Furosemide Withdrawal Improves Postprandial Hypotension in Elderly Patients With Heart Failure and Preserved Left Ventricular Systolic Function

Dave J. W. van Kraaij, MD; René W. M. M. Jansen, MD, PhD; Léon H. R. Bouwels, MD; Willibrord H. L. Hoefnagels, MD, PhD

Objective: To assess the effects of furosemide withdrawal on postprandial blood pressure (BP) in elderly patients with heart failure and preserved left ventricular systolic function.

Methods: Noninvasive measurement of blood pressure (BP) and heart rate, computation of stroke volume and cardiac output (after a 1247-kJ (297-kcal) meal, and Doppler echocardiography before and 3 months after placebo-controlled withdrawal of furosemide therapy.

Results: Of 20 patients with heart failure (mean ± SEM age, 75 ± 1 years; left ventricular ejection fraction, 61% ± 3%), 13 were successfully able to discontinue furosemide therapy. At baseline, 11 (55%) of the 20 patients (had maximum postprandial systolic BP declines of 20 mm Hg or more. In the withdrawal group, the maximum systolic BP decline was lessened from −25 ± 4 to −11 ± 2 mm Hg (P < .001) and the maximum diastolic BP from −18 ± 3 to −9 ± 1 mm Hg (P = .01), compared with no changes in the continuation group. In the withdrawal group, maximum postprandial declines in stroke volume and cardiac output decreased from −9 ± 1 to −4 ± 2 mL (P = .01) and from −0.6 ± 0.2 to −0.2 ± 0.1 L/min (P = .04), respectively. The baseline maximum postprandial systolic BP decrease was correlated with the ratio of early to late flow (n = 20; Spearman rank correlation coefficient, 0.58; P = .007). For patients in the withdrawal group, the changes in postprandial systolic BP response were independently related to changes in peak velocity of early flow (n = 13; r² = 0.61; P = .003).

Conclusions: Postprandial hypotension is common in elderly patients with heart failure and preserved left ventricular systolic function. The withdrawal of furosemide therapy ameliorates postprandial BP homeostasis in these patients, possibly by improving left ventricular diastolic filling.

Arch Intern Med. 1999;159:1599-1605

POSTPRANDIAL hypotension, which is a common and serious disorder of blood pressure (BP) regulation in older persons, is associated with falls and syncope. Also, meal-related declines in BP have been related to a higher incidence of coronary events, stroke, and total mortality. The pathogenesis of postprandial hypotension in the elderly is not fully understood, and several age- and disease-related factors appear to interact in different clinical conditions. An important new event in postprandial BP regulation seems to be a meal-induced splanchnic vasodilation with blood pooling in this area and reduced systemic vascular resistance. Postprandial hypotension may be caused by impairments in baroreflex function and inadequate compensatory responses of heart rate (HR), peripheral vasoconstriction, and sympathetic nervous system. An insufficient postprandial increase in cardiac output (CO) as a consequence of a reduced intravascular volume may also provoke or aggravate postprandial BP declines.

Maintenance of adequate intravascular volume and cardiac preload is especially critical for BP homeostasis in patients with diastolic heart failure. Approximately 40% to 50% of elderly patients with heart failure have a normal left ventricular systolic function, and heart failure in these patients is caused by an abnormal diastolic function of the left ventricle. Because of a decreased left ventricular compliance with impaired relaxation and left ventricular filling during diastole, older patients with diastolic heart failure are particularly dependent on intravascular volume and preload for maintaining CO and BP. In these patients, additional preload reduction by treatment with loop diuretics might further impair diastolic filling and provoke or aggravate postprandial hypotensive episodes.

