Quantification of Regional Left Ventricular Wall Motion in Newborns by Color Kinesis

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Background: Normal values for regional left ventricular wall motion, although documented in adults, have not been reported in healthy newborns.

Methods: This study prospectively evaluated global and segmental systolic and diastolic cardiac function by color kinesis in clinically asymptomatic healthy newborns.

Results: Eighty-eight asymptomatic infants who were less than 48 hours old were studied. Systolic and diastolic parameters of global and regional left ventricular function are reported as means ± SD, medians, 5th and 95th percentiles to establish the normative

values for newborns. The reported fractional area changes during systole and diastole are similar to the reported normal values for older subjects. Higher body surface area significantly correlated with an increased peak velocity during systole, and fractional area changes during filling of the lateral wall.

Conclusions: Our report of left ventricular regional wall-motion characteristics of healthy newborns, as evaluated by color kinesis, may help in the objective evaluation and management of newborns suspected to have global or segmental ventricular dysfunction.

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 ${f T}$ he importance of left ventricular (LV) diastolic function in various myocardial disease states has received increasing attention in infants and children. Doppler echocardiography has been the most widely used method to study diastolic function in neonates because of its ease of use and noninvasive nature. 1,2 The blood flow velocities measured with pulsed Doppler echocardiography reflect global LV diastolic function. Recent evidence, however, indicates that there may be differences in regional wall motion as seen by myocardial tissue velocity studies in children.³ A magnetic resonance imaging (MRI) study has demonstrated differences in regional diastolic strain and wall motion.⁴ The study of regional wall motion may also benefit infants undergoing arterial switch procedure, anomalous origin of the left coronary artery

from the pulmonary artery, cardiac transplantation, or newborns with prenatal cocaine exposure.⁵

Because noninvasive objective evaluation of the regional wall motion in newborns and infants has been difficult, there is a paucity of data in young children regarding normal LV regional wall-motion characteristics. In adults, color kinesis provides a realtime, color-coded display of LV endocardial motion. This enables an objective method for quantifying LV segmental wall motion.⁶ In a recent multicenter color kinesis study, normal values were published from 187 healthy subjects between the ages of 2 months to 79 years.⁷ Normal color kinesis values have not been established for the healthy newborns. The purpose of this study was to establish normal values for newborns and to study patterns of LV segmental wall motion with the help of color kinesis.

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METHODS

As part of a study on the effects of in utero cocaine exposure on the heart, healthy newborn infants were eligible for the study if they were less than 48 hours old, weighed more than 1500 g, and were between 33 and 42 weeks gestation. Infants were excluded if they had any significant medical problems (for example, receiving any medications including supplemental oxygen, birth asphyxia with 5-minute Apgar < 6); any illicit drug exposure in utero

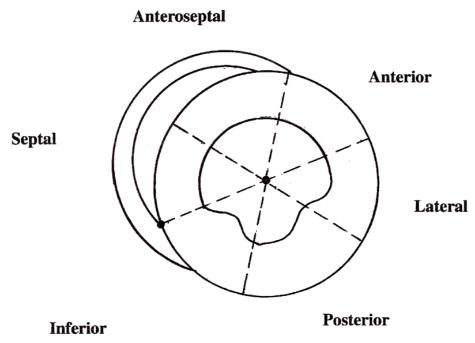


Figure 1 Schematic diagram outlining left ventricular segments in parasternal short axis.

Table 1 Demographics data

	Mean ± SD	Median
Infant characteristics		
Male (%)	52%	
Gestational age (wk)	39.45 ± 1.22	40
Birth weight (g)	3265.63 ± 431.78	3238
Birth length (cm)	49.95 ± 2.28	49.50
Head circumference (cm)	34.18 ± 1.34	34.00
Body surface area (mol/L ²)	0.21 ± 0.02	0.21
APGAR 1 min		9.00
APGAR 5 min		9.00
Age (h)	29.64 ± 17.73	27.83
Maternal characteristics		
Age (y)	21.61 ± 3.59	21.00
White (%)	20%	

N = 88.

Apgar scores are reported in medians only (at 1 min, 5th and 95th percentile scores were 7 and 9; at 5 min, 5th and 95th percentile scores were 9 and 9, respectively).

including alcohol, marijuana, cocaine, and nicotine (assessed by maternal drug interview and urine/meconium toxicology studies); and any significant maternal surgical or medical problems (ie, requiring pharmacologic treatment for hypertension, depression, or asthma). Newborns with associated congenital anomalies, including cardiac defects (except patent ductus arteriosus, patent foramen ovale, or physiologic mitral, tricuspid, or pulmonary regurgitation) were also excluded. A convenience sampling strategy was used to enroll these newborns.

