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The effect of meal size on postprandial increase in cardiac output

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Heart rate, stroke volume, cardiac output and mean arterial blood pressure were followed from the resting premeal situation and for 2 hours after intake of standardized meals in four healthy individuals. Continuous records of stroke volume and cardiac output were achieved with an improved method of Doppler ultrasonography. A smallish meal and one $2\frac{1}{2}$ times larger were both given twice and in random order to each of the four test persons.

The consumption of a meal invariably resulted in a cardiac output increase, which developed gradually to reach a maximum level 30 to 60 min after end of the meal. The postprandial cardiac output increase resulted from significant increases in both heart rate and stroke volume.

There were distinct and significant differences between the circulatory responses to small and large meals. The increase in cardiac output after a large meal was considerably larger and lasted for longer than the increase after a small meal. Two hours after a small meal cardiac output was nearly or fully back to pre-meal values, while cardiac output was still markedly elevated 2 hours after a large meal. Consequently, the total 'extra' amount of blood delivered by the heart over 2 post-meal hours was significantly – about 100% – larger after the large meal than after the small one.

Mean arterial blood pressure either fell or remained almost unchanged in the hour after a meal, so that total peripheral resistance was consistently and significantly reduced in the postprandial period – and considerably more so after a large meal than after a small one.

Key words: cardiac output, meal size, postprandial circulation, splanchnic circulation.

The blood vessels of the splanchnic organs are an interesting part of the circulatory system. The organs involved are richly perfused per unit weight and receive a large fraction of the cardiac output (CO) at rest. Furthermore, the process of food intake and the subsequent digestion causes marked local and general circulatory changes. Blood flow in arteries supplying the gastrointestinal organs has been shown to increase substantially after a meal in man (Norryd *et al.* 1975, Qamar & Read 1988, Waaler *et al.* 1990). CO has also been found to increase after food intake (Grollman 1929, Gladstone 1935, Waaler *et al.* 1990), and more so after a large meal than after a smallish one. Finally, marked reductions in blood flow to the gastrointestinal organs have been recorded during strenuous excercise in animals (Laughlin & Armstrong 1982, Armstrong *et al.* 1987), whereas the splanchnic area seems to retain its high postprandial blood flow during moderate exercise (Eriksen *et al.* 1990).

The digestive activity of the gastrointestinal organs is thus one of the factors which determine the setting and distribution of CO. However, the way CO changes after a meal *and its relation to*

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meal size are not known in detail, as earlier methods of measuring CO have only allowed single measurements separated by long intervals. By using improved Doppler ultrasonography, we have been able to follow the postprandial increase in CO in a continuous manner.

The aim of the present study was to reveal more precisely the time-course and pattern of the postprandial increase in CO and also to find out what relationship there might be between this pattern and meal size. To do this we used four subjects, each of whom received a smallish meal twice and a meal $2\frac{1}{2}$ times larger twice, arranged in a random order. We followed heart rate (HR), left ventricular stroke volume (SV), CO and mean arterial blood pressure (MAP) before the meals and for at least 2 h after meals.

MATERIALS AND METHODS

Measurements of CO were carried out as described by Eriksen & Walløe (1990), with Doppler ultrasonography, using a pulsed wave Doppler velocity-meter (SD-100), Vingmed Sound A/S, Horten, Norway), operated at 2.0 MHz. The transducer was positioned in the suprasternal notch, and the sampling volume was positioned about 20 mm upstream of the valvular orifice. Instantaneous maximum velocity was calculated by the built-in maximum velocity (V_{max}) estimator, and fed on-line to a microcomputer (Apricot XI, ACT Computers, Birmingham, UK) for further processing. During the measurements the computer calculated systolic velocity integrals for each cardiac cycle, gated by automatic ECG QRS complex detection.

Stroke volumes were calculated by multiplying velocity integrals by valvular cross-sectional area. This area was again calculated from internal aortic orifice diameters which were obtained by sector scan imaging (CFM-750, Vingmed Sound A/S, Horten, Norway). This calculation should give reliable estimates of stroke volumes according to the thorough methodological considerations of Eriksen & Walløe (1990), since the velocity profile at the valvular level is rectangular, and since this velocity is conserved as the maximum velocity in a jet some distance upwards from the aortic root.

