Vasovagal syncope, sympathetic mechanisms and prognosis: the shape of things to come

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This editorial refers to ‘Persistence of muscle sympathetic nerve activity during vasovagal syncope’1, by G. Vaddadi et al., on page 2027 and ‘Early and late outcome of treated patients referred for syncope to emergency department: the EGSYS 2 follow-up study’1, by A. Ungar et al., on page 2021

Vaddadi and co-workers, from the Baker Heart and Diabetes Research Institute of Melbourne, have examined, in a group of patients with a clinical history of recurrent postural vasovagal syncope, the behaviour of efferent postganglionic muscle sympathetic nerve traffic, directly assessed via the microneurographic technique in the peroneal nerve, during a fainting episode triggered by tilting.1 The background for this investigation is based on the hypothesis that neurally mediated syncope, and its related cardiovascular and neurohumoral alterations, has as a ‘primum movens’ the complete loss of sympathetic vasoconstrictor influences on the circulation (Figure 1).2–7 This pathophysiological view appears to be supported by the evidence, collected during the past few years, that sympathetic neural outflow is almost completely withdrawn during a neurally mediated syncopal episode.2–7 There are, however, two features of the neuroadrenergic responses to syncope that deserve to be highlighted. The first refers to the evidence that, despite the almost complete disappearance of the sympathetic neural discharge (so-called ‘neural silence’) reported during syncope, plasma norepinephrine and epinephrine concentrations, i.e. the adrenergic neurotransmitters, are only partially reduced in the blood reservoir.8,9 This implies that the hypothesis that neurogenic syncope might have been in some way related to methodological problems, i.e. the loss of the sympathetic traffic signal during the syncope. This was not the case, however, in the report of Vaddadi et al.,1 in which in 10 out of the 16 patients examined the nerve recording site was fully maintained, allowing the persistence of a normal sympathetic activity during syncope to be shown. Secondly, the fact that in the study of Vaddadi et al. the recruited patients had a clinical history of vasovagal syncope, at variance from other studies,2–7 allows the hypothesis to be advanced that the sympathetic neural responses to a fainting episode may be different according to the clinical history of recurrent vasovagal synapses. This implies that the ‘neuroadrenergic profile’ of people suffering from vasovagal syncope may not necessarily be homogeneous and that factors such as the genetic background may be important for triggering such heterogeneous behaviour.

In commenting on the results of the report by Vaddadi and co-workers,1 two other considerations should be taken into account. The first refers to the fact that the behaviour of sympathetic nerve traffic in the skeletal muscle area does not necessarily reflect the one seen in other districts. This has been shown, for example, in human obesity and in relation to the ageing process, in which some neural areas (the heart and the skin) do not display the same quantitative profile (sympathetic activation) reported in the muscle vascular area.10,11 The second consideration refers to
the behaviour of the arterial baroreflex function in subjects with neurogenic syndrome. In the report of Vaddadi et al., baroreflex modulation of vagal drive to the sinus node, as assessed via the so-called ‘sequence’ method, appears to be impaired, as compared with what was found in a group of healthy controls. This does not necessarily mean, however, that the baroreflex dysfunction in modulating heart rate should also apply to baroreceptor control of peripheral sympathetic neural outflow. However, evidence provided by Bèchir and co-workers conclusively shows that baroreceptor modulation of sympathetic outflow during the vasovagal episode is somewhat impaired, similarly to that reported for baroreflex heart rate control. Such a reflex alteration is not in contrast to the preservation of the sympathetic neural activity observed during the fainting episode and reported in the study of Vaddadi et al. This is because there might be several factors participating in guaranteeing a normal sympathetic function during vasovagal syncpe. This may be the case for metabolic factors, such as hyperinsulinaemia. This may also be the case for the renin–angiotensin activation occurring during syncope.

A second study on syncpe has also been published recently, reporting the follow-up of the Evaluation of Guidelines in Syncope Study 2 (EGIS 2). The main study aim was to define the short- and long-term prognosis of patients referred to an emergency ward for syncpe. The death rate was higher (17% of all deaths) in the first month of observation, while reoccurrence of the syncopal episode was low overall in both the short and the long term (0.3% and 0.8% in the first month and in the second year, respectively). Mortality was higher in patients with a clinical history of a previous cardiovascular disease or in those displaying electrocardiographic abnormalities. Both of these two factors represent the main predictors of short- or long-term mortality on multivariate analysis. The study results therefore reinforce the concept that particular attention should be paid in the emergency room to patients with syncpe and at high risk of fatal complications, for which hospitalization for further investigations should be highly recommended.

What is the common link between the two studies which should be regarded as the ‘take home message’ for the readership of the journal? There may be several, but I would like to underline that the major link could be the renaissance of interest in syncpe, which at present is regarded as an ‘independent disease’ with a complex pathophysiological background but also with a well-defined prognostic impact. Whether the different therapeutic approaches available for syncpe carry a different prognostic impact remains to be seen. This implies that the scientific and clinical interest in this disease will continue during the coming years.

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References


Figure 1 Schematic overview of the haemodynamic, neurohumoral, and reflex alterations occurring during vasovagal (neurogenic) syncpe. AVP, arginine vasopressin; All, angiotensin II.


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**CARDIOVASCULAR FLASHLIGHT**

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**Pneumopericardium**

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A 72-year-old man with hypertension presented with a 3-h chest pain, and an electrocardiogram (ECG) suggested acute inferior myocardial infarction (Panel A). He underwent emergency coronary angiography that showed non-significant epicardial coronary artery disease but presence of pneumopericardium (Panel B, arrows). A computed tomography scan confirmed the diagnosis, revealing a no-tension pneumopericardium (Panel C, arrows), and a limited posterior pneumomediastinum with air diffusion around the pulmonary vessels; just in front of the tracheal bifurcation, it also showed some tracheal wall irregularities and non-homogeneous tracheo-bronchial tissue (Panel C, x symbol), probably relating to a neoplastic proliferation.

An elective bronchoscopy showed an infiltrative tracheo-bronchial mass involving the tracheal bifurcation and right bronchus, in particular, with purulent secretions (Panel D). In the absence of other possible causes, the infiltrative tracheo-bronchial mass was the likely cause of pneumomediastinum and pneumopericardium through several microscopic direct communications.

During the first 2 days of hospitalization, we registered slightly increased troponin I and creatine phosphokinase-MB isoenzyme levels that subsequently decreased rapidly to normal values. In the course of observation, the patient did not present any sign of haemodynamic instability, and no pericardial aspiration or drainage was required. He was transferred to the Thoracic Surgery Division for specific intervention, but he refused surgery and died some weeks later.

We noted that diagnosis of pneumopericardium using angiography is unusual because pneumopericardium presentation with an ECG mimicking an acute myocardial infarction is uncommon. Moreover, it is even more infrequent for pneumopericardium to be the first clinical evidence of pulmonary neoplasm.

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