special communication

Ultrasound Doppler estimates of femoral artery blood flow during dynamic knee extensor exercise in humans

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Rådegran, G. Ultrasound Doppler estimates of femoral artery blood flow during dynamic knee extensor exercise in humans. *J. Appl. Physiol.* 83(4): 1383–1388, 1997.—Ultrasound Doppler has been used to measure arterial inflow to a human limb during intermittent static contractions. The technique, however, has neither been thoroughly validated nor used during dynamic exercise. In this study, the inherent problems of the technique have been addressed, and the accuracy was improved by storing the velocity tracings continuously and calculating the flow in relation to the muscle contraction-relaxation phases. The femoral arterial diameter measurements were reproducible with a mean coefficient of variation within the subjects of 1.2 ± 0.2%. The diameter was the same whether the probe was fixed or repositioned at rest (10.8 ± 0.2 mm) or measured during dynamic exercise. The blood velocity was sampled over the width of the diameter and the parabolic velocity profile, since sampling in the center resulted in an overestimation by 22.6 ± 9.1% ($P < 0.02$). The femoral arterial Doppler blood flow increased linearly ($r = 0.997$, $P < 0.001$) with increasing load [Doppler blood flow = 0.080·load (W) + 1.446 l/min] and was correlated positively with simultaneous thermodilution venous outflow measurements ($r = 0.996$, $P < 0.001$). The two techniques were linearly related (Doppler = thermodilution·0.985 + 0.071 l/min; $r = 0.996$, $P < 0.001$), with a coefficient of variation of ~6% for both methods.

blood velocity; flow profile; vessel diameter

DURING INTENSE DYNAMIC EXERCISE, human skeletal muscle blood flow rises markedly to meet the metabolic demand of active muscle tissue (13). Several methods have been utilized to estimate limb blood flow intermittently during or just after termination of exercise (2–5, 11, 15). Present measurements of blood velocity utilizing the noninvasive ultrasound Doppler provide an alternative method for continuously estimating regional arterial inflow (6, 7, 9). The method has been utilized previously to estimate leg blood flow at rest (12) and during intermittent static contractions of the human quadriceps muscle (14, 16, 17). In these exercise experiments, the mean blood velocity was averaged on a beat-by-beat basis triggered by the R wave or the QRS complex of the electrocardiogram (ECG). However, this ECG-averaged velocity varies markedly depending on its temporal relation to transient variations in intramuscular pressure during the muscle relaxation and contraction phases (16, 17). A further variability in the averaged values depends on whether cardiac systole or diastole is initiated at the beginning of the respective phases (16). Thus the ability of this procedure to follow the proper velocity and flow profile, as well as the precise transitional changes in blood velocity and flow during each kicking duty cycle (a muscular contraction and relaxation phase), is limited. Any failure in insonation (direction of the transmitted sound-wave beam at the site of measurement) of the artery may also contribute to the inherent variability of the procedure. Moreover, in the previous studies, fairly long contraction-relaxation phases (5–75, 30–195, 2–2, 4–4, and 4–1 s) have been used (14, 16, 17). Such exercise does not resemble normal action of muscle in daily life activities, where the contraction-relaxation phases are shorter and the contraction includes acceleration and retardation phases.

Therefore, the aim of the present study was to determine the validity and reliability of the ultrasound Doppler blood velocity and flow measurements during intense dynamic exercise in humans and to improve accuracy of the sampling procedure during transitional changes.

METHODS

Thirty-two healthy male volunteers with a mean (range) age of 26.1 (21–35) yr, height of 181.2 (174–193) cm, and body mass of 77.3 (59–96) kg participated in this study. Their anthropometrically estimated (2, 10) quadriceps muscle mass was 2.99 ± 0.08 (SE) kg, i.e., in the range of 2.83 ± 0.06 to 3.11 ± 0.13 kg for the five subgroups. The subjects were informed of the experimental procedures and that they were free to withdraw at any time without any consequences. They were allowed to participate after providing a signed informed consent. The study was approved by the Ethical Committee of Copenhagen and Fredriksberg (KF-01–013/96).