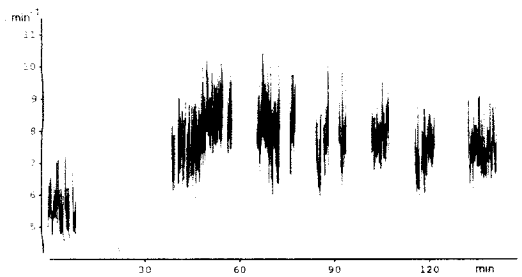

Fig. 1. Development of recorded beat by beat CO in a resting, supine person (TS) during 2 h after the ingestion of a large meal. The shaded rectangle indicates the period when the meal was consumed. The left part of the record shows CO during the last 10 min of the fasting, pre-meal situation.

Beat by beat CO (as shown in Fig. 1) was calculated by dividing stroke volumes by the corresponding beat durations found from QRS complex detections. Instantaneous heart rate was also calculated from the beat durations.

All these calculated values were stored in the computer for later plotting and statistical analysis.

The time integrated increase in CO during the 2 h period after end of a meal was also calculated. The 2 h period was divided into four successive 30 min periods, and a mean CO during each of these was found by taking the CO level as recorded during the four 2-min periods with their centres 15, 45, 75 and 105 min after end of the meal. The pre-meal CO level in a subject was measured as the mean CO level during the last 5 min of pre-meal rest. The extra cardiac output, above the pre-meal, resting CO, was calculated for each 30 min post-meal period, and the sum of these four amounts gave the integrated 2 h post-meal increase in CO.

Continuous records of mean arterial pressure (MAP) were derived from the output of a Finapres BP monitor (model 2300, Ohmeda, Madison, Wisconsin, USA), with its cuff placed around the middle phalanx of the third finger of the left hand. We have previously been able to confirm the finding of Imholz *et al.* (1990) and others that MAP derived in this way follows a simultaneous intra-arterial pressure record in a very close and precise manner.

Total peripheral resistance (PR) was calculated by dividing MAP (in mmHg) by CO (in l min^{-1}).

Subjects and experimental design. The experiments were carried out in four subjects, two male and two female (age 21–25), who were not known to have any cardiovascular disease. They all gave informed consent. Table 1 gives sex, age, weight, height, body surface area and plot symbols used for each of the four subjects. Each subject participated in four meal tests, carried out on separate days. Each person received a small meal twice and a large one twice. The succession of small and large meals could be arranged in four different ways, one of which was randomly assigned to each of the subjects. The subjects did not know which meal succession was assigned to them and therefore did not know which type of meal to expect on the first two or three occasions.

The experiments were carried out at a room temperature of about 22–23 °C, and the test persons were lightly clothed. The subjects arrived fasting and

Table 1. Sex, size parameters and the plot symbols used for each of the four test persons

Initials	Sex	Age	Weight (kg)	Height (cm)	Body surface area (m^2)	Plot symbol
GS	M	25	68	178	1.83	□
AS	F	24	54	167	1.59	△
TS	F	23	64	170	1.73	▽
AC	M	21	88	193	2.16	◇

without having eaten for the last 10–12 h. They rested in the supine position for at least 25 min, and CO, SV, HR and MAP were recorded for the last 7–10 min of this period. They were then served the meal, sitting at a table, and they were allowed to consume the food at their own pace; this took from 6–15 min. Afterwards, the subjects rested again, and measurements were made continuously from 5–7 min after end of the meal and for about 20 min. Thereafter, continuous measurements were made in 5–7 min bouts separated by 4–5 min periods when the experimenter holding the Doppler probe rested. The parameters recorded were followed using this scheme until CO was back to pre-meal level or until 2 h after the end of the meal.

The meal size was related to the size, expressed as body surface area, of each person. Body surface area (S) was calculated according to the formula of Dubois & Dubois (1916), whereby $S = W^{0.425} \times H^{0.725} \times 71.84$ (where S is body surface area in square cm, W weight in kg and H height in cm). All large meals had an energy content $2\frac{1}{2}$ times that of the small meal for the person in question. The meals given to the test person with smallest surface area (person AS) served as reference meals, composed so as to give her small meal an energy content of 2090 kJ (about 500 kcal) and her large meal an energy content of 5225 kJ. The small reference meal for person AS consisted of 65 g ham, 40 g brown bread, 8 g margarine, 85 g potato salad and 170 g milk with 2.5% fat. Her large meal contained $2\frac{1}{2}$ times as much of all the food components.

