● **Original** paper

SEGMENTAL MYOCARDIAL DISPLACEMENT AND TISSUE VELOCITY ANALYSIS OF THE RIGHT VENTRICLE IN HYPOPLASTIC LEFT HEART SYNDROME FETUSES AND CONTROLS USING COLOR TISSUE DOPPLER IMAGING (C-TDI)

Authors:
Oliver Graupner[1], Christian Enzensberger[2], Larissa Wieg[3], Aline Wolter[2], Can Yerebakan[4], Markus Khalil[5], Roland Axt-Fliedner[2]

1. Department of Obstetrics and Gynecology, Klinikum rechts der Isar, Technical University of Munich, German 2. Division of Prenatal Medicine, Department of Obstetrics and Gynecology, Justus-Liebig-University and UKGM, Giessen, Germany 3. Department of Cardiology, Klinikum rechts der Isar, Technical University of Munich, Germany 4. NCardiovascular Surgery, Children's National Heart Institute, George Washington University Medical Center, Washington, DC, USA 5. Department of Paediatric Cardiology, Justus-Liebig-University and UKGM, Giessen, Germany

Prenat Cardio 2017 Jan; 7(1):12-18
DOI: 10.1515/pcard-2017-0003

Abstract

Introduction: The long-term outcome of patients with HLHS (hypoplastic left heart syndrome) is mainly determined by right ventricular function. Our study examines, whether there are differences in segmental right ventricular myocardial displacement and tissue velocities of fetuses with HLHS compared to healthy fetuses during gestation.

Materials and methods: A prospective study was conducted including 20 fetuses with HLHS and 20 gestational age matched controls. c-TDI (colour tissue Doppler imaging) derived systolic and diastolic velocities as well as myocardial displacement were assessed in three different locations of the right ventricle (RV). A ROI (region of interest) was placed in the basal, middle and apical part of the myocardium. Possible changes of c-TDI indices in the course of pregnancy and between the three different segments were investigated in both groups.

Results: HLHS fetuses showed significantly lower e' velocities measured in the basal and middle part of the RV compared to healthy controls ($p < 0.05$). Basal displacement showed significantly lower values in HLHS fetuses compared to controls. In control fetuses but not in HLHS fetuses there was a significant increase of basal diastolic velocities and displacement in the course of pregnancy. According to myocardial velocities and displacement values there was a significant decrease from the base of the fetal heart to the apex pointed in both groups.

Conclusions: An altered right ventricular myocardial function in HLHS fetuses within different myocardial segments could be demonstrated. An apicobasal gradient with higher velocity and displacement values in the basal part of RV myocardium could be found in both groups. The technique may be of value in the prenatal assessment of myocardial function, however its role as a monitoring tool and outcome predictor needs to be defined.

Key words: *fetal echocardiography, color tissue Doppler imaging, c-TDI, hypoplastic left heart syndrome, fetal cardiac function*

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) is one of the most frequent forms of congenital heart disease. While it is generally well tolerated in utero, this cardiac anomaly is almost certainly lethal without postnatal treatment because the hypoplastic left ventricle is unable to support the systemic circulation and systemic blood supply entirely relies on a patent ductus arteriosus that is kept open after birth accomplished by prostaglandin in all patients until intervention.

How to cite this article:
Graupner O, Enzensberger C, Wieg L, Wolter A, Yerebakan C, Khalil M, Axt-Fliedner R.
Segmental myocardial displacement and tissue velocity analysis of the right ventricle in hypoplastic left heart syndrome fetuses and controls using color tissue Doppler imaging (c-TDI)
Prenat Cardio 2017 Jan; 7(1):12-18

Single ventricle palliation is performed and as a consequence the right ventricle becomes the systemic ventricle in HLHS. Myocardial function has been studied in HLHS using different techniques e.g. PW-Doppler, pulsed wave tissue Doppler imaging (PW-TDI) and color tissue Doppler imaging (c-TDI). Altered right ventricular function in HLHS has been reported to occur prenatally and it was speculated that these information might offer a link to right ventricular performance after surgical palliation[1-3].