Demographic and medical characteristics at the time of

infant birth were abstracted from the hospital record. These included maternal age, race, infant Apgar scores, birth weight, length, head circumference, and estimated gestational age. The study was approved by the Institutional Review Board for human investigation at MetroHealth Medical Center at Case Western Reserve University. Informed written consent was obtained from the legal guardians/parents of all participants.

Color Kinesis

All infants underwent echocardiography and Doppler studies, including color kinesis with a 5 MHz transducer (SONOS 5500 Ultrasonograph, Hewlett-Packard Company, Andover, Mass) by an experienced pediatric-trained sonographer. The parasternal short-axis view, at the level of papillary muscles, was used for the color kinesis studies. Color kinesis images were analyzed off line by a cardiologist (J.P.S.) trained in color kinesis. The analysis was performed with automated software (Quick Color Kinesis, EchoSoft Co, Wilmington, Del). The LV end-systolic and diastolic cavity was segmented into six 60-degree, wedge-shaped segments (clockwise: anterior, lateral, posterior, inferior, septal, and anteroseptal segments). The centroid and a manually determined anatomic landmark at the junction of the right ventricular posterior wall endocardium and the interventricular septum defined the zero line for the segments (Figure 1). Incremental area change was normalized from the end-diastolic area of the corresponding segment resulting in regional fractional area change (%) during systole and diastole. We analyzed global and regional, systolic and diastolic parameters. The following diastolic parameters

Table 2 Systolic parameters

	N	Mean ± SD	Median	Percentiles	
				5th	95th
Heart rate (bpm)	88	125.3 ± 12.4	125	104.2	146.3
Time to peak ejection rate (ms)	88	75.4 ± 20.6	66	66	99
Systolic duration or ejection time (ms)	88	247.1 ± 29.6	231	231	297
Peak ejection rate (EDA/s)	87	5.9 ± 0.9	5.9	4.4	7.4
Mean time of ejection (ms)	86	107.1 ± 10.4	107	92	125
Mean time to peak ejection rate (ms)	87	76.6 ± 19.6	66	49.5	116
Regional mean time of ejection (ms)					
Anterior	88	106.2 ± 15.9	106.7	79.5	135
Anteroseptal	88	101.8 ± 16.5	102	76	130
• Septal	88	106.7 ± 16.1	107.5	80	135
• Inferior	88	105.1 ± 13.2	104	86	128
• Posterior	88	109.6 ± 16.2	109	86	137
• Lateral	88	111.9 ± 19.1	111	85	145
Regional systolic fractional area change (%)					
Anterior	86	72.6 ± 9.8	72.9	55.5	86.6
Anteroseptal	88	76.3 ± 11.5	77.3	57.8	94.1
• Septal	88	76.6 ± 9.9	78.1	56	91.7
Inferior	87	77.3 ± 9.3	77	62.2	93.2
• Posterior	88	78.7 ± 9.7	79.5	61.9	92.2
• Lateral	87	78.4 ± 8.4	78.2	65.9	91.8
Global fractional area change—systole (% EDA)	87	76.5 ± 8.1	76.5	62	89
Index of asynchrony–systole	88	9.6 ± 3.8	9.5	3.7	16.4

bpm, Beats per minute; EDA, left ventricular end-diastolic area.

were also measured: ratio of peak velocity of early (E wave) and late (A wave) diastolic mitral flow (E/A), end-diastolic area (EDA), global fractional area change during filling (GFAC), and index of asynchrony. The index of asynchrony (IA) for LV filling was calculated as the standard deviation of the mean percentage of filling of all segments at 50% filling time.8 The global fractional area change was calculated by dividing the incremental area change by the end-diastolic area. The segmental fractional area change (%) for each segment was calculated by dividing the incremental area change of that segment by its end-diastolic area. Similar variables were measured for global and regional systolic function. A complete echocardiographic study (including M-mode, 2-dimensional, and Doppler) was performed at the same time with careful attention to the gain and filter settings to obtain clear images from endocardial and epicardial surfaces.

Statistical Analysis

All analyses were performed with SAS v8.1 software (SAS Institute, Cary, NC). Data on demographic characteristics are presented as mean ± SD. Linear regression models were used to evaluate body surface area, age in hours, and heart rate in relation to color kinesis measurements in healthy neonates. The results of the regression models are presented as intercept, slope of the regression line, and standard error of the slope. Scatter plots with a predicted line and corresponding 5th and 95th percentile regression lines are presented only for color kinesis parameters that were significantly correlated with body surface area at the .05 level.

