**Pediatric Echocardiographic Normal values** 

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# SIEC Firenze 18-20 Febbraio 2016



>An echocardiographic quantitative evaluation of the cardiac and vascular structures is often of critical importance for the diagnosis and management of congenital heart diseases.  $\succ$  In the pediatric age echocardiographic measurements, as well as any other measurements, need to be normalized according to range of normality for a given age and body size.

# How To Normalize

- ➢In the pediatric age data are commonly normalized according to:
- Age
  Weight/height
  BSA

BSA usually adopted for normalization in pediatric echocardiography

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< Previous Article January 2013 Volume	26, Issue 1, Pages 38–40 Next Article >				
The Why and How of Z Score	S				
Steven D. Colan, MD 2 20 Department of Cardiology, Boston Children's Hospital, Bo	oston, Massachusetts				
DOI: http://dx.doi.org/10.1016/j.echo.2012.11.005	🕂 f 💟 🗠 🕂				
Abstract Full Text References					
Editorial	Comment				
The Why and H	ow of Z Scores				
Steven D. Colan, MD	, Boston, Massachusetts				
The use of echocardiographic measurements to detect disease and predict outcomes can be confounded by a number of nondisease factors, including the effect of body size, that contribute to the variance of these measurements. The process of normal growth is associated with a nearly 200-fold increase in normal left ventricular end-diastolic volume (EDV) from premature infants up to large adolescents, making it imperative to account for changes in body size in pediatrics. Although this issue is often ignored in adult echocardiography, the sensitivity and specificity of parameters of left ventricular size are significantly improved when adjustment for body size in adults is performed. <sup>1</sup> The article by Mawad et al. <sup>2</sup> in this issue of JASE addresses an important aspect of this process, although it is likely a topic that is unfamiliar to most echocardiographers, even those in pediatric cardiology who rely heavily on Z scores. The concept of Z scores itself is often unfamiliar to adult echocardiographers.	cardiomyopathy that includes EDV as an end point (see Table 1). The study design involves recruiting 10 age-matched, sex-matched, and BSA-matched pairs of various ages and conducting a placebo- controlled trial lasting 2 years. As shown in the table, we are assuming perfect matching (age and BSA are identical in both groups) and sim- ilar growth in both groups, which is unrealistic, but these are well- recognized sources of variance, and by eliminating them as potential confounders in this example, recognition of other sources of variance is enhanced. The EDVs and EDV Z scores in the two groups are insig- nificantly different at baseline. Paired comparison of change in EDV between the treatment and control groups detects no statistically sig- nificant clinical benefit ( $P = .14$ ), whereas when adjustment for body size is performed by paired comparison of change in EDV Z score at the two time points, the effect is significant ( $P = .04$ ). Why was the analysis based on Z scores more effective in detecting				

# How to express normalized data: Z scores

Normalized data may be expressed in different ways, including the percentage of the mean normal value, percentile charts, and Z scores.
 The Z score of a measurement is the number of standard deviations of that value from the mean value. If a measurement is equal to the population mean, the

Z score is 0; a Z score of +2 or 2 corresponds to the 95th percentile (i.e., 2 standard deviations above or below the mean)

# Nomograms and Z scores

Thus to normalize in pediatric
 echocardiography we use nomograms
 Normalized data are expressed as z score
 i.e. a z score > 2 indicate dilatation while a z score <2 indicate hypoplasia</li>





# To trust in z scores?

Clinician often rely on z score to take very important clinical decision (i.e. biventricular versus single ventricle repair)
 Thus z scores should be accurate tools

≻BUT.....

## PART 1: dimensional Indexes

➢Basically 2d values

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#### Z-Scores of Cardiac Structures | Detroit Data

Calculate the z-scores of 21 common 2D and M-Mode echo measurements, related to body surface area. Measurement sites include the mitral valve, left ventricle, aortic valve, aortic arch, pulmonary valve, and pulmonary arteries. Data is from 782 patients evaluated at the Children's Hospital of Michigan.

Height (cm):	50	
Weight (kg):	3.5	
BSA formula:	DuBois	▼ 0.21 M <sup>2</sup>

Site	Measured (cm)	Mean	Range Z-Score
RVD:		1.02	(0.68 - 1.51)
IVSd:		0.36	(0.26 - 0.52)
IVSs:		0.48	(0.36 - 0.65)
LVIDd:		1.85	(1.57 - 2.18)
LVIDs:		1.14	(0.93 - 1.41)
LVPWd:		0.29	(0.21 - 0.39)
LVPWs:		0.55	(0.43 - 0.70)
Aortic Annulus:	0.5	0.68	(0.58 - 0.80) -3.08
Sinuses:		0.96	(0.80 - 1.15)
ST Junction:		0.75	(0.60 - 0.94)
Transverse Arch:		0.77	(0.60 - 0.99)
Isthmus:		0.54	(0.41 - 0.71)

#### Home

Aortic Root Z-Scores Ascending Aorta Z-Score: Halifax (Heart, 2006) Paris (AJC, 2010) Cardiac Valve Z-Scores Coronary Artery Z-Scores Boston (Circ., 2007) Washington, D.C. (JASE Montreal (JASE 2010) Fetal Echo Z-Scores Fetal Z-Score App Known EGA Known Femur Length Boston (Circ., 2009) OBSONO.org LVEDV Z-Scores LV Mass Z-Scores M-Mode Z-Scores TAPSE Z-Scores of... Detroit Z-Scores of ... Wessex About Mobile

Height (cm):	5		
Weight (kg):	3.5		
BSA formula:	Boyd	۲	0.12 m <sup>2</sup>

Location	Measured	Mean Range	Z-Score
Tricuspid Valve (cm):			
RV Inflow (cm):			
RV Outflow (cm):			
RV Area (cm <sup>2</sup> ):			
Pulmonary Valve (cm):			
MPA (cm):			
RPA (cm):			
LPA (cm):			
Mitral Valve (A-P) (cm):			
Mitral Valve (Lat) (cm):			
LV Inflow (cm):			
LV Area (cm <sup>2</sup> ):			
Aortic Valve (cm):	0.5	0.53 0.47 - 0.5	9 -0.83
Sinuses (cm):			
ST Junction (cm):			
	Update		

#### manington, 210, (01, 2000) Montreal (JASE 2010)

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## Structures evaluated

*We evaluated 31 published nomograms on 2 cardiac dimensions:* > *LVED and LVES* diameters in M-mode;

>*MV annulus* in apical 4CH-view and PLA view and the *TV annulus* in the apical 4CH-view;

Pulmonary annulus, MPA, and pulmonary arteries in the parasternal SA view;

Aorta: AO annulus, the AO root at the sinuses of Valsalva, the sinotubular junction, and the ascending aorta in the PLA view;
 AO Arch at different levels: the proximal transverse arch (between the IA and LCA), the distal transverse arch (LCA and LSA) and the aortic isthmus (narrowest aortic segment distal to LSA).

# RESULTS

➤The analysis highlights the accuracy of the latest studies but also underscores that some limitations remain.

# ☐2 major Limitations Numerical

- Methodological

# **Methodological Limitations**

➤ the lack of standardization in echo measurements (ASE guidelines only recently available)

 the different types of body size measurements used for normalization (BSA, weight, height)
 the various ways to express normalized data.

# **Numerical limitations**

- The number of healthy subjects was limited
- Poor differentiation among age subgroups
   Neonates poorly investigated
   Data for many cardiac structures were not numerous, especially for the aortic arch and pulmonary branches.

## Echo measurements

 For a long period of time it was not clear which moment of the cardiac cycle to employ for measurements
 ASE guidelines only recently available
 2D valvular and vessels diameters should be measured at the moment of maximum expansion (Ped Guidelines not Adult)

# Confounders

- Potential confounders have scarcely evaluated
- ➤Gender and race differences
- Interobserver and intra-observer variability
- Neonates: factor related to delivery

A huge heterogeneicity in estimation of the CHD

#### Case:

# A male child with a BSA of 0.3 m2 MV annulus of 11 mm

significantly different results can be obtained according to the nomogram used, from lower limits of normality (-1.63) up to a clear hypoplasia of -4.84.

