaluation. When the tilt test is positive in these patients, VVS could be diagnosed in the absence of any competing diagnosis.\textsuperscript{19} The treatment of VVS with a clinical presentation as a fall remains undefined, since published data are not available. In the 2013 European guidelines on cardiac pacing,\textsuperscript{27} the following recommendation dealing with patients with reflex syncope is reported: “Pacing should be considered in patients ≥40 years with recurrent, unpredictable reflex syncope and documented symptomatic pause/s due to sinus arrest or atioventricular block or the combination of the two” (class IIa, evidence B). It appears reasonable to assert that this recommendation is valid even for patients with VVS with a clinical presentation as a fall. However, in order to draw definite conclusions, large prospective studies using the ILR and cardiac pacing should be carried out; preliminary data seem to confirm a relationship between unexplained falls and bradyarrhythmias.\textsuperscript{28}

SYNCOPE DURING SLEEPING HOURS

VVS is rare in the supine position, with the exception of syncope triggered by venesection or medical procedures, because of gravitational relative preservation of cerebral perfusion. In studies dealing with typical VVS, syncope occurring in the horizontal position was observed in only 5% of subjects and was always triggered by emotional distress.\textsuperscript{3,29} When syncope occurs in the supine position, a cardiac cause of syncope should first be considered; if a cardiac cause is excluded, other examinations, chosen on the basis of the clinical presentation, should be performed.

Recently, a form of syncope which occurs in the supine position during the sleeping hours in the absence of any trigger has been recognised; this has been defined as ‘sleep syncope’.\textsuperscript{30–32} Most of the subjects involved were middle-aged women; they reported a history of waking up with abdominal discomfort and an urge to defecate, followed by TLoC. Autonomic symptoms, mainly sweating, nausea, palpitations and feeling warm were present in almost all patients. These symptoms always began in the supine position, but TLoC occurred in this position only in a third of subjects; in two-thirds it occurred after standing up to go to the bathroom. After regaining consciousness, most subjects felt intense weakness and could not remain in the upright position, but were oriented. The frequency of attacks varied from once a week to one episode a year and there was no relationship with alcohol. Some subjects had learned to partially abort the episodes by remaining supine in bed. Fifty-five per cent of these subjects also reported episodes of typical VVS during diurnal hours, and 74% had a history of specific phobia(s), mainly blood-injection-injury phobia. It is not clear whether the abdominal symptoms triggered the syncopal attack or whether they were part of the vagal response to the attack; the second hypothesis appears to be much more likely.\textsuperscript{30–32} Bradycardia was fortuitously documented in some subjects during the spontaneous syncopal episode. Basal testing was positive in 64% of subjects with sleep syncope—which appears to be a very high prevalence, considering the absence of pharmacological provocation—and in about half of these subjects an astyolic pause was recorded.

The mechanism of sleep syncope has not been elucidated. The possible underlying mechanisms include the circadian-modulated increase in parasympathetic nervous activity, decreased sympathetic nervous system activity, decreased systolic blood pressure and decreased cardiac output during the night. As some subjects have reported nightmares immediately before sleep syncope,\textsuperscript{30} some episodes might actually be emotional VVS. Sleep syncope can be diagnosed in the presence of typical autonomic prodromes and in the absence of structural heart disease or primary electrical disease. Some clinical features suggest that sleep syncope is a form of VVS with a different clinical presentation: high prevalence of autonomic prodromes, of diurnal episodes of typical VVS and specific phobias, and of positive tilt testing with severe cardioinhibition. The term ‘sleep syncope’ appears to be a misnomer and, after these considerations, the term ‘VVS during sleeping hours’ appears to be more appropriate.

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES


The different clinical presentations of vasovagal syncope

Paolo Alboni

*Heart* 2015 101: 674-678 originally published online March 19, 2015
doi: 10.1136/heartjnl-2014-307096

Updated information and services can be found at:
[http://heart.bmj.com/content/101/9/674](http://heart.bmj.com/content/101/9/674)

These include:

**References**
This article cites 32 articles, 12 of which you can access for free at:
[http://heart.bmj.com/content/101/9/674#BIBL](http://heart.bmj.com/content/101/9/674#BIBL)

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections
- Review articles (52)

**Notes**

To request permissions go to:
[http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to:
[http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to:
[http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)