The significance level was set a priori at .05 (2-tail). P values should be interpreted with some caution, however, as they need to be compared with an adjusted value because of multiple testing among related variables. To adjust the P value, we used the formula $\alpha^* = 1 - (1 - \alpha)^{\wedge}(1/k)$, where $\alpha = .05$ (significance level) and k is the number of tests in a group of related variables. 9,10 For example, there are 6 diastolic regional filling area change variables. Thus, the adjusted significance level is $\alpha^* = .0085$. Therefore, if any individual P value for a diastolic regional filling area change variable is less than or equal to α^* , then evidence exists that the regression parameter (slope) is statistically different from zero. However, we report all variables with a P value $\leq .05$ for completeness.

RESULTS

Eighty-eight asymptomatic infants who were less than 48 hours old were studied. The patient characteristics for these newborns and their maternal characteristics are reported in Table 1. Fifty-two percent of the infants were male and had a mean gestational age of 39.5 weeks. The color kinesis data are reported as mean \pm SD, medians, 5th and 95th percentiles for systolic (Table 2) and diastolic parameters (Table 3). Because of the rapid heart rate and technical difficulties, differentiation between early and late mitral valve filling was not reliable in many newborns; therefore, those

Table 3 Diastolic parameters

	N	Mean ± SD	Median	Percentiles	
				5th	95th
Heart rate (bpm)	88	125.3 ± 12.4	125	104.2	146.3
Peak filling rate (EDA/s)	82	6.8 ± 1.6	6.9	4.3	9
Time to peak filling rate (ms)	82	69.4 ± 36.7	66	33	132
Mean time of filling (ms)	81	108.1 ± 24.5	106	70	150
Mitral valve					
• Time to early peak filling rate (EDA/s)	82	63.9 ± 27.1	66	33	99
Peak velocity during early filling (E)	82	6.4 ± 1.5	6.5	4.1	8.6
• Early filling time (ms)	81	171.5 ± 53.1	165	99	264
• Time to late peak filling rate (EDA/s)	58	200.8 ± 50.3	198	132	297
• Peak velocity during late filling (A)	57	3.0 ± 1.1	2.9	1.5	5.3
• Late filling time (ms)	58	270.2 ± 59.7	264	165	396
• E/A	57	2.4 ± 1.1	2.2	0.9	4.7
Regional mean time of filling (ms)					
• Anterior	82	102.7 ± 21.7	105	69	139
Anteroseptal	82	104.9 ± 29.8	98.5	63	161.5
• Septal	81	106.0 ± 28.3	104	67	164
• Inferior	82	108.6 ± 28.3	106	68	157
• Posterior	82	107.0 ± 28.8	103	68.7	160
• Lateral	82	119.9 ± 33.0	119	70	182
Regional filling area change (%EDA)					
• Anterior	80	65.4 ± 13.1	65.8	45.6	88.9
Anteroseptal	78	73.1 ± 11.6	73	51.9	93.9
• Septal	80	71.9 ± 11.8	73.2	51.1	92.7
• Inferior	80	73.3 ± 11.1	73	53.4	92.6
• Posterior	80	72.0 ± 11.4	72.1	48.8	90.6
• Lateral	80	74.3 ± 11.9	76.2	52.7	92
Global fractional area change—diastole (% EDA)	81	72.0 ± 9.1	72.3	57	87
Index of asynchrony-diastole	82	11.6 ± 4.2	11.4	5.4	19.3

bpm, Beats per minute; EDA, left ventricular end-diastolic area.

Table 4 Regression coefficients for color kinesis data controlling for body surface area

	Intercept	Slope	Correlation (r)	
Index of asynchrony–systole	10.2	-2.8 (23.5)	-0.01	
Index of asynchrony-diastole	14.7	-14.5(26.4)	-0.06	
Global fractional area change during diastole (%)	59.1	60.8 (57.1)	0.12	
Global fractional area change during systole (%)	58.9	83.0 (50.1)	0.18	
Peak velocity during systole*	3.1	12.0 (5.9)	0.21	
E/A	2.7	-1.6(8.1)	0.03	
Regional filling area change				
• Anterior	35.8	139.7 (80.9)	0.19	
• Anteroseptal	56.9	76.6 (73.3)	0.12	
• Septal [†]	40.0	150.9 (72.3)	0.23	
• Inferior	54.8	87.3 (68.9)	0.14	
• Posterior	56.3	74.1 (71.4)	0.12	
• Lateral‡	29.4	211.6 (70.9)	0.32	

All data were acquired in parasternal short-axis view.

†P = .04 unadjusted (P > .0085 adjusted for test-wise error).

