Postprandial Hypotension in Elderly Patients With Unexplained Syncope

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Background: Syncope in older patients may be caused by a variety of disorders, including hypotension, but frequently remains unexplained. Postprandial hypotension is a common disorder of blood pressure regulation in the elderly.

Objective: To determine the pathogenic mechanisms and potential role of postprandial hypotension in elderly patients with otherwise unexplained syncope.

Methods: We studied 16 elderly patients with unexplained syncope and nine elderly controls. Blood pressure, heart rate, forearm vascular resistance, plasma norepinephrine level, and cardiac and splanchnic blood volumes were measured before and after a 1680-kJ meal.

Results: Eight elderly patients with syncope had postprandial hypotension, with a decline in supine mean arterial blood pressure of 17±2 mm Hg after a meal ($P<.001$). The blood pressure remained unchanged after the meal in the other patients with syncope and the controls. In patients with postprandial hypotension, systemic vascular resistance fell after the meal, while it remained unchanged in the other groups. Heart rate and plasma norepinephrine level increased to a similar extent in all three groups. Forearm vascular resistance increased only in the control subjects. Splanchnic blood volume increased by 26% ($P<.01$) in patients with syncope who had postprandial hypotension and by 22% ($P<.01$) in control subjects. Splanchnic blood volume remained unchanged in the patients with syncope without postprandial hypotension.

Conclusions: Postprandial hypotension may be an important causative factor in elderly patients with unexplained syncope. The evaluation of syncope in elderly patients should therefore include blood pressure measurements surrounding a meal. Elderly patients with syncope who have postprandial hypotension fail to maintain systemic vascular resistance, probably because of splanchnic blood pooling without a compensatory increase in peripheral vascular resistance.

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SYNCOPE IS a common symptom in elderly patients that remains unexplained in 30% to 50% of cases, despite extensive and expensive medical evaluations.[1-3] Elderly persons are particularly vulnerable to syncope because of the accumulation of multiple age- and disease-related abnormalities that impair cardiovascular adaptation to hypotensive stresses. Accordingly, hypotension and syncope may occur in response to seemingly minor stimuli not ordinarily expected to produce syncope. In more than one third of syncope cases, hypotension in response to common situational stresses, such as drug ingestion, posture change, meal digestion, defecation, and micturition, has been implicated as a causative factor.[4] These daily situations, alone or in combination with each other, and superimposed on comorbid diseases, may threaten cerebral oxygen delivery and subsequently result in a syncopal event.

During the past decade, postprandial hypotension (PH) has become recognized as a common disorder of blood pressure (BP) regulation in the elderly,[5-12] in patients with autonomic failure,[13-16] and in patients with end-stage renal disease during hemodialysis.[17] In most elderly persons, meal-associated declines in BP are modest and asymptomatic; however, in hypertensive elderly patients,[7,9,10] patients with Parkinson's disease[16] or autonomic

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SUBJECTS AND METHODS

SUBJECTS

Sixteen elderly patients with unexplained syncope were recruited from the Hebrew Rehabilitation Center for Aged, Boston, Mass, an academic long-term care facility (seven patients), from the Beth Israel Hospital, Boston (one patient), or from referrals by primary care physicians (eight patients). All patients underwent a full medical evaluation, including a careful history, physical examination, blood studies, an electrocardiogram, cardiac monitoring, and an echocardiogram and cardiac Doppler study. In all cases syncope remained unexplained after this evaluation.

Syncope was defined as a sudden transient loss of consciousness associated with an inability to maintain postural tone and with spontaneous recovery. All patients had one or more syncopal episodes, and all of these episodes occurred during a 2-hour period after a meal. Although several of the subjects were taking medications on a long-term basis, there was no temporal relationship between medication administration and syncope or other clinical evidence that syncope could be attributed to medication effects. None of the subjects had orthostatic hypotension. One patient with a demand pacemaker continued to have unexplained syncopal episodes and was included in this study. He was not in a paced rhythm during the study.

Subject characteristics are summarized in **Table 1**. The patients with syncope were divided into two groups according to their BP response after a meal. Eight of the patients with syncope had PH, defined as a decline in supine systolic BP of 20 mm Hg or more within the 90-minute study period. Nine healthy elderly subjects with no history of medical illness, smoking, or medication use were recruited from the local Boston community through newspaper advertisements. These healthy elderly subjects were also included in another study.[26]

The study was approved by the Institutional Review Boards of the Beth Israel Hospital and Hebrew Rehabilitation Center for Aged. All subjects provided written informed consent after the nature of the study had been fully explained.

STUDY PROTOCOL

Meal studies began at 7:30 AM after an overnight fast from midnight the night before. If subjects were taking long-term medications, these were withheld for as long as it was safe to do so: a minimum of 12 hours before the study for medications routinely given two to four times daily and 24 hours before the study for those given once daily.