### Nomograms for LV diameters: Example BSA 0.3 m2

	Nr	<b>BSA</b>	<i>R.E.</i>	Age	LVED (mm)	LVES (mm)
Gutgesell HP et al. (11)	145 (80 M, 65 F)			1 day-19 yrs 30 neonates	y=37.75+12.88*ln(BSA) 22.24 (18.91-25.58)	
Henry W.L. et al. (14)	105 (52 M, 53 F)			1 day-23 yrs 13 neonates	y=-6.6+45.2*(BSA) <sup>1/3</sup>	y=-3.8+28.3*(BSA) <sup>1/3</sup>
Akiba T. et al. (28)	110 (67 M, 43 F)			2-15 yrs	y=41.4*BSA <sup>0.49</sup>	y=28.1*BSA <sup>0.49</sup>
Ichida F. Et al. (31)	153 (97 M, 76 F)			1 day-15 yrs		y=3.861+1.365*ln(BSA) 22.2 (18.2-26.2)
Huwez F.U. et al. (45)	127 (77 M, 50 F)			7 month-19.5 yrs	y=1.3988+1.0295*BSA	y=2.2326+1.59*BSA
Kampmann C. et al. (57)	2036			0-18 yrs 450 neonates	y=38.537*BSA <sup>0.4509</sup> 22.9 (18.0-25.8)	y=24.231*BSA <sup>0.4469</sup> 14.8 (10.8-18.8)
Sluysman T. et al. (61)	496			0-20 yrs	y=3.935*BSA <sup>0.444</sup>	
Pettersen M. et al. (68)	782			1 day-18 yrs 82 neonates	Ln(y)=0.105+2.859*BSA- 2.119*BSA <sup>2</sup> +0.552*BSA <sup>3</sup> 22.0 (18.0-26.8)	ln(y)=-0.371+2.833*BSA- 2.081*BSA <sup>2</sup> +0.538*BSA <sup>3</sup> 13.6 (10.5-17.5)

### Nomograms for AV valves: Example BSA 0.3 m2

	Nr	Age	Mitral annulus 4-C (mm)	Mitral annulus PLA (mm)	Tricuspid annulus (mm)
King D.H. et al. (25)	103	1 day-15 yrs	y=32.3+12.47*ln(BSA)	y=23.9+8.56*ln(BSA)	y=32.4+12.29*ln(BSA)
			17.29 (13.71-20.86)	<u>13.59 (10.91-16.28)</u>	17.60 (13.92-21.29)
Hanseus K. et al. (35)	120 (58 M, 62	3 days-15.5 yrs	ln(y)=0.209+0.302*ln (BSA)		ln(y)=-0.209+0.302*ln(BSA)
	F)		<mark>5.6 (3.2-9.9)</mark>		5.6 (3.2-9.9)
Daubeney P.E. et al. (56)	125 (69 M, 56	0-17 yrs	ln(y)=0.9651+0.4658*ln(BS A)	ln(y)=0.9445+0.5022*ln(B SA)	ln(y)=1.084+0.4945*ln(BSA)
	F)		15.0 (12.5-18.0)	14.0 (11.6-17.0)	16.3 (13.9-19.2)
Sluysman T. et al. (61)	496	0-20 yrs	y=0.125+2.002*(BSA)1/2	y=0.117+1.844*(BSA) <sup>1/2</sup>	y=0.155+2.075*(BSA) <sup>1/2</sup>
Zillberman MV et	434	0-18 yrs	ln(y)=0.765+0.425*ln(BSA)		ln(y)=0.817+0.391*ln(BSA)
al. (03) Males			12.9 (9.2-18.1)		14.1 (10.0-19.9)
Zillberman MV et al. (63) Females	314	0-18 yrs	ln(y)=0.733+0.408*ln (BSA)		ln(y)=0.755+0.364*ln(BSA)
			12.7 (8.9-18.3)		13.7 (9.5-19.9)
Pettersen M. et al. (68)	782	1 day-18 yrs	ln(y)=-0.271+2.446*BSA- 1.70*BSA2+0.425*BSA3		Ln(y)=-0.164+2.341*BSA- 1.596*BSA <sup>2</sup> +0.387*BSA <sup>3</sup>
		82 neonates	13.8 (10.2-18.6)		15.0 (10.3-21.9)

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# Conclusions

➤The lack of valid nomograms based on a robust set of healthy children, using standardized approaches and formulas, substantially affects accuracy in estimating the severity of defects, especially in neonates.

Despite advances, the process of normalization of pediatric echocardiographic measures is still incomplete.

Indeed, differences between available nomograms may generate Z scores largely discordant for a given measurement.



#### Echocardiographic Nomograms for Ventricular, Valvular and Arterial Dimensions in Caucasian Children with a Special Focus on Neonates, Infants and Toddlers

Massimiliano Cantinotti, MD M., Marco Scalese, MS, Bruno Murzi, MD, Nadia Assanta, MD, Isabella Spadoni, MD, Pierluigi Festa, MD, Vittoria De Lucia, MD, Maura Crocetti, MD, Marco Marotta, MD, Sabrina Molinaro, PhD, Leo Lopez, MD, Giorgio Iervasi, MD

### **Structures evaluated**

♥22 cadiac structures ♥LVED and LVES diameters in M-mode; ♥ MV annulus in apical 4CH-view and PLA view and the *TV annulus* in the apical 4CH-view; • Pulmonary annulus, MPA, and pulmonary *arteries* in the parasternal SA view; ★ Aorta: AO annulus, the AO root at the sinuses of Valsalva, the sinotubular junction, and the ascending aorta in the PLA view; • AO Arch at different levels Ase Reccomendations (2010)

# Key points in the building of a z score..

To measure in a reproducible, standardized method

- ➤To use a rigorous statistical methods
- ➤The choice of the parameter to be used for normalization
- ≻Sample size
- Attention to confounders

### How to measure?

#### GUIDELINES AND STANDARDS

Recommendations for Quantification Methods During the Performance of a Pediatric Echocardiogram: A Report From the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council

 Leo Lopez, MD, FASE, Chair, Steven D. Colan, MD, FASE, Peter C. Frommelt, MD, FASE, Gregory J. Ensing, MD, FASE, Kathleen Kendall, RDCS, FASE, Adel K. Younoszai, MD, FASE,
 Wyman W. Lai, MD, MPH, FASE, and Tal Geva, MD, FASE, Bronx and New York, New York; Boston, Massachusetts; Milwaukee, Wisconsin; Ann Arbor, Michigan; Houston, Texas; Denver, Colorado

(J Am Soc Echocardiogr 2010;23:465-95.)

Keywords: Pediatric quantification, Measurements, Z scores, Normative database

#### Atrio-ventricular valve measurement



#### Semilunar valve measurement





#### **Aorta and Aortic arch measurement**





# **Statistical Methods**

♥Models using logarithmic, exponential, and square root relationship tested **vIndependent variables** used to normalize: age, weight, height and BSA Seven BSA formulas employed (Haycock, DuBois, Mosteller, Dreyer, Meban, Boyd, Gehan) Heteroscedasticity tested by White test and Breusch-Pagan Test

How to express normalized measurements: BSA issues

BSA, weight, height, age
BSA today accepted

However, some mathematical limitations in the use of BSA still persist, including a dependence of BSA-adjusted measurements on BSA and *high variability* 

of results according to the formula used, particularly for lower height and weight.

# **BSA** formula

#### ≻7 Formulas

The DuBois formula most used, but it has been recently challenged by the Haycock formula.
 The DuBois formula in particular tends to increasingly underestimate for BSAs < 0.7 m2 compared with the Haycock formula.</li>
 A similar problem of underestimation at low BSA values has also been observed for other formulas.

# **Population**

448 Italian healthy subjects
Age range 0 days -36 months
49% Female

BSA	N	%
[0.1-0.15)	5	1,1
[0.15-0.2)	77	17,2
[0.2-0.25)	111	24,8
[0.25-0.3)	63	14,0
[0.3-0.35)	34	7,6
[0.35-0.4)	46	10,3
[0.4-0.45)	38	8,5
[0.45-0.5)	28	6,2
[0.5-0.6)	33	7,4
[0.6-0.7)	13	2,9
Total	448	100,0

Measurements	N Valid
IVC	395
LVED M-mode	411
LVES M-mode	412
IVSd M-mode	405
LVPWd M-mode	406
Mass M-mode	382
Tricuspid annulus	436
Mitral annulus	434
Aortic annulus	431
<u>Sinuses of</u> Valsalva	432
Junction	424
Asc AO	414
Arch IA LCA	427
Arch LCA-LSA	431
Arch After LSA	401
Isthmus	363
Thorac AO	362
Abdominal Ao	396
Pulmonary annulus	347
MPA	428
LPA	432
RPA	434

# <u>Results</u>

- The Haycock formula provided the best results
- DuBois, Mosteller, Deryer and Meban understimated
- Boyd and Gehan overstimated
- The Haicock formula used when presenting data as predicted values (mean ±SD)

#### **Regression equations**

BSA HAYCO CHEATER BSA HAYCOCK. (h[y] = a + b\*h[x]); Z value = (h[Measurement] -(Intercept + B\*h[BSA]))//MSE (E

