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Blunted Chronotropic Response to Hypotension in Cough Syncope

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ABSTRACT

OBJECTIVES This study compared hemodynamic and chronotropic responses to cough in cough syncope (CS) patients to those in control subjects.

BACKGROUND Cough syncope is an uncommon form of situational fainting variously attributed to both reflex and mechanical causes. We hypothesized that if baroreflex responses contribute to CS, post-cough hypotension should be associated with cardioinhibition comparable to that observed in other reflex faints.

METHODS The study population consisted of 8 CS patients (group 1), 21 patients with vasovagal syncope (group 2), and 6 patients with nonvertiginous "lightheadedness" (group 3). Testing with patients seated included volitional coughing that achieved a transient blood pressure (BP) of ≥200 mm Hg. Beat-to-beat blood pressure (systolic blood pressure [SBP]) before cough, minimum cough-induced SBP and heart rate (HR) (beats/min) after cough, and HR change during cough-induced hypotension were recorded, along with SBP recovery time from SBP nadir after cough.

RESULTS Compared to controls, cough-induced SBP drop was greater in CS patients (CS patients: -48 ± 13.1 mm Hg vs. -29 ± 11.2 mm Hg for group 2 controls; $p = 0.005$; or -25 ± 10 mm Hg in group 3 controls; $p = 0.02$), and recovery time was longer (CS: 46 ± 19 s vs. 11 ± 3.6 s in group 1 controls; $p = 0.002$; or 12 ± 5 s in group 3 controls; $p = 0.01$). Furthermore, despite greater induced hypotension, post-cough chronotropic response was less in CS patients (+15% above baseline rate) than in either group 2 (+31% above baseline rate; $p < 0.001$) or group 3 (+28%; $p = 0.01$) controls.

CONCLUSIONS In CS patients, post-cough chronotropic response is blunted compared to that in controls despite greater cough-induced hypotension favoring baroreflex cardioinhibition contribution to the pathophysiology of cough syncope. (J Am Coll Cardiol EP 2016;■:■-■) © 2016 by the American College of Cardiology Foundation.

Cough syncope (CS) is a well-known but uncommon form of situational faint, the pathophysiology of which remains incompletely understood (1,2). CS has been variously attributed to both reflex and mechanical causes (3-11). The abrupt increase of systemic arterial pressure associated with forceful cough (**Figure 1**) has been hypothesized to cause loss of consciousness by 1 or more of the following mechanisms: baroreflex-induced bradycardia and vasodilation, or a mechanical cerebral concussive effect, or a transient venous obstruction with reduced cardiac output.

Previously, we observed that volition-induced cough in supine CS patients triggered a period of hypotension and that the duration of hypotension was greater than would be expected by venous obstruction alone (12). We concluded that CS was most likely due to a baroreflex-triggered response as originally proposed by Sharpey-Shafer (3).

In this study, we sought to further assess the concept that baroreflex responses contribute to cough-induced hypotension in CS patients. To this end, we compared the magnitude and duration of cough-induced hypotension with the resulting

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

BP = blood pressure

CS = cough syncope

ECG = electrocardiogram

HR = heart rate

SBP = systolic blood pressure

chronotropic response during the hypotensive phase after cough in upright, seated patients with clinical CS and in 2 sets of control subjects: 1 group with clinically diagnosed vasovagal syncope and a second group referred for evaluation of nonvertiginous "lightheadedness and dizziness." We hypothesized that if hypotension is principally mediated by reflex vasodilation, then it would be accompanied by a diminished chronotropic response (presumably on a parasympathetic basis) as is observed in other reflex faints (e.g., vasovagal syncope) (1).

METHODS

The patient population consisted of individuals referred between January 2012 and December 2015 for evaluation at the Cardiac Arrhythmia and Syncope Center at University of Minnesota (Minneapolis, Minnesota). Three patient groups were defined, as follows: group 1 included patients with a clinical history compatible with CS. These patients presented with a history of multiple syncope and/or near-syncope episodes closely associated with coughing (usually a spasm of coughing). Based on each individual's medical history, only 1 of these patients had experienced syncope unassociated with cough, and in that case the presumed faints had occurred more than 30 years earlier.

Group 2 included patients (syncope controls) without carotid sinus hypersensitivity or clinically significant structural cardiac or neurological disease, with reflex syncope of non-cough causes. Group 3 consisted of individuals without syncope or collapse but who were referred for evaluation of nonvertiginous lightheadedness or dizziness and in whom medical history and response to head-up tilt test was nondiagnostic (i.e., did not reproduce spontaneous symptoms).

Written informed consent was obtained after thorough discussion of the study plan with each subject, using an Institutional Review Board-approved consent form. Studies were undertaken after a 3-h fasting state, with intravenous saline (500 ml) administered over a 20-min period prior to initiating testing to attempt to achieve a euvolemic state. All cardioactive medications (primarily antihypertensive drugs in the CS group) had been withheld for approximately 48 h before testing. Prior to study, patients were asked to relax in a sitting position for 10 min in a quiet room with low-level lighting. Baseline heart rate (HR), continuous electrocardiography (ECG), and continuous beat-to-beat blood pressure (BP) (Finometer; Finapres Medical Systems or Nexfin, BMEYE, Amsterdam, the Netherlands) were recorded. In each case, the noninvasive BP recording system was calibrated using a standard sphygmomanometer.

The use of volitional cough as a diagnostic testing procedure has been previously reported (2,12). The cough maneuver was carefully explained to each patient. A practice maneuver was permitted in each case, and another 5 min was allowed prior to the actual test. The cough protocol was undertaken with patients in a seated position to diminish risk of falls.

Subjects were asked to undertake 2 to 3 vigorous coughs in quick succession with the goal of achieving a transient arterial pressure of 200 mm Hg or greater. Duration of the transient pressure >200 mm Hg was approximately 3 to 5 s (**Figures 1 and 2**). Continuous HR and beat-to-beat BP were recorded during coughing and for approximately 5 min after the completion of the coughing intervention. SBP and HR measurements were calculated as the average of 4 consecutive cardiac cycles. A cough test was deemed to have been effective if it induced a transient increase in systolic blood pressure (SBP) to ≥200 mm Hg.

The hemodynamic impact of cough was determined by measuring the change in mean beat-to-beat SBP before and after cough and the associated beat-to-beat HR prior to and immediately after the cough (**Figures 1 and 2**). Recorded hemodynamic responses included mean SBP before cough, mean minimum cough-induced SBP (mm Hg) immediately after the end of cough, mean HR (beats/min) before cough, and mean HR increase during cough-induced hypotensive period.

Time to SBP recovery was defined as duration (in seconds) from SBP nadir immediately after cough to the recovery of SBP to its value immediately prior to cough perturbation. All values are mean ± SD. Statistical significance of differences was assessed by Student *t*-test and ANOVA as appropriate. A p value of <0.05 was considered significant.

RESULTS

CLINICAL FEATURES. The study population consisted of 28 patients referred for diagnostic evaluation and treatment of suspected reflex syncope and an additional 6 individuals referred for evaluation of nonvertiginous lightheadedness or "dizziness" but without reported transient loss of consciousness and with nondiagnostic response to head-up tilt (i.e., study did not reproduce spontaneous symptoms).

The CS group included 8 individuals, 7 of whom were men (group 1). The syncope control group (group 2) included 21 individuals with a medical