Corresponding author: oliver.graupner@mri.tum.de

Submitted: 2017-05-27, accepted: 2017-10-19

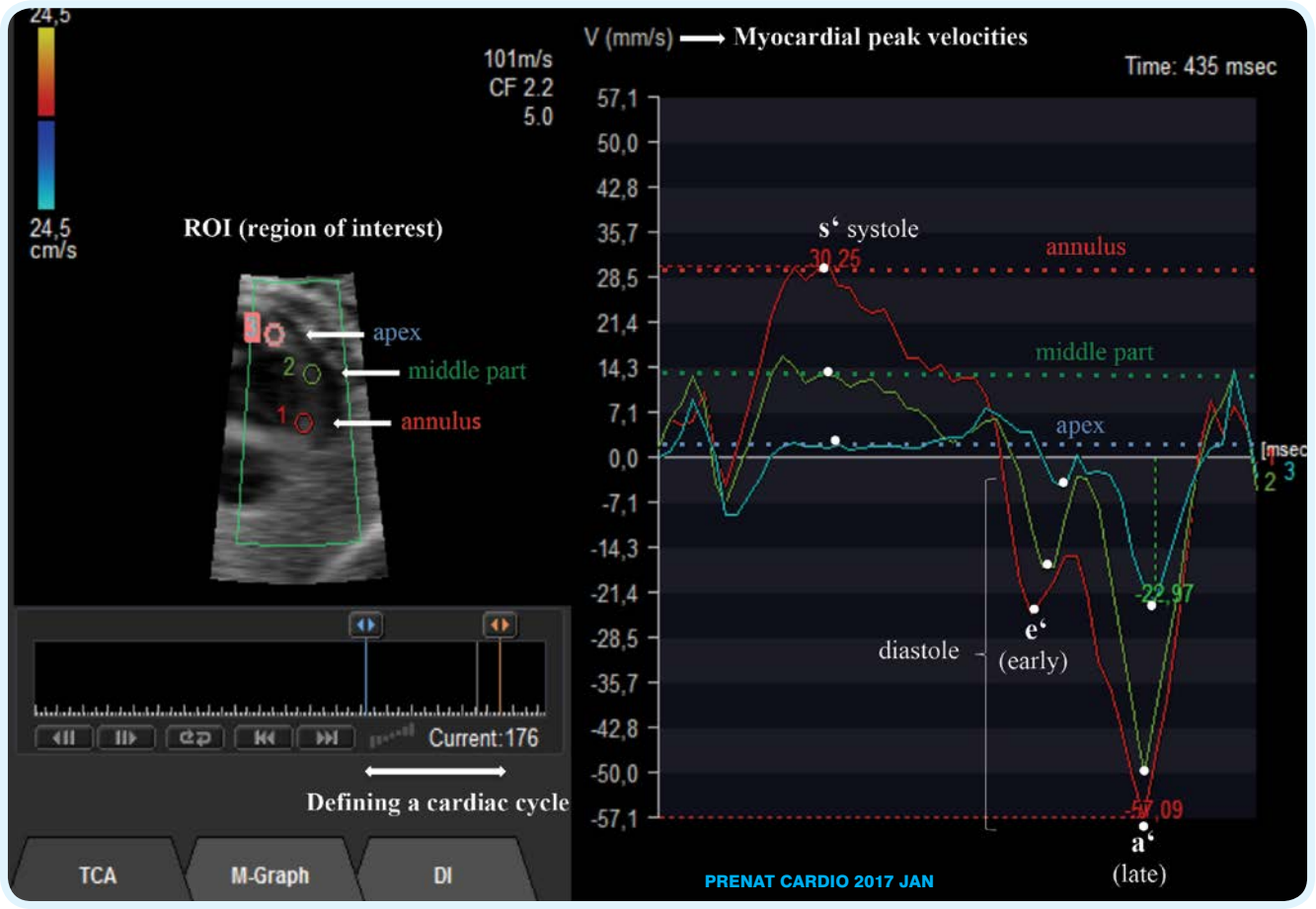

Figure 1. c-TDI (color-tissue Doppler imaging) of an HLHS fetus showing right ventricular peak velocity analysis. After defining one cardiac cycle three 3mm-ROIs (region of interest) are placed in the basal, middle and apical part of the right ventricular myocardium. The result is the typical TDI velocity curve with the systolic maximum s'and the two diastolic maxima e' (early diastole: passive filling of the ventricle) and a' (late diastole: atrial contraction) for each segment of the right ventricle (red: annulus, green: middle part, blue: apex).