The meal was a 1680-kJ drink (Carnation Instant Breakfast in lactose-free whole milk) that contained 40% carbohydrate, 45% fat, 15% protein, and 12 mEq of sodium. It was served at a temperature of 22°C to avoid potential temperature effects on BP.[24] This meal composition represents that of a mixed breakfast.

Each subject was studied in the nuclear medicine laboratory of the Beth Israel Hospital, where radionuclide imaging studies were performed to measure cardiac and splanchnic blood pools. A 21-gauge angiocatheter with heparin lock was placed in one antecubital vein for blood sampling throughout the study. This intravenous catheter was also used to withdraw a 3-mL blood sample during each radioventriculogram to determine biologic clearance of the tracer. A second temporary angiocatheter was placed in the opposite antecubital vein for collection and reinjection of autologous red blood cells that were labeled with 740 MBq of technetium Tc 99m. This line was removed after labeled red blood cell injection. After this injection and a minimum of 30 minutes of supine rest, 10 minutes of basal measurements were performed. Subjects then sat for 10 minutes to ingest the liquid meal, after which they resumed a supine position for the duration of the study. Room temperature remained constant (23±1°C) throughout the study.

The BP and heart rate (HR) were measured on one arm at 5-minute intervals throughout the study with an automated oscillometric device (Dinamap, Critikon, Tampa, Fla). The three BP and HR measurements at 10, 5, and 0 minutes before the meal were averaged and considered the baseline value. This value and the means of the three values around the 15-, 30-, 45-, 60-, 75-, and 90-minute time points

dysfunction,[13,14] and especially in the nursing home population,[5,12,18] postprandial declines in BP may be of sufficient magnitude to result in syncope.

In a previous study we found that in 31 of 97 elderly patients with syncope, fainting occurred within 1 hour of the beginning of meal ingestion.[4] In eight of these subjects, hypotension was documented immediately on fainting and marked PH was later reproduced.[18] Although these data suggest a causative relationship between PH and syncope, meal-related hypotension is rarely sought during the evaluation of syncope in the elderly. In a study that evaluated 210 elderly patients with syncope, no meal-associated syncope was reported.[3] In the absence of a careful search for PH, patients with syncope who have this problem may be inappropriately labeled as having "unexplained syncope" or subjected to unnecessary invasive tests. Therefore, one aim of the current investigation was to assess the potential clinical significance of PH in elderly patients with unexplained syncope.

Several pathophysiologic mechanisms of PH have been proposed, including age- and/or BP-related impairments in baroreflex function,[5,10,19] insulin-induced vasodilation or baroreflex impairment,[10,19] inadequate sympathetic nervous system compensation for meal ingestion,[5,10,13] excessive splanchnic blood pooling during digestion,[20] hypotensive effects of vasoactive gastrointestinal peptides,[14,20-25] and failure to maintain systemic vascular resistance after a meal.[26] In patients with autonomic dysfunction, impaired peripheral vascular responsiveness probably plays an important role.[26] Until now, no clear pathophysiologic mechanism of PH in the elderly has been defined. Therefore, the present study was designed also to determine the pathophysiologic mechanisms of PH in elderly patients with syncope. Accordingly, we compared the hemodynamic, neurohumoral, and splanchnic blood pool responses to a standardized mixed meal in elderly patients with syncope with and without PH, and in healthy elderly controls.

were used in the analyses. Upper-arm and wrist cuffs and a mercury-in-Silastic strain gauge were attached to the other arm for plethysmographic measurements of forearm blood flow taken during 3-minute periods. Circulation in the hand was excluded by application of a suprasystolic pressure to the wrist cuff. Blood flow was calculated by taking the average of three consecutive readings. Measurements were taken before the meal, then at 15-minute intervals beginning 15 minutes after the start of the meal.

Plasma norepinephrine samples were obtained twice before the meal (5 and 0 minutes), then 30, 45, 60, and 90 minutes after the meal. Blood was drawn from the antecubital intravenous catheter without the use of a tourniquet and was collected in specimen tubes that contained ethylene glycol-tetraacetic acid and reduced glutathione. The tubes were placed immediately on ice. Plasma was separated by refrigerated centrifugation, then fast-frozen in dry ice and acetone and stored at −70°C until assayed. Plasma norepinephrine concentrations were determined by the single-isotope radioenzymatic assay.[27] This assay is sensitive to within 0.12 nmol/L of plasma. The within-run coefficient of variation is less than 7.5%. Because interassay variability is 10% to 15%, all of each subject's samples were assayed at one time.

