Effects of gastric distension on blood pressure and superior mesenteric artery blood flow responses to intraduodenal glucose in healthy older subjects

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Vanis L, Gentilcore D, Hausken T, Pilichiewicz AN, Lange K, Rayner CK, Feinle-Bisset C, Meyer JH, Horowitz M, Jones KL. Effects of gastric distension on blood pressure and superior mesenteric artery blood flow responses to intraduodenal glucose in healthy older subjects. Am J Physiol Regul Integr Comp Physiol 299: R960–R967, 2010. First published June 16, 2010; doi:10.1152/ajpregu.00235.2010.—Postprandial hypotension occurs frequently and is associated with increased morbidity. Gastric distension may attenuate the postprandial fall in blood pressure (BP). Using a barostat, we sought to determine the effects of gastric distension on BP, heart rate (HR), and superior mesenteric artery (SMA) blood flow responses to intraduodenal glucose in eight (6 men, 2 women) healthy older (65–75 yr old) subjects. BP and HR were measured using an automated device and SMA blood flow was measured using Doppler ultrasound on 4 days in random order. SMA blood flow was calculated using the radius of the SMA and time-averaged mean velocity. Subjects were intubated with a nasoduodenal catheter incorporating a duodenal infusion port. On 2 of the 4 days, they were intubated orally with a second catheter, incorporating a barostat bag, positioned in the fundus and set at 8 mmHg above minimal distending pressure. Each subject received a 60-min (0–60 min) intraduodenal infusion of glucose (3 kcal/min) or saline (0.9%); therefore, the four study conditions were as follows: intraduodenal glucose + barostat (glucose + distension), intraduodenal saline + barostat (saline + distension), intraduodenal glucose (glucose), and intraduodenal saline (saline). Systolic and diastolic BP fell during glucose compared with saline (P = 0.05 and P = 0.003, respectively) and glucose + distension (P = 0.01 and P = 0.05, respectively) and increased during saline + distension compared with saline (P = 0.04 and P = 0.006, respectively). The maximum changes in systolic BP were −14 ± 5, +11 ± 2, −3 ± 4, and +15 ± 3 mmHg for glucose, saline, glucose + distension, and saline + distension, respectively. There was an increase in HR during glucose and glucose + distension (maximum rise = 14 ± 2 and 14 ± 3 beats/min, respectively), but not during saline or saline + distension. SMA blood flow increased during glucose and glucose + distension (2,388 ± 365 and 1,673 ± 187 ml/min, respectively), but not during saline and tended to decrease during saline + distension (821 ± 115 and 864 ± 116 ml/min, respectively). In conclusion, gastric distension has the capacity to abolish the fall in BP and attenuate the rise in SMA blood flow induced by intraduodenal glucose in healthy older subjects.

postprandial hypotension; barostat; small intestinal glucose

POSTPRANDIAL HYPOTENSION, defined as a ≥20-mmHg fall in systolic blood pressure within 2 h of a meal (16), is recognized as an important clinical problem, particularly in the elderly and in patients with autonomic dysfunction, the latter often secondary to diabetes mellitus (16, 23). Postprandial hypotension occurs in 30–40% of nursing home residents and is distinct from, and occurs more frequently than, orthostatic hypotension (16).

While the mechanisms underlying postprandial hypotension are poorly defined, the rate of small intestinal nutrient delivery, splanchic blood flow, and neural and hormonal mechanisms are important (15, 16, 23, 24). A series of studies performed by our group, primarily in healthy older subjects, have established that the postprandial fall in blood pressure is triggered by the interaction of nutrients (fat, carbohydrate, or protein) with the small intestine, presumably as a result of neural and humoral mediators (7, 18, 27). When gastric emptying is relatively more rapid, the magnitude of the fall in blood pressure is greater (18). In contrast, intragastric mechanisms, related to gastric distension, attenuate the postprandial fall in blood pressure (8, 17, 19, 30, 31, 33, 34). For example, consumption of water increases systolic blood pressure in healthy older subjects (19) and patients with autonomic failure (19, 31) and attenuates the hypotensive response to a meal (31). In healthy older subjects, the magnitude of the fall in systolic blood pressure is greater when glucose is ingested at a smaller volume (200 compared with 600 ml) but at the same concentration (17) and therefore, intragastric administration of 500 ml of water markedly attenuates the fall in systolic blood pressure induced by intraduodenal glucose (8), and when glucose is infused directly into the proximal small intestine at a rate comparable to gastric emptying of oral glucose, the magnitude of the fall in blood pressure is greater (9). Inherent limitations in these studies are as follows: 1) distension, with liquid nutrient or nonnutrient, cannot be well quantified, nor can it be sustained; i.e., with intragastric administration, gastric distension decreases as gastric emptying proceeds (8), and 2) if the distension stimulus includes nutrients, these nutrients may induce a fall in blood pressure (8). Moreover, the pressor effort of water may, in part, be mediated by its hyposmolarity (31).