Five different experimental protocols were performed: *1*) blood velocity distribution in the femoral artery ($n = 7$); *2*) arterial diameter at rest and during exercise ($n = 9$); *3*) variation in blood flow ($\dot{Q}$) during exercise ($n = 3$); *4*) ECG ($\dot{Q}_{ECG.av.UD}$, where av is average and UD is ultrasound Doppler; $n = 5$) vs. muscle contraction (cont) ($\dot{Q}_{cont.UD}$, $n = 10$) averaged Doppler blood flow during exercise; and *5*) simultaneous Doppler ($\dot{Q}_{cont.UD}$) and thermodilution (TD) ($\dot{Q}_{TD}$) blood flow measurements ($n = 7$). Before the experiments, the subjects were familiarized with the one-legged dynamic knee extensor exercise procedure, performed with the subjects maintained in the sitting position (1). The subjects trained at a rate of 60 contractions/min until they were comfortable and could fully relax the hamstring muscles so that the work was performed solely by the knee extensors (1). The exercise load

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was raised in 10-W increments every 10–20 min. In *protocol 3*, the intramuscular pressure was measured in the quadriceps muscle with a microtip catheter transducer (2-Fr, diffused semiconductor, model SPC-320, Millar Instruments, Houston, TX). The signal was amplified by a transducer control unit (Millar Instruments) and recorded simultaneously with the intra-arterial blood pressure (Kone Patient data monitor 565A, Medicoline, Valby, Denmark), the knee extensor force (strain gauge), and the mean Doppler blood velocity. In *protocol 5*, a straight 8-cm catheter (7-Fr diameter, Cook, Denmark) with perforating side holes as well as a thermistor (model 94–030–2.5-Fr, T. D. Probe, Edwards Edslab, Baxter, Irvine, CA) were inserted below the inguinal ligament in the proximal direction into a femoral vein. The thermistor was connected to a cardiac output computer (model 9520A, American Edwards Laboratories, Harvard Apparatus, Irvine, CA) for continuous blood temperature measurements and thermodilution blood flow measurements during constant infusion of a saline solution (0°C) utilizing a Harvard pump (Harvard Apparatus, Millis, MA) (2). The measured variables were recorded with a data-acquisition program (obtained from the Institute of Physiology, Oslo, Norway) on a personal computer (PC: IBM-compatible, Pentium based).

Ultrasound Doppler equipment. An ultrasound Doppler (model CFM 800, Vingmed Sound, Horten, Norway) equipped with an annular phased array transducer probe (11.5-mm diameter), operating at an imaging frequency of 7.5 MHz and variable Doppler frequencies of 4.0–6.0 MHz, was utilized to measure two-dimensional (2D) femoral arterial diameter and mean blood velocity at rest and during one-legged dynamic knee extensor exercise. The depth range of the ultrasound beam was greater than the anatomic location of the femoral artery. The Doppler signals and other data were processed via an external switch box and transferred to an eight-channel analog-to-digital converter mounted on the PC. The PC online system enabled continuous data storage with a frequency up to 300 Hz or averaging of the separate variables automatically on a beat-by-beat basis for each cardiac cycle triggered by the R wave of the ECG.

