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Acceleration of Blood Flow Velocity in the Carotid Artery and Myocardial Contractility in the Newborn Lamb

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ABSTRACT. We investigated the influence of quantitative changes in myocardial contractile state, reflected by changes in the end-systolic pressure-volume relationship (its slope and volume intercept) and by changes in the slope of the relationship between change in pressure per unit time and end-diastolic volume induced by β-adrenergic stimulation or inhibition, on the Doppler derived blood flow velocity wave form of the carotid artery, using a newborn lamb model. Acceleration time of the velocity wave form was investigated during control state I, during 4 and 8 μg/kg/min dobutamine infusion, during control state II, and during 0.5 mg/kg propranolol infusion, respectively. Using multiple linear regression analysis with dummy variables, confounding effects such as interanimal variability were removed. Acceleration time showed a strong relationship to both the slope and the volume intercept of the end-systolic pressure-volume relationship and to the change in pressure per unit time-end-diastolic volume relationship. The relations appeared to be independent of aortic pressure and relative resistance in the vascular bed of the carotid artery. These results indicate that acceleration of cerebral blood velocity may prove to be useful in assessing changes in myocardial contractile state of the newborn. (*Pediatr Res* 30: 375–380, 1991)

Abbreviations

acc-time, acceleration time
ESPVR, end-systolic pressure-volume relationship
Ees, slope of ESPVR
IVC, inferior vena cava
LV, left ventricle
MABP, mean aortic blood pressure
Rcar, relative resistance in the vascular bed of the carotid artery
dP/dt_{max}-EDV, change in pressure per unit time-end-diastolic volume relationship
V_{14}, volume intercept of ESPVR

LV myocardial dysfunction with reduced cardiac output and hypotension, which often occurs after birth asphyxia or during severe hyaline membrane disease, entails the risk for hypoxic-ischemic brain damage and/or periventricular hemorrhages (1, 2). Information about neonatal LV function could therefore be critical with respect to treatment strategies. In human adults and animal models, peak linear acceleration (peak slope of upstroke in the velocity wave form), the mean acceleration slope (ratio between peak velocity minus diastolic velocity and acc-time), and acc-time (time from onset of ejection to peak velocity) of velocity wave forms of peripheral arteries have been related to qualitative changes in LV contractility (3–6). No data are available yet for the relation between neonatal arterial blood flow velocity acceleration and a quantitative measure of myocardial contractility.

We therefore designed a study to investigate the relationship between acceleration of the velocity wave form of a peripheral artery and quantified myocardial contractile state in the newborn lamb. Serial transfontanellar determination of the velocity wave form of cerebral arteries, *e.g.* the carotid arteries, is feasible, even in the most unstable preterm baby, with minimal handling and without disturbing the infant (7–8). For this reason, we used the velocity wave form of the lamb's carotid artery in our study. Myocardial contractility was expressed by the slope and volume intercept of the ESPVR (9) using the conductance catheter (10–12) and was changed by β-adrenergic stimulation (dobutamine) and by β-adrenergic inhibition (propranolol). The acc-time of the carotid artery velocity wave form was preferred because it relies on the time component only, contrary to peak linear acceleration and acceleration slope, which are dependent on the angle between Doppler beam and blood stream for reliable measurement.

MATERIALS AND METHODS

Animal preparation. Surgical and experimental procedures were reviewed and approved by the committee on animal experiments at the University of Leiden and by the scientific board of the Department of Pediatrics.

Six newborn lambs, aged 3–9 d, were studied. After premedication with ketamine hydrochloride (3 mg/kg i.v.), general anesthesia was maintained using continuous infusion of ketamine hydrochloride (8–30 mg/kg/h), adjusted according to heart rate and blood pressure changes in response to external stimuli. After intubation, the lambs were ventilated with oxygen and air, using a pressure-regulated ventilator, adjusted to maintain arterial P_{O_2} and P_{CO_2} in the normal range throughout the study. Upon ventilation, pancuronium (0.2 mg/kg i.v.) was administered for muscle relaxation. An i.v. infusion of 10% dextrose in 0.5 N NaCl solution was continued throughout the study at about 100 mL/kg/24 h. $NaHCO_3$ was supplemented if the arterial pH was lower than 7.26.