In anesthetized cats, Longhurst et al. (22) demonstrated that gastric distension induces a sympathoexcitatory reflex, leading to an increase in blood pressure. Gastric distension at pre-defined volumes and/or pressures can be achieved using a barostat device (30, 33). In healthy, young adults, proximal gastric distension achieved with a barostat has been shown to increase blood pressure, heart rate, and muscle sympathetic nerve activity, the so-called “gastrovascular reflex” (30). In a study comparing healthy young and older subjects, gastric
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distension at 8 mmHg above minimal distending pressure (MDP) using a barostat increased mean arterial pressure, heart rate, and total peripheral arterial resistance more in the older subjects, while in both groups there was a slight rise in cardiac output (33). No studies have hitherto evaluated the effects of gastric distension achieved using a barostat on the hypotensive response to small intestinal nutrients.

Meal ingestion (9) and small intestinal nutrient infusion (7) increase superior mesenteric artery (SMA) blood flow, which can be measured by Doppler techniques (28). There is little information about the effects of gastric distension on SMA blood flow, with the majority of these studies in animals (26, 32) and only one study in humans (9). The outcome of these studies is inconsistent: no effect (32), increases (9, 21, 32), and decreases (26, 32) in SMA blood flow have been reported.

The aims of this study were to determine the effects of gastric distension achieved with a barostat on the blood pressure, heart rate, and SMA blood flow responses to intraduodenal glucose infusion in healthy older subjects. The broad hypothesis was that gastric distension would attenuate the hypotensive response and the increase in SMA blood flow induced by intraduodenal glucose.

MATERIALS AND METHODS

Subjects

Eight (6 men and 2 women) healthy older (median 70.5 yr, range 65–75 yr) subjects with body mass index of 23.5 kg/m² (range 20.4–27.1 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, nor was any subject taking medication known to influence blood pressure or gastrointestinal function.

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 their inclusion. All experiments were carried out in accordance with the Declaration of Helsinki.

Each subject was studied on four occasions in randomized order; each study was separated by 3 days. On each day, the subject arrived at 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). A silicone-rubber catheter (≈4 mm OD; Dentsleeve, Mui Scientific, Mississauga, ON, Canada) was introduced into the stomach via an anesthetized nostril (27). 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 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 antral (≈40 mV) and duodenal (0 mV) channels (12). For this purpose, an intravenous cannula filled with sterile saline was placed subcutaneously in the left forearm and used as a reference electrode (12).

On 2 of the 4 study days, the subject swallowed a single-lumen polyvinyl orogastric catheter (4 mm OD, 2 mm ID; Tygon tubing, Saint Gobain Performance Plastics, Akron, OH) equipped with an ultrathin, flaccid polyethylene bag (capacity 1,200 ml) that was tightly wrapped around the distal end. The proximal end of the catheter was connected via a three-way tap to a gastric barostat (Distender Series II, G & J Electronics, Willowdale, 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 adjusted to be positioned in the proximal stomach, just below the diaphragm. The bag was then deflated, and the barostat assembly was taped to the skin of the cheek (6, 30, 33).

