Effects of variations in intragastric volume on blood pressure and splanchnic blood flow during intraduodenal glucose infusion in healthy older subjects

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POSTPRANDIAL HYPOTENSION is an important clinical problem, particularly in the elderly (17, 27). It is distinct from, and may occur more frequently than, orthostatic hypotension and represents a substantial cause of morbidity and mortality (17). While the mechanisms underlying postprandial hypotension are poorly defined, several interrelated factors, including meal composition, gastric distension, the rate of small intestinal nutrient delivery, changes in splanchnic blood flow, and neural and hormonal mechanisms, have been identified (17, 39). In the elderly, it is likely that “normality” and postprandial hypotension represent a continuum, as is the case with many age-related phenomena. For example, after an oral glucose load, systolic blood pressure predictably falls in healthy older, but not young, subjects, and in the elderly the magnitude of this decrease is variable (18).

Our previous studies established that, in healthy older subjects and patients with type 2 diabetes, the magnitude of the fall in blood pressure in response to enteral glucose is dependent on the rate of nutrient delivery into the small intestine (20, 31, 47). For example, in healthy older subjects, when glucose is infused intraduodenally at rates within the physiological range for gastric emptying (i.e., 1–4 kcal/min) (4), infusions at 3 and 2 kcal/min induce a substantial fall in blood pressure, whereas infusion at 1 kcal/min has little, if any, effect (31, 47). In contrast, in healthy young subjects, intraduodenal glucose infusions at 1, 2, or 3 kcal/min have no effect on blood pressure (41). In contrast to the effects of small intestinal nutrients, gastric distension attenuates the postprandial fall in blood pressure (35, 38, 44, 46). It was initially reported that gastric distension with a balloon linked to a “barostat” device has the capacity to increase blood pressure in healthy young (35) and older (44, 46) subjects. More recently, using a barostat set to a pressure of 8 mmHg above minimal distending pressure (MDP), resulting in variable intragastric volumes ranging from 400 to 900 ml, we reported that gastric distension markedly attenuates the hypotensive response to a 3 kcal/min intraduodenal glucose infusion in healthy older subjects (46). This study did not provide information about the minimum volume or pressure required to attenuate the fall in blood pressure or the potential relationship between changes in blood pressure and changes in intragastric volume. This information has substantial implications for an understanding of the pathophysiology and rational management of postprandial hypotension.

Meal ingestion (11) and small intestinal nutrient infusion (9, 46, 47) increase superior mesenteric artery (SMA) blood flow, which may be important in mediating the postprandial hypotensive response (24) and can be measured by Doppler techniques (33). Information about the effects of gastric distension on SMA blood flow in animals and humans is limited and inconsistent, ranging from no effect (43) to increases (11, 25, 43) and decreases (30, 43, 46).

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The primary aims of this study were to determine, in healthy older subjects receiving an intraduodenal glucose infusion at 3 kcal/min, 1) whether low-volume (i.e., <400 ml) gastric distension attenuates the fall in blood pressure and 2) the relationship between blood pressure and SMA blood flow with intragastric volume.

MATERIALS AND METHODS

Subjects

Nine healthy older men [median age 68.6 yr (range 65–75 yr), body mass index 25.4 kg/m² (range 22.3–29.3 kg/m²)] were recruited by advertisement and enrolled in the study. All subjects were nonsmokers. None had a history of gastrointestinal disease or surgery, diabetes, significant respiratory, renal, hepatic, or cardiac disease, intake of >20 g alcohol/day, or epilepsy or was taking medication known to influence blood pressure or gastrointestinal function. Two of the nine subjects had participated previously in studies involving gastrointestinal intubation.

Protocol

The protocol was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital, and each subject provided written, informed consent prior to inclusion in the study. All experiments were carried out in accordance with the Declaration of Helsinki.

