Changes in regional blood volume and blood flow during static handgrip

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Stewart JM, Montgomery LD, Glover JI., Medow MS. Changes in regional blood volume and blood flow during static handgrip. Am J Physiol Heart Circ Physiol 292: H215-H223, 2007. First published August 25, 2006; doi:10.1152/ajpheart.00681.2006.—Increased blood pressure (BP) and heart rate during exercise characterizes the exercise pressor reflex. When evoked by static handgrip, mechanoreceptors and metaboreceptors produce regional changes in blood volume and blood flow, which are incompletely characterized in humans. We studied 16 healthy subjects aged 20–27 yr using segmental impedance plethysmography validated against dye dilution and venous occlusion plethysmography to noninvasively measure changes in regional blood volumes and blood flows. Static handgrip while in supine position was performed for 2 min without postexercise ischemia. Measurements of heart rate and BP variability and coherence analyses were used to examine baroreflex-mediated autonomic effects. During handgrip exercise, systolic BP increased from 120 ± 10 to 148 ± 14 mmHg, whereas heart rate increased from 60 ± 8 to 82 ± 12 beats/min. Heart rate variability decreased, whereas BP variability increased, and transfer function amplitude was reduced from 18 to 0.76 at low frequencies of 0.05 indicative of uncoupling of heart rate regulation by the baroreflex. Cardiac output increased by 18% with a 4.5% increase in central blood volume and an 8.5% increase in total peripheral resistance, suggesting increased cardiac preload and contractility. Splanchnic blood volume decreased reciprocally with smaller decreases in pelvic and leg volumes, increased splanchic, pelvic and calf peripheral resistance, and evidence for splanchic venoconstriction. We conclude that the exercise pressor reflex is associated with reduced baroreflex cardiogual regulation and driven by increased cardiac output related to enhanced preload, cardiac contractility, and splanchnic blood mobilization.

MATERIALS AND METHODS

Subjects and Experimental Outline

To test this hypothesis we studied 16 healthy volunteer subjects aged 20–27 yr (median = 24.5 yr, 7 male, 9 female). Average weight (±SD) was 70 ± 14 kg, average height was 169 ± 10 cm, average body mass index was 24 ± 4 kg/m². Patients were normotensive. All measurements were made supine. Resting supine systolic blood pressure was 118 ± 10 mmHg, resting supine diastolic blood pressure was 63 ± 8 mmHg, and resting heart rate was 59 ± 9 beats/min.

All subjects were free from systemic illnesses. Subjects were not taking medications and were nonsmokers. All subjects had no evidence of cardiovascular or systemic illness. There were no competitive athletes or bedridden subjects. Informed consent was obtained. All protocols were approved by the Committee for the Protection of Human Subjects (IRB) of New York Medical College.

Laboratory Evaluation

We monitored blood pressure and heart rate continuously and estimated changes in thoracic, splanchnic, pelvic, and calf segmental blood volume and splanchnic blood flow.

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blood volumes and blood flows by impedance plethysmography while the subjects were supine and throughout static handgrip as explained below. All subjects had blood volume and resting cardiac output measured by indocyanine green (ICG) dye dilution methods, and results were compared between impedance measurements and venous occlusion plethysmography, green dye cardiac output, and dye estimates of splanchnic blood flow (see Dye dilution measurement of blood volume and cardiac output).

Protocol

Tests began at least 2 h after a light breakfast. An intravenous catheter was placed in the right antecubital fossa. After a 30-min acclimatization period, we used supine impedance plethysmography (IPG) to continuously measure resistance (R), and beat-to-beat change in resistance (∆R) of thoracic, splanchnic, pelvic, and leg segments (terms defined below) while we simultaneously estimated supine cardiac output, blood volume, and effective portal vein blood flow by the ICG dye dilution technique. Next, calf blood flow was measured by strain-gauge plethysmography (SPG). We verified respective correlations of impedance measurements of thoracic blood flow, calf blood flow, and splanchnic blood flow with dye dilution cardiac output, SPG calf blood flow, and the exponential decay coefficient of the concentration of ICG, which approximates portal blood flow divided by blood volume within a constant representing hepatic dye extraction (see Dye dilution measurement of blood volume and cardiac output). We also compared impedance methods with reference methods for measuring blood flow using Bland-Altman Plots (3). These results appear in Fig. 1. On this basis we used impedance measurements to continuously estimate changes in segmental blood flows throughout the handgrip evaluation.