The present study was designed to evaluate the potential pathophysiologic role of impaired left ventricular filling in postprandial BP regulation in elderly patients with diastolic heart failure and to determine whether withdrawal of furosemide therapy in these patients can ameliorate BP declines after meals. Loop diuretics are very fre-
PATIENTS AND METHODS

PATIENTS

Patients aged 70 years or older and using furosemide were recruited through advertisements in local newspapers and asked to participate in a randomized controlled double-blind trial of furosemide withdrawal. For responders, a questionnaire was sent to the treating general practitioner and/or cardiologist to inquire after relevant medical history, particularly heart failure diagnosis and current treatment. Pre-defined inclusion criteria for participation in the trial were a diagnosis of heart failure (New York Heart Association functional class I to III), the use of furosemide at a dosage of 20 and 80 mg/d, and a history of congestive heart failure, as documented by the presence of at least 2 prior symptoms (eg, dyspnea on exertion or at rest, orthopnea, paroxysmal nocturnal dyspnea, and/or peripheral edema), and 1 prior sign (jugal venous distention, rales, or pulmonary congestion on chest radiograph).

In total, 55 patients were invited for a screening visit, during which a medical history was obtained and a physical examination and laboratory testing (ie, blood chemistry studies, hematologic tests, urinalysis, and electrocardiography) were performed. Preset exclusion criteria for participation in the withdrawal trial were the presence of a systolic BP higher than 170 mm Hg and/or diastolic BP higher than 90 mm Hg, absence of regular sinus rhythm, symptoms of angina pectoris (New York Heart Association class II or higher), or the presence of overt congestion. Congestion was determined by means of a scoring list, including rest dyspnea (4 points); orthopnea (4 points); paroxysmal nocturnal dyspnea (3 points); dyspnea on walking on a level plane (2 points); dyspnea on climbing (1 point); increased resting HR (91-110 beats/min, 1 point; >110 beats/min, 2 points); elevated jugular venous pressure (2 points; plus hepatomegaly or edema, 3 points); pulmonary rales (basilar, 1 point; more than basilar, 2 points); and wheezing (3 points). Overt congestion was defined by a heart failure classification score of more than 7 points and verified by the results of chest radiography.

After screening, 13 patients were excluded from participation because of a heart failure classification score of more than 7 (n = 5), elevated BP (n = 4), chronic atrial fibrillation (n = 3), and second-degree atrioventricular block (n = 1). One patient had already stopped using furosemide, and 3 patients decided not to participate in the study after screening. A cardiologist subsequently evaluated 38 patients with such conditions, prescribing furosemide, and examining the postprandial changes of 2 noninvasively measured hemodynamic parameters: stroke volume and CO. Finally, we examined the relationship between cardiovascular response to a meal and Doppler echocardiographic parameters of diastolic filling, as measured before and 3 months after the withdrawal of furosemide therapy.

RESULTS

The patients (11 male, 9 female) had a mean age of 75 ± 1 years. They were using furosemide in an average daily dose of 31 ± 2 mg for an average preceding period of 3.6 ± 0.7 years. During the 3-month follow-up, furosemide therapy was successfully withdrawn in 13 patients, whereas 7 patients continued to take a constant dose of furosemide.
STUDY DESIGN

The study was designed as a randomized, placebo-controlled, double-blind trial of furosemide withdrawal. After a run-in phase of 2 weeks, in which baseline data were collected, the patients were randomly assigned in a 2:1 ratio to a withdrawal group and a continuation group, respectively, balancing for age, sex, cardiovascular co-medications, and daily furosemide dose. Immediately after randomization, they started taking double-blind study medication, consisting of a 1-week dose-halving regimen followed by placebo in the withdrawal group and of matching daily furosemide dosages in identical capsules in the continuation group. Drug compliance was assessed by means of tablet counts. No other medication was administered during the study to substitute for loop diuretic withdrawal (eg, thiazides or angiotensin-converting enzyme inhibitors).

Six follow-up visits took place 1, 2, and 3 weeks and 1, 2, and 3 months after randomization. Heart failure score, body weight to the nearest 0.1 kg (SECA Electronic Scale; SECA, Hamburg, Germany), and BP (sphygmomanometrically) were determined at baseline and at all follow-up visits. Chest x-ray films were obtained to verify pulmonary congestion in case of a heart failure score of greater than 5 points or an increase of more than 3 points. Predefined criteria for unblinding and restarting or augmentation of furosemide therapy were a heart failure score of more than 7 points with verified pulmonary congestion on the chest x-ray film and/or 2 consecutive systolic or diastolic BP measurements of more than 180 or more than 100 mm Hg, respectively. In case of unsuccessful withdrawal, unblinded follow-up and treatment were carried out until a clinically stable condition was reestablished.