The bag was then inflated in 1-mmHg steps at 5-min intervals to determine the MDP, which represents the minimal pressure required to overcome the intra-abdominal pressure, defined as the pressure required to achieve a volume >30 ml in the bag (6). The stomach was then distended using a single-“staircase” protocol, in which intragastric pressure was increased by 2 mmHg every 3 min, in four steps, to achieve a distension of 8 mmHg above MDP (36). The intraballoonal volume was recorded at 3-min intervals commencing immediately prior to the intraduodenal infusion. Perceptions of fullness, nausea, and bloating were assessed using the seven-point Likert scale (30), commencing immediately prior to the distension and during the last minute of each distension step. The subject was asked to quantify these sensations on a scale of 1 (no sensation) to 7 (unbearable sensation) (30, 33).

After the catheters were positioned correctly and stepwise distension was completed, at 0 min, the subject received 1) an intraduodenal infusion of glucose at 3 kcal/min (glucose), 2) an intraduodenal infusion of 0.9% saline (saline), 3) an intraduodenal infusion of glucose at 3 kcal/min with intraballoon pressure set to 8 mmHg above MDP (glucose + distension), or 4) an intraduodenal infusion of saline with intraballoon pressure set to 8 mmHg above MDP (saline + distension) for 60 min (i.e., 0–60 min). The barostat bag was deflated at 60 min. Between 60 and 120 min, saline (0.9%) was infused intraduodenally at an identical rate (27). 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 positioned 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. At 120 min, the catheters were removed and the subject was given a light meal and then allowed to leave the laboratory. On 1 day, cardiovascular autonomic nerve function was evaluated immediately after the completion of the study (5, 29).

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 −9, −6, and −3 min prior to commencement of the intraduodenal infusions and then every 3 min between 0 and 120 min (27). “Baseline” (0 min) blood pressure and heart rate were calculated as the mean of measurements at −9, −6, and −3 min. Postprandial hypotension was defined as a ≥20-mmHg fall in systolic blood pressure that was sustained for ≥30 min (16).

SMA blood flow. 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) (28). The subject was scanned using a 3.5C broadband-spectrum 2.5- to 4-MHz convex transducer before (−2 min) the commencement of the intraduodenal infusion and then at 15-min intervals between 0 and 120 min. Blood flow (ml/min) was calculated instantaneously using the following formula: π × r² × TAMV × 60, where r is the radius of the SMA and TAMV is the time-averaged mean velocity (7, 28).

Blood glucose concentrations. Venous blood samples were obtained prior to the commencement of the intraduodenal infusion (i.e., −2 min) and at 15-min intervals between 0 and 120 min. Blood glucose concentrations (mmol/l) were determined immediately using a portable blood glucose meter (Precision Q1-D System, Abbott Laboratories, Medisense Products, Bedford, MA).
Perceptions of distension. Perceptions of nausea, bloating, and fullness were assessed by the seven-point Likert scale, where 1 is no sensation and 7 is unbearable sensation (30).

Autonomic function. Autonomic nerve function was assessed using standardized cardiovascular reflex tests (5, 29). Parasympathetic function was evaluated by the variation (R-R 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 0 (normal), 1 (borderline), and 2 (abnormal) for a total maximum score of 6. A score ≥3 was considered to indicate autonomic dysfunction (5, 29).

Statistical Analysis

Systolic and diastolic blood pressure, heart rate, and perception scores were analyzed as changes in absolute values from baseline. Intragastric volume, SMA blood flow, and blood glucose concentrations were analyzed as absolute values. One-way ANOVA was used to analyze the effects of “time” on intragastric volume, systolic and diastolic blood pressure, heart rate, SMA blood flow, blood glucose concentrations, and perception scores. The maximum change in systolic and diastolic blood pressure, heart rate, SMA blood flow, and blood glucose concentrations was defined as the greatest change from baseline in each subject at any given time for each treatment. Areas under the curve (AUC) for intraballoon volume to be greater during glucose distension than saline could not be obtained adequately during glucose distension. At 60 min, SMA blood flow measurements were not included.

The studies were well tolerated, and there were no adverse events. No subject had definite autonomic neuropathy (mean score 0.9, range 0–2). One subject had postprandial hypotension (i.e., a ≥20-mmHg fall in systolic blood pressure that was sustained for ≥30 min) following glucose. In one of the remaining eight subjects, SMA blood flow measurements could not be obtained adequately during glucose + distension, because the vessel was obscured by abdominal gas; these data were not included.