Instrumentation and methodological considerations. All measurements were performed below the inguinal ligament on the common femoral artery, ~2–3 cm above its bifurcation into the superficial and profundus branch. The position was chosen to minimize turbulence from the bifurcation and interference of blood flow to the inguinal region; also, the arterial diameter is unaffected by the contraction and relaxations per se at this site proximal to the muscle location. The muscular arterial wall and the high arterial pressure allowed positioning of the transducer without deformation of its circular shape. The femoral artery was insonated with 7.5 MHz at a fixed perpendicular angle. Longitudinal 2D images of 25 frames/s were stored in the image buffer and on magneto-optical discs. The systolic and diastolic diameters were subsequently determined over the cardiac cycles along the central path of the ultrasound beam, where optimal spatial resolution occurs. An average diameter corresponding to the relative time periods of the systolic (1/3) and the diastolic (2/3) blood pressure phases [$D_{(\text{systole}/3)+(\text{diastole}2/3)}$] was selected as the most representative diameter estimate. These diameter measurements were used to calculate the circular cross-sectional area ($A = \pi \cdot r^2$) of the artery. Blood velocity measurements were obtained at the lowest possible insonation angle. Special care was taken to ensure that the probe position was stable, that the insonation angle did not vary, and that the sample volume was positioned in the center of the vessel and adjusted to cover the width of the diameter and the blood velocity distribution. Contributions to the signal by turbulence occurring at the vascular wall were reduced with a low-velocity rejection filter. Guided by the longitudinal ultrasound 2D image and the rotatable flow-directional axis of the sample volume, a correction for the external angle of insonation was performed continuously. The blood velocity was then measured in the artery at a Doppler frequency of 4.0–6.0 MHz, operated in the high-pulsed repetition frequency mode (4–36 kHz), during simultaneous real time 2D vessel visualization, together with audiovisual feedback from the velocity spectra. The velocity display was adjusted to a level where the maximum velocity predicted to occur in the artery during exercise would not exceed the Nyquist limit. The PC system was calibrated within this velocity range. To avoid motion artifacts during intense incremental exercise, the subjects were strapped tightly to the seat and positioned so that the femoral arterial inflow to the leg would not be impeded. To eliminate calf muscle blood flow contributions, all blood flow measurements were performed with a cuff around the lower leg, temporarily inflated to a suprasystolic blood pressure.

In previous exercise studies, the blood flow velocity has been averaged on a beat-by-beat basis for each cardiac cycle, rendering great variability in the mean blood velocity values (14, 16, 17). Because the blood velocity and flow variation during exercise may be more dependent on the muscle contraction and relaxation phases, rather than on the cardiac cycle and the pulse pressure, the effect on the blood velocity over the kicking duty cycle was considered. Thus the blood velocity was sampled continuously, stored with a frequency of 100 Hz, and, subsequently, after a quality control of the velocity spectra, averaged for each duty cycle in relation to the knee extensor force tracing representing the impact of the muscle contraction profile. Velocity spectra of poor quality, i.e., with an irregular envelope tracing and a loss in signal intensity that could not be accounted for by the impact of the muscle contraction but rather insonation failures, were excluded from the analysis. Blood flow ($\dot{Q} = v_{\text{mean}} \cdot A \cdot 6 \times 10^4$, where v_{mean} is mean blood velocity; l/min) was calculated from the amplitude (signal intensity)-weighted, time- and spatial-averaged v_{mean} (m/s), corrected for its angle of insonation, and multiplied by A (m^2) of the femoral artery.

Statistical analysis. Parametric statistics (linear regression, Pearson correlation, paired *t*-test when comparing two groups, analysis of variance when comparing more than two groups) was used for data analysis. A P value <0.05 was considered as statistically significant. The values are means ± SE unless otherwise indicated.

RESULTS

Blood velocity distribution in the femoral artery. Mean blood velocity at rest was 52.1 ± 10.1% higher ($P < 0.02$) in the center of compared with in the periphery of the artery, whereas the velocities in the two peripheral locations were similar [P = not significant (NS)] (Fig. 1). Mean blood velocity in the center of the vessel measured with the smallest sample volume (0.8 mm) was 22.6 ± 9.1% higher ($P < 0.02$) than with the largest sample covering the width of the arterial diameter.