Assessment of myocardial contractility. LV contractility was quantified by the ESPVR, represented by the slope (Ees) of a straight line connecting the upper left-hand corners of the pressure-volume loops when loading conditions are changed by

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inflow occlusion (10, 13, 14) and by the volume intercept of the relation at a fixed pressure of 14 kPa (V_{14}). We used this value to quantify its position along the volume axis as explained elsewhere (15). From each loading intervention, we also calculated the left ventricle dP/dt_{max}-EDV. We used the slope of the dP/dt_{max}-EDV as an additional index of myocardial performance in subsequent data analysis, because of its alleged superior sensitivity to changes in inotropic state (12). Figure 1 shows LV-pressure-volume loops induced by IVC occlusion. Both an increase in Ees and a leftward shift of the ESPVR (decrease of V_{14}) have been shown to reflect an increase in LV contractility (13, 16). The method used to measure LV-volume by means of the conductance catheter in dogs and also in newborn lambs have been described earlier (11, 15, 17, 18). Briefly, via percutaneous approaches, 6 or 7F self-sealing sheaths were placed in both right and left femoral arteries and veins. Two 5F atrial septostomy catheters (Fogarty, Gould Statham model SP 5005) were advanced via a femoral artery and vein to the midthoracic aorta and the IVC-right atrial junction, respectively, under fluoroscopic guidance. A 5F Berman angiographic catheter (American Edwards Laboratories, Irvine, CA) was advanced via the other femoral vein to the main pulmonary artery, and an eight-electrode pig-tailed conductance catheter (size 6F, custom made by Webster Labs, Baldwin Park, CA) was advanced via the other femoral artery to the apex of the left ventricle. LV conductance was measured and converted to LV volume using a Sigma-5 signal conditioner-processor (Leycom, Oegstgeest, the Netherlands). For determination of parallel conductance, necessary to obtain absolute volumes, a balloon-flotation catheter (size 5F, Gould Statham model SP 5005) was advanced into the pulmonary artery via the left jugular vein for injection of hypertonic saline (1 mL). Because of its possible dependence on volume, calibration for parallel conductance was repeated after each intervention that changed LV volume (16, 19), such as dobutamine or propanolol-infusion (see below). In addition, blood samples were taken to determine blood conductivity (using the Sigma-5) and repeated at least every half hour or after infusion of fluids that might alter its value.

Via an incision in the neck, a 5F sheath was inserted into the right carotid artery and a 5F micro manometer catheter (Millar Instruments, Houston, TX) was advanced into the LV just below the aortic valve.

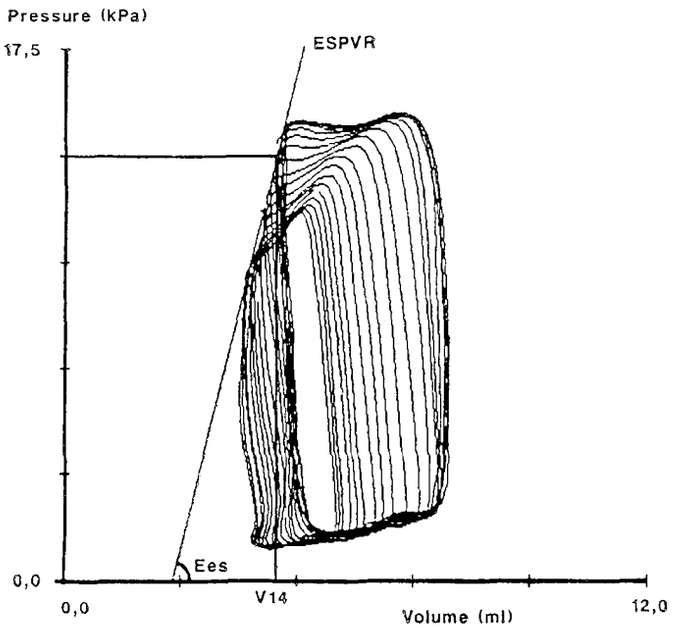

Fig. 1. Left ventricular pressure-volume loops. Variation in pressure and volume were produced by occlusion of the IVC. Ees and V_{14} have been shown to reflect left ventricular contractility.