c-TDI in contrast to pulsed wave TDI (PW-TDI) which only evaluates one region of interest within the fetal myocardium, offers the possibility of simultaneous offline analysis of multiple areas of interest in both ventricles in a single cardiac cycle[4,5]. To date published data regarding tissue velocities in fetal hearts are scarce[4-6]. c-TDI and PW-TDI use different post processing and temporal resolution methods and can therefore not be used interchangeably. Also, maximum instantaneous myocardial velocity is evaluated by PW-TDI, whereas c-TDI measures the regional mean velocities.

Quantification of myocardial motion (displacement) allows description of regional cardiac function[7]. The sum of longitudinal shortening of all myocardial segments results in the basal part being moved closer towards the apex. Because the apex is stationary within the thorax, the atrioventricular valve plane consecutive moves towards the apex. The displacement of basal myocardial wall, measured at the level of the tricuspid annulus, gives information about the total change in length of that RV wall and thus corresponds to the overall shortening of the wall[8].

Annular displacement of the tricuspid valve - often referred to as TAPSE (tricuspid annular plane systolic excursion) measured by M-Mode - is reported as a sensitive parameter for myocardial dysfunction[9-11]. Any change in any segment will be reflected in the amount and the timing of displacement[8]. However less is known about TDI based displacement analysis especially in pathological conditions like congenital heart failure.

This work represents a secondary analysis of prior work from our study group concerning evaluation of right ventricular function in fetal HLHS by c-TDI[13]. The purpose of this study was to evaluate individual myocardial displacement and tissue Doppler velocities within three different regions of the right ventricle (base, middle part, apex) and to look for a possible gradient from base to apex from which is known that it normally exists in adult heart corresponding to the stationarity of the apex within the thorax while the base moves towards it. As known from echocardiographic measurements in adults these patterns can be altered in certain cardiac pathologies as coronary artery disease and volume or pressure overload[7].

MATERIALS AND METHODS

This prospective study consisted of women referred for fetal echocardiography to the fetal heart program at the department of fetal diagnosis&therapy, University of Giessen and Marburg from 2011-2014. The institutional review board approved this study (protocol number 209/11). Inclusion and exclusion criterias for control and HLHS fetuses were as previously described[12]. For the final analysis, a total of 20 HLHS fetuses (of a total