Each subject was studied in single-blind order on four occasions, each separated by ≥3 days. The study days were randomized using the online Random Integer Set Generator program (RANDOM.org). On each day, the subject attended the University of Adelaide Discipline of Medicine at the Royal Adelaide Hospital at 0800 following an overnight fast (10 h for solids, 8 h for liquids) (46). A silicone-rubber catheter (~4 mm OD; Dentsleeve International, Mui Scientific, Mississauga, ON, Canada) was introduced into the stomach via an anesthetized nostril (31). The assembly included an infusion channel (~1 mm ID) and was positioned so that the infusion port was located ~10 cm distal to the pylorus (i.e., in the duodenum). Two other channels were positioned in the antrum (2.5 cm proximal to the pylorus) and the duodenum (2.5 cm distal to the pylorus), respectively, and were perfused with 0.9% saline. The correct positioning of the catheter was maintained by continuous measurement of the transmucosal potential difference at the antrum (~40 mV) and duodenal (0 mV) channels (13). For this purpose, an intravenous cannula filled with sterile saline was placed subcutaneously in the left forearm and used as a reference electrode (13).

The subject also swallowed a single-lumen polyvinyl orogastric catheter (4-mm-OD, intraduodenal 2-mm Tygon tubing, Saint Gobain Performance Plastics, Akron, OH). An ultrathin, flaccid polyethylene bag (600-ml capacity) was wrapped tightly around the distal end, and the proximal end of the catheter was connected via a three-way tap to a gastric barostat (Distender Series II, G & J Electronics, Toronto, ON, Canada). The bag was unfolded by inflation with 400 ml of air, with care taken to ensure that the pressure did not exceed 20 mmHg, and the bag was positioned in the proximal stomach, just below the diaphragm. The bag was then deflated, and the orogastric tube was taped to the skin of the cheek to fix its position (7, 35, 44).

After the catheters were positioned correctly (at t = −2 min), the barostat balloon was inflated over 2 min to a volume of 0 ml (V0), 100 ml (V100), 300 ml (V300), or 500 ml (V500). At t = 0 min, an intraduodenal glucose infusion (3 kcal/min at 3 ml/min) was commenced and continued for 60 min (i.e., t = 0–60 min). At t = 60 min, the barostat bag was deflated. Intraballooon pressure and volumes were measured and recorded using a computer-based system running commercially available software (Protocol Plus, G & J Electronics) and stored for subsequent analysis. Intraduodenal infusions were performed using a volumetric infusion pump (Gemini PC-1, IMED, San Diego, CA). An intravenous cannula was positioned in a left antecubital vein for blood sampling, and an automated blood pressure cuff was placed around the right arm. Each subject remained in a supine position during blood sampling and measurements of blood pressure, heart rate, and SMA blood flow. Upon completion of the study, the catheters were removed, and the subject was given a light meal and allowed to leave the laboratory. On one day, cardiovascular autonomic nerve function was evaluated immediately after the completion of the study (6, 34).

Measurements

Blood pressure and heart rate. Blood pressure (systolic and diastolic) and heart rate were measured using an automated oscillometric blood pressure monitor (DINAMAP ProCare 100, GE Medical Systems, Milwaukee, WI) at t = −12, −9, and −6 min prior to commencement of any intervention, i.e., gastric distension or intraduodenal infusions and then every 3 min between t = 0 and 60 min (31). “Baseline” blood pressure and heart rate were calculated as the mean of measurements taken at t = −12, −9, and −6 min. Postprandial hypotension was defined as a fall in systolic blood pressure of ≥20 mmHg that was sustained for ≥30 min (17).