Five-minute images for gated cardiac blood pool determinations were obtained before and at 30-minute intervals after the meal.[28,29] The left ventricular ejection fraction was calculated with a fixed region of interest method. The area and longest axis of the region of interest was used to calculate absolute left ventricular end-diastolic volume (EDV).[28] Cardiac index, stroke volume index, and EDV index were calculated by dividing the cardiac output (stroke volume×HR), stroke volume (EDV×ejection fraction), or EDV by body surface area, which was estimated according to the equation of DuBois and DuBois from the measured height and weight.[30] Peak filling rate was calculated from a third-order polynomial fit to the rapid filling portion of diastole.[29] As the absolute value of EDV was known, we were able to express peak filling rate as milliliters per second.

Changes in splanchnic blood volume were determined by measuring the relative changes in radionuclide activity from a region of interest overlying the bowel.[31] Compared with Doppler measurements of superior mesenteric blood flow, this method has the advantage of assessing splanchnic blood pooling, which is more directly related to the pathophysiologic basis of PH. A cobalt 57 marker was attached to the lower part of the abdomen to aid in repositioning the patient and to align the images during analysis. Two sequential 2-minute images of the abdomen were obtained during the baseline period to establish that equilibrium had been adequately achieved. Images were obtained at 15, 30, 60, and 90 minutes in the anterior position to decrease the contribution from excreted activity. An attempt was made to exclude the urinary system from the region of interest when it could be identified. The counts were corrected for background, biologic clearance, and physical decay. The intraindividual variability of the radionuclide technique has been reported to be 1% to 3%.[31]

ANALYSIS

Forearm vascular resistance was calculated as mean arterial BP divided by the forearm blood flow, and systemic vascular resistance was calculated as mean arterial BP divided by cardiac output. Splanchnic blood volume was calculated as a percentage of the baseline value.

The Kruskall-Wallis test was used to compare baseline values in the three groups. Changes over time for the different variables were examined by means of repeated-measures analysis of variance. Changes for each variable over time were compared between two groups at a time with the use of a two-factor (group and time) repeated-measures analysis of variance.[32] When an overall time effect was found, the postmeal measures at each time point were individually compared with baseline by means of Student's *t* test for parametric data and Wilcoxon's Rank Sum Test for nonparametric data. To study the effects of splanchnic blood volume and peak filling rate on the change in mean arterial BP, a linear regression analysis model was used. A *P* value of .05 was used as the criterion for determining statistical significance. Data are presented as mean±SEM, unless otherwise indicated.

RESULTS

Mean arterial BP declined significantly after the meal, with a maximum of −8±3 mm Hg by 90 minutes in the 16 elderly patients with syncope, compared with a nonsignificant change of −1±2 mm Hg in the healthy elderly subjects. The HR increased to a similar extent in both groups, by 6±1 beats per minute and 5±1 beats per minute, respectively. The difference in BP and HR response between the two groups was not significant. Eight of the patients with syncope had PH. Therefore, the results were further analyzed by comparing the eight patients with syncope who had PH with the eight patients with syncope who did not have a postprandial decline in supine BP. Baseline cardiovascular characteristics of both syncope groups and the healthy elderly control subjects are shown in **Table 2**. Baseline measurements did not differ significantly among these three groups.

Hemodynamic, plasma norepinephrine, and splanchnic blood pool responses to meal ingestion for the three groups of subjects are shown in **Figure 1**, **Figure 2**, and **Figure 3**. **Table 3** summarizes the directional changes of all the variables for the three different groups. In the elderly patients with syncope who had PH, supine BP declined significantly, falling a maximum of 25/12±2/2 mm Hg by 90 minutes after the meal. In no subject did the supine BP decrease cause subjective symptoms. In both the elderly syncope patients without PH and the healthy elderly subjects, supine BP remained unchanged.

The HR (Figure 1, bottom right) and plasma norepinephrine level (Figure 2, top left) increased significantly in each group after the meal, without any difference between the groups.

Cardiac index increased a maximum of 879±360 $mL \cdot min^{-1} \cdot m^{-2}$ ($P<.05$) 30 minutes after the meal in the patients with syncope with PH and remained elevated during the duration of the study (Figure 2, bottom left). There was a tendency for a transient increase in cardiac index