Arterial diameter at rest and during exercise. The common femoral arterial diameters measured at similar locations in nine subjects at rest were the same (P =

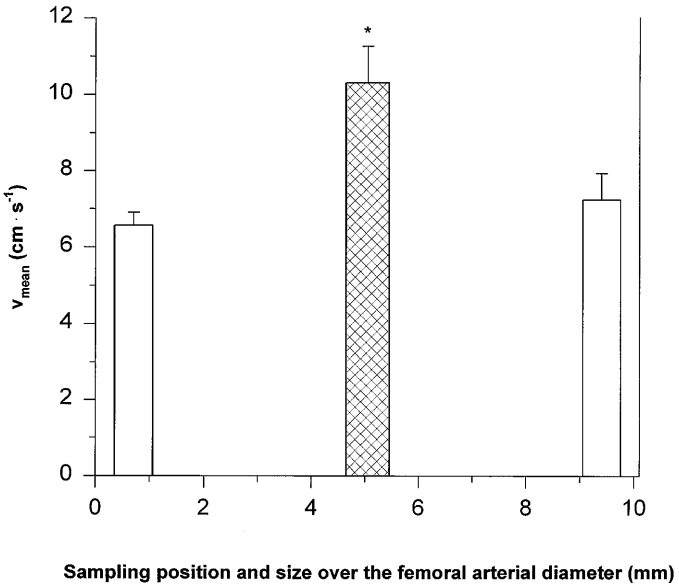

Fig. 1. Mean blood velocity (v_{mean}, cm/s) at rest in femoral artery of 7 subjects with a mean arterial diameter of 10.1 ± 0.3 mm; v_{mean} was 52.1 ± 10.1% larger (*significantly different, $P < 0.02$) in center compared with that in 2 peripheral positions along vascular wall. Width of bar corresponds to sample volume size (0.8 mm). Values are means ± SE.

NS) whether made with six repetitive repositionings of the probe (10.8 ± 0.2 mm) or when six measurements were made with a fixed probe positioning (10.8 ± 0.2 mm). The individual values for the averaged diameters were the same (P = NS) at rest (10.8 ± 0.2 mm) compared with during exercise at 10 W (10.6 ± 0.2 mm), 30 W (10.7 ± 0.2 mm), and 50 W (10.7 ± 0.2 mm) (Fig. 2). The systolic diameters (10.8 ± 0.2 mm) were the same (P = NS) at rest and during exercise. The diastolic diameters were slightly smaller ($P < 0.05$) during exercise at 10 W (10.6 ± 0.2 mm) compared with those at rest (10.8 ± 0.2 mm) and during exercise at 30 W (10.7 ± 0.2 mm) (Fig. 2). The systolic diameters were the same (P = NS) compared with the diastolic ones under all conditions, except for those at 10-W exercise where they appeared to be slightly larger ($P < 0.05$). The mean coefficients of variation within the subjects for the systolic, diastolic, and averaged [$D_{(systole/3)+(diastole2/3)}$] diameter measurements were 1.5 ± 0.2, 1.6 ± 0.2, and 1.2 ± 0.2%, respectively. The range of the mean femoral arterial diameters for the subjects was from 8.5 to 11.8 mm.

Variation in blood flow during exercise. Two subjects, with a mean femoral arterial diameter of 9.7 ± 0 mm, exercised for 60 min at 20 W. Blood velocity and flow values of the same magnitude were found when the beat-by-beat triggered blood velocity was compared (analyzed over 15- to 60-s segments) with the velocity spectra temporarily stored in the Doppler image buffer (analyzed over 2–3 s only). For the first subject, the corresponding mean blood flow, coefficient of variation, and number of measurements for each procedure were 2.88 ± 0.07 l/min (9.9%, n = 18) vs. 2.85 ± 0.10 l/min (9.3%, n = 7), respectively, and for the second subject were 2.65 ± 0.07 l/min (14%, n = 30) vs. 2.56 ± 0.31 l/min (24%, n = 4), respectively. The somewhat larger variation in the second subject, when analyzed over the short period of a few seconds, reflects the variability in blood flow between duty cycles and may, during steady-state exercise, be reduced by averaging values over longer time periods.