SMA blood flow and mesenteric vascular resistance. SMA blood flow was measured by Duplex ultrasonography (i.e., B-mode and Doppler imaging) using a Logiq 9 ultrasonography system (GE Healthcare Technologies, Sydney, Australia). The subject was scanned using a 3.5C broad-spectrum 2.5- to 4-MHz convex transducer before (i.e., t = −5 min) commencement of the intraduodenal infusion and then at 15-min intervals between t = 0 and 60 min. Blood flow (ml/min) was calculated instantaneously using the following formula: \(\pi \times r^2 \times TAMV \times 60\), where \(r\) is the radius of the SMA and TAMV is the time-averaged mean velocity (9, 33). The investigator who performed the SMA blood flow measurements was not blinded to the study conditions, given that the ultrasound technique allows inferences about gastric distension. Mesenteric vascular resistance (MVR) was calculated subsequently using the systolic and diastolic blood flow velocities to determine the resistance index (RI) (40) based on a calculation of Pourcelot \([RI = (S - D)/S]\, where \(S\) and \(D\) represent systolic and diastolic blood flow velocity). The RI has been validated as a reliable measurement of MVR (36, 40).

Blood glucose and plasma norepinephrine concentrations. Venous blood samples were obtained prior to commencement of the intraduodenal infusion (i.e., t = −5 min) and then at 15-min intervals between t = 0 and 60 min. Blood glucose concentrations (mmol/l) were determined immediately using a portable blood glucose meter (Precision Q-I-D System, Abbott Laboratories, Medicense Products, Bedford, MA). Plasma norepinephrine (NE) was measured at t = −5, 30, and 60 min using high-performance liquid chromatography coupled with electrochemical detection (Waters, Milford, MA) (16).

Perceptions of gastric distension. Perceptions of gastric distension, i.e., nausea and fullness, were measured using a validated visual analog scale questionnaire. Other perceptions, including anxiety, drowsiness, and dizziness, were also assessed to distract the subject from the main purpose of the questionnaire but were not evaluated formally. Each visual analog scale consisted of a 100-mm horizontal line, where 0 mm represented “sensation not felt at all” and 100 mm represented “sensation was felt the greatest.” Subjects were asked to place a vertical mark on the 100-mm line to indicate how they felt at a particular point in time. Measurements were obtained prior to the commencement of the intraduodenal infusion (i.e., t = −5 min) and at 15-min intervals between t = 0 and 60 min (32).

Cardiovascular autonomic nerve function. Autonomic nerve function was assessed using standardized cardiovascular reflex tests (6, 34). Parasympathetic function was evaluated by the variation (RR interval) of the heart rate during deep breathing and the response to standing (‘30:15’ ratio). Sympathetic function was assessed by the fall in systolic blood pressure in response to standing. Each of the test
results was scored according to age-adjusted predefined criteria as follows: 0 = normal, 1 = borderline, and 2 = abnormal, for a total maximum score of 6. A score ≥3 was considered to indicate autonomic dysfunction (6, 34).

**Statistical Analysis**

Systolic and diastolic blood pressure, heart rate, and effects of distension were analyzed as changes in absolute values from baseline. Intragastric pressure, SMA blood flow, MVR, and blood glucose were analyzed as absolute values. The maximum changes in heart rate, SMA blood flow, MVR, and blood glucose were defined as the greatest change from baseline in each subject at any time point for each treatment. Differences between baseline levels on each study visit were analyzed using one-way repeated-measures ANOVA. Areas under the curve (AUCs) were calculated using the trapezoidal rule and analyzed by a maximum-likelihood mixed-effects model, including the fixed effect of volume with Bonferroni-adjusted post hoc tests following a significant volume effect. A planned contrast of volume of 0 ml vs. the average of the volumes 100, 300, and 500 ml was also included in the mixed model to test for an overall effect of distension. Differences between baseline and t = 60 min were analyzed using paired t-tests for each treatment. Changes in plasma NE at t = 30 and 60 min were evaluated using Student’s paired t-test, and differences between treatments were assessed with a maximum-likelihood mixed-effects model, with fixed effects for time, treatment, and their interaction. Relationships between AUCs for systolic blood pressure, SMA blood flow, and intragastric pressure with intragastric volume were calculated using within-subject correlations (3). Multiple within-subject regressions were used to assess the independent effects of intragastric volume and intragastric pressure on the AUCs and maximum fall of systolic blood pressure. All analyses were performed using SPSS versions 16.0.2 and 17.0 (SPSS, Chicago, IL). Data are shown as changes from baseline and means ± SE, unless stated otherwise. Based on our previous study, we calculated that a minimum of six subjects would be required to detect a difference of ~14 mmHg in systolic blood pressure between V0 and V500, with the power of 0.80 and at a significance level of P < 0.05 (46). P < 0.05 was considered statistically significant in all analyses.