Blood flow velocity wave form of carotid artery. The left carotid artery was used to obtain the Doppler derived velocity wave form in this artery. An appropriately sized 20-MHz Doppler flow probe was applied to fit around the vessel and connected to a range-gated pulsed Doppler flow meter (Crystal Biotech, Hollliston, MA). The range-gate was adjusted to detect the highest possible velocity for subsequent determination of the optimal blood flow velocity wave form. The following indices were derived from 20–30 consecutive wave forms of the carotid artery: peak velocity and temporal mean velocity in cm/s, and acc-time in ms. Figure 2 shows a schematic velocity wave form of the carotid artery of the newborn lamb in which the investigated Doppler variables are indicated.

Physiologic measurements. Arterial blood gases were measured using a Corning 178 pH/blood gas analyzer (Corning, Halstead, UK). Rcar was assessed by dividing MABP, as a measure of effective pressure difference over this vascular bed, by the temporal mean velocity of the carotid artery. Because we were not concerned about the absolute values of this resistance, nor about absolute flow values, but only about changes in these quantities, we made no attempt to calibrate the velocity signal for volume flow nor to correct the pressure difference for the (low) venous pressure value.

Study protocol. To avoid reflex changes in heart rate induced by IVC occlusion, we performed the studies under parasympathetic blockade (atropine, 0.1 mg/kg i.v. approximately every hour). ESPVR were obtained in five conditions: control I, during two levels of dobutamine infusion (4 and 8 μg/kg/min), control II, and after propranolol administration (0.5 mg/kg). The IVC occlusions were performed by slowly inflating the Fogarty balloon with 1.5 mL of NaCl solution over about 10 s. Doppler tracings of the blood flow velocity wave form of the carotid artery were recorded just before the IVC occlusions during periods of suspended respiration at end-expiration (maximally 20 s), to exclude the influence of respiration and variation in lung volume on LV volume and/or LV parallel conductance. Dobutamine was chosen for its positive inotropic effect on the myocardium (20) and negligible chronotropic or vascular effects in the dosages used (21). After condition 3 (dobutamine 8 μg/kg/min) measurements, dobutamine infusion was discontinued and, after steady state was reached, we repeated blood flow velocity wave forms and ESPVR determinations (control II). Then we administered 0.5 mg/kg propranolol. No efforts were made to keep aortic pressures constant between the respective conditions. However, to investigate further possible dependency of acc-time on arterial pressure, we artificially created high pressure conditions by slow inflation of the aortic balloon and compared the preinflation values of acc-time with the values during maximal inflation. In the same manner, we compared pre-IVC occlusion values of this Doppler variable with those measured during

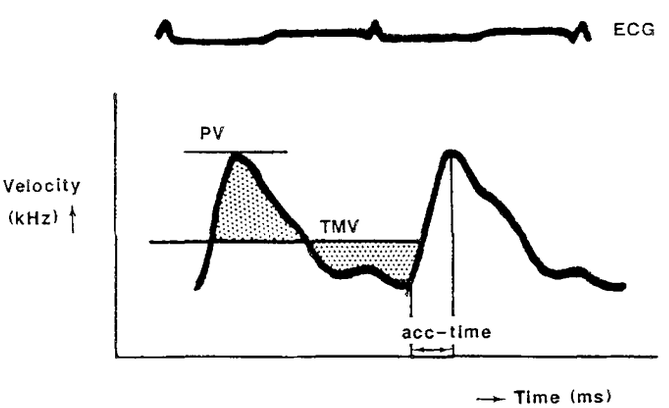

Fig. 2. Schematical representation of a characteristic blood flow velocity wave form from a lamb's carotid artery. *TMV*, temporal mean velocity; *PV*, peak velocity.

maximal IVC occlusion (*i.e.* during low aortic pressure). Arterial O_2 tension and arterial CO_2 tension were kept within physiologic ranges by adjusting the respirator. Pressure-volume loops as well as the aortic pressure and the Doppler velocity signal of the carotid artery were continuously displayed on two memory oscilloscopes (Gould OS 4100; Hainault, UK). The following signals were digitized with 12-bit accuracy on a personal computer at a sample frequency of 200 Hz; blood flow velocity wave form of the carotid artery, ECG, LV pressure, aortic pressure, and LV volume by conductance catheter. Data were stored on a hard disk for subsequent analysis. For comparison between velocity wave form variables on one hand, and Ees, V_{14}, and dP/dt_{max}-EDV on the other hand, only the pressure-volume loops and carotid artery velocity wave forms of good quality were used for analysis. All pressure values and the derived variables are given in units of kPa (13 kPa = 100 mm Hg).