The arterial inflow to the contracting muscle, as monitored by continuous recording of the blood velocity spectra during exercise in one of the subjects, appeared to be markedly affected by the transient variations in intramuscular pressure, indicating the importance of the continuous velocity sampling procedure (Fig. 3). The muscle contraction-relaxation phases were closely related to the variation in blood velocity, with mechanical hindrance to blood flow and a high intramuscular pressure during the contraction phase and with an unimpeded blood flow and low intramuscular pressure during the relaxation phase (Fig. 3). As indicated at *peaks A-I*, peak blood velocity occurs during the relaxation phase when low intramuscular pressure and knee extensor force coincide with peak arterial pressure (*A*); a velocity plateau occurs as the second dicrotic blood pressure notch (8) occurs during the relaxation phase (*B*); no or retrograde velocity occurs as the intramuscular pressure and knee extensor force peak during minimum arterial pressure (*C, G*); a slight velocity increase to only 50% of peak velocity occurs when peak arterial pressure coincides with the peak intramuscular pressure and knee extensor force (*D, I*); a somewhat greater velocity increase to ~70–75% of the peak velocity follows when the second dicrotic blood pressure notch (8) occurs early (*E*) or when peak arterial pressure occurs late (*F*) during the muscle relaxation phase.

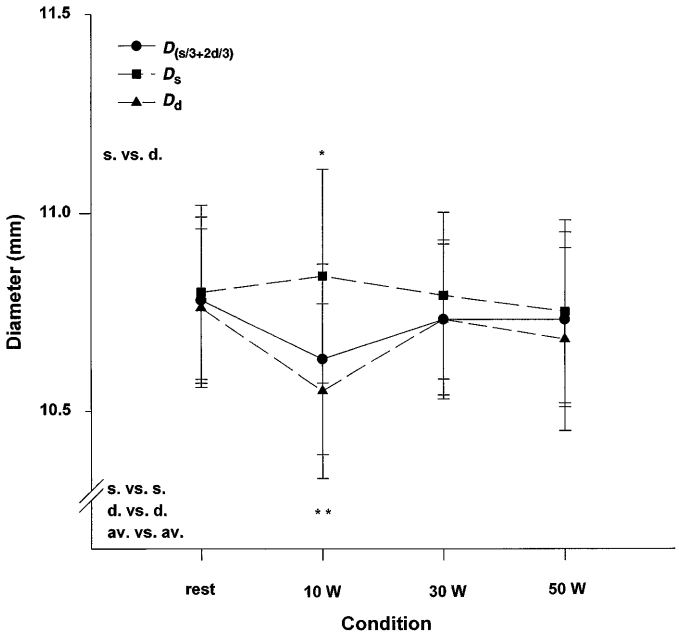

Fig. 2. Mean systolic (s), diastolic (d), and averaged [av.; $D_{(systole/3)+(diastole2/3)}$] femoral arterial diameter D in 6 subjects, measured at rest as well as during exercise at 10, 30, and 50 W. Values are means ± SE. *Significantly different between systole and diastole at 10 W; **significantly different between diastole at 10 W compared with diastole at rest and at 30 W ($P < 0.05$)