DOMINALOVO		CALL AND				Color Barrowski Color		
Measurement	Intercept	В	SEE (√MSE)	R <sup>2</sup>	SW	KS	BP	W
IVC	2.100	0.609	0.239	0.495	0.554	0.200	0.614	0.577
LVPWd M-mode	1.832	0.464	0.179	0.511	0.000	0.001	0.645	0.684
Tricuspid annulus	3.135	0.428	0.100	0.729	0.498	0.200	0.665	0.918
Aortic annulus	2.805	0.562	0.085	0.866	0.176	0.200	0.837	0.869
Sinuses of Valsalva	3.059	0.491	0.092	0.807	0.438	0.200	0.424	0.815
Junction	2.806	0.528	0.097	0.811	0.119	0.200	0.704	0.375
Asc AO	2.922	0.466	0.095	0.776	0.451	0.200	0.855	0.608
Arch IALCA	2.719	0.495	0.121	0.703	0.660	0.200	0.776	0.242
Arch LCA-LSA	2.554	0.503	0.122	0.709	0.862	0.200	0.996	0.294
Arch After LSA	2.518	0.544	0.125	0.722	0.691	0.200	0.353	0.026
Isthmus	2.450	0.625	0.146	0.706	0.518	0.200	0.194	0.268
Thorac AO	2.552	0.520	0.127	0.695	0.106	0.200	0.923	0.458
Pulmonary annulus	2.916	0.543	0.108	0.779	0.897	0.200	0.934	0.995
RPA	2.516	0.656	0.150	0.738	0.651	0.200	0.109	0.318
BSAHAYCOCK. BSAH.	AYCOCK. (√y=	• a + b * √x); Z	Z value = (\Measurei	nent –(Inter	cept + B*√B	SA))//MSE		
Measurement	Intercept	В	SEE (√MSE)	R <sup>2</sup>	SW	KS	BP	W
LVED M-mode	2.414	4.040	0.209	0.820	0.270	0.200	0.571	0.704

BSAHAYCOCK. (y	= a BSA HAYCOCK	. (y = a + b *x); /	Z value = (Measure	ement –(Intercej	ot + B*BSA))/	MSE		
LPA	0.844	2.716	0.190	0.702	0.754	0.200	0.364	0.324
MPA	1.632	2.947	0.186	0.734	0.024	0.200	0.997	0.428
<u>Mitral annulus</u>	1.948	3.088	0.164	0.800	0.798	0.200	0.774	0.075
Mass M-mode	-1.316	0.918	0.412	0.863	0.106	0.007	0.186	0.782
<u>IVSd</u> M-mode	1.115	1.669	0.188	0.492	0.066	0.200	0.807	0.764

V		Constant of the second second second second		and the second second second second				
Measurement	Intercept	В	SEE (√MSE)	$\mathbb{R}^2$	SW	KS	BP	W
LVES M-mode	7.483	18.321	1.785	0.638	0.091	0.140	0.132	0.099
Abdominal Ao	3.471	7.857	0.755	0.624	0.178	0.200	0.512	0.540
	UTO.	0.15	0.20	0.20	0.30	0.35	0.40	0.20
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	1.25	1.59	190	2.18	2.43	2.67	2.90	3.32
IVC	2.01	2.57	3.06	351	3.92	4.31	467	5.35
	3.24	4.15	494	5.66	6.33	695	7.54	8.64
	3.82	4.80	5.64	6.40	7.09	7.73	8.33	9.44
Aortic annulus	4.53	5.69	6.69	7.58	8.40	9.16	9.88	11.19
	5.37	6.75	793	899	9.96	10.86	11.71	13.27
	5.72	6.98	8.04	897	9.81	10.59	11.30	12.61
Sinuses of Valsalva	6.88	8.39	9.67	10.79	11.80	12.72	13.59	15.16
	8.27	10.09	11.62	1297	14.18	15.30	16.33	18.22
	4.04	5.00	5.83	655	7.22	7.83	8.40	9.45
Junction	4.90	6.08	7.07	7.96	8.76	9.50	10.20	11.47
	5.96	7.38	8.59	9.66	10.64	11.54	12.38	13.93
	5.25	6.35	7.26	8.05	8.77	9.42	10.02	11.12
Asc AO	6.35	7.67	8.78	9.74	10.60	11.39	12.12	13.45
	7.68	9.28	10.61	11.78	12.82	13.77	14.66	16.26
	3.81	4.65	537	599	6.56	7.08	7.56	8.45
Arch IA LCA	4.85	5.93	6.84	7.64	8.36	9.02	9.64	10.76
	6.18	7.55	8.71	9.73	10.64	11.49	12.27	13.71
	3.16	3.88	4,48	5.02	<i>5.5</i> 0	594	6.35	7.11
Arch LCA-LSA	4.04	4.95	5.72	6.40	7.02	7.58	8.11	9.07
	5.15	6.32	730	8.17	8.96	9,68	10.35	11.58
	2,76	3,44	4,02	4,54	5,02	5,46	5,87	6,63
Arch After LSA	3,54	4,42	5,17	5,83	6,44	7,01	7,53	8,51
	4,55	5,67	6,64	7,49	8,27	9,00	9,67	10,92
	2.05	2.64	3.16	3.64	4.08	4.49	4.88	5.61
Isthmus	2.75	3.54	4.24	4.87	5.46	6.01	6.54	7.51
	3.68	4.74	5.68	6.52	7.31	8.05	8.75	10.06
	3,01	3,71	4,31	4,84	5,32	5,77	6,18	6,94
Thorac AO	3,88	4,79	5,56	6,24	6,86	7,43	7,97	8,95
	5,00	6,17	7,16	8,05	8,85	9,58	10,27	11,54
	2,75	3,14	3,53	3,93	4,32	4,71	5,10	5,89
Abdominal Ao	4,26	4,65	5,04	5,44	5,83	6,22	6,61	7,40
	5,77	6,16	د کړه	6,95	7,34	7,73	8,12	8,91



### Comparison with other nomograms BSA 0.3 m2

	Cantinotti	Pettersen	Zilberman	Gautier
Mitral annulus 4 C	13.24 (10.97-15.74)	13.8(10.2-18.6)	12.9 (9.2-18.1)	
Tricuspid annulus 4 C	13.73(11.24-16.77)	13,8(10.2-18.6)	12.7 (8.9-18.3)	
Aortic annulus	8.40 (7.09-9.96)	8.1 (6.6-9.9)		M 9.2 (7.5-11.2) F 9.2 (7.5-11.3)
Sinuses of Valsalva	11.80 (9.81-14.18)	11.3 (9.0-14.0)		M 12.3 (10.1-15.0) F 13.1 (10.9-15.7)
Junction	8.76 (7.22-10.64)	8.9 (6.8-11.6)		M 10.3(8.4-12.6) F 10.9(9.2-13.1)
Arch IALCA	8.36 (6.56-10.64)	9.2(6.8-12.4)		
Arch L CA-L SA	7.02(5.5-8.96)	6.4 (4.6-8.9)		
Arch After L SA	6.44 (5.02-8.27)	6.8 (5.0-9.4)		
Pulmonary annulus	9.60 (7.74-11.92)	9.2(6.8-12.5)		
MPA	10.54 (8.26-13.09)	9.7 (7.1-13.2)		l l
RPA	5.62 (4.16-7.59)	5.8 (4.2-8.0)		
LPA	5.44 (3.81-7.35)	5.2 (3.8-7.3)		
LVED M-mode	21,41 (17.71-25.45)	22.0(18.0-28.6)		
LVES M-mode	12.98 (9.41-16.55)	13.6(10.5-17.5)		

### **Conclusions**

•We report new, reliable echocardiography Zscores derived from a large population of Caucasian neonates, infants and toddlers calculated using a rigorous statistical design Our nomograms represent a valid diagnostic tool for echo quantification in this age group Further studies are required to evaluate other parameters as well as the effects of race and ethnicity on reference values.

# 2D Nomograms

Pettersen 0-18 yrs and Cantinotti 0-3 yrs acceptable

Not all 2D measures covered, in partciular chamber area and diameters lacking (only M-mode)



### Echocardiographic Nomograms for Chamber Diameters and Areas in Caucasian Children

Massimiliano Cantinotti, MD Marco Scalese, MS, Bruno Murzi, MD, Nadia Assanta, MD, Isabella Spadoni, MD, Vittoria De Lucia, MD, Maura Crocetti, MD, Alberto Cresti, MD, Milena Gallotta, MD, Marco Marotta, MD, Karin Tyack, PhD, Sabrina Molinaro, PhD, Giorgio Iervasi, MD Echocardiographic nomograms for chamber diameters and areas in Caucasian children.