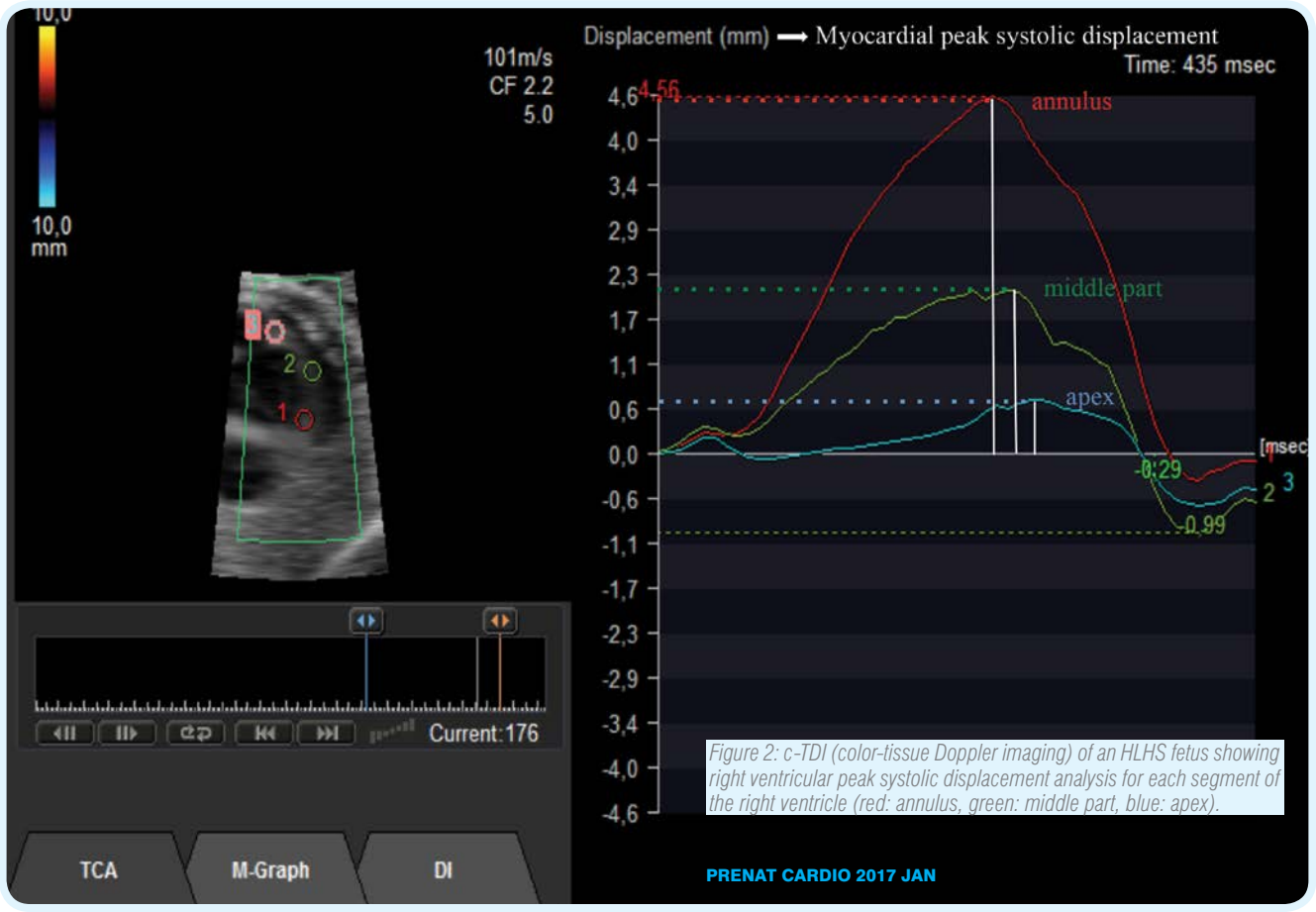

Figure 2: c-TDI (color-tissue Doppler imaging) of an HLHS fetus showing right ventricular peak systolic displacement analysis for each segment of the right ventricle (red: annulus, green: middle part, blue: apex).

cohort of 32 HLHS fetuses during the study period) and 20 gestational age-matched controls were included. The cohort was in part analysed previously describing PW-TDI and c-TDI techniques, demographic data were described before[12,13].

FETAL ECHOCARDIOGRAPHY

Transabdominal echocardiograms were performed in a standardized manner as previously described[13].

Offline analysis was performed with the TDI-Q software (Toshiba Medical Systems Corporation, Otawa, Tochigi, Japan). In the four chamber view a circular 3mm diameter sample volume was placed within the basal part of the right ventricular wall (just beneath the tricuspid valve annulus) and secondly, a 3mm diameter region of interest (ROI) covering middle and apical part of the right ventricular free wall was used.

The peak tissue velocities along the axis at systole (s´), early filling phase of diastole (e´) and during atrial contraction (a´) were averaged from three consecutive cardiac cycles as previously described[13].