Table 1. Clinical Characteristics of Subjects*

	Subject Group		
	With PH (N=4)	Without PH (N=8)	Healthy Elderly (N=9)
Age, yr	63±2	62±2	80±2
Sex, No. M/F	3/5	3/5	2/7
BMI, kg/m²†	27.0±1.7	26.8±2.3	23.9±1.7
Disease history, No.			
CAD	3	4	...
Hypertension	5	4	...
MI >6 mo ago	2	3	...
CHF	1	3	...
Parkinson's disease	2	1	...
PMR	2	0	...
Paget's disease	0	1	...
Demand pacemaker	1	0	...
COPD	0	1	...
Depression	1	0	...
Malignant neoplasm in remission	3	2	...
Osteoarthritis	0	1	...
Hypothyroidism	2	0	...
Medications, No.			
Diuretics	2	4	...
ACE inhibitors	2	1	...
β-Blockers	0	1	...
Calcium antagonists	1	2	...
Nitrates	2	2	...
Clonidine	0	1	...
Levodopa/carbidopa	2	1	...
Digoxin	3	2	...
Histamine, antagonist	1	2	...
Prednisone	2	0	...
Benzodiazepines	1	3	...
Aspirin	3	2	...
Antidepressant	1	0	...
Levothyroxine	2	0	...
NSAID	1	0	...
Mean No. of syncopal episodes ≤1 y before study	2.3	1.8	...

*PH indicates postprandial hypotension; BMI, body mass index; CAD, coronary artery disease; MI, myocardial infarction; CHF, congestive heart failure; PMR, polymyalgia rheumatica; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; and NSAID, nonsteroidal anti-inflammatory drug.

†Values are mean±SE.

Table 2. Baseline Cardiovascular Characteristics*

	Subject Group (Mean±SE)		
	With PH	Without PH	Healthy Elderly
Blood pressure, mm Hg			
Systolic	164±6	156±11	146±4
Diastolic	84±4	79±5	74±3
Mean arterial pressure, mm Hg	111±4	105±7	98±3
Heart rate, beats/min	62±4	67±4	57±3
FVR, U	65±12	79±19	63±5
SVR, U	29±3	24±2	30±3
Plasma norepinephrine, nmol/L	2.12±0.31	2.32±0.47	1.59±0.14
EDV index, mL/m²	64±5	61±5	57±4
SV index, mL/m²	44±5	42±4	36±4
Cardiac index, $mL \cdot min^{-1} \cdot m^{-2}$	2616±259	2844±304	2019±169
Ejection fraction, %	68±4	69±5	62±4
PFR, mL/s	185±28	269±52	182±24

*PH indicates postprandial hypotension; FVR, forearm vascular resistance; SVR, systemic vascular resistance; EDV, end-diastolic volume; SV, stroke volume; and PFR, peak filling rate.

at 30 minutes (P=.07) in healthy elderly subjects and no change in patients with syncope without PH. Baseline peak filling rate was not different between any of the groups. There was a weak relationship between baseline peak filling rate and the change in mean arterial BP 60 minutes after the meal (r=.44, n=25, P=.09).

Systemic vascular resistance declined by 8±2 U (P<.01) in the patients with syncope with PH, remained unchanged in patients with syncope without PH, and increased significantly by 4±2 U (P<.05) 90 minutes after the meal in the healthy elderly subjects (Figure 2, top right).

Between the patients with syncope with PH and the healthy elderly subjects, this difference in systemic vascular resistance response was significant (P=.008). Forearm vascular resistance increased significantly only in the healthy older subjects, with a maximum change of 39 U (P<.05) 45 minutes after the meal. Both syncope groups had no significant changes in forearm vascular resistance after the meal (Figure 2, bottom right). There was no difference in forearm vascular resistance responses after the meal between the three groups.

Splanchnic blood volume increased a maximum of 26%±7% (P<.01) 90 minutes after the meal in the patients with syncope with PH (Figure 3). A similar increase was found in the healthy elderly subjects, with a maximum increase of 22%±8% (P<.05) by 90 minutes. In the patients with syncope without PH, only a small, nonsignificant increase in splanchnic blood volume was found. Comparisons between each of the three groups disclosed no significant differences.

In **Figure 4** the individual changes for splanchnic blood volume and mean arterial BP 60 minutes after the meal are given for the three groups of subjects. The change in mean arterial BP was inversely related to the change in splanchnic blood volume (r=−.67, n=24, P<.001). This relationship explains 47% of the variance. In one of the healthy elderly subjects we were not able to measure splanchnic blood volume at the 60-minute time point.

COMMENT

The main finding of this study is that half of the patients with postprandial syncope that was unexplained after a conventional evaluation had marked meal-related supine systolic BP reduction that could contribute to the pathogenesis of syncope. This decline in BP was associated with pooling of blood in the splanchnic circulation and no change in forearm vascular resistance, resulting in a fall in systemic vascular resistance.