>A total of **1,091 Caucasian Italian healthy children** (age range, 0 days to 17 years; 44.8% female) with body surface areas (BSAs) ranging from 0.12 to 1.8 m(2) were prospectively enrolled.

Echocardiographic reference values are presented for chamber area and diameters, derived from a large population of healthy children.

>These data partly cover a gap in actual pediatric echocardiographic nomograms.

 $\succ$ Further studies are required to reinforce these data, as well as to evaluate other parameters and ethnicities.

### New parameterz.com



# Z-Scores and Reference Values for Pediatric Echocardiography.

#### Sites

View z-scores calculated by multiple references for common collections, like the aortic root and coronary arteries.

View the sites  $\rightarrow$ 

#### Refs

Calculate z-scores of cardiac structures using a large collection of references, from Bhatla to Zilberman.

View the refs  $\rightarrow$ 

#### Boston

Wait. What? Yep, the famous and celebrated Boston z-scores just dropped on the web.

Boom.  $\rightarrow$ 



C 
www.parameterz.com/sites/aortic-arch

7

#### 8

### **Aortic Arch**

Calculate and compare z-scores of the aortic arch, including the aortic isthmus. Data from multiple references including recent data particularly suited for infants with arch hypoplasia or coarctation. References included conform to ASE Guideline methodology: measurements are made in systole, from inside edge to inside edge. (See the methods page for further details.)

SITES

REFERENCES

**NEWS** 

>	Aortic Arch
	Aortic Root
	Coronary Arteries
	M-Mode
	Pulmonary Arteries
	Valves

Patient Demographics		
leight (cm):		
Veight (kg):		
3SA (N/A): N/A		
Gender: Female •		
Age: ye	ars •	
leasurements		
Site	Z-Score	Range
Site	Z-Score	Range



Bhatla et al.

Campens et al.

Cantinotti et al.

Cantinotti et al.

Dallaire and Dahdah

Colan et al.

### Cantinotti et al., JASE 2014

BSA-adjusted Z scores derived from a large population of Caucasian neonates, infants, and toddlers calculated using "*a rigorous statistical design*": particular attention was paid to matters of skew/distribution and heteroscedasticity.

and the second second second second second			Dunin e unu Duniu
Patient Demographics			Dallaire et al.
Height (cm):			
Weight (kg):			Daubeney et al.
BSA ("Haycock"):			Eidem et al.
Measurements			Foster et al.
Site	Z-Score	Range	Gautier et al.
Interventricular Sentum			Gentles et al.
Diastole (mm):			Jain et al.
			Kampmann et al

### **PART 2: Functional Indexes**

Diastolic values
Deformation indexes
Others

### Nomograms for Blood Flow and Tissue Doppler Velocities to Evaluate Diastolic Function in Children: A Critical Review

Massimiliano Cantinotti, MD, and Leo Lopez, MD, Massa and Pisa, Italy; Bronx, New York

Interest in diastolic function in children has increased recently. However, the strengths and limitations of published pediatric nomograms for echocardiographic diastolic parameters have not been critically evaluated, especially in the neonatal population. A literature search was performed within the National Library of Medicine using the keywords normal/reference values, power Doppler/tissue Doppler velocities, and children/neonates. The search was further refined by adding the keywords diastolic function, myocardial, mitral/tricuspid inflow, pulmonary vein, and Tei index. Thirty-three published studies evaluating diastolic function in normal children were included in this review. In many studies, sample sizes were limited, particularly in terms of neonates. There was heterogeneity in the methodologies to perform and normalize measurements and to express normalized data (Z scores, percentiles, and mean values). Although most studies adjusted measurements for age, classification by specific age subgroups varied, and few addressed the relationships of measurements to body size and heart rate (especially with higher neonatal heart rates). Although reference values were reproducible in older children, they varied significantly in neonates and infants. Pediatric diastolic nomograms are limited by small sample sizes and inconsistent methodologies for the performance and normalization of measurements, with few data on neonates. Some studies do reveal reproducible patterns in diastolic function in older children. A comprehensive pediatric nomogram of diastolic function involving a large population of normal infants and older children and using standardized methodology is warranted and would have tremendous impact in the care of children with acquired and congenital heart disease. (J Am Soc Echocardiogr 2013:26:126-41.)

Keywords: Echocardiography, Children, Neonates, Diastolic function

### **Materials and Methods**

≻Mitral and Tricuspid Inflow: E wave, the E/A ratio, DT,

IVRT

≻Mitral Velocities e' and a';

➤Tei index for LV and RV

➤33 studies evaluating diastolic function in children were

included in this review.

# **Methodological Limitations**

There was significant heterogeneity in the methodologies to perform and

normalize measurements and to express normalized data (Z-scores,

percentiles, and mean values).

>Although *most studies adjusted measurements for age,* the classification systems dividing age into specific subgroups varied, and few addressed the relationships of measurements to body size and to **heart rate** (especially with the higher heart rates in neonates).

## RESULTS

➢As a results various nomograms showed quite different results

For children >2-3 years references intervals were quite reproducible and not dissimilar from the ones published for young adults

In neonates instead data were limited, often discordant and strongly influenced by various factors including age, prematurity and HR

### Normal neonatal reference values for MV inflow velocities and other diastolic parameters

Study	Subject *	N	MIE	Rady Ste	HR (hn m)*	F (em/e)*	à (comie)*	DT (me)*	FIA+	IVRT
oluuy	awjers	1	WEL	Dody and	(op m)	L (CHUS)	A (CHUS)	(IIIS)	D'A	(iiis)
Schmitz, 2004	lõtal	104								
	$\underline{\text{Preterm}} (0.5 - 1 \text{ kg}): 13 \pm 10 \underline{\text{ da}}$	34		093 ±0.3kg	151±15	$32.7 \pm 123$	$36.9 \pm 10$	)	1 1	53 ± 5
	<u>Pretern (1 - 1.5 kg) 12 ± 9 da</u>	29		134 ±0.4 kg	156±13	38.5 ± 11.4	$43.6 \pm 11.9$	]		54 ± 5
	Tenn: 15 ± 14 <u>da</u>	74		3.66 ±0.6 kg	134±16	$56.2 \pm 16.4$	50.8 ± 13.9			54 ± 8
	<u>Preterm (0.5 – 1 kg): 132 ± 33 da</u>	22		3.28 ±0.8kg	150±24	82 ± 14.5	66.5 ± 24.5	]		41 ± 4
	Preterm (1 – 1.5 kg): 138 ± 70 <u>da</u>	25		3.86 ± 1.4 kg	143±11	79 ± 10.9	75.1 ± 10.7	Į.		41 ± 5
	Term: 135 ± 36 <u>da</u>	28		6.46 ±1.2kg	140±13	86.2 ± 10.5	70.6 ± 13.1	Į.	e	41 ± 4
Schmitz, 2004	Total	127				The second second		-		
	Wé ek 1 (3 ± 2 <u>da</u> )	53	33/20	3.4±0.4kg 51±2 cm	2	46.1 (34.4,63.8)	42.1 (27.4, 56.7)	88 ± 23	6	59 ± 7
	Week 2 (10 ± 2 <u>da</u> )	45	25/20	3.6±0.5kg 51±2 cm		493 (34.6,67.2)	45.9 (32.5,73)	74 ± 24		55 ± 5
	Week 3 - 4 (21 ± 4 <u>da</u> )	29	19/10	3.7±0.4kg 52±2 cm	2	63.1 (39,85.4)	57.3 (37.8, 78.6)	66 ± 21		54 ± 7
Ekici, 2007	1 - 5 <u>da</u>	50				57.6 ± 10.2 (30 - 83)	52.4 ± 10.7 (33 - 85)			
Jahnson, 1988	<u>Preterm</u> 32 <u>wk</u> : 28 – 35 <u>da</u>	18			2	55 ± 10	55 ± 13	5	$1.01 \pm 0.11$	
	Term: 2 - 5 <u>da</u>	10	1		G	53 ± 19	47 ± 11		1.13 ± 0.30	
Kozak, 2001	<u>Pretern: 1 -4 da</u>	15		2.52 ± 0.27 kg 46.2 ± 1.8 cm		40.1 ± 5.6	43.2 ± 6.0	83 ±1 2	0.93 ± 0.03	
	Preterm: 1 mo		5 - S		3	61.5 ± 5.2	56.9 ± 4.8	73 ± 10	1.08 ± 0.04	
	Tenn: 1 – 5 <u>da</u>	19		3.32 ± 0.44 kg 49.7 ± 2.3 cm		46.9 ± 5.2	44.3 ± 5.7	87 ± 10	1.06 ± 0.05	
	Term: 1 mo					62.8 ± 6.1	56.9 ± 5.4	80 ± 12	1.11 ±0.05	
<u>Ciccone</u> , 2011	<u>Pretern: 3.8 ± 2.1 da</u>	20		2.15 ± 0.50 kg 44.5 ± 2.3 cm		45.3 ±8.4	45.6 ± 7.8		1±0.1	
	Term: 29 ± 0.01 <u>da</u>	53		3.19±0.44 kg		53.4 ±7.8	46.7±79		1.16±0.1	