MEASUREMENTS

Meal studies were performed within 1 week after echocardiography on the day before randomization and were repeated after 3 months. All studies began at 8 AM after an overnight fast from midnight the night before. The patients’ usual medications were administered with 100 mL of water at least 30 minutes before the start of the study. The tests were performed in quiet surroundings. All patients voided before the study began. After a supine rest for 20 minutes, the patients sat upright for 10 minutes to ingest a standardized liquid 1226-kJ (292-kcal) test meal (100 mL of Nutrical; [Nutricia, Zoetermeer, the Netherlands] in 100 mL of lactose-free whole milk) containing 65 g of carbohydrate, 2 g of fat, and 4 g of protein. This meal was served at a temperature of 22°C to avoid potential temperature effects on BP. After 10 minutes, the patients resumed supine rest for 90 minutes.

Noninvasive beat-by-beat BP and HR recordings were provided by a volume clamp device (Finapres) TNO-BMI, connected to the middle finger of the non-dominant hand. The BP and HR responses were sampled at 100 Hz and stored digitally. In subsequent analyses, we calculated postprandial changes in left ventricular SV and CO from the volume clamp arterial pressure signal. We used a commercially available continuous CO software package (Modelflow; Dutch Organization for Applied Technology, Biomedical Instrumentation Unit) that computes aortic flow from arterial pressure and aortic impedance, using a nonlinear and time-varying 3-element model of aortic input impedance. The SV is derived by integrating flow during systole, and the CO is computed by multiplying the SV by the instantaneous HR. This model has been previously validated and has demonstrated reliable tracking of changes in SV, compared with invasive measurements in several settings. During all experiments, the patients were instructed to keep the measuring finger cuff at heart level, thus avoiding hydrostatic pressure artifacts. A correct position of the cuff was checked by the examiner (D.J.W.v.K.) during all maneuvers.

STATISTICAL ANALYSIS

Average BP, HR, SV, and CO values of the last 10 minutes of supine rest preceding meal ingestion were computed as baseline values. Five-minute average values of the volume clamp device recordings during the ensuing 90 minutes were used in all subsequent analyses. Data are presented as mean ± SEM. Appropriate independent randomization was tested with the χ² and Fisher exact tests for proportions and the Student t test for continuous variables. Two-way repeated-measures analysis of variance (ANOVA) was used to examine the effects of time and test (ie, before and after diuretic withdrawal) and their interaction on changes in BP, HR, SV, and CO during meal studies. Student t tests were applied post hoc to check for differences between groups. Dependence of BP and HR responses on diastolic filling parameters was initially explored by univariate correlation, with subsequent use of stepwise linear regression analysis, incorporating age, sex, and baseline BP and HR values as independent variables. A P value of less than .05 was considered significant. Analysis was carried out using a commercially available software package (SPSS for Windows 6.1; SPSS Inc, Chicago, Ill).

Table 1 shows no differences between the withdrawal group and the continuation group with regard to age, sex, medical history, and number and type of cardiovascular medications in use. It also demonstrates that baseline measurements of systolic and diastolic BP, HR, SV, CO, and Doppler echocardiographic parameters were not different for both groups. After 3 months of furosemide withdrawal, there was a small improvement in the E/A ratio by 0.12 ± 0.04, compared with a decrease of 0.05 ± 0.06 in the group continuing to take furosemide (P = .04). Peak E also tended to increase in the withdrawal group from 62 to 70 milliseconds (difference, 8 ± 4 milliseconds; P = .07). There was no change in any other clinical or echocardiographic parameters. Figure 1 and Figure 2 demonstrate comparisons of postprandial changes in BP and HR (Figure 1) and changes in SV and CO (Figure 2) for patients before and after furosemide withdrawal (n = 13) and for patients who continued to take furosemide (n = 7).