Splanchnic blood pooling appears to be an important initial event in the development of PH. This is supported by the observation that somatostatin and its analogue octreotide prevent postprandial BP reduction in elderly subjects and patients with autonomic dysfunc-

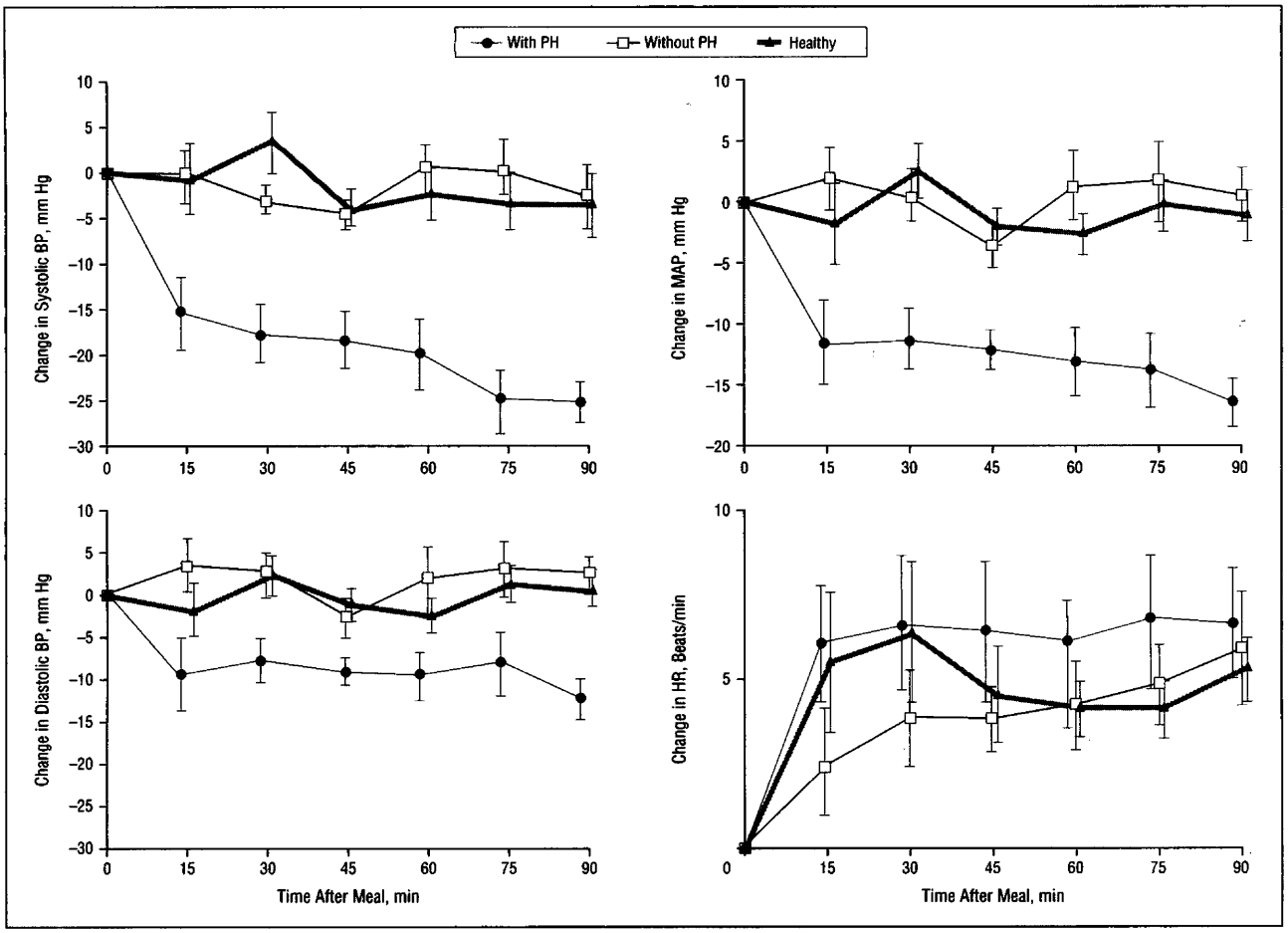

Figure 1. *Changes in systolic blood pressure (BP), diastolic BP, mean arterial pressure (MAP), and heart rate (HR) after meal ingestion for elderly patients with syncope who had postprandial hypotension (PH), elderly patients with syncope without PH, and healthy elderly subjects. Each value represents the mean±SE. Group effects were significant for subjects with PH compared with the other groups for all variables (P<.001) except change in HR (P=.06).*

tion[20-23] because of an increase in splanchnic vascular resistance.[21] However, the present study does not support previous suggestions that *excessive* splanchnic blood pooling during digestion is the principal mechanism of PH.[20] The increase in splanchnic blood volume after the meal was similar for the patients with syncope with PH and the healthy elderly subjects in whom BP remained unchanged. Furthermore, two healthy subjects were able to maintain their mean arterial BP despite marked increases in splanchnic blood volume.

