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# Predictive models of syncope causes in an outpatient clinic

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**Abstract**

The investigation of unexplained syncope remains a challenging clinical problem. In the present study we sought to evaluate the diagnostic value of a standardized work-up focusing on non invasive tests in patients with unexplained syncope referred to a syncope clinic, and whether certain combinations of clinical parameters are characteristic of rhythmic and reflex causes of syncope.

*Methods and results:* 317 consecutive patients underwent a standardized work-up including a 12-lead ECG, physical examination, detailed history with screening for syncope-related symptoms using a structured questionnaire followed by carotid sinus massage (CSM), and head-up tilt test. Invasive testings including an electrophysiological study and implantation of a loop recorder were only performed in those with structural heart disease or traumatic syncope. Our work-up identified an etiology in 81% of the patients. Importantly, three quarters of the causes were established non invasively combining head-up tilt test, CSM and hyperventilation testing. Invasive tests yielded an additional 7% of diagnoses. Logistic analysis identified age and number of significant prodromes as the only predictive factors of rhythmic syncope. The same two factors, in addition to the duration of the ECG P-wave, were also predictive of vasovagal and psychogenic syncope. These factors, optimally combined in predictive models, showed a high negative and a modest positive predictive value.

*Conclusion:* A standardized work-up focusing on non invasive tests allows to establish more than three quarters of syncope causes. Predictive models based on simple clinical parameters may help to distinguish between rhythmic and other causes of syncope.


*Keywords:* Syncope; Diagnostic yield; Diagnosis; Syncope unit

## 1. Introduction

Syncope, a common and challenging symptom, remains unexplained in up to 60% of the cases [1–6]. Some investigators have recently shown the superiority of simple investigation strategies over usual practice in patients with syncope addressed to emergency departments [1,6–8]. The development of syncope clinics has dramatically changed the evaluation of syncope by re-orienting patients toward functional investigations; however, little is known about the true diagnostic performance of these dedicated facilities. Moreover, patients with syncope often present with multiple symptoms before and/or after the event. Syncope-related symptoms have been traditionally used to separate vasovagal from rhythmic causes [9–11] but predictive models of syncope causes are still lacking.

In the present work we investigated a population of patients referred to a syncope unit for unexplained syncope. We sought first to evaluate the diagnostic yield of a standardized work-up, which turned out to correspond closely to later published guidelines [12], and second, whether a certain combination of clinical parameters based on history, ECG and syncope-related symptoms were characteristics of either rhythmic or reflex causes of syncope.

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## 2. Materials and methods

### 2.1. Setting

This single center study was conducted in the syncope clinic of the Service of Cardiology at the Lausanne University hospital in Switzerland. On average, one patient is referred daily to the clinic for the investigation of unexplained syncope or presyncope. The study complies with the Declaration of Helsinki, and has been approved by our local ethics committee. Syncope was defined as a brief, self-limited loss of consciousness with the inability to maintain postural tone. Presyncope was defined as a near syncopal event. Patients with symptoms compatible with other non syncopal conditions such as seizure disorders, vertigo, dizziness or coma were excluded.

### 2.2. Study design

Consecutive outpatients referred to our syncope clinic were prospectively included between December 1st 1999 and October 30th 2001. Patients underwent a standardized work-up (Fig. 1) consisting of a history, physical examination and 12-lead ECG analyzed by two of the investigators (E.P. and E.G.). Patients underwent a 30-min head-up tilt test (HUT) followed by upright and supine CSM in absence of contra-indications [12], with continuous non invasive blood pressure measurement (Finapres, Ohmeda). Drug challenges with intravenous adenosine triphosphate [13] and sublingual dinitrate isosorbide [14] were performed following a negative baseline HUT and CSM. Hyperventilation testing was performed only in patients with phobic, anxious and/or depressive features. Evaluation by a psychiatrist was required in all clinically suspect cases. Structural heart disease was ruled out on the basis of history, physical examination and ECG [12]. When the initial evaluation confirmed or suggested an underlying cardiac disease, a stress test and an echocardiogram were usually performed. The latter was also performed before any invasive study in patients not previously evaluated. Patients then re-integrated the common work-up. Coronary angiography was performed when indicated. Electrophysiological (EP) study was performed only in patients with an underlying structural heart disease, or in those whose non invasive work-up was negative but who required further testing because of major trauma and/or for medico-legal purposes. Importantly, a positive test was considered diagnostic when the test-induced symptom(s) matched the presentation of the clinical syncope, otherwise the test was considered abnormal but non diagnostic.

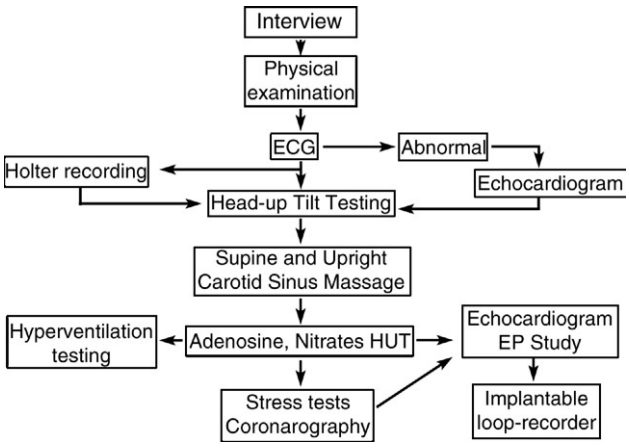


Fig. 1. Standardized work-up.

### 2.3. Measurements

In order to maximize the reliability of data acquisition, physicians in charge of the patients were trained to use a 600 items database (FileMaker Pro 5) specifically developed for the management of syncope patients. The initial interview focused on the number of syncopal episodes, precipitating factors, occurrence and duration of prodromal and recovery symptoms. The following 23 symptoms were systematically investigated: diaphoresis, nausea and/or vomiting, visual changes, dyspnea, headache, chest pain, abdominal pain, palpitations, vertigo, asthenia, incontinence, neurologic deficit, impression of imminent death, diarrhea, sudation, tinnitus, paresthesia, anxiety, tongue biting, difficulty to concentrate, confusion, disorientation and tremor. Syncope-related trauma was classified as: (1) major, defined as any fractures, head injury or internal organ damage, or syncope resulting in a car accident; or (2) minor, defined as any bruise, cut, or soft tissue injury. The duration of the P-wave of the ECG was determined by averaging the P-wave value from three consecutive beats, from at least two derivations (D2 and V1) [15]. Importantly, P-wave duration was measured and reported in a database before any investigations in order to avoid methodological bias.

### 2.4. Diagnostic criteria for causes of syncope

Diagnostic criteria for causes of syncope were established before the study and adhered strictly to published data [12]. The diagnosis was assigned by one of the investigators (E.P.) at the end of the standardized work-up which turned out to follow the guidelines of the European Society of Cardiology [12]. We did not establish final diagnoses on history alone or as a part, but always using results of investigational tests. Prodromes (i.e. history) were only used to establish that the syncopal event taking place during a specific test did reproduce the clinical event. However, the nature of prodromes (i.e. nausea, diaphoresis, etc) in itself was not used to establish final diagnoses.

For statistical analysis, final causes of syncope were grouped into 5 categories: (1) Rhythmic causes included bradyarrhythmias (AV block and cardio-inhibitory carotid sinus syndrome, CSS) and tachyarrhythmias (supra- and ventricular tachycardia); (2) VV/Psy causes included vasovagal (VV, i.e. tilt induced) syncope and psychogenic pseudo-