Intraballoon Volume and Pressure During Gastric Distension

There was no significant difference in baseline (−2 min) intraballoon volume between the 2 days (Fig. 1): 443 ± 60 and 410 ± 80 ml for glucose + distension and saline + distension, respectively (P = 0.59). Between 0 and 60 min, there was a prompt rise in intraballoon volume during glucose + distension (P < 0.001) and saline + distension (P = 0.002), with a plateau from ~15 min. There was a trend (P = 0.07) for the AUC for intraballoon volume to be greater during glucose + distension than saline + distension. At 60 min, intragastric volume was greater than baseline after glucose + distension (790 ± 71 ml, P = 0.001) and tended to be greater after saline + distension (637 ± 80 ml, P = 0.07) without any difference between them.

During distension, MDP was 3–6 mmHg, so that pressures within the barostat bag were 11–14 mmHg (MDP + 8 mmHg). During the intraduodenal infusions, barostat bag volumes were 300–950 ml.

There was no significant difference in baseline (0 min) blood pressure or heart rate between the 4 days (Fig. 2, A–C, and Fig. 3): systolic blood pressure was 119 ± 7, 117 ± 5, 121 ± 5, and 122 ± 5 mmHg (P = 0.52) for glucose, saline, glucose + distension, and saline + distension, respectively; diastolic blood pressure was 69 ± 3, 68 ± 2, 71 ± 2, and 69 ± 2 mmHg (P = 0.43) for glucose, saline, glucose + distension, and saline + distension, respectively; and heart rate was 58 ± 3, 59 ± 3, 59 ± 3, and 60 ± 2 beats/min (P = 0.45) for glucose, saline, glucose + distension, and saline + distension, respectively.

Between 0 and 60 min, there was a substantial fall in systolic blood pressure during glucose (P < 0.05), no overall change during saline (P = 0.19) or glucose + distension (P = 0.20), and a rise during saline + distension (P = 0.008). The maximum change in systolic blood pressure from baseline during glucose was −14 ± 5 mmHg, while there was minimal change following glucose + distension (−3 ± 4 mmHg) and a maximum change of +11 ± 2 and +15 ± 3 mmHg during saline and saline + distension, respectively. There was a significant treatment effect (P = 0.01) for the AUC for the change in systolic blood pressure between 0 and 60 min. Systolic blood pressure was less during glucose than during saline (P = 0.05), glucose + distension (P = 0.01), and saline + distension (P = 0.03). Systolic blood pressure was greater during saline + distension than during saline (P = 0.04), with no significant difference between glucose + distension and saline + distension (P = 0.56). At 120 min, systolic blood pressure was not different from baseline after glucose (116 ± 5 mmHg, P = 0.40), saline (123 ± 6 mmHg, P = 0.26), and glucose + distension (125 ± 5 mmHg, P = 0.15) but was greater after saline + distension (132 ± 7 mmHg, P = 0.01).

Between 0 and 60 min, there was a substantial fall in diastolic blood pressure during glucose (P = 0.001), a slight fall during glucose + distension (P = 0.02), a rise during saline + distension (P = 0.02), and no overall change during saline (P = 0.48). The maximum fall in diastolic blood pressure from baseline was 12 ± 2 mmHg during glucose (at 43 ± 5 min) and 9 ± 1 mmHg during glucose + distension (at 45 ± 5 min). There was a significant treatment effect (P < 0.001) for the AUC for the change in diastolic blood pressure between 0 and 60 min. The magnitude of the fall in diastolic

Fig. 1. Intrabag (barostat) volumes during glucose + distension and saline + distension. Values are means ± SE (n = 8).

During the intraduodenal infusions, barostat bag volumes were 300–950 ml.