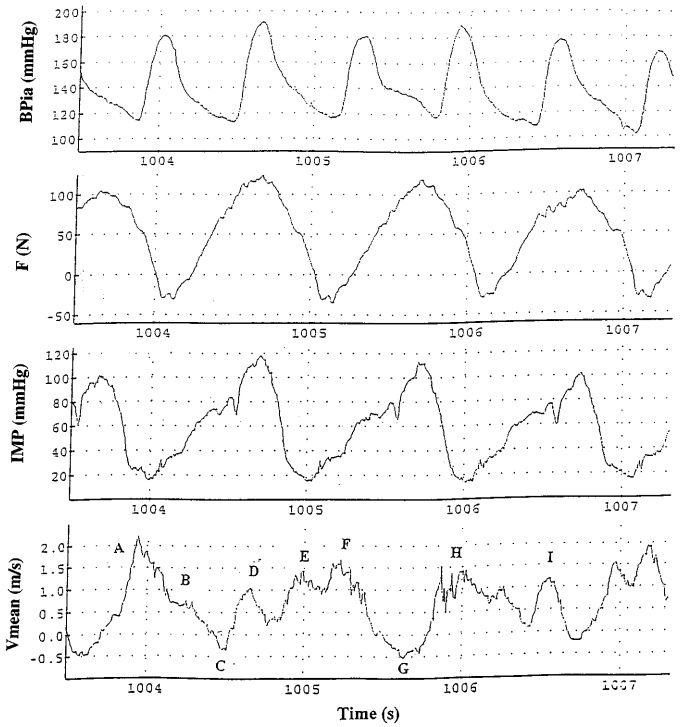

Fig. 3. Intra-arterial blood pressure (BPia), knee extensor kicking force (F), intramuscular pressure (IMP), and v_{mean} vs. time during 1-legged dynamic knee extensor exercise at 50 W. Note the temporal association between intramuscular pressure and blood velocity as well as dissociation between blood pressure and blood velocity (indicated by *A-I*). *H* denotes a period of insonation failure.

At *H* in Fig. 3, a clear insonation failure is detected with loss of signal intensity in the continuously stored velocity tracing. Such a signal loss must be excluded from the blood flow analysis. This type of insonation failure is obscured, however, in the normal inherent variability of the beat-by-beat procedure when the blood velocity is averaged for each ECG automatically.

ECG vs. muscle contraction-averaged Doppler blood flow during exercise. The beat-by-beat mean blood flow increased linearly ($r = 0.998$, $P < 0.001$) during exercise from a mean resting value of 0.28 ± 0.03 l/min with increasing load [$\dot{Q}_{ECG.av.UD} = 0.084 \cdot$load (W) + 1.317 l/min] (Fig. 4). The mean within-subject coefficient of variation of the blood flow was 7.2 ± 1.2%. The mean muscle contraction-related blood flow from the continuous velocity measurements also increased linearly ($r = 0.997$, $P < 0.001$) during exercise from a mean resting value of 0.28 ± 0.03 l/min with increasing load [$\dot{Q}_{cont.UD} = 0.080 \cdot$load (W) + 1.446 l/min] (Fig. 4). The mean within-subject coefficient of variation of the blood flow was 6.2 ± 0.6%. These arterial inflow values were on the same order of magnitude as well as correlated positively ($r = 0.985$, $P < 0.02$) with thermodilution blood flow measurements in the femoral vein [$\dot{Q}_{TD} = 0.065 \cdot$load (W) + 1.941 l/min], as reported previously by Andersen and Saltin (2) under similar experimental conditions (Fig. 4).

Simultaneous Doppler and thermodilution blood flow measurements. The Doppler arterial inflow data, averaged from the continuous velocity tracings, correlated positively ($r = 0.974$, $P < 0.001$) with and were similar (P = NS) to simultaneous thermodilution venous outflow; resting measurements with values of 0.31 ± 0.071 and 0.26 ± 0.024 l/min, respectively; as well as during submaximal exercise up to 70 W with flows of 7.22 and 7.07 l/min, respectively (Fig. 5). The two methods were linearly related ($\dot{Q}_{cont.UD} = \dot{Q}_{TD} \cdot 0.985 + 0.071$ l/min, $r = 0.996$, $P < 0.001$). Six repeated simultaneous measurements in one subject during submaximal exercise at 40 W also showed good agreement between the two methods: the mean values were 5.12 ± 0.06 and 4.96 ± 0.12 l/min, respectively; and coefficients of variation were 6.2 and 6.1%, respectively. The mean arterial diameter of these subjects was 11.3 ± 0.4 mm.