Early in the experiment, each subject performed two brief maximal voluntary contractions (MVCs) with their left hand using a handgrip dynamometer (Lafayette Instruments, Lafayette, IN). Subsequently, subjects performed static handgrip while impedance, heart rate, and blood pressure monitoring continued. Handgrip was preceded by a baseline phase lasting 5 min, during which impedance, heart rate, and blood pressure data were collected. Subjects then performed 120 s of sustained isometric handgrip at 35% MVC, which we typically exhaused exercise. Posthandgrip circulatory arrest was not performed because we were interested in the exercise pressor reflex rather than measurements made after exercise. A feedback system allowed subjects to maintain force near constant. Blood pressure, electrocardiogram, and IPG flow and volume measurements were made continuously but are reported at baseline, 1 min, and 2 min of sustained handgrip and during a recovery period.

Details of Method

Heart rate and blood pressure monitoring. A single electrocardiogram lead was recorded for rhythm. Upper extremity blood pressure was continuously monitored with a finger arterial plethysmograph (Finometer, FMS, Amsterdam, The Netherlands) placed on the right middle or index finger. Electrocardiogram and Finometer pressure data were interfaced to a personal computer through an analog-to-digital converter (DI-720 DataQ Ind, Milwaukee, WI). Heart rate was derived from arterial pressure data. Finometer data were calibrated to a brachial artery oscillographic pressure. All data were multiplexed with strain gauge and impedance data and were thereby synchronized. Continuous blood pressure data were used to identify pulses and to compute heart rate and blood pressure variability indexes and to perform and compare coherence analyses among the subject groups.

Heart rate and blood pressure variability, coherence analysis. To investigate the effects of handgrip on the carotidovagal baroreflex regulation of heart rate, we measured indexes of heart rate and blood pressure variability. There is evidence for important effects of both the mechanoreflex and the metaboreflex components of the exercise pressor reflex on baroreflex function (18, 24, 54). The transfer function between blood pressure and heart rate at middle frequency (~0.1 Hz) relates to sympathetic modulation of blood pressure transduced to heart rate changes primarily by way of vagal efferents of the baroreflex (28). We examined coherence and transfer function phase and amplitude (baroreflex gain) during handgrip: baseline heart rate and blood pressure data were captured during the 5-min resting period. Beats were acquired for the first minute and second minute of handgrip. Data were analyzed for each minute separately and for both minutes combined as a single beat sequence. Data were also collected for a 1-min period during recovery from handgrip centered on the time of minimum blood pressure for comparison. We used custom software to collect digital sequences containing RR interval and systolic, diastolic, and mean blood pressures for each heartbeat, as previously described (47). The coherence function was also calculated at low frequencies. Usually a coherence of at least 0.5 is used to indicate a significant baroreceptor-mediated relationship between changes in blood pressure and changes in heart rate (38). Coherence less than 0.5 suggests an “uncoupling” of the baroreflex modulation of heart rate by blood pressure (28).

Dye dilution measurement of blood volume and cardiac output. We used ICG dye dilution technique to measure blood volume and cardiac output (3) and to estimate splanchnic blood flow in terms of portal uptake of the dye (44). We used a spectrophotometric photosensor (DDG2000, Nihon-Kohden) previously validated in clinical studies (16, 19). The dye decay curve fits a monoexponential V0 exp (−Kt), where K represents clearance by the liver divided by blood volume and clearance = (1 − hematocrit) × Q × E (44).