Statistical analysis. Simple linear regression analysis was performed to illustrate the individual relationship between acc-time and myocardial contractility parameters (Ees, V_{14}, and dP/dt_{max}-EDV). The correlation coefficients are shown for descriptive purposes only. To investigate whether changes in myocardial contractility (as reflected by changes in Ees, V_{14}, and dP/dt_{max}-EDV) and changes in MABP and Rcar affected the acc-time of the velocity wave form of the carotid artery, we performed multiple linear regression analysis with acc-time as the dependent variable. Five equations for the dependent variable (acc-time) were solved using sequentially the parameters Ees, V_{14}, dP/dt_{max}-EDV, MABP, and Rcar (independent variables), and sets of dummy variables representing interanimal variability [five variables for the six lambs and four condition dummy variables for the five conditions, using the effects coding technique (22)]. The latter set was included to investigate whether there were additional independent effects of dobutamine and propranolol on the dependent variables (such as vasoactive effects) from their effects on myocardial contractility. A more detailed explanation of the analysis has been given elsewhere (18). The regression equations were:

$$Y = b_{o1} + b_{Ees} \cdot Ees + \sum b_{iv} \cdot IV + \sum b_{dp} \cdot DP \quad (1)$$

$$Y = b_{o2} + b_{V14} + \sum b_{iv} \cdot IV + \sum b_{dp} \cdot DP \quad (2)$$

$$Y = b_{o3} + b_{dP/dt} \cdot dP/dt + \sum b_{iv} IV + \sum b_{dp} \cdot DP \quad (3)$$

$$Y = b_{o4} + b_{MABP} \cdot MABP + \sum b_{iv} \cdot IV + \sum b_{dp} \cdot DP \quad (4)$$

$$Y = b_{o5} + b_{Rcar} \cdot Rcar + \sum b_{iv} \cdot IV + \sum b_{dp} \cdot DP \quad (5)$$

where Y is the dependent variable (acc-time), b_{oi} (the intercepts of the equations) are their overall mean values, IV and DP represent the dummy variables for interanimal variability (IV) and additional independent effects of dobutamine and propranolol (DP), and the "b" associated with each dummy variable represents its coefficient. To determine the statistical significance of any variable or set of variables, an F test was performed by dividing the mean square of that variable or set of variables by the mean square residual.

Differences in MABP, heart rate, Rcar, stroke volume, pH, and blood gases, and in Ees, V_{14}, and dP/dt_{max}-EDV between the various conditions were also investigated by multiple linear regression analysis followed by the Newman-Keuls test if statistically significant differences were obtained. Finally, comparisons between pre-IVC and preaortic occlusion values of acc-time and MABP and those during maximum IVC and aortic occlusion were made using the t test for paired observations. Statistical significance was assumed for $p < 0.05$. Groups of data are summarized as mean ± 1 SD.

RESULTS

Each intervention was performed after steady state had been reached. After the start or change of dobutamine or propranolol infusion, it usually took 10–15 min before this was the case. After discontinuation of dobutamine, it took 15–20 min before a steady state was reached and the interventions for control II state could be performed. The interventions themselves lasted usually 5–10 min. During each condition, pH and blood gases were determined. because of pressure-volume loops of insufficient quality, two measurement values of Ees, V_{14}, and dP/dt_{max}-EDV (control I or control II in two lambs) were not available.

Physiologic measurements. Mean values of MABP, heart rate, Rcar, stroke volume, pH, and blood gas values during the different conditions are shown in Table 1. Blood gases were always within physiologic range. Table 2 summarizes the effects of the different conditions on Ees, V_{14}, and dP/dt_{max}-EDV of the newborn lambs. Each level of dobutamine caused an increase in Ees and dP/dt_{max}-EDV, and leftward shift of the ESPVR (decrease of V_{14}), but only changes in dP/dt_{max}-EDV at a dobutamine infusion rate of 8 μg/kg/min approached statistical significance. Propranolol caused a decrease in Ees and dP/dt_{max}-EDV, and an increase of V_{14} (compared to control II), which was statistically significant for Ees (only *versus* control II) and for dP/dt_{max}-EDV, but not for V_{14}.