	HLHS	Controls	P-value
Gestational age (weeks)	28.6 ± 4.6 (20)	29.2 ± 4.9 (20)	0.68
Tricuspid valve annulus			
s´ (mm/s)	23.68 ± 10.20 (20)	28.91 ± 9.53 (20)	0.10
e´ (mm/s)	18.55 ± 8.55 (19)	28.65 ± 15.39 (20)	0.02*
a´ (mm/s)	38.55 ± 19.66 (20)	38.69 ± 17.04 (20)	0.98
displacement (mm)	2.02 ± 1.29 (20)	2.99 ± 1.59 (20)	0.04*
RV free wall (middle)			
s´ (mm/s)	12.45 ± 8.79 (20)	15.80 ± 7.27 (20)	0.20
e´ (mm/s)	10.72 ± 5.06 (19)	20.76 ± 15.47 (20)	0.01*
a´ (mm/s)	25.43 ± 16.49 (20)	27.14 ± 19.0 (20)	0.76
displacement (mm)	0.92 ± 0.83 (20)	1.54 ± 1.38 (20)	0.09
RV free wall (apex)			
s´ (mm/s)	8.54 ± 5.11 (20)	9.53 ± 5.03 (20)	0.54
e´ (mm/s)	5.30 ± 3.69 (19)	8.58 ± 7.09 (20)	0.08
a´ (mm/s)	16.14 ± 8.33 (20)	16.84 ± 11.88 (20)	0.83
displacement (mm)	0.40 ± 0.41 (20)	0.91 ± 1.09 (20)	0.06

Table 1: Right ventricular colour tissue Doppler imaging (c-TDI) findings of myocardial segmental velocities and displacement for HLHS fetuses and healthy controls; s': Peak velocity during ventricular systole, e': Peak early diastolic relaxation velocity, a´: Peak late diastolic relaxation velocity

By definition displacement or motion of a point is the distance a point covers over a certain period of time. It is the temporal integral of the velocity. When using TDI, the motion towards the transducer is quantified[8] (Fig. 1). In our study two-dimensional longitudinal peak systolic displacement was examined.