BASELINE POSTPRANDIAL CHANGES

Before withdrawal, maximum declines in systolic BP of 15 ± 3 mm Hg and in diastolic BP of 12 ± 2 mm Hg occurred on average 55 minutes after the meal. The HR in-
increased by 6 ± 1 beats/min 40 minutes postprandially. There were no differences between the 2 groups in BP and HR responses, or in the timing of these responses after the meal, before withdrawal. There were also no differences at baseline between both groups in postprandial changes in SV or CO. The baseline measurements demonstrated postprandial decreases in SV and CO (maximum, 4 ± 1 mL and 0.3 ± 0.1 L/min, respectively).

POSTPRANDIAL CHANGES AFTER FUROSEMIDE WITHDRAWAL

After 3 months, postprandial declines in BP diminished in the withdrawal group. Systolic BP declined by 6 ± 2 mm Hg and diastolic BP by 4 ± 2 mm Hg after 40 minutes, compared with unchanged declines in systolic BP of 11 ± 4 mm Hg and in diastolic BP of 9 ± 2 mm Hg diastolic after 35 and 45 minutes, respectively, in the continuation group. After 3 months of follow-up, postprandial systolic BP responses were significantly different when both patient groups were compared (P = .006, ANOVA for repeated measurements). The differences in diastolic BP did not reach significance (P = .06). The HR response did not change in either group and also did not differ in either group on follow-up (P = .27, ANOVA): the maximum HR response was +7 ± 2 beats/min for patients in the withdrawal group, compared with +4 ± 1 beats/min for patients in the continuation group.

Postprandial decreases in SV diminished in the withdrawal group (decrease, 1 ± 2 mL), compared with no change in the continuation group (decrease, 6 ± 3 mL), and both patient groups were significantly different with regard to postprandial SV response after furosemide withdrawal (P = .002, ANOVA). In the withdrawal group, the CO increased after the meal, with a maximum increase of 0.5 ± 0.1 L/min, compared with an unchanged decrease in CO of 0.4 ± 0.1 mL in the continuation group. The postprandial changes in CO also differed significantly between both patient groups after 3 months (P = .009, ANOVA).

MAXIMUM POSTPRANDIAL CARDIOVASCULAR RESPONSES

The timing of maximum changes in postprandial cardiovascular responses varied considerably between individuals. During the first (baseline) meal test, 4 subjects had their maximal decline in systolic BP within 30 minutes after the meal, 3 subjects between 30 and 45 minutes, 5 subjects between 45 and 60 minutes, and 8 sub-

---

**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>Furosemide Therapy</th>
<th>Withdrawal Group (n = 13)</th>
<th>Continuation Group (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y*</td>
<td>76 ± 1</td>
<td>75 ± 1</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>8/5</td>
<td>3/4</td>
</tr>
<tr>
<td>Medical history, total No. of diagnoses*</td>
<td>4.4 ± 0.4</td>
<td>4.9 ± 1.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Non–insulin-dependent diabetes mellitus</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Medication use, total No.*</td>
<td>5.3 ± 0.5</td>
<td>4.6 ± 0.8</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Nitrates</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>β-Receptor blockers</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Heart failure score, points*</td>
<td>1.4 ± 0.4</td>
<td>2.9 ± 0.7</td>
</tr>
<tr>
<td>Furosemide dose, mg*</td>
<td>32 ± 10</td>
<td>29 ± 11</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg*</td>
<td>143 ± 5</td>
<td>151 ± 8</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg*</td>
<td>77 ± 2</td>
<td>80 ± 3</td>
</tr>
<tr>
<td>Heart rate, beats/min*</td>
<td>76 ± 3</td>
<td>71 ± 4</td>
</tr>
<tr>
<td>Stroke volume, mL*</td>
<td>42 ± 3</td>
<td>43 ± 5</td>
</tr>
<tr>
<td>Cardiac output, L/min*</td>
<td>3.3 ± 0.2</td>
<td>3.1 ± 0.3</td>
</tr>
<tr>
<td>Echocardiographic parameters*</td>
<td>左心室射血分数, %</td>
<td>60 ± 4</td>
</tr>
<tr>
<td>Doppler characteristics†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak E, cm/s</td>
<td>63 ± 5</td>
<td>57 ± 8</td>
</tr>
<tr>
<td>Peak A, cm/s</td>
<td>97 ± 5</td>
<td>80 ± 10</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>0.85 ± 0.03</td>
<td>0.72 ± 0.04</td>
</tr>
<tr>
<td>Deceleration time, msec</td>
<td>200 ± 16</td>
<td>192 ± 28</td>
</tr>
</tbody>
</table>

* Values are mean ± SEM.
† Peak E indicates peak velocity of early flow; peak A, peak velocity of late flow; and E/A ratio, ratio of early to late flow.