Another important finding is the absence of vasoconstriction despite the decline in BP in patients with syncope who had PH. The healthy elderly subjects demonstrated postprandial increases in HR, plasma norepinephrine level, cardiac index, and forearm vascular resistance, thus compensating for splanchnic blood pooling and resulting in a stable BP after the meal. The patients with syncope with PH also had an increase in HR, plasma norepinephrine level, and cardiac index but did not show an increase in forearm vascular resistance. This resulted in a decline in systemic vascular resistance and hypotension. These results were even more impressive given the small sample size because patients with syncope were subdivided into those with and without PH.

It is notable that both syncope groups failed to show an increase in forearm vascular resistance after the meal. However, in patients with syncope without PH, the changes in splanchnic blood volume were apparently too small to affect systemic vascular resistance and BP. It is possible that prolonged medication effects were responsible for the observed decline in systemic vascular resistance in patients with syncope who had PH. However, medications were similar in patients with and without meal-related BP declines. On the other hand, withholding medications for 12 to 24 hours before the study may have prevented discovery of some meal-drug interactions. Regardless of whether medications played a role in the pathogenesis of this syndrome, the common physiologic mechanism underlying the development of PH appears to be a failure to maintain compensatory vasoconstriction after a meal. Therefore, future investigative and therapeutic efforts should be aimed toward elucidating the cause of the vascular impairment and restoring vascular responsiveness in patients with this phenomenon.

Our findings are consistent with previous studies of patients with autonomic failure who showed no postprandial changes in forearm[26] or skin blood flow after a meal.[21,33] It is known that the early forearm vascular response to active standing is attenuated in many elderly subjects.[34] In addition, a recent study demonstrated impaired forearm vascular resistance in patients aged 11 to 92 years with tilt-induced syncope compared with pa-