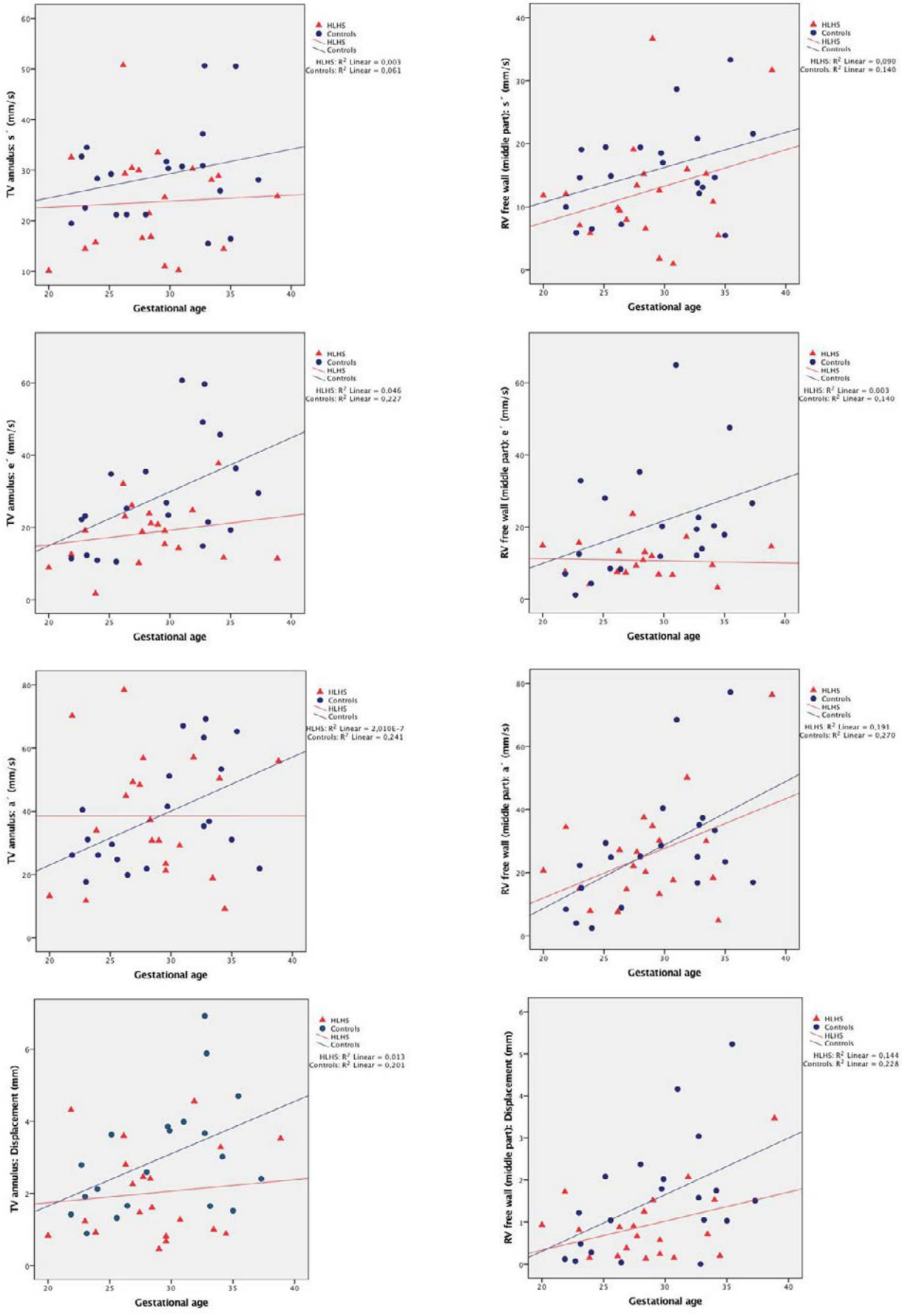

Figure 3: Impact of gestational age on segmental c-TDI-derived systolic (s') and diastolic (e',a') peak velocities as well as peak systolic displacement for HLHS fetuses (red squares) and controls (blue circles). [part 1 of 2]

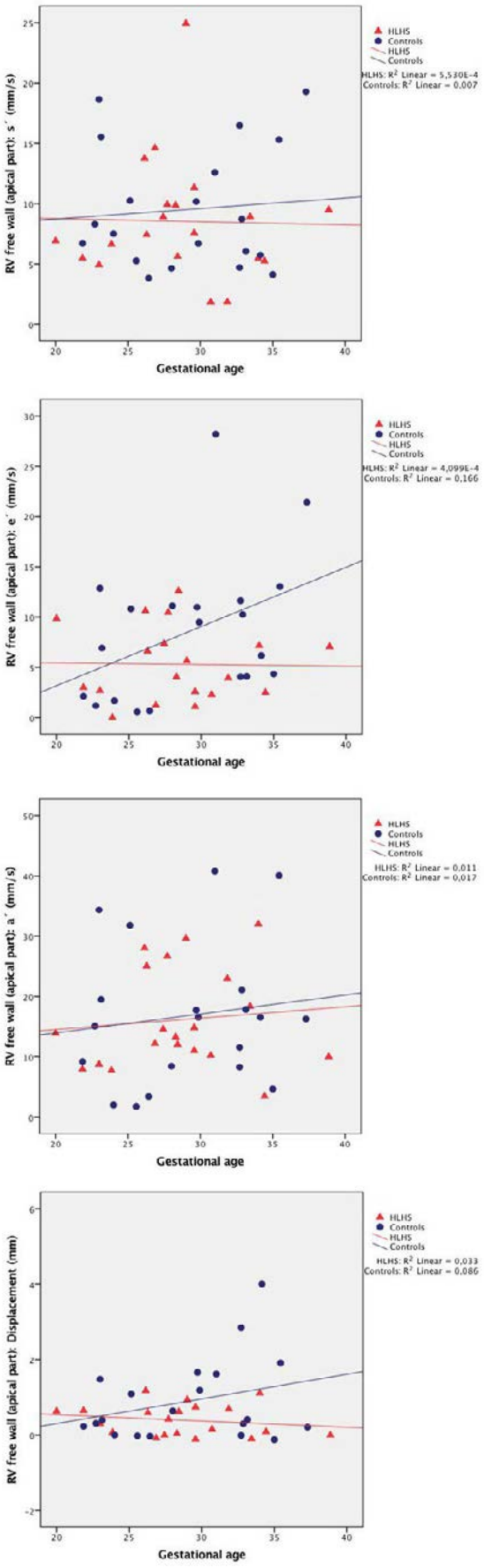

Figure 3: Impact of gestational age on segmental c-TDI-derived systolic (s') and diastolic (e',a') peak velocities as well as peak systolic displacement for HLHS fetuses (red squares) and controls (blue circles). [part 2 of 2]

