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Temporal Relationship of Asystole to Onset of Transient Loss of Consciousness in Tilt-Induced Reflex Syncope

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ABSTRACT

OBJECTIVES The purpose of this study was to investigate the relationship between the onset of asystole and transient loss of consciousness (TLOC) in tilt-induced reflex syncope and estimate how often asystole was the principal cause of TLOC.

BACKGROUND The presence of asystole in vasovagal syncope (VVS) may prompt physicians to consider pacemaker therapy for syncope prevention, but the benefit of pacing is limited in VVS.

METHODS We evaluated electrocardiography, electroencephalography, blood pressure, and clinical findings during tilt-table tests. Inclusion required TLOC (video), electroencephalographic slowing, accelerating blood pressure decrease, and an RR interval ≥3 s. We excluded cases with nitroglycerin provocation. Asystole after onset of TLOC (group A) or within 3 seconds before TLOC (group B) was unlikely to cause TLOC, but an earlier start of asystole (group C) could be the cause of TLOC.

RESULTS In one-third of 35 cases (groups A [n = 9] and B [n = 3]), asystole was unlikely to be the primary cause of TLOC. The median of the mean arterial pressure at the onset of asystole was higher when asystole occurred early (45.5 mm Hg, group C) than when it occurred late (32.0 mm Hg, groups A and B), which suggests that vasodepression was not prominent at the start of asystole in early asystole, further suggesting that early asystole was the prime mechanism of syncope.

CONCLUSIONS In one-third of cases of tilt-induced asystolic reflex syncope, asystole occurred too late to have been the primary cause of TLOC. Reliance on electrocardiography data only is likely to overestimate the importance of asystole. (J Am Coll Cardiol EP 2017;■:■-■) © 2017 by the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Syncope is the form of transient loss of consciousness (TLOC) that is caused by brief and self-terminating diminution of global cerebral hypoperfusion (1). The term *reflex syncope* refers to those forms of syncope in which neural reflex responses play a key role in causing transient hypotension and consequent diminution of cerebral blood flow. Vasovagal syncope (VVS) is by far the most common cause of reflex syncope. In many instances, susceptibility to VVS can be unmasked by head-up tilt-table testing (2).

Reflex syncope encompasses both vasodepressor and cardioinhibitory mechanisms. Although either mechanism can cause syncope, in most cases both

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ABBREVIATIONS AND ACRONYMS

BP = blood pressure

ECG = electrocardiography

EEG = electroencephalography

LUMC = Leiden University Medical Centre

MAP = mean arterial pressure

SEIN = Stichting Epilepsy Instellingen Nederland

TLOC = transient loss of consciousness

tend to occur together in reflex syncope (i.e., the mixed pattern). The basis by which the vasodepressor response contributes to syncope remains controversial, but it has been considered to be primarily due to venous pooling in the lower parts of the body, resulting in decreased cardiac venous return and a reduced cardiac output (3,4). The cardioinhibitory mechanism is effected primarily through an increase in vagal tone (5,6). Its most extreme expression is abrupt prolonged asystole (usually defined as a cardiac pause ≥3 s), which on its own causes blood pressure (BP) to fall precipitously. If asystole is sustained for a sufficiently long period of time, the resulting cerebral hypoperfusion causes unconsciousness about 6 to 8 s after the last heartbeat (7,8).

The presence of asystole in VVS might prompt physicians to consider pacemaker therapy to prevent syncope recurrence; however, it is increasingly recognized (2) that the benefit of pacing is limited in VVS patients. In fact, recent observations from the ISSUE-3 (third International Study on Syncope of Uncertain Etiology) (9) and SUP-2 (Syncope Unit Project 2) (10) suggest that among patients with documented spontaneous asystole during VVS, pacing efficacy was primarily of value in those individuals without evident vasodepressor susceptibility (i.e., the latter observation implies that the VVS origin was truly due to cardioinhibition). Unfortunately, when vasodepression and cardioinhibition act at the same time, it is not usually feasible to quantify how much each contributes to cerebral hypoperfusion. However, during head-up tilt-induced syncope with continuous electroencephalographic (EEG) monitoring, it is possible to determine both when asystole starts and when onset of TLOC occurs; thus, if asystole starts after the onset of TLOC, it cannot have been the principal cause of TLOC. Similarly, if asystole starts within 3 s of TLOC, the bradycardia is unlikely to be the cause of syncope. On the other hand, if asystole begins >3 s before TLOC, there is a reasonable likelihood that the bradycardia did contribute to TLOC.

The objective of this study, using head-up tilt testing with continuous video-EEG recording, was to describe the temporal relation between the onset of asystole and of TLOC during tilt-induced syncope. A second goal was to use the observed temporal relationship to estimate how often asystole could be the prime cause of TLOC in tilt-induced syncope.

METHODS

PATIENTS. This report is based on all tilt-table tests performed between 2006 and 2015 for evaluation of TLOC at 2 tertiary syncope referral centers: the Department of Neurology of the Leiden University Medical Centre (LUMC), and the syncope clinic of Stichting Epilepsie Instellingen Nederland (SEIN). These institutions share expertise, use the same indications and protocols for tilt-table testing, use the same brand of tilt table, and have collaborated on studies assessing the semiology and pathophysiology of tilt-induced syncope and psychogenic pseudosyncope (11–15).

Suspected susceptibility to vasovagal syncope is the most common indication for tilt-table tests in both centers. Part of the present patient group has been described previously (14). In that study, tilt-induced reflex syncope was defined using the following triad: video records compatible with loss of consciousness, EEG changes showing a slow or slow-flat-slow pattern, and BP showing the pattern of tilt-induced reflex syncope, that is, an increasing rate of decline with or without bradycardia. We now incorporated 1 additional inclusion criterion: the electrocardiogram (ECG) showed asystole, defined as an RR interval of ≥3 s. We also added 1 exclusion criterion: tilt tests in which syncope developed after administration of sublingual nitroglycerin were excluded on the assumption that nitroglycerin administration might influence the relative contribution of vasodepression and cardioinhibition.

CLINICAL TILT PROTOCOL AND DATA EXTRACTION. We used EEG machines to store data sampled at 200 Hz. Recordings comprised continuous video, EEG, BP (derived from finger plethysmography), and a 1- or 2-lead ECG. In the LUMC, the video camera is attached to the tilt table and is aimed at the head and shoulders, whereas at SEIN, a ceiling-mounted camera covers the entire tilt table.

Tilt-table tests were performed with a modified Italian protocol (16). The usual test protocol consisted of 10 min of supine rest followed by 20 min of head-up tilt to 70°, after which, if syncope did not occur, sublingual nitroglycerin was used and patients were observed for another 20 min. However, as noted previously, the present study included only tests in which TLOC occurred in the drug-free first 20 min after head-up tilt. Reasons to tilt patients back before the expiration of the allotted protocol time included the presence of syncope (i.e., the circulatory pattern of reflex syncope with clinical TLOC); presyncope