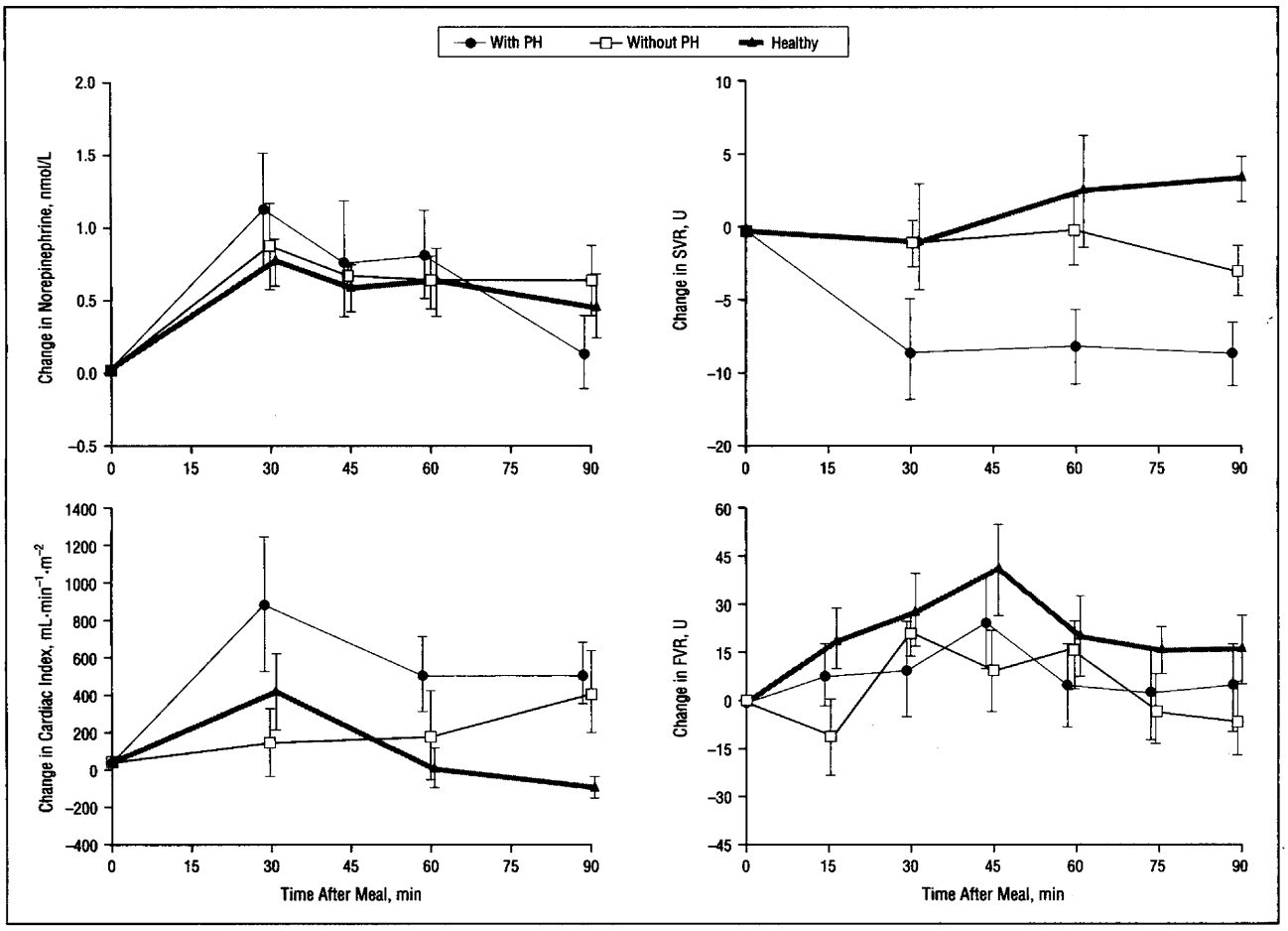

Figure 2. *Changes in plasma norepinephrine level, cardiac index, systemic vascular resistance (SVR), and forearm vascular resistance (FVR) after meal ingestion for elderly patients with syncope who had postprandial hypotension (PH), elderly patients with syncope without PH, and healthy elderly subjects. Each value represents the mean±SE. Group effects were significant for subjects with PH compared with the other groups for change in SVR (P<.001) and compared with healthy subjects for changes in cardiac index (P<.001) and FVR (P<.001).*

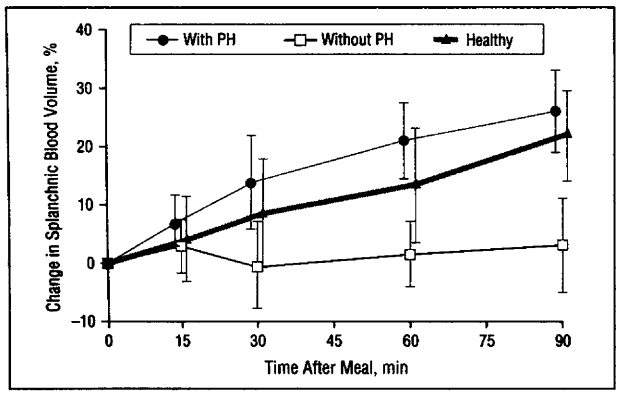

Figure 3. *Change in splanchnic blood volume in response to meal ingestion for the elderly patients with syncope who had postprandial hypotension (PH), elderly patients with syncope without PH, and healthy elderly subjects. Each value represents the mean±SE. There was a significant group effect between patients with syncope without PH and the other two groups (P<.05).*

tients without tilt-induced syncope.[35] Forearm blood flow is largely under cardiopulmonary baroreceptor control, in contrast to splanchnic blood flow, which is mainly modulated by carotid baroreceptors.[36] The failure of forearm vasoconstriction in elderly patients with syncope who have PH might also be related to impaired cardiopulmonary baroreceptor control caused by decreased diastolic distensibility of the ventricle and increased filling pressures.[37] We did not find a difference in peak filling rate at rest between the elderly patients with syncope and the healthy elderly subjects. However, there was a weak linear relationship between peak filling rate and the decline in mean arterial BP after the meal.

Another proposed contributor to PH is an impairment in baroreflex function. Both aging and hypertension are associated with impaired baroreflex function.[19,38] Previous studies have shown greater postprandial declines in BP in hypertensive than normotensive elderly subjects.[7,10,19] Indeed, six of the elderly patients with PH and four without PH had a history of hypertension. Furthermore, baseline BP was higher in patients with PH than in those without it.

The increase in HR and plasma norepinephrine level suggest intact cardiac responsiveness to activation of the sympathetic nervous system. However, in previous studies that used spectral analysis of HR variability, we found that elderly subjects with and without PH did not have changes in their low- and high-frequency HR power after a meal (representing sympathetic and parasympathetic nervous system activity), despite an increase in

Table 3. Summary of Changes for All Variables

	Subject Group*		
	With PH	Without PH	Healthy Elderly
Systolic blood pressure	↓	↔	↔
Diastolic blood pressure	↓	↔	↔
Mean arterial pressure	↓	↔	↔
Heart rate	↑	↑	↑
Forearm vascular resistance	↔	↔	↑
Systemic vascular resistance	↓	↔	↔
Plasma norepinephrine	↑	↑	↑
Cardiac index	↑	↔	↔
Splanchnic blood volume	↑	↔	↑