**RESULTS**

The studies were generally well tolerated. One subject experienced nausea and subsequently vomited during V500, and

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**Table 1. Systolic and diastolic blood pressure and heart rate at baseline, immediately in response to gastric distension, and at 60 min after commencement of intraduodenal glucose infusion**

<table>
<thead>
<tr>
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<th>V0</th>
<th>V100</th>
<th>V300</th>
<th>V500</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>SBP, mmHg</td>
<td>124 ± 4</td>
<td>124 ± 5</td>
<td>122 ± 4</td>
<td>119 ± 4</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>71 ± 2</td>
<td>69 ± 3</td>
<td>71 ± 2</td>
<td>69 ± 2</td>
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<tr>
<td>HR, beats/min</td>
<td>58 ± 3</td>
<td>59 ± 3</td>
<td>58 ± 3</td>
<td>57 ± 3</td>
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<tr>
<td><strong>Postdistension (t = 0 min)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>124 ± 4</td>
<td>125 ± 5</td>
<td>124 ± 4</td>
<td>122 ± 4</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>70 ± 3</td>
<td>70 ± 3</td>
<td>71 ± 2</td>
<td>72 ± 3</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>59 ± 3</td>
<td>60 ± 3</td>
<td>59 ± 4</td>
<td>57 ± 3</td>
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<tr>
<td><strong>t = 60 min</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>122 ± 4</td>
<td>123 ± 5</td>
<td>126 ± 5</td>
<td>123 ± 6</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>66 ± 3*</td>
<td>67 ± 3*</td>
<td>70 ± 3</td>
<td>68 ± 3</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>65 ± 4†</td>
<td>67 ± 4†</td>
<td>65 ± 4†</td>
<td>64 ± 4†</td>
</tr>
</tbody>
</table>

Values are means ± SE. V0, no distension (0 ml); V100, V300, and V500, 100, 300, and 500 ml, respectively; SBP and DBP, systolic and diastolic blood pressure; HR, heart rate. Significantly different from baseline: *P < 0.001; †P < 0.05.
that study day was, accordingly, excluded in all analyses. No subject had definite autonomic neuropathy (mean score 0.78, range 0–2) or postprandial hypotension.

**Intragastric Pressures During Gastric Distension**

There were significant differences in intragastric pressure between the 4 days immediately following the gastric distension (i.e., t = 0 min); 1.7 ± 0.4 (V0) vs. 5.2 ± 0.6 (V100) vs. 10.3 ± 1.3 (V300) vs. 16.0 ± 1.1 (V500) mmHg (P < 0.001). Between t = 0 and 60 min, there was a treatment effect (P < 0.001) for no distension (V0) vs. the average of the volume distensions (V100, V300, and V500). In the mixed model comparing all conditions, there was a significant treatment effect (P = 0.01), so that intragastric pressure was less during V0 than during V300 (P = 0.008) and V500 (P = 0.01), with a trend for a difference compared with V100 (P = 0.09). There was no significant difference in systolic blood pressure during V300 compared with V100 (P = 0.36) or V500 (P = 0.72); however, there was a trend for a difference in systolic blood pressure between V100 and V500 (P = 0.10; Fig. 2A).

**Systolic and Diastolic Blood Pressure and Heart Rate**

There was no difference in predistension (baseline) or post-distension (t = 0 min) blood pressure or heart rate between the 4 days (Table 1).