Acc-time of carotid artery and cardiac contractility. Figure 3 shows the individual relationships between acc-time and the different parameters for myocardial contractility. In the final data analysis and presentation, the dummy variable representing additional dobutamine/propranolol effects was removed from the equation, because it was found to be insignificant in all situations and, by increasing the number of degrees of freedom, decreased the significance of the effects of any variable, thus impairing the regression equation. Acc-time showed a strong relation with myocardial contractility (as reflected by both Ees and V_{14}) after correction for interanimal variability and became significantly shorter with increasing myocardial contractility (Table 3). As expected, we also found a highly significant positive correlation between acc-time and dP/dt_{max}-EDV used as an index of global myocardial performance (Table 3). There was a substantial amount of interanimal variability (as demonstrated by rather large F_{set} values). It appears that the acc-time of the carotid artery was not influenced by the spontaneous changes in MABP or Rcar (Table 3). Moreover, acc-time measured during maximum IVC (hypotension) or aortic occlusion (hypertension) did not differ from pre-IVC and preaortic occlusion values ($p = 0.82$ and $p = 0.35$, respectively, t test for pair observations).

DISCUSSION

Indices of the Doppler derived velocity wave form of arteries supplying the neonatal brain, especially the temporal mean velocity, have been validated and used extensively as markers of changes of blood supply to this organ (23, 24). The noninvasive character of this bedside method, which uses the anterior fontanel as an acoustic window, enables reliable serial determinations of cerebral artery velocity wave forms, even in the sickest and most unstable preterm baby. On the contrary, determination of velocity wave forms in other peripheral arteries or aorta (3, 4, 6) often requires transthoracic or transabdominal Doppler/ultrasound studies. These procedures are known to provoke apnea and/or hypothermia, both associated with a less favorable outcome, especially in the very preterm infant. These techniques are therefore less suitable for serial investigations.

In the present study, we investigated the relation between quantitative measures of myocardial contractile state and the blood velocity acceleration time (acc-time) derived from the carotid artery of the newborn lamb. Contrary to most clinical Doppler studies in newborn infants, we used the velocity wave form of the extracranially situated part of the carotid artery. The arterial blood supply of the lamb's brain is different from that in the human baby: arterial supply comes via the (common) carotid arteries, which enter the skull as several branches and form a plexus. A short, large caliber artery formed by this plexus even-

Table 1. *MABP, heart rate, stroke volume (SV), Rcar (mean ± 1 SD), arterial pH, and arterial blood gases during different conditions (mean ± 1 SD, range)*

	Control I	Dobutamine (4 μg/kg/min)	Dobutamine (8 μg/kg/min)	Control II	Propranolol (0.5 mg/kg)
MABP (kPa)	11.6 ± 0.6	13.2 ± 3*	11.6 ± 3	13.3 ± 4	9.9 ± 1*†
SV (mL)	4.7 ± 0.5	4.4 ± 0.8	4.3 ± 1.17	4.3 ± 1.2	4.0 ± 2.3
Heart rate	233 ± 8	221 ± 23	247 ± 25	221 ± 28	156 ± 9*†
Rcar (kPa/kHz)	1.74 ± 1.08	2.55 ± 0.45*	2.38 ± 1.0	2.46 ± 1.14	2.43 ± 1.18
pH	7.31 ± 0.09	7.32 ± 0.07	7.33 ± 0.06	7.30 ± 0.11	7.38 ± 0.13
(range)	(7.27–7.45)	(7.28–7.43)	(7.30–7.38)	(7.27–7.38)	(7.31–7.49)
Pa_{O_2} (kPa)‡	16.2 ± 11.2	11.7 ± 7.9	12.0 ± 7.0	14.7 ± 7.6	13.4 ± 9.3
(range)	(8.5–17.1)	(7.9–16.8)	(10.6–15.6)	(10.2–18.2)	(8.9–17.6)
Pa_{CO_2} (kPa)§	5.1 ± 2.1	4.7 ± 0.7	4.9 ± 0.5	5.9 ± 1.6	5.3 ± 0.9
(range)	(3.9–6.7)	(4.0–5.4)	(4.5–6.6)	(4.6–6.5)	(4.2–6.3)

* $p < 0.05$ *vs* control I.
† $p < 0.05$ *vs* control II.
‡ Pa_{O_2}, arterial O_2 tension.
§ Pa_{CO_2}, arterial CO_2 tension.