STATISTICAL ANALYSIS

To carry out comparisons between the two groups, a case–control design was used. Every HLHS and control fetus was included only once (at first evaluation). Every HLHS case was compared against one control of approximately the same gestational age (maximum two weeks gestational age difference). For final analysis, Student's *t*-test was performed to demonstrate significant differences in cardiac function parameters between the 20 HLHS and 20 control fetuses. In addition, a linear regression analysis was carried out to investigate the relationship of the c-TDI-based regional velocity and displacement values and gestational age in both the HLHS and control groups. The level of statistical significance was $p < 0.05$.

RESULTS

HLHS fetuses showed significantly lower e' velocities measured in the tricuspid annulus and the right ventricular free wall compared to healthy control fetuses (18.55 vs. 28.65 mm/s; p=0.02, 10.71 vs. 20.76 mm/s; p=0.01, Tab. 1).

In the apex area HLHS fetuses also showed lower e' velocities but without statistical significance (5.30 vs. 8.58 mm/s; p=0.08, Tab. 1).

Annular displacement showed significantly lower values in the HLHS group compared to the control group (2.02 vs. 2.99 mm; p=0.04, Tab. 1).

Also in the right ventricular free wall and in the apex area displacement values were significantly lower in the HLHS group compared to controls but without reaching statistical significance (0.92 vs. 1.54 mm; p=0.09, 0.40 vs. 0.91 mm, p = 0.06, Tab. 1).

Healthy control fetuses showed a significant increase of annular e' and a' velocity (R2=0.23; p=0.03; R2=0.24; p=0.03) in the course of pregnancy (Fig. 2).

Likewise, there was a significant increase in right ventricular free wall a' velocity in healthy control fetuses (R2=0.27; p=0.02, Fig. 2). Right ventricular free wall and annular displacement values also showed a significant increase in the course of pregnancy in the control group (R2=0.20; p=0.048; R2=0.23; p=0.03, Fig. 2).

In HLHS fetuses there were no significant changes of velocities and displacement values during pregnancy (Fig. 2).

According to myocardial velocity and displacement values there was a significant decrease from the base of the fetal heart to the apex pointed (apicobasal gradient) in both groups (p<0.05) (Tab. 2-3).

HLHS	Myocardial function	Segment	Mean values	Difference	P-value
RIGHT VENTRICLE	s´ (mm/s)	annulus vs. middle	23.68 vs. 12.45	11.23	< 0.001*
		middle vs. apex	12.45 vs. 8.54	3.91	0.025*
		annulus vs. apex	23.68 vs. 8.54	15.14	< 0.001*
	e´ (mm/s)	annulus vs. middle	18.55 vs. 10.72	7.83	0.003*
		middle vs. apex	10.72 vs. 5.31	5.41	< 0.001*
		annulus vs. apex	18.55 vs. 5.31	13.24	< 0.001*
	a´ (mm/s)	annulus vs. middle	38.55 vs. 25.43	13.12	< 0.001*
		middle vs. apex	25.43 vs. 16.13	9.30	0.032*
		annulus vs. apex	38.55 vs. 16.13	22.42	< 0.001*
	Displacement (mm)	annulus vs. middle	2.02 vs. 0.92	1.10	< 0.001*
		middle vs. apex	0.92 vs. 0.40	0.52	0.02*
		annulus vs. apex	2.02 vs. 0.40	1.62	< 0.001*

Table 2. Comparison of myocardial velocities and displacement between the different segments for for HLHS fetuses; s': Peak velocity during ventricular systole, e': Peak early diastolic relaxation velocity, a': Peak late diastolic relaxation velocity