Systolic and Diastolic Blood Pressure and Heart Rate
blood pressure was greater during glucose than during saline ($P = 0.003$), glucose + distension ($P = 0.05$), and saline + distension ($P = 0.002$). Diastolic blood pressure was greater during saline + distension than during saline ($P = 0.006$) and glucose + distension ($P = 0.01$). At 120 min, diastolic blood pressure was not significantly different from baseline after glucose ($68 \pm 3$ mmHg, $P = 0.26$), glucose + distension ($73 \pm 3$ mmHg, $P = 0.17$), and saline + distension ($71 \pm 2$ mmHg, $P = 0.28$) but was slightly greater than baseline after saline ($71 \pm 2$ mmHg, $P = 0.03$).

Between 0 and 60 min, there was a progressive rise in heart rate during glucose ($P < 0.001$) and glucose + distension ($P < 0.001$) but no overall change during saline ($P = 0.42$) or saline + distension ($P = 0.41$). The maximum rises in heart rate from baseline during glucose (14 ± 2 beats/min at 45 ± 4 min) and glucose + distension (14 ± 3 beats/min at 44 ± 5 min) were similar, with no significant difference between them ($P = 0.99$). There was a significant treatment effect ($P = 0.002$) for the AUC for the change in heart rate between 0 and 60 min. The magnitude of the rise in heart rate was greater during glucose than during saline ($P = 0.005$) but not during glucose + distension ($P = 0.94$). Similarly, the magnitude of the increase in heart rate was greater during glucose + distension than during saline + distension ($P = 0.02$). There was no difference in heart rate following saline compared with saline + distension ($P = 0.43$). At 120 min, heart rate was not significantly different from baseline after saline (60 ± 3 beats/min, $P = 0.56$) and saline + distension (61 ± 3 beats/min, $P = 0.13$) but higher than baseline following glucose (56 ± 3 beats/min, $P = 0.007$) and glucose + distension (64 ± 2 beats/min, $P = 0.02$).

**SMA Blood Flow**

There was no significant difference in baseline (−2 min) SMA blood flow between the 4 days (Fig. 2D): 798 ± 132, 844 ± 91, 770 ± 121, and 829 ± 120 ml/min ($P = 0.81$) for glucose, saline, glucose + distension, and saline + distension, respectively.

Between −2 and 60 min, there was a rise in SMA blood flow during glucose ($P = 0.004$) and glucose + distension ($P = 0.001$) but no overall change during saline ($P = 0.13$) and a trend for a decrease during saline + distension ($P = 0.07$). The maximum rise in SMA blood flow from baseline during glucose (2,388 ± 365 ml/min at 43 ± 6 min) was greater ($P = 0.05$) than the maximum rise during glucose + distension (1,673 ± 187 ml/min at 41 ± 9 min). There was a significant treatment effect ($P < 0.001$) for the AUC for the change in SMA blood flow between −2 and 60 min, so that the magnitude of the rise in SMA blood flow was greater during glucose than during saline ($P = 0.001$), glucose + distension ($P = 0.03$), and saline + distension ($P = 0.001$). There was a trend for a rise in SMA blood flow to be greater during glucose + distension than during saline + distension ($P = 0.09$) and no significant difference during saline compared with saline + distension ($P = 0.14$). At 120 min, SMA blood flow had returned to baseline after glucose (848 ± 134 ml/min, $P = 0.73$), saline (747 ± 116 ml/min, $P = 0.19$), glucose + distension (894 ± 120 ml/min, $P = 0.16$), and saline + distension (839 ± 142 ml/min, $P = 0.92$).

**Blood Glucose Concentrations**

There was no significant difference in baseline (−2 min) blood glucose concentration between the 4 days (Fig. 4): 6.0 ± 0.2, 6.1 ± 0.1, 6.1 ± 0.1, and 6.2 ± 0.1 mmol/l ($P = 0.78$) for glucose, saline, glucose + distension, and saline + distension, respectively.