We defined effective portal blood flow = Q × E = (K × BV)/(1 − hematocrit), where BV is blood volume, Q is portal blood flow, and E is the hepatic dye extraction ratio.

We measured the hematocrit from antecubital venous blood, and extrapolated the dye decay curve to the time of dye injection (t = 0) yielding estimated blood volume. A semilogarithmic fit to the exponential decay yields the parameter K, which was used to estimate portal blood flow and thus splanchnic blood flow within a constant. Echo-Doppler measurements of portal venous blood flow and ICG clearance methods compare favorably (5).

Calf blood flow by SPG. We used venous occlusion strain-gauge plethysmography in all subjects to measure calf blood flow. SPG measurements were made at the beginning of experiments, and measurements were compared with impedance estimates of blood flow. We have previously employed these techniques (48, 50).

Impedance plethysmography to measure changes in segmental blood volumes and blood flows. Impedance plethysmography (IPG) has been used to detect internal volume shifts during orthostatic stress (8, 11, 33, 53). IPG is routinely used to measure changes in cardiac output in the form of impedance cardiography (8, 11). We have used this technique extensively before with repeatable and physiologically reasonable outcomes (49, 51). Our device employs a Tetrapolar High Resolution Impedance Monitor (THIRM) four-channel digital impedance plethysmograph (UFI) applied to four anatomic segments defined in practice by electrode placement. These are designated the thoracic segment (supraclavicular area to xyphoid process), the splanchnic segment (xyphoid process to iliac crest), the pelvic segment incorporating lower pelvis to the knee (iliac crest to knee), and the leg or calf segment (upper calf just below the knee to the ankle) (49, 51). Ag/AgCl electrocardiograph electrodes were attached at these segmental boundaries and also to the right foot and right hand, where they served as current injectors. The IPG uses a 50-kHz, 0.1 mA RMS constant current signal between the foot and hand electrodes. Electrical resistance values were measured using the segmental pairs as sampling electrodes. The midline distance between the sampling electrodes (L) was measured with a tape measure. We also measured the circumferences of calf, thigh, hips, waist, and chest to obtain approximate volume contents of each anatomic segment. We estimated the change in blood volume in each segment during handgrip from the formula:
where \( \rho \) is electrical conductivity of blood estimated as \( 53.2 \times \exp(\text{hematocrit} \times 0.022) \) given by Geddes and Sadler (12). \( R_0 \) is the resistance of a specific segment before handgrip, \( R_1 \) is the resistance during handgrip, and \( \Delta R \) is the change in resistance \((R_1 - R_0)\) in a specific segment during handgrip. \( \rho \) was regarded as constant during the maneuver.

IPG was also used to measure segmental blood flows (33). Transient blood flows have been similarly quantitated during orthostasis (49) and during the Valsalva maneuver (51). Pulsatile changes in electrical resistance for each segment were employed to compute the time derivative \( \partial R/\partial t \), which we used to obtain the blood flow responses of each body segment during handgrip.

Blood flow was estimated for an entire anatomic segment from the formula:

\[
\text{Flow} = [\text{HR} \times \rho \times L^2 \times T \times \partial R/\partial t \times \text{max}]/R_0^2
\]

where HR is heart rate, \( T \) is the ejection period, \( R \) is the pulsatile resistance, and \( R_0 \) is the baseline resistance at a given angle of tilt. Respiratory artifact was removed from the signal using a custom,

\[
\Delta \text{segmental blood volume (ml = } \rho \times (L^2/R_0R_1) \times \Delta R \text{ (11, 13)),}
\]

Fig. 1. Top left: estimated cardiac index (CI) calculated using indocyanine green (ICG) dye dilution technique on the abscissa compared with CI calculated using impedance methods; top right: corresponding Bland-Altman plot. Middle left: estimated splanchnic blood using ICG dye dilution technique (ordinate) compared with splanchnic blood flow using impedance plethysmography (abscissa); middle right: corresponding Bland-Altman plot. Bottom left: calf blood flow measured by venous occlusion plethysmography (ordinate) and estimated by IPG (abscissa); bottom right: corresponding Bland-Altman plot. Correlation coefficients are shown. There are small fixed errors in thoracic blood flow, as well as fixed and proportional biases in splanchnic and calf blood flows, but no nonuniformities of error.
Fourier-based frequency selection technique. IPG flows are expressed in milliliters per minute for anatomic segment and can be normalized by dividing by estimated segmental volume.