The meals given to the 3 other subjects had the same relative content of the various food components, but were increased in relation to the greater surface area of the individual. (e.g. increased by a factor of 1.36 for the largest test person, AC).

Statistical methods. The values for the time integrated postprandial increases in CO were handled as such. In addition the meal-induced changes in CO, SV and PR were converted to relative values by dividing the maximal change caused by the meal intervention by the pre-meal value. The CO, SV and PR values used in these conversions were arrived at by averaging records over 1 min periods. The relative values, as well as absolute time integrated CO values, were subsequently analysed by the BMDP3V programme (general mixed model analysis of variance). The difference in response to a small versus a large meal was considered to be a fixed effect, and the inter-individual responses to meals were assumed to be normally distributed. The programme estimates the two-tailed level of significance by which the effect of meals is different from zero, and also the two-tailed level of significance for the difference in effect between small and large meals. The magnitudes of the meal effects are also calculated.

RESULTS

Definite postprandial increases in CO were seen after all 16 meal tests in the four test persons, whose sex and size parameters are given in Table 1. Figure 1 illustrates a typical development of recorded CO after a large meal (person TS). In this particular test CO is seen to increase from a pre-meal level of about $5\frac{1}{2}$ l min^{-1} to a maximum

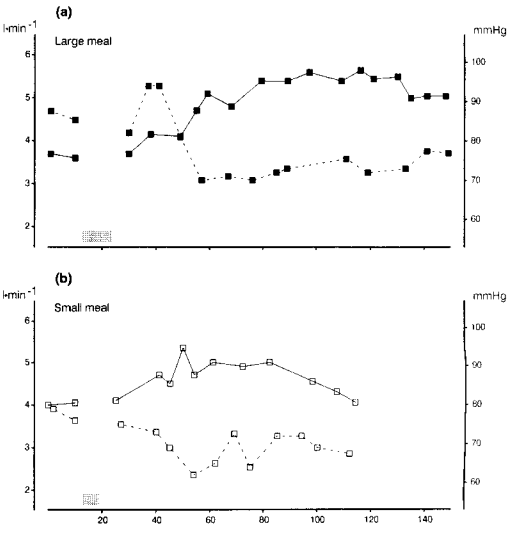

Fig. 2. Graphical illustration of the development of CO (continuous lines) and MAP (dotted lines) in the 2 h after ingestion of a large (a) and a small (b) meal by the same person (GS). Shaded rectangles indicate the periods when the meals were consumed.

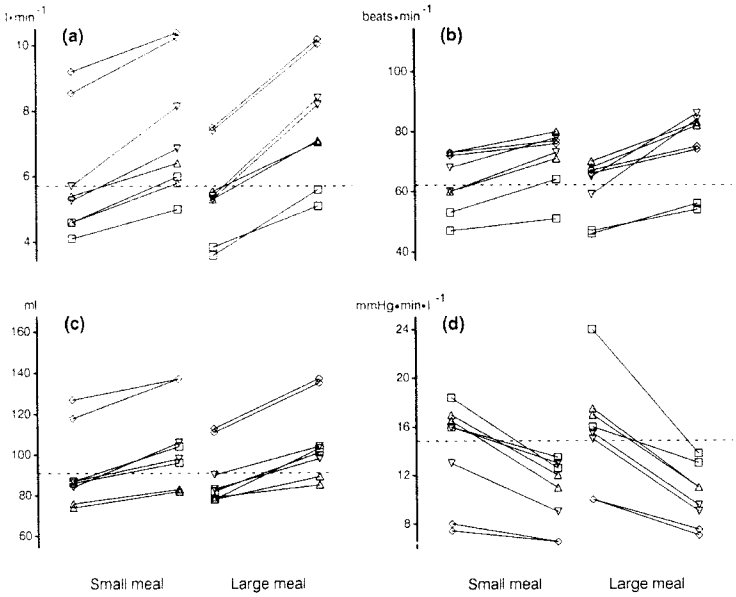

Fig. 3. Absolute values from all 16 meal tests for pre-meal and maximum (minimum for PR) post-meal levels of CO (panel a), HR (panel b), SV (panel c) and PR (panel d). Lines connect the pre and post-meal values for the same meal test. The test persons have the plot symbols assigned to them in Table 1. The dotted lines represent mean levels for pre-meal values. The ranges of the vertical axes in panels a, b and c have been selected so as to allow comparison of the degree of relative changes.

postprandial level of about 8.5 l min^{-1}. CO can be seen to fluctuate considerably around its mean levels with spontaneous fluctuations that are more marked after than before the meal. The postprandial increase in CO developed gradually and the maximum post-meal level in the various tests was reached from 30–60 min after the end of the meal (Figs 1 & 2).