Table 2. *Ees, V_{14}, and dP/dt_{max}-EDV (mean ± 1 SD) during different conditions*

	Control I	Dobutamine (4 μg/kg/min)	Dobutamine (8 μg/kg/min)	Control II	Propranolol (0.5 mg/kg)
Ees (kPa/mL)	2.73 ± 1.39	3.78 ± 2.72	3.67 ± 1.50	2.81 ± 1.09	2.28 ± 0.68†
V_{14} (mL)	4.05 ± 2.30	2.72 ± 1.36	3.10 ± 0.66	3.42 ± 1.18	4.00 ± 1.62
dP/dt_{max}-EDV (kPa^{-1}/mL)	36.6 ± 29.1	45.7 ± 19.1	99.9 ± 38.7*†	33.4 ± 21.2	15.1 ± 9.8*†

* $p < 0.05$ *vs* control I.
† $p < 0.05$ *vs* control II.

tually supplies all the blood flow to the circle of Willis. An earlier study in newborn lambs reported a close correlation between the extracranially derived carotid artery velocity wave form, using electromagnetic flow probes, and the velocity wave form from an intracranially situated major artery with a hand-held Doppler probe using an artificial fontanel (25). We therefore assume that the obtained velocity wave forms in the present study are indicative for those normally found in the large intracranial arteries of the newborn lamb.

Assessment of the contractile state of the left ventricle of the heart is the subject of many controversies. Several indices of left ventricular contractility have been advocated, but most of them are related to qualitative changes in the contractile state (3–6). The ESPVR has been shown to be a reliable and reproducible quantitative measure for myocardial contractility as investigated in dogs. This holds also for the quantity dP/dt_{max}-EDV. Although some dependence, especially of V_{14}, on afterload conditions has been found (15), such load dependency is certainly less than that which prevails for other indices, *e.g.* ejection fraction (26). The ESPVR is sensitive to changes in contractile state, and its sensitivity for loading conditions is of lesser importance in the present study because the same type of loading intervention was used during the different conditions. Repeated measurements in different control situations have demonstrated its reproducibility in dogs (15). Teitel *et al.* (18) investigated the use of the ESPVR in the heart of the newborn lamb. Their study showed that ESPVR measurements were reliable and reproducible as well. We therefore considered it unnecessary to repeat validation and reproducibility studies in the present study.

Although we used β-adrenergic stimulation and inhibition to alter myocardial contractility, it has been reported that the neonatal heart is stimulated by a high level of circulating catecholamines (27). We indeed found that dobutamine increased myocardial contractility only slightly, which is most probably related to the high resting β-adrenergic state in the newborn lamb (28). We expected a larger effect of inhibition of β-adrenergic stimulation with propanolol. This was indeed the case: dP/dt_{max}-EDV and Ees were decreased significantly compared with control states I and II, and control state II, respectively, indicating a decrease in myocardial contractility. The effect of propanolol on V_{14} was less clear, probably because of a larger interanimal variability of this parameter, reflected by a smaller F value compared with those for Ees and dP/dt_{max}-EDV (Table 3). Despite the fact that we did not always succeed in creating significant increases in myocardial contractility by a dobutamine-induced stimulation of β-adrenergic state (as indicated by the absence of significance in changes of the overall values of Ees, V_{14}, and dP/dt_{max}-EDV), individual differences between these parameters (Fig. 3) were sufficient to study the relationship between acc-time and myocardial contractility. We found a significant relationship between cerebral blood flow velocity acc-time measured in the carotid artery and contractile state of the heart in the newborn lamb. In adult humans, it has already been shown that the acceleration of blood tends to be a constant quantity along the peripheral arterial tree and is related to myocardial performance (3). Although studies that investigated acc-time of blood in the aorta and pulmonary artery of older children and adults indicated that acc-time became shorter as arterial blood pressure increased (29, 30), this is not confirmed by our results for the acc-time in the carotid artery. In the present study, there was an increase in MABP and Rcar at the low dobutamine infusion regime, suggesting a vasoconstriction compared with control state I, but not with control state II. Indeed, α-receptor stimulation at low dobutamine infusion rates have been reported (20). This might challenge the causal relationship between acc-time and myocardial contractility. However, as stated before, neither MABP nor Rcar showed a dependency when each of these parameters was introduced as an independent variable in the regression equations 4 and 5, respectively. Moreover, acc-time appeared to be independent of major intentional changes in aortic pressure brought about by aortic or venous occlusions. In most studies dealing with animals and adult humans, peak acceleration or the acceleration slope of the arterial blood velocity wave form were compared to a qualitative measure of contractility without any attempt to control peripheral resistance. We state, however, that the acc-time of the peripheral artery velocity wave form is preferred because of its independence of the angle