Statistics
All tabular and text results are reported as means ± SD. Graphics are presented as means ± SE. Changes in heart rate and blood pressure variability and in impedance estimates of regional blood flow and regional blood volume, heart rate, and mean and systolic blood pressures were compared by analysis of variance for repeated measures at baseline before handgrip, 1 min after the start of handgrip, 2 min after the start of handgrip, and during recovery using the minimum of blood pressure during recovery as the time of comparison. Results were calculated using SPSS (Statistical Package for the Social Sciences) software version 11.0.

RESULTS
All subjects completed the protocol successfully. Blood volume for each subject was normal, and the mean was 5.2 ± 1.5 liter (73 ± 12 ml/kg) and the mean hematocrit was 41 ± 3%. Data were similar for males and females and pooled gender data are presented.

Heart Rate and Blood Pressure During Handgrip
Heart rate and blood pressure are shown in Fig. 2. Data from a representative subject shows the approximately linear increase in blood pressure as a function of time during handgrip. This linearity was observed in all subjects. Heart rate increased rapidly during the early course of static handgrip and more slowly thereafter. Percent changes in heart rate and blood pressure are based on paired data assessments and are also shown in Fig. 2. Absolute blood pressures (systolic and mean) and heart rates at stages of handgrip are shown in Table 1. On average systolic and mean arterial blood pressure increased significantly from baseline at 1 min of handgrip (P < 0.0001) and increased further at 2 min of handgrip (P < 0.0001) returning at recovery to a pressure that was slightly lower than baseline (P < 0.001). Heart rate increased significantly from baseline at 1 min (P < 0.0005) and further at 2 min (P < 0.005), returning at recovery to a heart rate that was similar to baseline.

Heart Rate and Blood Pressure Variability, Coherence Analysis
Decreased HRV during handgrip varied BPV. Data are shown in Table 1. Total heart rate variability (HRV) was significantly decreased compared with baseline (P < 0.001) at 1 and 2 min of handgrip and returned to baseline values during recovery. Low-frequency HRV power decreased (P < 0.01) during the first minute of handgrip but then was similar to baseline during the second minute of handgrip. High-frequency HRV power was decreased during both 1 and 2 min of handgrip but was similar to baseline during recovery. The ratio of low-frequency to high-frequency power (LF/HF) was increased during the second minute of handgrip compared with baseline (P < 0.001). Blood pressure variability (BPV) was decreased in the first minute of handgrip (P < 0.01) and was
increased during the second minute \( (P < 0.05) \) compared with baseline.

**Lack of significant low-frequency HRV-BPV coherence during handgrip.** Although transfer function gain (transfer magnitude) was markedly reduced \( (P < 0.001) \) throughout handgrip and recovery, this was associated with a reduction of coherence \( (P < 0.001) \) well below the 0.5-cutoff for significant coherence. Thus changes in transfer magnitude (i.e., baroreflex gain) may not be strictly interpretable under these circumstances. The data suggest an uncoupling of baroreflex mediation of heart rate and blood pressure during handgrip.

**Impedance Plethysmographic Changes in Segmental Blood Volumes and Blood Flows**

Reciprocal thoracic (central)–splanchnic blood volume changes during handgrip. Representative changes in segmental impedance and in the percent change in blood volume during handgrip are shown in Fig. 3. There are opposite changes within the thoracic and splanchnic segments. Significant increases in impedance also occur within pelvic and calf segments but are of much smaller magnitude than splanchnic increments.