**SMA Blood Flow and MVR**

There was no difference in predistension (baseline) SMA blood flow or MVR between the 4 days (Table 2).
There was no significant treatment effect \( (P = 0.16) \) for the AUCs of SMA blood flow between baseline and 60 min for no distension \((V0)\) vs. the average of the volume distensions \((V100, V300, \text{ and } V500)\). There was also no difference \( (P = 0.15) \) in maximum SMA blood flow from baseline during \( V0 \) \((2,080 \pm 228 \text{ ml/min at } 45 \pm 4 \text{ min})\), \( V100 \) \((1,806 \pm 184 \text{ ml/min at } 47 \pm 6 \text{ min})\), \( V300 \) \((1,748 \pm 187 \text{ ml/min at } 32 \pm 6 \text{ min})\), and \( V500 \) \((1,555 \pm 280 \text{ ml/min at } 34 \pm 5 \text{ min}; \text{Fig. 4A})\). At \( t = 60 \text{ min} \), SMA blood flow was greater \( (P < 0.005) \) than baseline after \( V0 \), \( V100 \), \( V300 \), and \( V500 \) (Table 2).

There was no significant treatment effect \( (P = 0.07) \) for the AUCs of MVR between baseline and 60 min for no distension \((V0)\) vs. the average of the volume distensions \((V100, V300, \text{ and } V500)\). There was a significant difference \( (P = 0.03) \) in the maximum fall in MVR from baseline during \( V0 \) \((0.058 \pm 0.010) \) and \( V500 \) \((0.089 \pm 0.012) \), but no differences with \( V100 \) \((0.041 \pm 0.008) \) or \( V300 \) \((0.085 \pm 0.017; \text{Fig. 4B})\). At \( t = 60 \text{ min} \), MVR was slightly less \( (P < 0.05) \) than baseline after \( V0 \), \( V300 \), and \( V500 \) (Table 2), but not \( V100 \).

**Blood Glucose and Plasma NE Concentrations**

There was no difference in predistension (baseline) blood glucose concentrations between the 4 days (Table 2). There was also no significant treatment effect \( (P = 0.99) \) for the AUCs of blood glucose between baseline and 60 min for no distension \((V0)\) vs. the average of the volume distensions \((V100, V300, \text{ and } V500)\; \text{Fig. 5} \). At \( t = 60 \text{ min} \), blood glucose was greater \( (P < 0.001) \) than baseline after \( V0 \), \( V100 \), \( V300 \), and \( V500 \) (Table 2).

There was no significant difference in the predistension (baseline) plasma NE between the 4 days \( (P = 0.88) \). Plasma NE increased from baseline at \( t = 30 \text{ min} \) \((P < 0.01) \) and \( t = 60 \text{ min} \) \((P < 0.005) \). There was no difference between the four treatments \( (P = 0.76; \text{Fig. 6}) \).

**Perceptions of Distension**

There was no difference at predistension (baseline) for perceptions of distension (nausea and fullness) between the 4 days (Table 2). Between baseline and 60 min, there was no treatment effect for the AUCs of the scores for nausea \( (P = 0.89; \text{Fig. 7A}) \) or fullness \( (P = 0.86; \text{Fig. 7B}) \) for no distension \((V0)\) vs. the average of the volume distensions \((V100, V300, \text{ and } V500)\). At \( t = 60 \text{ min} \), scores for nausea and fullness did not differ from baseline after \( V0 \), \( V100 \), \( V300 \), or \( V500 \) (Table 2).

**Within-Subject Relationships Between Blood Pressure and SMA Blood Flow With Intragastric Pressure and Volume**

There was a positive relationship \( (r = 0.60, P = 0.001) \) between the AUCs of the change in systolic blood pressure \((t = 0–60 \text{ min}) \) from baseline and intragastric volume \((t = 0–60 \text{ min}) \). There was also a positive relationship \( (r = 0.64, P < 0.001) \) between the AUCs of the change in systolic blood pressure \((t = 0–60 \text{ min}) \) from baseline and the AUCs of intragastric pressure \((t = 0–60 \text{ min}) \). Furthermore, there was a positive relationship \( (r = 0.50, P = 0.008) \) between the maximum fall in systolic blood pressure and the AUCs of intragastric pressure \((t = 0–60 \text{ min}) \).