DISCUSSION

The results demonstrate that a noninvasive Doppler can be used to measure arterial inflow of blood to skeletal muscle in humans continuously during intense dynamic exercise. The temporal resolution is sufficient for determination of variations in blood flow between and within the contraction and relaxation phases, respectively. The in vivo measurements were reproducible and had the same order of magnitude, as well as similar accuracy, as the thermodilution venous outflow measurements. Both methods have coefficients of variation of ~6%.

The arterial diameter measurements were reproducible and were not affected by repetitive repositioning of the probe. The individual values for the averaged

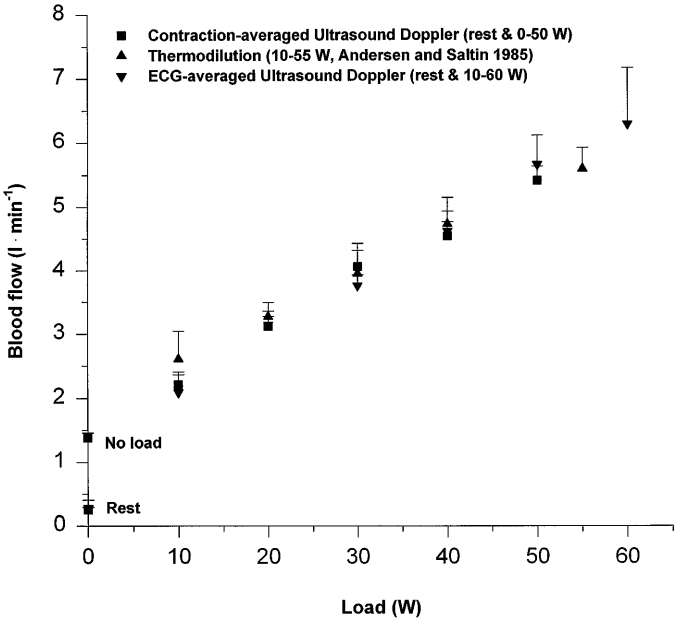

Fig. 4. Blood flow during incremental 1-legged dynamic knee extensor exercise, estimated from v_{mean} and averaged on a beat-by-beat basis in 5 subjects with a mean femoral arterial diameter of 9.9 ± 0.3 mm or continuously measured and analyzed in relation to muscle contraction profile in 10 subjects with a mean femoral arterial diameter of 10.4 ± 0.2 mm. Values are means ± SE. Results are plotted together with Andersen and Saltin's (2) thermodilution blood flow measurements obtained under similar experimental conditions. Different blood flow estimates were similar and correlated positively ($r > 0.985$, $P < 0.02$).