### Published normal paediatric reference values and regression equations for tissue Doppler diastolic parameters at the septal mitral annulus

Study	Subjects*	N	M/F	Body Size <sup>+</sup>	HR (bpm)*	e' (cm/s)*	a' (cm/s)*	E/e**
<u>Eidem</u> , 2004 (18)	Total	325	177/148			y = 9.629 +0.380*Age y = 20.190 + 0.083*HR	y = 5.049 + 0.020*Age y = 5.108 + 0.011*HR	
	<1 yr (0.40 ±0.30 yr)	63	29/34	6.6 ± 2.7 kg 0.34 ± 0.08 m <sup>2</sup>	124 ± 16	8.1 ± 2.5 (7.5 - 8.7)	6.1 ± 1.5 (5.7 - 6.4)	10.3 ± 2.7 (9.7 - 11.0)
	<mark>1 – 5 yr</mark> (3.05 ±1.51 yr)	68	39/29	$15.1 \pm 5.4 \text{ kg}$ $0.62 \pm 0.14 \text{ m}^2$	105 ± 17	11.8 ± 2.0 (11.3 - 12.3)	6.0 ± 1.3 (5.7 – 6.4)	8.1 ±1.8 (7.7 -8.5)
	<mark>6 - 9 yr</mark> (7.91 ±1.12 yr)	55	27/28	33.8 ± 14.9 kg 1.07 ± 0.27 m <sup>2</sup>	80 ± 11	13.4 ± 1.9 (12.8 - 13.9)	59 ± 1.3 (5.5 – 6.3)	7.2 ±1.6 (6.8 – 7.7)
	10 – 13 yr (11.9 ±1.11 yr)	58	38/20	47.2 ± 16.3 kg 1.37 ± 0.29 m <sup>3</sup>	75±12	14.5 ± 2.6 (13.8 - 15.2)	6.1 ± 2.3 (5.6 - 6.7)	6.6 ±1.4 (6.3 - 7.0)
	14 – 18 yr (16.0 ±1.40 yr)	81	44/37	66.1 ± 15.5 kg 1.73 ± 0.25 m <sup>2</sup>	69±16	14.9 ± 2.4 (14.3 - 15.4)	6.2 ± 1.5 (5.9 - 6.6)	6.4±1.5 (6.1-6.8)
<u>Ekici,</u> 2007 (23)	<mark>5 - 16 yr</mark>	54				17.9 ± 2.8	<mark>9.6 ± 2.5</mark>	4.2 ± 1.1
<u>Kapusta,</u> 2000 (25)	<mark>4 - 17.9 yr</mark>	160	77/83	17.5 – 83.5 kg		14.3 (11.2 – 18.5)	5.8 (4.4 – 7.9)	
<u>Mori,</u> 2000 (30)	2 <u>mo</u> – 19 yr (7.5 ±5.5 yr)	131	69/62			13.5 ± 2.4 (5.9 – 18.0)	6.5 ±1.4 (4.0 – 10.6)	X

# CONCLUSIONS

>Diastolic nomograms for children are limited by small

sample sizes and inconsistent methodologies for

performance and normalization of measurements, and

there are few data on neonates.

However, some studies do reveal some reproducible

patterns in diastolic function in older children.

J Cardiol. 2015 Nov 9. pii: S0914-5087(15)00321-4. doi: 10.1016/j.jjcc.2015.10.004. [Epub ahead of print]

### Nomograms for mitral inflow Doppler and tissue Doppler velocities in Caucasian children.

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#### Author information

#### Abstract

BACKGROUND: Pediatric echocardiographic nomograms for systolic/diastolic functional indices are limited by small sample size and inconsistent methodologies. Our aim was to establish pediatric nomograms for mitral valve (MV) pulsed wave Doppler (PWD) and tissue Doppler imaging (TDI) velocities.

METHODS: We performed PWD/TDI measurements of MV velocities and generated models testing for linear/logarithmic/exponential/square root relationships. Heteroscedasticity was accounted for by White test or Breusch-Pagan test. Age, weight, height, heart rate (HR), and body surface area (BSA) were used as independent variables in different analyses to predict the mean values of each measurement.

**RESULTS:** In all, 904 Caucasian Italian healthy children (age 0 days-17 years; 45.5% females; BSA 0.12-2.12m<sup>2</sup>) were prospectively studied. No individual variable provided equations with an acceptable coefficient of determination (R<sup>2</sup>) and even the inclusion of multiple variables in the model resulted in only a partial amelioration of the R<sup>2</sup>. Higher R<sup>2</sup> were obtained for PWD-E deceleration time (0.53), septal (Se') and lateral (Le') MV-TDI e' velocity (Se': 0.54; Le': 0.55). Variability was higher at lower age and BSA. In older children patterns were more reproducible; however, the exclusion of neonates did not substantially improve the final models. The low R<sup>2</sup> hampered building of z-scores and calculation of estimated percentiles. Thus normative data have been presented as observed percentile according to age for all measurements.

CONCLUSIONS: We report normal ranges for PWD and TDI mitral velocities derived from a large population of Caucasian children. Variability of diastolic patterns especially at lower ages needs to be taken into account.

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### Results

➢In all, 904 Caucasian Italian healthy children (age 0 days-17 years; 45.5% females; BSA 0.12-2.12 m2) were prospectively studied.

➢ No individual variable provided equations with an acceptable coefficient of determination (R2) and even the inclusion of multiple variables in the model resulted in only a partial amelioration of the R2.

➢ Higher R2 were obtained for PWD-E deceleration time (0.53), septal (Se') and lateral (Le') MV-TDI e' velocity (Se':0.54; Le':0.55).

➢ Variability was higher at lower age and BSA. In older children patterns were more reproducible, however the exclusion of neonates did not substantially improve the final models.

The low R2 hampered building of z-scores and calculation of estimated percentiles.

Thus normative data have been presented as observed percentile according to age and BSA for all measurements.

Table . Coefficients for regression equations relating echocardiographicmeasurements and body surface area, heart rate and age. The Standard Errorof the Estimate, the determination coefficient. Normality test: Shapiro-Wilk.Heteroscedasticity test (White test and Breusch-Pagan test).

Measurement	Intercept	B(BS.4)	B(HR)	B(AGE)	$ADJ R^2$	SEE	BP	W	SW
Mitral A	0.604	0.131	0.791	NS	0.376	0.193	0.273	< 0.001	< 0.001
Dec ms	6.264	0.226	-0.319	NS	0.510	0.223	<0.001	< 0.001	<0.001
SM	1.691	0.208	0.129	NS	0.337	0.145	0.952	< 0.001	0.362
A'M	-0.718	0.093	0.609	NS	0.236	0.212	0.323	0.182	0.341
S'1	1.732	0.237	0.137	NS	0.334	0.165	0.063	< 0.001	<0.001
All	-0.336	0.065	0.519	NS	0.184	0.220	0.551	0.291	0.039
E/e'	1.258	-0.140	0.157	NS	0.236	0.222	< 0.001	0.099	<0.001

#### rad(y)=intercept+B1\*ln(BSA)+B2\*rad(HR)+B3\*AGE

Measurement	Intercept	B(BS.4)	B <sub>(HR)</sub>	B(AGE)	SEE	ADJ R <sup>2</sup>	BP	W	SW
Mitral E	10.483	1.658	0.084	-0.010	0.314	0.819	< 0.001	< 0.001	< 0.001
E'M	4.596	0.712	-0.048	-0.003	0.526	0.349	0.008	< 0.001	0.063
E1	4.726	0.717	-0.045	NS	0.552	0.355	0.104	<0.001	0.088