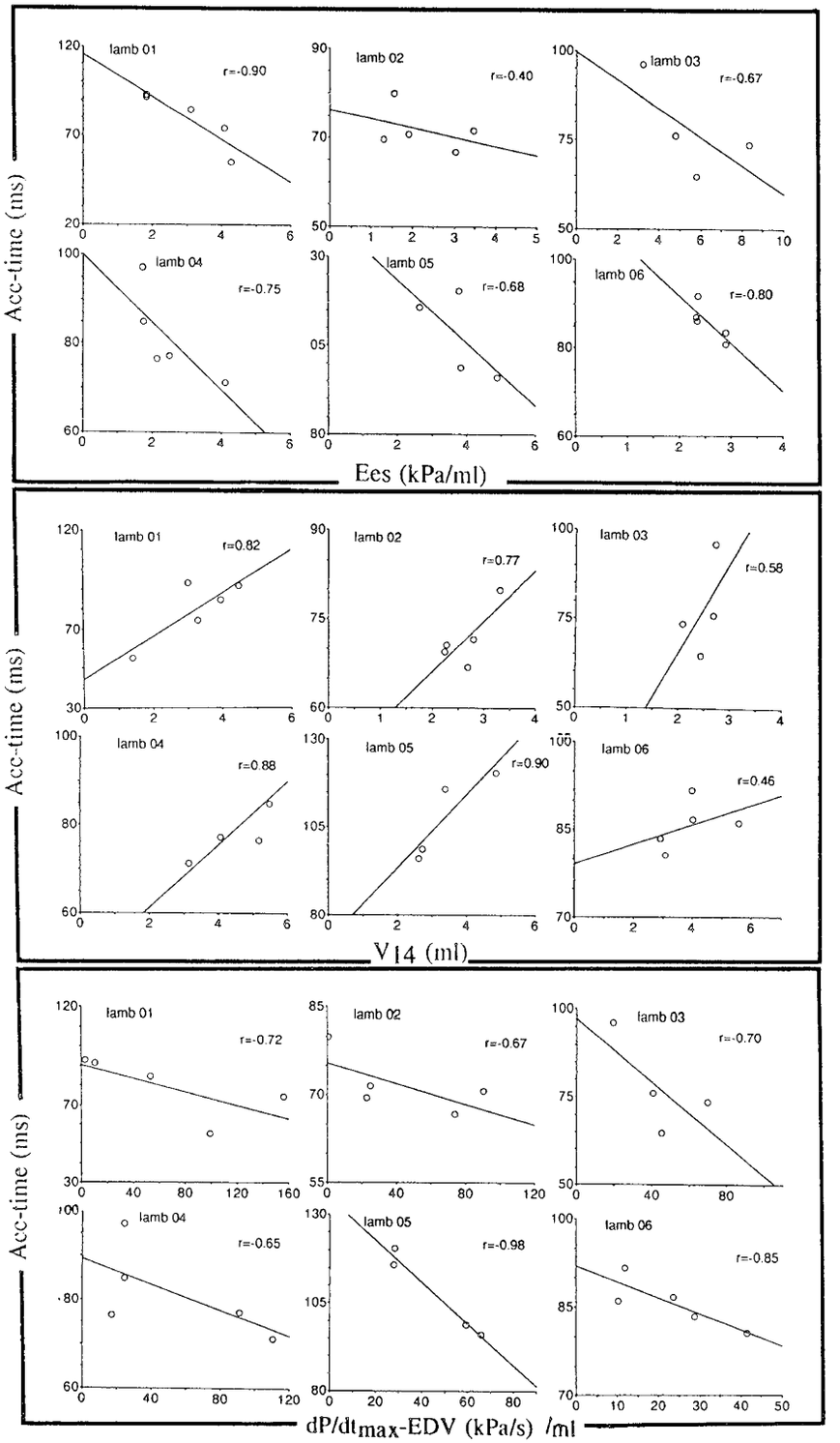

Fig. 3. Individual regression plots between acc-time and Ees, V_{14}, or dP/dt_{max}-EDV.

between the Doppler beam and the bloodstream (5), which enhances the accuracy of the measurement.

As far as we know, the present study is the first to investigate the relationship between neonatal cerebral blood velocity acc-time and quantitative measurements of myocardial contractility. Raju and Kim (30) analyzed acceleration and deceleration characteristics in different cerebral arteries in newborn babies using Doppler ultrasound and found that these Doppler variables could diverge among these vessels. This should be due to different viscoelastic properties of the investigated cerebral vessels. Other investigators have found an association between acc-time of the blood velocities in cerebral arteries and gestational age and birth weight in preterm and full-term neonates (32). The latter results, however, might be based on developmental changes in LV contractility (33).

That ketamine hydrochloride or pancuronium used for anesthesia and muscle relaxation or atropine could have influenced the study results is not very likely, because their cardiovascular effects are only transient (34). Moreover, all lambs had approximately the same dosage schedule, and measurements were only performed after hemodynamic steady state.

Although the acc-time in the carotid artery is a relative measure

Table 3. *Results of multiple linear regression analyses of acc-time in carotid artery (dependent variable) on independent variables Ees, V_{14}, dP/dt_{max}-EDV, MABP, and Rcar**

	Acc-time (dependent variable)				Interanimal variable	
Independent variable	Intercept	Coefficient	*F* value	*p*	F_{set}	*p*
Ees	+99.7	−5.6	11.77	<0.01	9.78	<0.01
V_{14}	+63.7	+5.8	6.28	<0.02	4.67	<0.05
dP/dt_{max}-EDV	+114.1	−0.1	19.71	<0.01	7.66	<0.01
MABP	+107.6	−2.0	3.16	NS	6.24	<0.01
Rcar	+77.7	+2.1	0.04	NS	6.24	<0.01