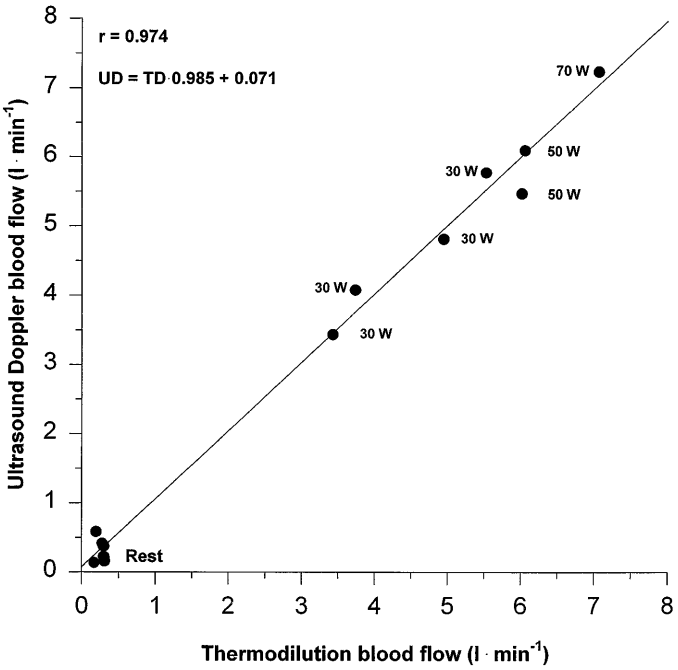

Fig. 5. Blood flow in femoral artery at rest (n = 6) and during incremental 1-legged dynamic knee extensor exercise at 30 W (n = 4), 50 W (n = 2), and 70 W (n = 1), measured simultaneously with ultrasound Doppler (UD) and thermodilution (TD). Individual measurements of the 2 methods were similar and correlated positively (r = 0.974, $P < 0.001$).

diameters were the same at rest compared with those during exercise. The mean within-subject coefficient of variation for the averaged diameter measurements was ~1.0%. Thus, within the limits of the spatial resolution in the 2D mode of the Doppler, these results indicate that the averaged femoral arterial diameter size is not altered during exercise. Thus blood flow during exercise can be based on resting diameter measurements. This bypasses the potential measurement errors that may be introduced by frequently altering the insonation angle of the probe. It also indicates that it is not necessary to use two different probes simultaneously to obtain independent measurements of diameter and velocity. This latter procedure is not the best option because it does not allow for measurements of the blood velocity and diameter at the exact same position and because the sound waves of the two probes may interfere with each other. The femoral artery is, indeed, very suitable for blood flow measurement because it is easily accessible, because its relatively large diameter reduces errors in the flow estimates introduced by small errors in the diameter measurements, and because the site of measurement located outside the muscle is not compressed by the muscle contractions.

The arterial inflow to contracting muscle during dynamic exercise appears to be markedly affected by the transient variations in intramuscular pressure. Therefore, accurate quantification of transitional changes in blood velocity and flow during dynamic exercise requires continuous measurement of the blood velocity in relation to the muscle contraction forces or intramuscular pressure, rather than that averaged for each ECG. The results show a close relationship between the muscle contraction-relaxation phases and the variation in blood velocity, with mechanical hindrance to blood flow and a high intramuscular pressure during the contraction phase and with an unimpeded blood flow and low intramuscular pressure during the relaxation phase (Fig. 3).

However, for determination of steady-state blood flow at a certain exercise load rather than variations and absolute values during each contraction-relaxation cycle, the mean values over time with the ECG-averaging analysis are satisfactory as long as perfect insonation can be guaranteed. Due to the great variability in the ECG-averaged blood velocity values, which depends on whether the heart rate is in or out of phase with the muscle contractions as well as whether cardiac systole or diastole is initiated in the beginning of the contraction or relaxation phase, respectively (16), any insonation failure (*H* in Fig. 3) may thus be conveyed and obscured in the normal variability of the procedure (16, 17). Thus the most precise measurements are obtained by sampling the blood velocity continuously, thereby allowing for a direct visual quality control of the signal intensity of the original tracings after the experiments. Any loss in signal intensity of the blood velocity due to poor vessel insonation (*H* in Fig. 3) will then be evident on the tracings and can thus be edited in the blood flow anaysis. Moreover, the temporary fluctuations in blood flow during steady-state exercise can be minimized by analyzing tracings over long durations (10–60 s). Nonetheless, to obtain the most accurate blood flow, the mean blood velocity should be measured continuously during simultaneous vessel visualization and audiovisual blood velocity feedback. This procedure ensures a continuous check that the sample volume is positioned in the center of the vessel, that it is covering the spatial width of the arterial diameter and the velocity distribution, and that it is allowing for continuous control and correction of the angle of insonation.

In conclusion, results from this study demonstrate that an ultrasound Doppler integrated with a PC can be used *1*) to accurately measure blood flow during intense steady-state dynamic knee extensor exercise and *2*) to measure transient changes in blood flow with high temporal resolution to define the temporal course and magnitude of changes in blood flow at onset of exercise of different intensities.

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