Between −2 and 60 min, there was a progressive rise in blood glucose concentrations during glucose ($P < 0.001$) and glucose + distension ($P < 0.001$) but no overall change during saline ($P = 0.55$) or saline + distension ($P = 0.48$). The maximum rises in blood glucose during glucose (11.3 ± 0.7 mmol/l at 56 ± 3 min) and glucose + distension (11.5 ± 0.8 mmol/l at 60 ± 0 min) were not different ($P = 0.69$). There was a significant treatment effect ($P < 0.001$) for the AUC for the blood glucose concentration between −2 and 60 min. The magnitude of the rise in blood glucose concentration was
greater during glucose than during saline \((P < 0.001)\) but not different from glucose + distension \((P = 0.94)\). At 120 min, blood glucose concentrations were not different from baseline after glucose \((5.8 \pm 0.8 \text{ mmol/l}, P = 0.74)\), saline \((6.0 \pm 0.2 \text{ mmol/l}, P = 0.28)\), glucose + distension \((6.9 \pm 0.8 \text{ mmol/l}, P = 0.31)\), or saline + distension \((6.1 \pm 0.1 \text{ mmol/l}, P = 0.43)\).

**Perceptions of Distension**

Baseline (at MDP) perceptions on the 2 days (glucose + distension vs. saline + distension) were \(1.3 \pm 0.2 \text{ vs. } 1.1 \pm 0.1 (P = 0.35)\) for nausea, \(1.6 \pm 0.4 \text{ vs. } 1.1 \pm 0.19 (P = 0.35)\) for bloating, and \(1.6 \pm 0.5 \text{ vs. } 1.5 \pm 0.4 (P = 0.23)\) for fullness. Prior to the glucose infusion, the stepwise distension (glucose + distension), there was no change in nausea \((P = 0.21)\) or fullness \((P = 0.12)\) and a trend for an increase in bloating \((P = 0.08)\). On the day that subjects received saline (saline + distension), there were no changes in sensations of nausea (P = 0.42), bloating \((P = 0.52)\), or fullness \((P = 0.25)\). There were no differences in perceptions between the 2 days, i.e., glucose + distension and saline + distension.

**DISCUSSION**

This study establishes that gastric distension achieved by a barostat has the capacity to abolish the fall in systolic
blood pressure and attenuate the rise in SMA blood flow but has no effect on the rise in heart rate induced by intraduodenal glucose infusion at 3 kcal/min in healthy older subjects. These observations have implications for the nonpharmacological management of postprandial hypotension.

There is increasing evidence that gastric distension plays a protective role in the regulation of postprandial blood pressure (3, 8, 17, 19, 20, 30, 31, 33). In a recent study in healthy older subjects, we demonstrated that the hypotensive response to intraduodenal infusion of glucose at 3 kcal/min was markedly attenuated by the presence of as little as ~300 ml of intragastric water; during intraduodenal saline infusion, the presence of ~100 ml of intragastric water increased systolic blood pressure by 6–8 mmHg above baseline (8). In that study, gastric distension could not be sustained, and it is possible that distension of the small intestine due to gastric emptying of the intragastric water could have influenced the response. In the current study, we were able to address these limitations by the use of a gastric barostat (30, 33). We distended the stomach to a fixed pressure of 8 mmHg above MDP, as this has been shown to be well tolerated (as proved to be the case) and to increase blood pressure in healthy young (30, 33) and older (33) subjects, in the absence of intraduodenal nutrients. In the current study, there was a trend for a rise in blood pressure (~12–18 mmHg above baseline) during intraduodenal saline when air (300–950 ml) was present within the barostat bag, consistent with previous observations (8). Also, in the presence of intraduodenal glucose, there was a trend for intraballoon volume to be greater. This is not surprising, as intraduodenal carbohydrate is known to be associated with greater gastric relaxation than intraduodenal saline as a result of feedback from small intestinal chemoreceptors (1), and acute hyperglycemia is known to induce proximal stomach relaxation (10, 11, 35). Hence, while the intragastric pressures were matched in both distension experiments, the distending volume should be considered comparable, rather than identical. It has been reported that consumption of 480 ml of water increases systolic blood pressure in healthy older subjects and patients with multiple-system atrophy and autonomic failure (19) and attenuates the fall in blood pressure following a high-carbohydrate meal in patients with autonomic failure (31). Furthermore, in healthy older subjects, the magnitude of the fall in systolic blood pressure is greater when glucose is ingested at a smaller volume (200 ml compared with 600 ml), at the same glucose concentration (17). The latter study also provided evidence that proximal, rather than distal, gastric distension may be primarily responsible for this effect (17). If this proves to be the case, it would be possible to modify the intragastric meal distribution and, hence, the regional gastric distension by changes in meal composition and/or “posture” for therapeutic purposes (4, 13).