*↓ *indicated decreased;* ↔, *unchanged; and* ↑, *increased.*

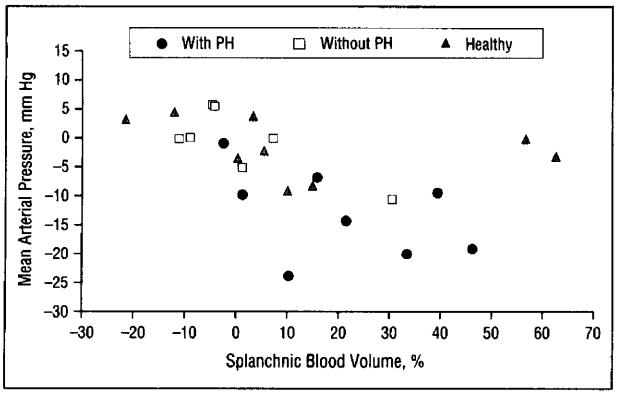

Figure 4. *Individual changes for splanchnic blood volume and mean arterial blood pressure 60 minutes after the meal for subjects with and without postprandial hypotension (PH) and in healthy elderly subjects.*

HR.[26,39] It was therefore suggested that this cardioacceleration is caused by other, unknown, factors rather than sympathetic activation or parasympathetic withdrawal. Furthermore, the activity of the sympathetic nervous system remains difficult to determine from overall changes in plasma norepinephrine level. The sympathetic outflow to all organs is not uniform, and regional, organ-specific increases or decreases in sympathetic nervous system activity can occur with different reflexes.[40] In a previous study we found that the normal increase in plasma norepinephrine level after a meal in healthy elderly subjects is not sustained in those with PH.[18] In the current study, when BP declined between 30 and 90 minutes after the meal, plasma norepinephrine levels inappropriately decreased to baseline levels. These data suggest that elderly patients with syncope with PH are unable to maintain activation of the sympathetic nervous system after a meal.

Syncope in elderly patients is usually a manifestation of serious underlying disease, associated with substantial morbidity and mortality.[1,41] Approximately 30% to 50% of patients with syncope are never given a clear diagnosis, which leads to repeated expensive workups. In 1990, the nationwide inpatient cost for the evaluation of syncope was estimated to be close to $750 million.[42] Evaluation of syncope in the elderly patient is especially difficult because there are often coexistent multisystem abnormalities. In this study, all of the patients were carefully examined, some of them more than once. Nonetheless, syncope remained unexplained. Careful history taking disclosed that all syncopal episodes occurred shortly after meals.

Syncope in association with PH in the elderly has received little attention in the literature since the first publications that described it.[5,18] A study of elderly nursing home patients demonstrated that patients with a history of syncope had a postprandial decline in systolic BP of 31 mm Hg, compared with 17 mm Hg in elderly patients without such a history.[12] Although the incidence of meal-related syncope is unknown, the current study suggests that it may occur in a substantial proportion of elderly patients with unexplained syncope. Even when other identifiable causes of syncope are established, postprandial declines in BP may act synergistically to cause syncope, especially in the elderly.[43]

The workup of syncope in the elderly patient should pay attention to the relationship with meals. A careful history surrounding the syncopal event and BP measurements taken before and 60 to 90 minutes after a meal are easy to collect, are inexpensive, and might reveal important information.

There are a few limitations to the present study. Identification of a causative role of PH in syncope is complicated by the fact that no BP data were available at the time consciousness was lost. Also, patients with postprandial declines in BP were asymptomatic during this study, and, although they had a mean maximal systolic BP decline of 25±2 mm Hg compared with baseline, their BP did not fall into a clinically hypotensive range. They might have become more profoundly hypotensive and symptomatic if they had been studied in the sitting position. However, we were interested in distinguishing mechanisms of postprandial from orthostatic hypotension and therefore chose to study our subjects while they were supine.

Since many patients were taking potentially hypotensive medications, these too may have played a causative role. Nevertheless, medication effects were not identified as potential causes of syncope during the clinical study of these patients. This would require a different study. We have shown that PH is a common, yet often overlooked impairment in BP regulation in patients with unexplained syncope, regardless of whether they are taking medications. Further studies are needed to identify appropriate treatments for these patients, such as medication withdrawal, alterations in meal composition, or the addition of vasoconstrictor agents to increase systemic vascular resistance.

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Conversions From Système International (SI) Units to Traditional Units (Modified From *The SI Manual in Health Care*)

System	Component	SI Reference Interval*	SI Unit	Conversion Factor (Divide by)	Traditional Reference Interval*	Traditional Unit
Plasma	Norepinephrine (radioenzymatic procedure)	1.27-2.81 (at rest for 15 min)	nmol/L	0.005911	215-475 (at rest for 15 min)	pg/mL

**These reference values are not intended to be definitive since each laboratory determines its own values. They are provided for illustration only.*