 $\ddagger P = .004$ unadjusted (P < .0085 adjusted for test-wise error).

cases were eliminated from the analysis of late filling time, rate and peak velocity (Table 3). Hence, our E/A ratio is based on data from 57 patients. The mean values of regional mean time of ejection, systolic fractional area change, and mean time of filling are similar

among all 6 segments with similar variability. The mean regional filling area change for the anterior wall is slightly lower than the rest of the 5 LV segments, which have similar means and standard deviations. The lateral wall has the highest mean of regional mean

^{*}P = .04

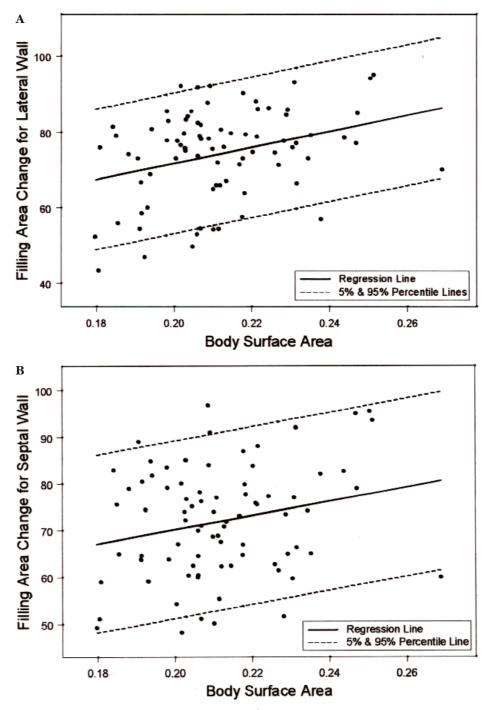


Figure 2 A, Regression plots of body surface area (m^2) and filling area changes for lateral wall (P = .004) of left ventricle. **B,** Regression plots of body surface area and filling area changes for septal wall (P = .04) of left ventricle.

filling time and filling area change; such a change is not apparent during systole (Tables 3 and 4).

Among the various color kinesis parameters measured, lateral (r = 0.32: unadjusted for possible testwise error P = .004; adjusted P < .0085) and septal wall (r = 0.23: unadjusted for possible test-wise error

P=.04; adjusted P>.0085) filling area change increases with increasing body surface area (Table 4). An increase of $0.01~\text{m}^2$ in body surface area increases the lateral and septal wall filling area change by 2.12% (SE = 0.71) and 1.51% (SE = 0.72), respectively (Figure 2, A and B). A similar relationship was noted

for peak velocity during systole and body surface area (P = .04) (Table 4). The body surface area does not significantly influence other systolic and diastolic parameters such as global fractional area changes and IA. In addition, regional and global area changes for systole and diastole were unrelated to heart rate.

DISCUSSION

With the help of color kinesis, we have established normal regional systolic and diastolic parameters that will permit an objective evaluation of regional wall-motion abnormalities in newborns. We have also observed that higher body surface area significantly increases lateral and septal wall fractional area changes during filling in healthy newborns during the first 48 hours of postnatal period.

In adults, the role of color kinesis in the study of qualitative and quantitative evaluation of global and regional wall motion has been well documented. 11 It permits fast, objective, and automated evaluation of regional wall motion with high sensitivity. Wall-motion abnormalities detected by color kinesis have been confirmed in subjects with dobutamine-induced regional wall-motion abnormalities. 12 Color kinesis also provides an objective quantitative assessment of decreased global LV function. 13 Quantitative analysis of color kinesis images was also used to identify diastolic dysfunction in 25 patients with cardiac hypertrophy whose systolic function was preserved. In addition to decreased filling seen during the first half of diastole, these subjects had increased IA with wide intersegmental variability in the regional LV filling times.8

It is of interest to note that means and SD of regional systolic fractional area changes noted in our newborns are similar to the normal data reported in 187 subjects aged 2 months to 79 years by Mor-Avi et al.⁷ Except for the slightly lower means for the anterior wall, diastolic filling fractions were also similar, indicating that these parameters are independent of the heart rate and age. These finding are similar to other color kinesis studies reported in adults.8,11-13 The lower regional mean time of ejection and filling observed in the current study are probably due to the higher heart rate in newborns. In contrast to adults, the healthy newborn LV myocardium has immature calcium transport and is subject to wide variations in right ventricular hemodynamics. This is reflected in an elevated IA compared with the data reported in older children and healthy adults.7

Our reported normal values of newborns would

be helpful in obtaining objective information about regional wall-motion abnormalities in several clinical conditions. Baseline regional wall-motion abnormalities were noted in 80% of patients during the first year of cardiac transplantation. If Infants who have undergone arterial switch procedure may have transmural perfusion defects that may lead to segmental abnormalities. Although global myocardial function of newborns has been studied in clinical conditions such as infants of diabetic mothers (including gestational diabetes), and neonatal asphyxia, it is unknown whether these conditions have selective segmental involvement or affinity for certain segments of the left ventricle.