The normal overall rate of gastric emptying of glucose in healthy young and older subjects is 1–4 kcal/min (2, 14), and we have shown that, in healthy older subjects, administration of intraduodenal glucose at 3 kcal/min induces a substantially greater fall in blood pressure than 1 kcal/min (27, 34). In contrast, infusion of glucose intraduodenally at 3 kcal/min has a minimal effect on blood pressure in young adults (34), whereas preliminary data indicate that, in patients with post-prandial hypotension, the response is exaggerated (34). The differential response to intraduodenal glucose in healthy young and older subjects has been attributed to alterations in baroreceptor function (34). As in previous studies (8), the magnitude of the fall in systolic blood pressure during intraduodenal glucose without gastric distension was substantial (14 ± 5 mmHg), and it is, accordingly, remarkable that gastric distension completely abolished the fall. Interestingly, heart rate increased progressively in response to intraduodenal glucose, and this was not influenced by gastric distension. The latter observation was surprising, and while it could reflect the greater variability of heart rate, it suggests that this response may not represent an effect of splanchnic vasodilation and a fall in blood pressure, but some form of “enterocardiac” reflex.

The mechanism(s) mediating the effects of gastric distension on the hypotensive response to intraduodenal glucose remains uncertain, and a number of possibilities warrant further exploration. The glycemic responses to intraduodenal glucose were comparable in studies with and without gastric distension (8). Furthermore, insulin is 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 (23, 25), who are, by definition, insulin-deficient. The observed effects of gastric distension on the stimulation of SMA blood flow are of considerable interest, particularly given the paucity of previous information. The current study establishes that gastric distension markedly attenuates the increase in SMA blood flow induced by intraduodenal glucose. In both cases, the pattern of SMA blood flow response differed from that of heart rate: the increase in heart rate was progressive, whereas SMA blood flow plateaued. During gastric distension, the plateau occurred substantially earlier, a response that may contribute to the maintenance of blood pressure. While this may suggest the existence of a gastrovascular reflex in the peripheral, somatic circulation, gastric distension had no effect on SMA blood flow during intraduodenal saline. Further studies are indicated to explore this issue. In the pig, fasting SMA blood flow has been reported to be decreased (26, 32), increased (32), or unchanged (32) by gastric distension, whereas in the cat, a modest increase has been reported (21). A recent study by our group reported that the rise in SMA blood flow was greater after oral than after intraduodenal glucose (9), which may reflect differences in the method of gastric distension: the barostat distends primarily the proximal stomach, while an intragastric load distends the whole stomach. There is no information relating to the potential regional effects of gastric distension on SMA blood flow, which would be of interest. It should be recognized that measurement of SMA blood flow using Doppler ultrasound is affected by the presence of abdominal gas, which may compromise location and imaging of the vessel, thereby degrading image quality, and that this may represent an issue with the barostat bag. For logistical reasons, we did not perform studies with the barostat bag deflated. The minimal intragastric pressure required to attenuate the fall in blood pressure induced by intraduodenal glucose and whether the effect is volume- and/or pressure-dependent remain to be determined. We elected to study healthy older subjects, not those with known postprandial hypotension, given that the latter occurs frequently in these individuals (16), who also exhibit a fall in blood pressure in response to intraduodenal glucose, a response that is substan-
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Preliminary data also indicate that the magnitude of the fall may be precipitous in patients with known postprandial hypotension (34). Studies in this latter group are now indicated, given that they represent the target population.

In summary, in healthy older subjects, the fall in systolic blood pressure and rise in SMA blood flow induced by intraduodenal glucose are markedly attenuated by modest gastric distension, supporting the concept that maximizing nonnutrient gastric distension may represent a simple approach to the management of postprandial hypotension (e.g., consumption of water prior to a meal).

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GRANTS

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DISCLOSURES

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

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