In multiple within-subject regressions, the AUC of the change in systolic blood pressure \((t = 0–60 \text{ min}) \) from baseline was not independently associated with the AUCs of intragastric pressure \((t = 0–60 \text{ min}, P = 0.18) \) or intragastric volume \((t = 0–60 \text{ min}, P = 0.63) \). There was, however, a significant independent association between the maximum change in systolic blood pressure and intragastric volume \( (P = 0.03) \), but not pressure \( (P = 0.46) \).

There was an inverse relationship \( (r = -0.44, P = 0.01) \) between the AUCs of the change in systolic blood pressure \((t = 0–60 \text{ min}) \) from baseline and the AUCs of SMA blood flow \((t = 0–60 \text{ min}) \).

**DISCUSSION**

This study evaluated the effects of gastric balloon distension at volumes of 100, 300, and 500 ml on the blood...
pressure and SMA blood flow responses to intraduodenal glucose infusion in healthy older subjects. In the absence of gastric distension, systolic blood pressure predictably fell and SMA blood flow rose (9). Gastric distension at all volumes prevented the fall in blood pressure, and the magnitude of this attenuation was related to the intragastric distension volume. In contrast to its substantial effect on blood pressure, gastric distension had no effect on heart rate or SMA blood flow, although the latter was related to the change in blood pressure. The capacity of low-volume (≈100 ml) gastric distension to markedly attenuate the fall in blood pressure induced by small intestinal nutrients has implications for the nonpharmacological management of postprandial hypotension; e.g., drinking a small volume of liquid is likely to be effective.

There is persuasive evidence that gastric distension plays a protective role in the maintenance of postprandial blood pressure (5, 10, 19, 21, 22, 35, 38, 44, 46). Consumption of 480 ml of water increases systolic blood pressure in healthy older subjects, as well as patients with multiple-system atrophy and autonomic failure (21), and attenuates the fall in blood pressure induced by a high-carbohydrate meal in patients with autonomic failure (38). In healthy older subjects, the magnitude of the fall in systolic blood pressure is known to be greater when motility. While elevations in blood glucose and insulin appear unlikely to play a major role in postprandial hypotension, since intravenous glucose has little, if any, effect on blood pressure and rise in heart rate observed during the control study were comparable to that reported elsewhere (31, 47).

The mechanism(s) mediating the effects of gastric distension on the hypotensive response to intraduodenal glucose remain(s) uncertain. In autonomic failure patients, water drinking appears to have a peak effect on blood pressure at ≈30 min after ingestion (38), whereas the effect of gastric distension obtained with the barostat seems almost immediate, suggesting that different mechanisms may be involved. Given that small intestinal glucose delivery was standardized, the absence of any effect of distension on the rise in blood glucose was predictable. This was, however, important to exclude, as hyperglycemia (2, 26), including variations in blood glucose that are within the normal postprandial range (1, 37), affects gastric motility. While elevations in blood glucose and insulin appear unlikely to play a major role in postprandial hypotension, since intravenous glucose has little, if any, effect on blood pressure and postprandial hypotension occurs in type 1 diabetic patients, who are, by definition, insulin-deficient (27, 28), this does not discount the relevance of potential hormonal factors. An increase in sympathetic activity may potentially account for the effects of gastric distension, particularly as gastric distension has been shown to increase muscle sympathetic nerve activity in healthy young and older subjects, although the magnitude of the increase was less in the elderly (44). It is not known whether this sympathetic activation is mediated by brain stem
and/or spinal reflex mechanisms. The effects of gastric distension on sympathetic nerve activity in response to water drinking may be related to stretch (44) and osmolarity (38), although the hypotensive response to intraduodenal glucose is apparently independent of osmolarity (8). In mice, recent evidence suggests that the rise in blood pressure induced by water ingestion is mediated via osmoreceptive afferent nerves in the portal tract through transient receptor potential vanilloid 4 channel activation (23, 29). Oral (49) and intraduodenal (41) glucose have been reported to increase plasma NE in healthy humans, as shown in the present study, but this response was not modified by gastric distension. It should, however, be recognized that plasma NE response was only assessed at two time points, so the data should be viewed circumspectly. Moreover, the plasma NE concentrations are likely to be primarily a reflection of sympathetic nerve activity in the forearm muscles (14).