#### $\pm \ln(y) = intercept + B_1 + \ln(BSA) + B_2 + \ln(HR) + B_3 + AGE$

Measurement	Intercept	B(BS.4)	B(HR)	B(AGE)	$ADJ R^2$	SEE	BP	W	SW
Α	0.604	0.131	0.791	NS	0.376	0.193	0.273	< 0.001	< 0.001
EDT	6.146	0.224	-0.292	NS	0.530	0.206	<0.001	< 0.001	< 0.001
Ss'	1.691	0.208	0.129	NS	0.337	0.145	0.952	< 0.001	0.362
Sa'	-0.718	0.093	0.609	NS	0.236	0.212	0.323	0.182	0.341
Ls'	1.732	0.237	0.137	NS	0.334	0.165	0.063	<0.001	<0.001
La'	-0.336	0.065	0.519	NS	0.184	0.220	0.551	0.291	0.039
E/e'	1.258	-0.140	0.157	NS	0.236	0.222	< 0.001	0.099	< 0.001

#### rad(y)=intercept+B1\*ln(BSA)+B2\*rad(HR)+B3\*AGE

Measurement	Intercept	B(BSA)	B <sub>(HR)</sub>	B(AGE)	$ADJ R^2$	SEE	BP	W	SW
E	10.483	1.658	0.084	-0.010	0.314	0.819	< 0.001	<0.001	<0.001
Se'	4.641	0.714	-0.052	-0.003	0.537	0.344	0.049	< 0.001	0.059
Le'	4.726	0.717	-0.045	NS	0.552	0.355	0.104	< 0.001	0.088

Coefficients for regression equations relating echo measurements and BSA, the SSE, the determination coefficient and normality test: Shapiro-Wilk and Lilliefors

Heteroscedasticitv test (White test and BreuschPagan test).



# *Examples of p*redicted values (Mean $\pm 2$ SD) of measured echocardiography variables expressed by BSA (Haycock).

percentiles	0.15-0.20	0.20-0.25	0.25-0.30	0.30-0.35	0.35-0.40	0.40-0.45	0.45-0.50	0.50-0.55	0.55-0.60	percentiles	0.60-0.65	0.65-0.70	0.70-0.75	0.75-0.80	0.80-0.85	0.85-0.90	0.90-0.95	0.95-1.00	1.00-1.05
E										E									
10	42.8	52.6	68.3	76.1	70.9	92.1	80.3	83.6	86.9	10	86.2	85.8	83.4	86.4	84.2	84.6	92.8	84.2	84.0
25	51.1	60.9	82.3	87.7	83.4	100.0	88.3	92.1	94.1	25	94.5	94.6	92.8	94.0	93.4	87.9	95.8	94.8	95.6
50	64.9	75.7	98.7	99.1	95.8	109.0	106.5	105.0	104.0	50	107.5	105.0	101.0	105.0	98.0	103.5	103.0	103.0	105.0
75	72.4	88.0	107.0	109.0	109.0	118.0	122.0	113.0	121.0	75	113.5	116.0	116.0	118.0	107.0	110.0	114.0	107.0	114.0
90	83.9	103.0	118.0	118.5	115.0	132.0	135.0	129.0	128.0	90	120.0	120.0	126.0	123.0	118.0	118.0	121.0	119.0	125.5
Α										Α									
10	45.0	50.7	63.3	67.1	57.0	69.0	45.0	53.7	48.7	10	49.4	53.3	47.0	48.4	47.0	49.5	49.9	45.9	45.9
25	51.3	57.6	74.0	76.0	64.3	73.1	55.6	62.7	56.9	25	54.3	59.4	54.6	54.4	52.1	52.1	53.2	49.5	52.1
50	64.2	72.4	88.2	90.3	77.3	78.2	71.4	70.0	67.1	50	63.2	67.1	62.3	61.1	61.1	57.8	57.3	60.3	57.0
75	80.6	84.7	97.9	97.9	88.5	84.8	88.2	81.6	79.6	75	72.3	73.5	73.5	66.1	69.3	61.1	65.8	66.5	66.5
90	97.9	96.7	105.0	104.5	104.0	91.6	100.0	91.5	80.9	90	80.9	77.9	82.9	77.0	74.2	68.4	78.5	73.4	79.0
EDT										EDT									
10	48.0	48.0	42.0	50.0	74.0	61.0	69.0	79.0	82.0	10	90.0	85.0	92.0	95.0	87.0	90.0	109.0	111.0	100.5
25	53.0	66.0	77.0	79.0	82.0	92.0	79.0	87.0	98.0	25	99.0	98.0	98.0	103.0	103.0	106.0	116.0	116.0	111.0
50	72.0	74.0	90.0	92.0	98.0	106.0	93.5	95.0	108.0	50	108.0	116.0	116.0	114.0	116.0	119.0	120.0	137.0	127.0
75	95.0	87.0	98.0	106.0	106.0	116.0	100.0	108.0	116.0	75	125.5	129.0	128.0	129.0	140.0	137.0	145.0	151.0	151.0
90	132.0	103.0	106.0	111.0	114.0	137.0	114.0	116.0	127.0	90	135.0	137.0	158.0	148.0	156.0	169.0	158.0	165.0	156.5
Ss'										Ss'									
10	5.5	5.8	6.9	7.7	7.6	7.7	7.1	7.3	6.8	10	7.9	7.6	8.3	7.5	8.1	8.0	7.9	7.7	7.9
25	6.1	6.6	7.4	8.2	8.2	8.0	8.3	7.7	8.3	25	8.4	8.4	8.7	8.5	9.0	8.8	8.7	8.5	8.4
50	6.6	7.1	7.8	8.6	8.9	8.9	8.7	8.8	9.3	50	9.3	9.1	9.6	9.2	10.3	9.4	9.2	9.4	9.1
75	8.0	7.7	8.5	9.2	9.7	10.2	9.7	9.6	9.7	75	10.2	9.9	10.1	10.5	11.4	10.1	10.0	10.4	10.1
90	8.9	8.8	9.1	10.4	10.4	12.4	10.1	9.8	10.0	90	10.9	11.0	10.8	12.0	11.8	10.4	10.7	10.9	10.5
Se'										Se'									
10	4.5	5.6	5.6	7.2	8.8	9.6	10.2	11.7	11.1	10	12.6	12.2	12.9	12.7	12.7	12.7	12.6	12.3	12.3
25	5.6	6.2	7.6	8.1	10.5	10.7	11.2	12.3	12.7	25	13.1	13.5	13.7	13.8	14.6	13.5	13.7	13.9	13.4
50	6.8	7.1	8.5	10.1	11.2	12.3	13.0	13.2	15.7	50	14.6	14.9	14.5	14.7	15.1	14.8	15.8	15.0	14.9
75	8.4	8.4	9.9	10.9	12.3	14.4	14.7	15.1	16.6	75	15.7	15.6	15.8	16.9	17.0	16.3	17.1	17.1	16.6
90	12.0	11.4	11.3	12.7	14.0	16.1	16.0	15.8	17.2	90	18.1	16.1	16.8	17.8	18.8	17.5	18.4	18.1	17.5
Sa'										Sa'									
10	6.4	6.3	8.2	6.7	6.4	6.3	6.3	5.2	5.3	10	5.9	5.6	5.5	5.3	6.0	6.2	4.9	5.2	5.0
25	6.8	8.3	8.4	7.6	7.5	7.3	7.1	6.2	6.9	25	6.6	6.5	6.4	6.3	7.0	6.5	5.7	5.8	6.0
50	7.9	8.9	9.9	9.4	8.8	9.2	7.8	7.7	8.2	50	7.2	7.0	7.0	7.0	8.0	7.2	6.7	6.8	6.8
75	9.7	10.9	11.7	11.6	10.9	11.5	9.1	8.6	8.8	75	7.9	8.1	8.4	8.0	8.6	8.3	7.8	7.9	8.1
90	12.0	11.4	12.2	12.8	14.2	14.3	12.0	9.6	10.1	90	9.1	9.0	9.5	9.5	9.5	9.2	9.4	10.0	9.2
LS			7.0	2.6	7.6		2.6	7.0	0.0	Ls'									
10	5.0	0.4	7.2	7.5	7.0	1.1	7.5	/.8	8.3	10	8.5	8.5	7.8	7.7	8.4	8.7	8.6	7.5	8.4
20	0.8 6.5	7.1	/.9	8.1	7.9	8.0	8.3	8.2	9.1	25	9.1	9.0	8.5	8.4	9.1	9.2	9.1	8.7	9.2
20	0.0	/.0	8.5	8.3	9.1	9.0	9.2	8.8	10.0	50	9.5	9.8	9.5	9.8	10.1	10.1	10.2	10.1	9.9
73	1.5	8.5	9.2	8.8	9.7	11.0	10.4	9.5	10.3	75	10.5	11.0	10.2	11.6	11.0	11.1	11.1	10.8	10.6
	V 11					14.5													

### Conclusions

♥We report normal ranges for PWD and TDI mitral velocities derived from a large population of Caucasian children.