**Figure 1.** Postprandial changes (mean ± SEM) for systolic blood pressure and heart rate in patients in whom furosemide therapy was withdrawn (n = 13, left panels) and in patients who continued to take furosemide (n = 7, right panels) before (circles) and after (triangles) the withdrawal trial. The P values represent within-group comparisons (analysis of variance for repeated measurements).
jects after more than 60 minutes. Likewise, 5 subjects had maximum increases in HR within 30 minutes after the meal, 4 subjects between 30 and 45 minutes, and the remaining 11 subjects after more than 60 minutes. Table 2 lists the maximum decreases in systolic and diastolic BP, SV, and CO, as well as the maximum increases in HR, that occurred during the first and second meal test.

There were no differences in maximum changes for all parameters between withdrawal and continuation groups on baseline testing. However, the changes in postprandial systolic BP response were significantly different between the 2 groups ($P = .03$). In the withdrawal group, the maximum systolic and diastolic BP decreases after the meal diminished significantly from $-25 \pm 4$ to $-11 \pm 2$ mm Hg ($P < .001$) and from $-18 \pm 3$ to $-9 \pm 1$ mm Hg ($P = .01$), respectively. Likewise, the maximum postprandial decreases in CO and SV lessened after withdrawal, from $-0.6 \pm 0.2$ to $-0.2 \pm 0.1$ L/min ($P = .01$) and from $-9 \pm 1$ to $-4 \pm 2$ mL ($P = .04$), respectively. The HR response after the meal did not change. In the continuation group, none of the hemodynamic parameters demonstrated significant changes in maximum postprandial declines or increases.

**DOPPLER INDICES OF DIASTOLIC FILLING**

Analysis of the Doppler parameters of left ventricular diastolic filling demonstrated a correlation between the E/A ratio and sex, ratios for women being higher than those for men ($0.74 \pm 0.02$ vs $0.62 \pm 0.03$; $P = .008$). Figure 3 demonstrates the correlation of the E/A ratio and the maximum postprandial systolic BP decline at baseline for all patients ($N = 20$; Spearman rank correlation coefficient, $0.58$; $P = .007$). Linear regression analysis demonstrated this relationship to be independent of age, sex, and premeal BP and HR levels, with an $r^2$ of 0.22. No correlations between echo parameters and baseline diastolic BP, HR, SV, or CO values were found.

Analyzing the determinants of the improvement in postprandial BP response after withdrawal of furosemide therapy, we found that the improvement of systolic BP decline was univariately correlated to increases in E/A ratio ($n = 13$; Spearman rank correlation coefficient, $0.66$; $P = .02$) and particularly to peak E increases ($n = 13$; Spearman rank correlation coefficient, $0.80$; $P = .002$) (Figure 4). Subsequent regression analysis demonstrated that the improvement in postprandial systolic BP response in the withdrawal group was independently related to the increase in peak E in these patients (Spearman rank correlation coefficient, $0.61$; $P = .003$).

**SYMPTOMS**

In the baseline meal tests, 11 of 20 patients experienced systolic BP reductions of $20$ mm Hg or more. Three patients, all in the withdrawal group, experienced symptoms of light-headedness, dizziness, and near-fainting during the first test. These symptoms were related to postprandial declines in systolic BP from 150 to 115, 160 to 120, and 150 to 100 mm Hg, respectively, 50, 75, and 75 minutes after the meal. In 2 of these patients, an anti-Trendelenburg maneuver was successfully applied to elevate BP and reduce symptoms. After furosemide withdrawal, the maximum systolic BP declines were 12, 17, and 23 mm Hg, respectively, for these patients, and none of them experienced adverse symptoms on this occasion. One patient in the continuation group had a symptomatic systolic BP decline of 20 mm Hg on the first occasion to a minimum BP level of 118 mm Hg and felt dizzy at that moment. During the second meal test, the patient’s BP decreased 18 mm Hg to a minimum level of 110 mm Hg. However, the patient did not report symptoms on this occasion.