In the present study, gastric distension had no effect on the stimulation of SMA blood flow or the fall of MVR induced by small intestinal glucose. In the pig, fasting SMA blood flow has been reported to be decreased (30, 43), increased (43), or unchanged (43) by gastric distension; in the cat, however, a modest increase has been reported (25). We have reported, in healthy older subjects, that gastric distension with a barostat set to 8 mmHg above MDP attenuated the rise in SMA blood flow observed in response to an identical intraduodenal infusion (46), an observation that is apparently discrepant from that in the present study and likely to reflect methodological differences. In particular, as discussed in the previous study (46), the intragastric volumes resulting from the distension were substantially greater (mean volume ~750 ml). It is, accordingly, likely that a “threshold” volume and/or pressure needs to be exceeded for a reduction in SMA blood flow, and this is >500 ml. The relationship between the magnitude of the fall in blood pressure and rise in SMA blood flow is consistent with previous observations (11, 46) and with the concept that the latter is integral to the hypotensive response. While gastric distension has been shown to elevate MVR in the cat (25), to our knowledge this is the first study to evaluate the effects of variations in intragastric volume on MVR in humans. MVR predictably fell in response to intraduodenal glucose infusion, but this was not influenced by gastric distension. Hence, MVR does not appear to be increased by gastric distension.

Our study does not allow the potential effects of intragastric volume or pressure to be clearly discriminated, but based on the outcome of the multiple regression analysis and the lack of a significant difference in the effects of the three volumes on blood pressure (there was only a trend) for a difference in the systolic blood pressure responses to the 100- and 500-ml distensions, it appears that volume is relatively more important, although it would certainly be of interest to evaluate the effects of different pressures. The 100-, 300-, and 500-ml volumes we studied can be considered representative of small- to moderate-sized meals. Given that the 100-ml volume was effective, it would be of interest to evaluate lower volumes. There is also evidence that the site of gastric distension (proximal vs. distal) may be important (19, 35), and given that the barostat bag was positioned proximally in our study, evaluation of the effects of distal stomach would be of interest. It should also be recognized that we studied healthy older subjects, not those with known postprandial hypotension, and studies in the latter group are indicated, given that they represent the target population for therapy. However, characterization of responses in healthy elderly subjects was a prerequisite to initiating comparable studies in elderly patients known to have postprandial hypotension, particularly as there is evidence that the hypotensive response to small intestinal nutrients is exaggerated in the latter group (45). The finding that a low-volume gastric distension was effective in abolishing the hypotensive response to small intestinal glucose in healthy older subjects suggests that gastric distension will also be effective in patients with postprandial hypotension, although the volume required may be larger. This information may be of major relevance to the management of postprandial hypotension. Some of the clinical symptoms of postprandial hypotension may reflect reduced cerebral hypoperfusion, implying a defect in cerebral autoregulation. It has been suggested that patients with chronic orthostatic hypotension may have an expansion of their autoregulated range to lower blood pressure (15, 42). Cerebral autoregulation in response to reductions in blood pressure associated with postprandial hypotension has not been evaluated, nor have the potential effects of gastric distension on cerebral blood flow in this group.

**Perspectives and Significance**

This study establishes that the fall in systolic blood pressure induced by intraduodenal glucose in healthy older subjects is abolished by low-volume gastric distension, supporting the concept that nonnutrient gastric distension immediately before a meal, possibly with volumes of ~100 ml, is likely to represent a simple approach to the management of postprandial hypotension.

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**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the authors.

**AUTHOR CONTRIBUTIONS**


**REFERENCES**