♥There was no ideal body size variable for normalization and the inclusion of multiple variables (BSA, HR and age) resulted only in a partial amelioration of the final models.

♥The high variability in the regression analyses hampered the possibility of z score calculations, so data are presented as percentiles mean values (plus/minus standard deviation).

♥The highest variability was seen in the lowest age groups, while satisfactory reproducibility was observed in older children, so we recommend caution in the use of diastolic functional indices in the lower age groups.

♥Further studies are required to reinforce these data, as well to evaluate other parameters of pediatric systolic and diastolic function.

### Other functional index

**RVOT escursion** Koestenberger M et al. Reference values of the right ventricular outflow tract systolic excursion in 711 healthy childrenand calculation of z-score values. Eur Heart J Cardiovasc Imaging. 2014 Sep;15(9):980-6 **TAPSE** Koestenberger M, Systolic right ventricular function in children and young adults with pulmonary artery hypertension secondary to congenital heart disease and tetralogy of Fallot: tricuspid annular plane systolic excursion (TAPSE) and magnetic resonance imaging data. Congenit Heart Dis. 2012 May-Jun;7(3):250-8. **TV s' TDI** Weismann CG, Normal pediatric data for isovolumic acceleration at the lateral tricuspid valve annulus-a heart rate dependent measure of right ventricular contractility. Echocardiography. 2015 Mar;32(3):541-7.

>ETC.....

### **Deformation indexes**

Heart Fail Rev. 2015 Sep;20(5):601-12. doi: 10.1007/s10741-015-9492-9.

Review and status report of pediatric left ventricular systolic strain and strain rate nomograms.

Cantinotti M1, Kutty S, Giordano R, Assanta N, Murzi B, Crocetti M, Marotta M, Iervasi G.

Author information

#### Abstract

Interest in strain (ε) and strain rate (SR) for the assessment of pediatric left ventricular (LV) myocardial function has increased. However, the strengths and limitations of published pediatric nomograms have not been critically evaluated. A literature search was conducted accessing the National Library of Medicine using the keywords myocardial velocity, strain, strain rate, pediatric, reference values, and nomograms. Adding the following keywords, the results were further refined: neonates, infants, adolescents, range/intervals, and speckle tracking. Ten published studies evaluating myocardial velocities, ε, or SR nomograms were analyzed. Sample sizes were limited in most of these studies, particularly in terms of neonates. Heterogeneous methods-tissue Doppler imaging, two- and three-dimensional speckle tracking-were used to perform and normalize measurements. Although most studies adjusted measurements for age, classification by specific age subgroups varied. Few studies addressed the relationships of ε and SR measurements to body size and heart rate. Data have been generally expressed by mean values and standard deviations; Z scores and percentiles that are commonly employed for pediatric echocardiographic quantification have been never used. Reference values for ε and SR were found to be reproducible in older children; however, they varied significantly in neonates and infants. Pediatric nomograms for LV ε and SR are limited by (a) small sample sizes, (b) inconsistent methodology used for derivation and normalization, and (c) scarcity of neonatal data. Some of the studies demonstrate reproducible patterns for systolic deformation in older children. There is need for comprehensive nomograms of myocardial ε and SR involving a large population of normal children obtained using standardized methodology.

### LV strain normal values children

Author	Population	Global longitudinal strain	Global circumferential strain	Global radial strain	Global S
3d					
<u>Thang_L</u> 2013_China (4)	< 1 n 23 (M 13) 0.56 ±0.23 yrs	-17.31 ±2.27	-16.87 ±2.73	61.58 ±18.82	-29.77 ±4.45
	1-5 n 83 (M 45) 2.7 ±1.19 <u>yrs</u>	-17.34 ±2.56	-17.06 ±3.25	60.28 ±13.37	30.13 ±3.47
	5-9 n 61 (M 33) 6.88 ±1.16 <u>yrs</u>	-17.56 ±2.221	-17 ±3.43	59.49 ±13.29	-30.24 ±3.61
	9-13 n 36(M 17) 10.86 ±1.23 <u>yrs</u>	-18.75 ±1.72	-18.83 ±3.32	64.65 ±8.42	-31.52 ±2.65
	13-18 n 25 (M 11) 14.83± 1.88 <u>yrs</u>	-16.64 ±2.8	-16.26 ±4.11	56.62 ±14.89	-28.96 ±4.53
Speckle tracking		Septal			
<u>Macus</u> K 2011 USA (7)	0 yrs n 24 (13 M) 0.3 ±0.3 yrs	- 18.3 ± 1.9 P5 - 14.5 P 95 - 22.1	PM     MV       -18.6 ± 3.3     -17.5 ± 2.5       P5 -12     P5 -12.5       P95 -25.2     P95 -22.5	PM     MV       52.0 ± 9.9     49.9 ± 4.3       P5 32.2     P5_41.3       P95 71.8     P95 58.5	
	1-4 yrs n 34 (19 M) 2.9 ± 1.0 yrs	-20.7 ±1.3 P5 -18.1 P95 -23.3	PM     MV       -21.3 ± 2.0     -19.7 ± 2.0       P5 -17.3     P5 -15.7       P95 -25.3     P95 -23.7	PM     MV       53.5 ± 6.7     50.0 ± 5.7       P5_40.1     P5 38.6       P95 66.9     P95 61.4	
	5-9 Yrs n 36 (25 M) 7.2 ± 1.2 yrs	-21 ± 1.3 P5 - 18.4 P95 - 23.6	PM     MV       -23.4 ± 1.7     -20.9 ± 2.0       P5 -20     P5 -16.9       P95 -26.8     P95 -24.9	PM     MV       54.9 ± 5.5     52.3 ± 4.5       P5 43.9     P5_43.3       P95_65.9     P95_61.3	
	10-14 y n 29 (16 M)	-21.8 ± 1.3 P5 -19 2	PM MV	PM MV	

# Part 3:Other field of application and future prospective

Other imaging techniques: MRI, CT, angio
Easy approach to z scores: app, web site implementation

### MRI z scores

J Cardiovasc Magn Reson. 2015 Apr 18;17:29. doi: 10.1186/s12968-015-0111-7.

#### Normal values for cardiovascular magnetic resonance in adults and children.

Kawel-Boehm N<sup>1</sup>, Maceira A<sup>2</sup>, Valsangiacomo-Buechel ER<sup>3</sup>, Vogel-Claussen J<sup>4</sup>, Turkbey EB<sup>5</sup>, Williams R<sup>6</sup>, Plein S<sup>7</sup>, Tee M<sup>8</sup>, Eng J<sup>9</sup>, Bluem

#### Author information

#### Abstract

Morphological and functional parameters such as chamber size and function, aortic diameters and distensibility, flow and T1 and T2\* can be assessed and quantified by cardiovascular magnetic resonance (CMR). Knowledge of normal values for quantitative CMR is c interpretation of results and to distinguish normal from disease. In this review, we present normal reference values for morphological a CMR parameters of the cardiovascular system based on the peer-reviewed literature and current CMR techniques and sequences.

PMID: 25928314 [PubMed - in process] PMCID: PMC4403942 Free PMC Article





Baby Norm Calculator Pediatric Normal Values and Drug Doses

### COMING SOON!!!!!

# **Applications**

Cardiac

- EchocardiographyFetal Echocardiography
- ≻MRI
- ≻ECG
- ≻Stress Test

Basic

Vital Parameters, Anthropomorphic Data, Blood pressure, Drug Doses, laboratory tests

## Home page: Patient detail



	🛜 📶 67% 🖬 12:58				
🮲 Baby Norm Calculator					
	Patient List				
Filte	er _				
	<b>CS000001</b> 4 years 15 Kg 90 cm				
<b>S</b>	<b>CS000002</b> 0 day 0 Kg 0 cm				
<b>*</b>	<b>CS000003</b> 5 years 20 Kg 110 cm				
2 2 2	CS000004 30 gest week				
Ş	<b>CS000005</b> 1 years 9 Kg 70 cm				

### Home page 66% 13:00



**Baby Norm Calculator** 



**Child Growth Standards** 



Vital parameters/Anesthesia



**Blood Pressure** 



Laboratory Tests



Drug doses



Echocardiography



Fetal Echocardiography



Cardiac MRI



ECG



Stress Tests



Nutrition

### Blood pressure/Laboratory tests

		t.0)	67%	12:58
🎲 Baby	/ Norm Ca		+	Q
Patient Generalities				
ID	CS00000	5		
Туре	Child	Fetal		
Height	70	cm		
Weight	9.0	Kg		
Age	1	years	;	
Gender	<b>M</b>	) F		