Central blood volume increases and peripheral volume decreases during handgrip. Percent changes in all segmental blood volumes are shown in Fig. 4. There is an increase in thoracic volume noted during the first minute of handgrip, which reaches significance \( (P < 0.025) \) during the second minute. Splanchnic volume changes in reciprocal fashion with smaller changes noted in pelvic and calf volumes, which both decreased significantly \( (P < 0.05) \) during the second minute of handgrip. Comparable changes in the percent volume of the calf diameter were measured by SPG.

Segmental blood flow changes during handgrip: stable splanchnic blood flow suggests vеноconstriction. Changes in segmental blood flow are shown in Fig. 5. Cardiac output is increased by nearly 20% \( (P < 0.01) \) throughout handgrip, whereas splanchnic blood flow tends to be unchanged during handgrip, and pelvic and calf blood flows are increased at 2 min \( (P < 0.025) \). Stable splanchnic blood flow with decreasing splanchnic volume may indicate active splanchnic vеноconstriction (see DISCUSSION).

### Table 1. Heart rate and blood pressure data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>1 min</th>
<th>2 min</th>
<th>1&amp;2 min</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>59 ± 8</td>
<td>76 ± 12*</td>
<td>82 ± 12*</td>
<td>58 ± 6</td>
<td></td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>118 ± 10</td>
<td>134 ± 12*</td>
<td>148 ± 14*</td>
<td>116 ± 8*</td>
<td></td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>90 ± 7</td>
<td>102 ± 11*</td>
<td>114 ± 14*</td>
<td>87 ± 7*</td>
<td></td>
</tr>
<tr>
<td>Total HRV Power, ms²/Hz</td>
<td>3,213 ± 836</td>
<td>1,683 ± 714*</td>
<td>2,207 ± 1156*</td>
<td>2,156 ± 895</td>
<td>3,245 ± 906</td>
</tr>
<tr>
<td>Low-frequency HRV Power, ms²/Hz</td>
<td>1,071 ± 310</td>
<td>562 ± 279*</td>
<td>1,061 ± 710</td>
<td>769 ± 326</td>
<td>1,197 ± 367</td>
</tr>
<tr>
<td>High-frequency HRV Power, ms²/Hz</td>
<td>1,476 ± 498</td>
<td>827 ± 417</td>
<td>847 ± 389</td>
<td>843 ± 377</td>
<td>1,546 ± 243</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>0.90 ± 0.19</td>
<td>0.80 ± 0.17</td>
<td>1.76 ± 0.63*</td>
<td>1.02 ± 0.31</td>
<td>1.12 ± 0.20</td>
</tr>
<tr>
<td>Total BVP Power, mmHg²/Hz</td>
<td>8.4 ± 2.0</td>
<td>6.8 ± 0.8*</td>
<td>9.8 ± 1.5*</td>
<td>9.5 ± 1.6</td>
<td>10.0 ± 2.3</td>
</tr>
<tr>
<td>Transfer coherence</td>
<td>0.76 ± 0.10</td>
<td>0.41 ± 0.06*</td>
<td>0.26 ± 0.05*</td>
<td>0.34 ± 0.05</td>
<td>0.42 ± 0.06</td>
</tr>
<tr>
<td>Transfer magnitude, gain/mmHg⁻¹</td>
<td>18 ± 2</td>
<td>11 ± 2*</td>
<td>8 ± 2*</td>
<td>10 ± 2*</td>
<td>11 ± 2*</td>
</tr>
<tr>
<td>Transfer phase (degrees)</td>
<td>24 ± 12</td>
<td>80 ± 46*</td>
<td>90 ± 40*</td>
<td>88 ± 42*</td>
<td>80 ± 17*</td>
</tr>
</tbody>
</table>

Values are means ± SD. HR, heart rate; BP, blood pressure; MAP, mean arterial resistance; HRV, HR variability; BVP, BP variability. *\( P < 0.05 \) compared with baseline.
peripheral resistance is modestly increased ($P < 0.025$) during the second minute of handgrip but returns to baseline during recovery. Similar increases in splanchnic, pelvic and calf resistances were noted.