**COMMENT**

The main findings of this study are 3-fold: First, we demonstrated postprandial systolic BP reductions of $20$ mm Hg or more in 11 (55%) of 20 elderly patients with heart failure and preserved left ventricular systolic function, a figure considerably higher than the prevalences of 24% to 36% reported earlier.1,2 Second, postprandial BP declines were accompanied by reductions or minimal increases in SV and CO. The BP declines were also correlated to impaired left ventricular filling as quantified by Doppler echocardiography. Finally, after furosemide with-

---

**Figure 3.** Asymptomatic systolic BP declines (mean ± SEM) for repeated measurements.

**Figure 4.** Postprandial changes (mean ± SEM) for modelflow stroke volume and cardiac output in patients in whom furosemide therapy was withdrawn ($n = 12$, left panels) and in patients who continued to take furosemide ($n = 7$, right panels) before (circles) and after (triangles) the withdrawal trial.
After meal ingestion in healthy elderly subjects, bowel blood volume increases by approximately 20%. Splanchnic blood pooling, which reduces systemic vascular resistance, appears to be an important initial event in the development of postprandial hypotension. Increases in HR, plasma norepinephrine, CO, and peripheral vascular resistance compensate for this pooling and may prevent declines in BP. Patients with impaired left ventricular diastolic filling are particularly dependent on adequate preload to maintain CO and BP. Furosemide therapy reduces intravascular volume and decreases preload. This decrease might impair postprandial augmentation of CO and exacerbate postprandial hypotension. The findings of the present study appear to support this hypothesis: We found postprandial reductions in CO and SV, in contrast to previous findings in healthy elderly subjects, in whom increases in CO after meals were demonstrated. This finding suggests that the subjects in the present study were unable to maintain or augment CO after the meal might thus have contributed to the significant postprandial BP declines noted.

Postprandial BP declines diminished significantly after withdrawal of furosemide therapy. This outcome appears to contrast to previous findings, which demonstrated an amelioration of postprandial BP homeostasis after antihypertensive treatment in patients with hypertension or antianginal treatment in patients with angina pectoris. However, in both studies, baseline BP levels decreased as a consequence of treatment. Postprandial hypotension is related to baseline BP levels, and an improvement of baseline BP may thus have lessened subjective relationship between the Doppler ratio of early to late flow (E/A ratio) and maximum postprandial systolic blood pressure (BP) reductions at baseline for all 20 patients combined.

Figure 4. Univariate relationship between the changes in postprandial blood pressure (BP) reductions and the changes in Doppler peak velocity of early flow (peak E) before and after withdrawal of furosemide therapy in 13 patients.

<table>
<thead>
<tr>
<th></th>
<th>Furosemide Withdrawal (n = 13)</th>
<th>Furosemide Continuation (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔSystolic</td>
<td>−25 ± 4</td>
<td>−11 ± 2</td>
</tr>
<tr>
<td>ΔDiastolic</td>
<td>−18 ± 3</td>
<td>−9 ± 1</td>
</tr>
<tr>
<td>ΔHR, beats/min</td>
<td>13 ± 2</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>ΔSV, mL</td>
<td>−9 ± 1</td>
<td>−4 ± 2</td>
</tr>
<tr>
<td>ΔCO, L/min</td>
<td>−0.6 ± 0.2</td>
<td>−0.2 ± 0.1</td>
</tr>
</tbody>
</table>