₽ 11 94% <b>U</b> 9:33			
🎲 Baby Norm Calculator			
PRESSURE			
ID = CS00002 H = 120 cm W = 22.0 Kg BMA = 0,85 Sex = M Age = 6 years			
Reference Fouth Report 2004 (USA)			
DBP (mmHg)= 55 (P95= 57.0)			
SBP (mmHg)= 96 (P95= 100.0)			
Reference Details <u>THE FOURTH REPORT ON THE Diagnosis,</u> <u>Evaluation, and Treatment of High Blood Pressure</u> in Children and Adolescents. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health National Heart, Lung, and <u>Blood Institute</u>			

家 📶 66% 💼 12:59				
🤔 Baby Norm Calculator				
Laboratory Tests				
blood gas				
Met Hb (venous blood) = none blood gas				
O2Hb (arterial blood) = 95-98 % blood gas				
O2Hb (venous blood) = none				
pCO2 (arterial blood) = 27-41 mmHg				
pCO2 (venous blood) = 32-66 mmHg blood gas				
pH (arterial blood) = 7.35-7.45 blood gas				
pH (venous blood) = 7.32-7.42				
pO2 (arterial blood) = 80-100 mmHg				
pO2 (venous blood) = 6-30 mmHg <sup>blood</sup> gas				

# Drug doses

🗊 📶 66% 🖬 12:59	🛜 📶 66% 🛑 13:00			
🎲 Baby Norm Calculator	🤔 Baby Norm Calculator 🛛 🗐			
DRUGS LIST	DRUG INFORMATIONS			
Name	ID = CS000005 H = 70 cm W = 9.0 Kg BMA = 0,43 Sex = M Age = 1 years			
Group All	Name: Albumin			
Aciclovir	Group: Vasopressin			
Antiviral	User information:			
Adenosine Antiarrhythmic	20% 18-45 ml IV. 4%: 90-180 ml If no loss from plasma: dose (ml/kg)=5x			
Adrenaline	(increase g/l) (%albumin)			
Emergency/IV	Dose normalized to weight and/or age.			
Albumin Vasopressin				
Aldactone Diuretics				
Alginic acid Gastroprotective/pro-cynetic				
Allopurinol Antiinflammatory				
Altenlase				

# Echocardiography: a high level application

🗊 📶 66% 💼 13:00	🗊 📶 66% 💼 13:02		🛜 📶 64% 🖬 13:09	
🎲 Baby Norm Calculator	🮲 Baby Norm Calculator		🮲 Baby Norm Calculator	
Pulmonary Outflow Short	Aorta Long Axis		Global Strain	
Aorta Long Axis	ID = CS000005 H = 70 cm W = 9.0 Kg BMA = 0,43 Sex = M Age = 1 years		V = 9.0 Kg = 1 years	ID = CS000005 H = 70 cm W = 9.0 Kg BMA = 0,43 Sex = M Age = 1 years
Aortic Arch Suprasternal	Reference Warren 2006 (Canada)			Reference Zhang 2013 (China)
M-mode	Valve (mm)			Longitudinal strain = -17.34 (2.56)
LV 4 and 2 Ch	1,2 (1 - 1,5)	1	Z = -0,49	Circumf. strain = -17.06 (3.25)
BV 4 and 2 Ch	Sinuses (mm)			Radial strain = 60.28 (13.37)
	1 (0,8 - 1,1)	1.2	Z = 0,5	Global Strain = 30.13 (3.47)
Atrial	Junction (mm)			
Coronary artery	1,1 (1 - 1,4)	1.5	Z = 0,62	Reference Details Zhang L, Gao J, Xie M, Yin P, Liu W, Li Y, et al. Left ventricular three-dimensional global systelic strain
	Ascending Aorta (mm)			by real-time three-dimensional global system strain hy real-time three-dimensional speckle-tracking in phildrap foesibility, reproducibility, meturational
PW/TDI Mitrai/Tric/P.vein	11(09-12)	1	7 = -0 12	changes, and normal ranges. J Am Soc
TAPSE/MAPSE Interference   Banging Age = 0 - 18 years		Echocardiogr 2013,20.853-9		
Cardiac Output	Dutput Reference detail			
	bilatation of the accellulity a	ond in puce	and the particility	


	¥- 1			
🎲 Baby Norm Calculator				
Cardiac Chamber M-mode				
ID = CS000005 H = 70 cm W = 9.0 Kg BMA = 0,43 Sex = M Age = 1 years				
Reference Cantinotti 2014 (Italy)				
LVED diameter M-mode (mm)				
25,5 (21,5 - 29,8)	25	Z = -0,23		
LVES diameter M-mode, (mm)				
15,2 (11,7 - 18,7)	16	Z = 0,43		
IVSd M-mode (mm)				
4,2 (3 - 6)	5	Z = 0,93		
LWPd mode (mm)				
0,7 (0,5 - 1)	0.6	Z = -0,94		
Reference detail				

165% 13:04

Echocardiographic Nomograms for Ventricular, Valvular and Arterial Dimensions in Caucasian Children with a Special Focus on Neonates, Infants and Toddlers,

🗊 📶 65% 🛑 13:06



🎲 Baby Norm Calculator

#### **Right ventricle 4 and 2 Ch**

ID = CS000005 H = 70 cm W = 9.0 KgBMA = 0,43 Sex = M Age = 1 years

Reference Cantinotti 2014 (Italy)

RVED area (cm2)			
5,1 (3,6 - 7,1)	6	Z = 0,96	
RVES area (cm2)			
2 (1,2 - 3,1)	3		
RVED lenght (mm	)		
33,8 (27,9 - 41)	35	Z = 0,35	
RVES lenght (mm	)		
20,5 (14,9 - 27,1)	21	Z = 0,15	
RVED basal diameter (RV1) (mm)			
20,5 (16,4 - 25,6)	22	Z = 0,63	

### ECG/Fetal echo/Stress Test

s 👔 54% 🖬 13:12	🗊 📶 64% 🗖 13:10		
🎲 Baby Norm Calculator	🎲 Baby Norm Calculator		
ECG	Fetal Echo		
ID = CS000005 H = 70 cm W = 9.0 Kg BMA = 0.43 Sex = M Age = 1 years	Reference: Schneider 2007 (UK)		
	Parameter: Gestational week1		
Reference Garson 1983 (USA)	Aortic Valve (cm)		
QRS vector = 55 (da 7 a 101)	1,2 (1 - 1,5) 1.5 <b>Z</b> =		
PR (sec) = 0.11 (0.08 - 0.15)	24,35		
	Pulmonary Valve (cm)		
QRS(sec) = 0.06(0.04 - 0.08)	1.4 (1.1 - 1.7) 2 7 =		
Q DIII (mm) = 8.5	29,01		
Q V6 (mm) = 3.0	Ascending Aorta (cm)		
$P_{1}(1) = 0.0(2.5 - 17.0)$	1,4 (1,1 - 1,7) <u>1</u> Z =		
(iiiii) = 9.0 (2.3 - 17.0)	19,42		
SV1 (mm) = 8.0 (0.5 - 21.0)	MPA (cm)		
R/SV1 = 1.4 (0.05 - 4.3)	1,5 (1,1 - 1,9) 2 Z = 21,76		
RV6 (mm) = 13.0 (6.5 - 22.5)	TV (cm)		

		i≈i #*∎ 10:4
Baby Norm Calculator		
RV 4 and 2 Ch	Stress Tests	
📏 Atrial	BMA = 1,64 Sex = M Age = 11 years	
Coronary artery		
> Pw/TDI Mitral/Tric/		
TAPSE/MAPSE	Reference Harkel T 2011 (Netherlands)	
Cardiac Output	V02 max = 47.7 (7.0) ml/min/kg	
> Strain	V02 VAT = 28.0 (2.0) ml/kg/min	
🥙 Fetal	VEV C02 = 30.4 (4.0) slope	
Cardiac MRI	RER = 1.13 (0.08)	
👽 ECG	Ten Harkel AD, Takken T, Van Osch-Gevers M, Hebing WA Normal values for cardiopulmonary exercise testing in children Eur J Cardiovasc Prev Rehabil population Euro	
👿 Stress Tests		
Dutrition		
Copyright		
	r Ó	a

## **Future prospective**

### >3D z scores

- Deformation index z scores
- ➤Z scores also for other imaging modalities
- Not only actual pediatric nomograms need to be reinforced and completed
- Pediatric normal values need to be implemented and/or created according to the development new diagnostic tools

## Conclusions

- Nomograms are useful but not perfect tools
- >Knowledge of the problem: how to
- interpret nomograms
- Substantial improvement have been made
- Effort ongoing both in Europe and North America
- >A never ending research

# Thank you for your attention!