**DISCUSSION**

**Main Findings**

Regional blood volume redistribution and hemodynamics during handgrip. Our results demonstrate an integrated approach by which changes in hemodynamically important regional circulations contribute to the redistribution of blood volume and blood flow during static handgrip. The most significant new finding is that the increase in central blood volume and cardiac output evoked by the exercise pressor reflex is produced in large part by emptying of the splanchnic segment.
vascular bed through splanchnic venoconstriction and arterial vasoconstriction. We observed a 4.5% increase in central blood volume associated with a 2.5% decrease in splanchnic volume. Since the splanchnic vascular bed receives ~25% of the cardiac output and contains ~30% of the blood volume, it is reasonable that the splanchnic vasculature is able to rapidly transfer its blood to the central circulation (41). Relatively smaller but directionally similar decreases in segmental blood volume occur within the pelvic and calf segments. The finding of splanchnic emptying at relatively constant splanchnic blood flow implies the active contribution of venoconstriction. In addition, there is an increase in total peripheral resistance and therefore cardiac afterload. The magnitude of the increase in cardiac output, the increase in central blood volume, and the increase in end-systolic pressure suggest that there is also an increase in cardiac contractility.

Baroreflex regulation of heart rate during handgrip (cardiovagal regulation).

Cardiovagal baroreflex regulation is calculated in the present work. This technique mainly estimates parasympathetic control of heart rate. If usual coherence criteria are employed, our data also imply that parasympathetic baroreflex regulation of heart rate may become relatively less important during handgrip. Note that the data do not inform on baroreflex effects on peripheral resistance or on cardiac contractility (28).

Comparisons with the Literature

Heart rate and blood pressure during handgrip. Our observations are consistent with the literature showing changes in both blood pressure and heart rate during and after release of hand grip. The time course and magnitude of increases in heart rate and blood pressure are similar to data observed elsewhere in healthy human subjects (1, 6, 10, 21).

Variability analyses. Our measurements of heart rate variability are consistent with past data of Kluess et al. (25) and with the extended analyses of Iellamo et al. (18) in showing a relative increase in low-frequency to high-frequency spectral components and a reduction in baroreflex gain. We would, however, interpret such data differently in light of the progressive decrease in coherence between heart rate and blood pressure, which falls well below the 0.5 threshold for significance of coherence (Table 1) and is synchronous with the reduction in baroreflex gain. This can be interpreted as resulting from an uncoupling of heart rate from blood pressure modulation of the baroreflex during the isometric static exercise pressor reflex.

Segmental hemodynamics. These data, showing segmental changes in blood volume during hand grip measured by impedance plethysmography, are new in humans and are consistent with other findings in both human and animal literature. They are also unique because these measurements are noninvasive. Thus, for example, O’Leary’s laboratory (45) have demonstrated the increase in central blood volume and ventricular performance (37) with consequent increased cardiac output (2), which occurs during the metaboreflex. This is in agreement with our measurements and with the observations on heart rate and stroke volume of Crisafulli et al. (7) during rhythmic handgrip contraction followed by local ischemic occlusion.

Increases in total peripheral resistance have also been shown in humans (17, 27) but not in normal dogs (2) during submaximal exercise. Thus in humans the increase in blood pressure during the pressor reflex has often been ascribed to vasoconstriction alone. This species difference in vasoconstriction may

Fig. 6. Percent changes in segmental arterial resistance. From top to bottom: changes in thoracic, splanchnic, pelvic, and leg (calf). Total peripheral resistance (TPR, thoracic resistance) was increased by the second minute of handgrip and was increased in splanchnic, pelvic and calf segments during the entire handgrip period. All resistances returned to baseline during recovery.