The increase in CO was considerably larger and more long-lasting after large meals than after small ones. This is illustrated in Figure 2, which shows postprandial development after two meals given to the same person. After a small meal CO was back to the pre-meal level in 2 h, at a time when CO after a large meal was still considerably elevated. When the maximum levels were reached after large meals, CO values had increased by 1.2 to 3 l min^{-1}, or by 30 to 55% (mean increase 38%). The maximum CO increases after small meals ranged from 1 to 2.4 l min^{-1}, or from 13 to 42% (mean increase 26%).

MAP developed somewhat differently in the various persons and tests. In eight tests (4 in person GS, 3 in person AS and 1 in person AC) there was a lasting postprandial fall in MAP. This type of development, from two of the tests in person GS, is illustrated in Figure 2. In the other eight tests only small reductions or no significant changes at all were observed in postprandial MAP. In five tests the postprandial fall in MAP was preceeded by a shortlasting increase in MAP (Fig. 2a). However, as CO invariably increased in the post-meal periods, there was always a marked postprandial reduction in total peripheral resistance (PR).

The meal-induced augmentations in CO resulted from definite increases in HR as well as in SV. This is illustrated in Figure 3, where the absolute values for CO, SV, HR and PR for all the 16 meal tests are summarized. Pre-meal levels and maximum (minimum for PR) levels in the post-meal periods are given, with small meals in the left part of the panels, large meals to the right. The meal-induced changes in CO, SV, HR and PR shown in Figure 3 were statistically evaluated after conversion of absolute values to relative changes (see Methods).

For the group of 16 meal tests as a whole the induced changes in CO, HR, SV and PR were all

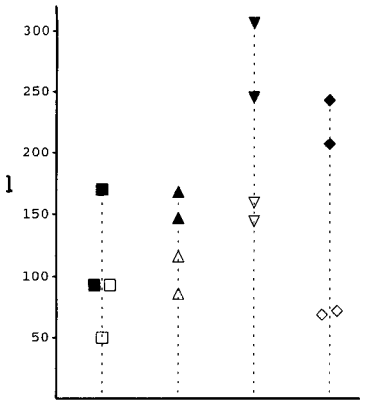

Fig. 4. Total post-meal increases in CO (in l) integrated (see Methods) over the 2 h periods following the end of meals. The plot symbols used for the test persons are the same as in Table 1. Open symbols give values from small meals, closed symbols values from large meals.

highly significant ($P < 0.001$). The changes in CO, HR and PR caused by large meals were also significantly ($P < 0.001$) larger than those caused by small meals. Large meals also caused greater change in SV than small meals (Fig. 3), but this difference was not significant ($P = 0.077$).

Figure 4 shows the total post-meal increases in CO integrated over the 120 min period following the end of a meal. Open symbols give values for small meals, closed ones for large meals. It can be seen that the left ventricle pumped 50–150 l of blood 'extra' during the 2 h period after a small meal, and 100–300 l 'extra' during the 2 h periods after a large meal. The mean value for the 'extra' CO during the 2 h postprandial period was 98.6 l for the small meals, and about twice as much, 197.4 l, for the large ones. This difference was highly significant ($P < 0.001$).

DISCUSSION

Most of the information we were looking for was obtained through the present series of 16 meal tests, where the circulatory parameters could be followed continuously. Firstly, a postprandial increase in CO was invariably observed, after both large and small meals. This is in agreement with observations by Grollman (1929), Gladstone (1935) and Fagan *et al.* (1986), whereas Norryd *et al.* (1975) reported that only two of their five test persons showed a post-meal increase in CO.