* In all equations, interanimal variability was represented by an independent dummy variable. All regression equations were statistically significant ($p < 0.005$). F_{set} is the *F* value for the set of interanimal coefficients.

in that it only estimates changes in (individual) myocardial contractility, this finding may be of clinical relevance because it provides the possibility for serial assessment of changes in contractile state of the heart of the newborn baby. Moreover, Doppler-derived acc-time may be an important variable for serial estimation of myocardial contractility in the newborn because of its ease and accuracy of assessment (see above) and because it appears unaffected by arterial blood pressure or by resistance of the vascular bed under investigation. Especially in asphyxiated neonates and those with severe hyaline membrane disease who are suspected to have suboptimal cardiac function on clinical grounds, additional information about LV contractility, which is often impaired by ischemic myocardiopathy (35–37), can be an important tool to assess and monitor the effect of positive inotropic support of the heart.

In conclusion, acc-time of blood velocity in the carotid artery of the newborn lamb is significantly related to changes in quantitative measures of LV contractility. This finding can be of clinical relevance for the (preterm) newborn baby, because serial measurements of the acc-time in the easily accessible intracranial arteries of the neonate can help to assess the effectiveness of instituted therapy to support suboptimal neonatal myocardial contractility. However, it is important to realize that there may be differences in acceleration of blood velocity in the different neonatal intracranially situated arterial vessels. For the application of this method to be effective, serial measurements should be done in the same vessel and at a fixed location.

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