*BP indicates blood pressure; HR, heart rate; SV, stroke volume; and CO, cardiac output. Values other than Ps are expressed as mean ± SEM. †P values represent comparison of changes in hemodynamic parameters from before and after between both groups. ‡P < .05 for within-group comparisons.
sequent postprandial decreases.23-24 Also, postprandial BP reductions were less pronounced in this study, whereas half of our patients experienced systolic BP reductions of 20 mm Hg or more. The mechanisms involved in postprandial cardiovascular homeostasis might also differ; Connelly et al demonstrated increases in CO after meals on baseline testing. In contrast, we found that postprandial CO decreases and that this decline improved after withdrawal of furosemide therapy. The high prevalence of postprandial hypotension in the study population and the correlations of postprandial BP reductions with diastolic filling strongly suggest that impaired left ventricular filling is an important factor in the pathogenesis of postprandial hypotension in patients with diastolic heart failure. Furosemide withdrawal may improve intravascular volume status and ventricular preload, and thus enable improvement of postprandial BP homeostasis.

Invasive hemodynamic studies were not feasible in our patients. Instead, we used aortic modelflow computations of SV and CO, for which reliable recordings of changes in SV and CO have been demonstrated.20,21 The observed changes in SV and CO are consistent with our hypotheses and provide insight into the pathogenesis underlying BP homeostasis after meals as well as its improvement after furosemide withdrawal. Cardiovascular medications, which were consistently used by several patients during the entire study, may have influenced results by interacting with HR or vascular resistance. Because of the small numbers involved, we were unable to correct for this confounder, and the possible effect that angiotensin-converting enzyme inhibitors or nitrates have on postprandial hypotension in diastolic heart failure

In conclusion, we identified an important group of patients at risk for serious and symptomatic postprandial hypotension. Both heart failure with an intact systolic left ventricular function and long-term furosemide use are very prevalent among elderly patients. Declines in BP after meal ingestion improve significantly after 3 months of furosemide withdrawal in such patients, possibly by improvement of diastolic filling. Given the association of postprandial hypotension with cardiovascular morbidity and mortality found in previous studies, our results imply that furosemide should not be prescribed for elderly patients with left ventricular diastolic impairment unless such treatment is proved necessary to treat or prevent congestive heart failure. A carefully guided intermittent diuretic treatment modality, withdrawing furosemide therapy when possible, seems preferable for elderly patients with delayed diastolic filling.

Accepted for publication November 3, 1998.

This study was supported by the Netherlands Program for Research on Aging (NESTOR), funded by the Ministry of Education, Culture and Science and the Ministry of Health, Welfare, and Sports.

The authors thank Henk J. J. van Lier, MSc, Department of Medical Statistics and Epidemiology, University of Nijmegen, for his help with the statistical analyses; Hans E. J. Vollaard, PharmD, Canisius-Wilhelmina Hospital, for preparing blinded medication sets; Roy I. H. Go, MD, PhD, and nurses and staff of the Departments of Internal Medicine and Cardiology, Canisius-Wilhelmina Hospital, for their help in performing this study.

Reprints: Rene W. M. M. Jansen, MD, PhD, Department of Geriatric Medicine, University Hospital Nijmegen, PO Box 9101, 6500 HB Nijmegen, the Netherlands.

REFERENCES


15. Kraaij van DJW, Jansen RWMM, Brujinis E, Gribnau FW, Hoefnagels WHL. Di-
16. Carlson KJ, Lee DCS, Goroll AH, Leathy M, Johnson RA. An analysis of physi-
18. Kuipers HM, Jansen RWMM, Peeters TL, Hoefnagels WHL. The influence of food temperature on postprandial blood pressure reduction and its relation to sub-
22. Vaiškevičius PV, Esserwein DM, Maynard AK, O'Connor FC, Fleg JL. Frequency and importance of postprandial blood pressure reduction in elderly nursing-
23. Limptiz LA, Fullerton JK. Postprandial blood pressure reduction in healthy el-
26. Jansen RWMM, van Lier HJJ, Hoefnagels WHL. Effects of nitrendipine and hy-
drochlorothiazide on postprandial blood pressure reduction and carbohydrate metabolism in hypertensive patients over 70 years of age. J Cardiovasc Phar-
27. Connelly CM, Waksmonski C, Gagnon MM, Limptiz LA. Effects of isosorbide di-
itrato and nicardipine hydrochloride on postprandial blood pressure in elderly patients with stable angina pectoris or healed myocardial infarction. Am J Car-