Our finding of increased septal fractional area change during filling may be related to altered right ventricular pressure because of a drop in pulmonary vascular resistance during the postnatal period. Earlier experimental studies indicate that diastolic properties of the left ventricle can be modified by changes in right ventricular pressure and compliance even without a change in right ventricular volume. 16 Furthermore, diastolic ventricular interaction has been associated with septal shift and deformation.¹⁷ At birth, normal newborns have pulmonary hypertension that is known to cause flattening of the interventricular septum. 18 A rapid drop in the pulmonary vascular resistance and pulmonary artery pressure during the postnatal period has been well documented in humans and in various animal studies. The pulmonary arterial pressure remains elevated if the ductus arteriosus is still widely patent (PDA).¹⁹ A drop in pulmonary artery pressure would permit increased septal motion. It is likely that this change is accentuated in larger newborns (with higher body surface area) by earlier closure of the PDA. It is unclear whether increased septal fractional area changes during filling are due to changes in the right ventricular pressures or LV diastolic compliance with increasing body surface area.

The lateral wall of the left ventricle appears to be most affected by strain. The possible mechanism may be that lateral wall is farthest away from the right ventricle, and therefore is less restricted and less influenced by the right ventricular myocardium and its mechanics. A recent study of the regional differences in ventricular shape and load in patients with hypertrophic cardiomyopathy and right ventricular pressure overload, as demonstrated by 3-dimensional tagged MRI, demonstrated significantly higher lateral wall motion than other segments when compared with normal hearts. Non-uniformity in temporal and regional distribution of load and inactivation is one of the major factors

influencing LV relaxation.²¹ Because multiple interconnected factors may influence LV myocardium, particularly during the postnatal period, the cause of our finding of increased lateral wall fractional area change during filling remains speculative. It could be the result of postnatal hemodynamic changes and or maturational changes in the myocardium as reflected by the body surface area.

In contrast to adults, in whom delineation of the endocardium may be difficult, we had optimal delineation of the endocardial surface of the left ventricle in all infants. In our pilot study, the parasternal shortaxis view in infants had more consistent landmarks than the apical 4-chamber view. In addition, the parasternal short-axis view in infants is easier to acquire with higher reproducibility. In adults, there is also greater intrasubject variability in the 4-chamber view in contrast to the short-axis view.²² In addition, MRI studies have shown less rotational error in the parasternal short-axis view than in the 4-chamber view.⁴ Therefore, we elected to study and report the color kinesis data only in the parasternal short-axis view. In older healthy individuals, compared with the other 3 views (parasternal long-axis, apical 4- and 2chamber views), parasternal short-axis view yielded the maximum fractional area changes during systole and diastole. Furthermore, mean times of ejection and filling showed minor differences between the 4 standard views.⁷

It should be noted that fractional area changes do not necessarily reflect volume changes or the cardiac output. These area changes, measured only in the short-axis view, may or may not be reflective of changes in the long-axis view or in other LV dimensions. The possible contribution of LV rotational changes to our measurements of global or regional fractional area changes during the relaxation period cannot be estimated by the current noninvasive methods. Therefore, the above parameters for the evaluation of possible segmental wall-motion abnormalities should be compared with data obtained only in the parasternal short-axis view. We have concerns regarding temporal resolution, which may not be high enough for accurate measurements of the endocardial velocity rates at the high heart rates seen in our subjects. This needs further study before our data of mitral inflow peak velocity rate and velocity rate at E wave can be compared with other clinical

Color kinesis is an evolving technology that offers objective evaluation of wall-motion abnormalities. Similar to other technologies, there is a learning curve, but a major challenge is in obtaining the optimum images in a moving newborn infant. It is rela-

tively easy to perform in parasternal short-axis view; however, before considering its routine use to evaluate the cardiac status of all newborn infants, more studies are needed to define its contributions and limitations in the diagnosis of various cardiovascular abnormalities—specifically conditions that are expected to alter myocardial wall motion.

In summary, color kinesis provides a quantitative method for the analysis of segmental wall-motion abnormalities in newborns. By using color kinesis, we observed that maturational changes, as reflected by increasing body surface area, have a significant effect on septal and lateral wall motion. By establishing normal values, our study will aid in the diagnosis and management of numerous pathologic conditions of the newborn myocardium.

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