*P < 0.05 compared with baseline.
represent a more situational than qualitative difference: thus
pronounced vasoconstriction does occur by metaboreflex if
cardiac output is held constant by ventricular pacing + β-block
(45), during maximal exercise wherein cardiac output cannot
increase further (2), during heart failure (15), or in normal dogs
after arterial baroreceptor denervation (24).

Whereas a modest increase in total peripheral resistance was
observed during our studies, it was combined with a propor-
tionately greater increase in cardiac output related at least in
part to an increase in central volume. Whereas an accurate
calculation of ventricular elastance was not feasible using
current data, the results suggest an increase in cardiac contract-
tility as observed in dogs by Sala-Mercado and coworkers (43).

In addition, we found that arterial resistance increased in
splanchnic, pelvic, and calf segments to a similar degree,
although blood flow did not change in the splanchnic segment
and actually increased in the pelvic and calf segments due to
the increase in blood pressure. Similar observations concerning
splanchnic resistance have been made by Waaler and associ-
ates (52). Since neither blood flow changes nor blood volume
shifts were reported, it was not possible to draw conclusions
concerning regional blood volume changes from their data.
However, the lack of change in splanchnic blood flow with
decreasing splanchnic segmental blood volume in our data may
support the hypothesis of venoconstriction. Active vено-
constriction is confirmed if there is a decrease in venous volume
while venous pressure is kept constant. This may also be true
if there is perfusion at constant flow provided there is no
reduction in central venous pressure (40). Canine data suggest
that there is actually an increase in right atrial pressure during
ischemic exercise (45), which should result in an increase in
central venous pressure. Taken together the data and literature
support the proposal of active splanchnic venoconstriction
during static handgrip in humans.

Limitations

Impedance plethysmography is an indirect measurement of
blood flow, and the accuracy and validity of its use for such
measurements may be questioned. We tried to resolve this
issue by comparing impedance measurements to standard ref-
ERENCE methods such as ICG dye dilution (for cardiac output
and for portal venous blood flow) and venous occlusion pleth-
ysmography (for calf blood flow). Comparisons show reason-
able albeit imperfect correlations between reference standard
and impedance measurements. There are both fixed and pro-
portional biases but no nonuniformities of error. Thus, within
limits, and for purposes of continuous monitoring, we believe
invasive testing can be replaced by noninvasive testing. How-
ever, whereas the ICG method can yield accurate cardiac
outputs, neither this reference standard method (as imple-
mented in the current study) nor impedance methods are
capable of giving true splanchnic flow results. Thus with ICG
dye we calculated dye clearance rather than portal or hepatic
blood flow, whereas impedance methods are best suited for
detecting relative or percent changes in blood volume. Invasive
measures to obtain hepatic extraction ratios in each subject are
beyond the scope of current studies and would need repeated
reassessments throughout static handgrip.

ICG estimates of portal blood flow were hampered by the
lack of computation of the hepatic dye extraction ratio. As
explained in MATERIALS AND METHODS, there is an implicit
assumption of equal extraction in all patients with an extraction
ratio of 1.0. Similar extraction ratios seem to be a reasonable
assumption among healthy subjects.

Heart rate and blood pressure variability indexes are not
reference standards for autonomic or metaboreflex measurements.
However, measured indexes have been consistent with inva-
sive forms of measurement such as microneurography. (39)

Our aim was to assess the hemodynamic responses induced
by exercise pressure reflex during exercise. Other confounding
factors, such as central command, humoral changes, physical
factors, and other blood-borne biochemical factors may be
present during exercise. This leads many investigators to per-
form measures immediately after peak exercise during periph-
eral circulatory occlusion ischemia, which was not done here.
However, central command, whereas responsible for much of
the increase in heart rate and respirations during exercise, does
not appear to increase sympathetic outflow unless the intensity
of the exercise is near maximal (20), and humoral contributions
appear to require a more sustained form of exercise to achieve
importance (34). Nevertheless, central command, in particular
may contribute to measured changes in heart rate.

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