Secondly, the postprandial increase in CO developed gradually and rather slowly, so that CO reached its maximum level from 30–60 min after the end of the meal. This is a somewhat slower development towards the maximum CO level than has previously been reported both by others (Grollman 1929) and by us (Waaler *et al.* 1990). Qamar & Read (1988) have shown that the speed of postprandial flow increase in the superior mesenteric artery depends on the food components given, and develops much more slowly after fat and protein meals than after carbohydrate meals. It therefore seems reasonable to assume that the slower increase in CO in the present experiments is related to meal composition; there were larger fractions of protein and fat in the meals served this time than in those given in our previous investigation (Waaler *et al.* 1990).

The gradual increase of CO over $\frac{1}{2}$ to 1 h might reflect the course of the digestive processes, in which organs and sections enter digestive activity consecutively, as food and chyme reach new levels in the gastrointestinal tract.

A third and important observation is the definite relationship between meal size and subsequent CO increase. Thus, the maximum postprandial CO elevation above the pre-meal level was significantly larger for big meals than for small ones. This is in agreement with the careful, but much less continuous, measurements made 61 years ago by Grollman (1929). However, a more interesting measure of postprandial cardiac performance would be the 'extra' meal-induced CO, integrated over the 2 h period after a meal. We found a highly significant difference between small and large meals as regards this 'extra' amount of post-meal CO. The mean values found for this 2 hourly excess CO, 98.6 and 197.4 l respectively, give a 1 to 2 relationship between this type of response to small and large meals. This corresponds reasonably well to the 1 to $2\frac{1}{2}$ relationship in meal energy (kJ) levels. It would be interesting to know from some future experiments if this 'dose-response' relationship can be extended to meals smaller and larger than the ones chosen by us.

The calculated 'extra' CO of 98 and 197 l indicates that the left heart pumps 16% or 33% more blood during the 2 h post-meal period than the 600 l resulting from a steady, resting rate of 5 l min^{-1}. It is also interesting to note that the post-meal increase in CO results from increments

in both HR and SV, and that the two components contribute roughly equal amounts. The increase in SV indicates that an inotropic effect is included in the response of the heart to the consumption of a meal.

The previously reported spontaneous fluctuations in CO (Eriksen *et al.* 1990) were also observed in this series of experiments. Again, such fluctuations appeared to be most marked in the post-meal situation, a phenomenon possibly related to some sort of intermittence in the digestive process (Waaler *et al.* 1990).

One puzzling finding was that of the marked differences in postprandial MAP development, with a significant and lasting fall in eight tests as opposed to no or only small changes in the remaining eight. Also in five tests, but not in the other 11, we observed an initial, shortlasting increase in MAP. We have no ready explanation for these differences in postprandial MAP development. Nor can we explain why in the eight former tests MAP remained at the low level for such a long period of time. Exploration of mechanisms behind the variable postprandial development in MAP would require a search for possible circulation-influencing signals from the splanchnic area and an evaluation of the integration of such signals with other ones, e.g. those from the arterial baroreceptors.

The question also arises as to how much of the increased postprandial CO the splanchnic circulation does receive, and correspondingly how much of the marked postprandial reduction in PR can be ascribed to vasodilatation in this area. The splanchnic circulation has been found to receive about 25% of CO at rest (Donald 1983). In a previous investigation, with meals smaller than the large ones presently used (Waaler *et al.* 1990), we recorded a postprandial doubling of flow in the superior mesenteric artery, one of the arteries supplying the splanchnic organs. In animals food intake has been found to increase mesenteric flow by as much as 100 to 300% (Donald 1983). It seems reasonable to assume that postprandial flow in the various arteries supplying the splanchnic area increases in the same manner, and thus that total splanchnic flow after our large meals increases by a good 100%. It follows that the whole of our maximal postprandial CO increase of from 30–55% might reach the splanchnic organs, in which case the reduction seen in PR would be due to vasodilatation in this area only.

Since large meals cause both a greater postprandial increase in CO and a more marked reduction in PR than small meals, one would again presume that the splanchnic area is more intensely perfused after a large meal than after a small one. A direct analysis of the possible relationship between meal size and flow to the splanchnic area through one of its supplying arteries would be an interesting theme for a future investigation.

The main conclusions from this series of experiments is that the gradual increase in CO, which invariably occurs after food intake, is closely related to meal size and is a result of increments in both HR and SV. Together with these central circulatory changes peripheral changes also occur, as indicated by the reduction in PR, the extent of which is also related to meal size.

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