Controls	Myocardial function	Segment	Mean values	Difference	P-value
RIGHT VENTRICLE	s´ (mm/s)	annulus vs. middle	28.91 vs. 15.80	13.11	< 0.001*
		middle vs. apex	15.80 vs. 9.53	6.27	< 0.001*
		annulus vs. apex	28.91 vs. 9.53	19.38	< 0.001*
	e´ (mm/s)	annulus vs. middle	28.66 vs. 20.76	7.90	0.03*
		middle vs. apex	20.76 vs. 8.58	12.18	< 0.001*
		annulus vs. apex	28.66 vs. 8.58	20.08	< 0.001*
	a´ (mm/s)	annulus vs. middle	38.69 vs. 27.14	11.55	< 0.001*
		middle vs. apex	27.14 vs. 16.85	10.29	< 0.001*
		annulus vs. apex	38.69 vs. 16.85	21.86	< 0.001*
	Displacement (mm)	annulus vs. middle	2.99 vs. 1.54	1.45	< 0.001*
		middle vs. apex	1.54 vs. 0.91	0.63	0.03*
		annulus vs. apex	2.99 vs. 0.91	2.08	< 0.001*

Table 3. Comparison of myocardial velocities and displacement between the different segments for healthy control fetuses; s': Peak velocity during ventricular systole, e': Peak early diastolic relaxation velocity, a': Peak late diastolic relaxation velocity

DISCUSSION

This study demonstrates, that in fetuses with HLHS right ventricular myocardial function differs from normal controls. First, lower e' velocities measured in the tricuspid annulus and the right ventricular free wall in HLHS compared to healthy control fetuses might provide further evidence of altered ventricular diastolic function. We previously described a lower e´ velocity and e´/a´ ratio reflecting an impaired ventricular relaxation during early diastole in fetuses with HLHS using a drawn ROI, which covers the middle and basal part of the right ventricular wall[13]. In comparison to our previous findings we observed an increase in diastolic velocities (e´, a´) of the basal part in control fetuses during gestation. Natarajan et al. described a significant increase of RV free wall (measured just beneath the tricuspid annulus) diastolic velocities in HLHS and control fetuses. Similar to our results they also described lower e´ velocities in case of HLHS[1]. Other color tissue Doppler studies reported about increasing annular velocities during gestation in normal fetuses placing the ROI in the RV free wall or annulus[14,15]. We think, that measurements of tissue velocities are highly dependent on region of interest placement (even close to the atrioventricular level), the basically undefined ROI size (in the literature this ranges between 1 and 3mm) and the different ultrasound machines with post-processing algorithms[14-20]. Therefore, published tissue velocities vary and cannot be used interchangeably. Absolut values of s´ velocities in both groups were comparable, suggesting a preserved systolic function of the right ventricle in fetuses with HLHS, which is in line with our previous results[12,13].

Second, we found highest tissue velocities at the base of the heart at the atrioventricular valve level significantly decreasing towards the apex of the heart within the right ventricle in HLHS and normal fetuses. This finding has not been described before by c-TDI techniques and compares well to postnatal data[21,22]. Further investigations of fetal cardiac function using Velocity Vector Imaging (VVI) techniques showed decreasing global RV myocardial longitudinal peak systolic velocities from the base towards the apex[23].

Third, we investigated displacement, which is the integral of the velocity over time within the right ventricular myocardium and found a significant decrease of values from the base to the apex of the RV in normal fetuses and in cases with HLHS. To our knowledge this is the first study reflecting c-TDI based RV displacement analysis in fetal HLHS. We found significantly lower values of annular displacement in the HLHS group compared to the control group and a significant increase of RV free wall and annular displacement values in the course of pregnancy only in control fetuses. Brooks et al. who examined RV function in HLHS fetuses using VVI techniques reported about reduced peak global RV longitudinal displacement values in HLHS fetuses, while radial displacement was increased compared to controls. The authors concluded that fetal RV in HLHS becomes more spherical with reduced ratio of longitudinal to circumferential deformation[2].

Limitations of the study include angle dependency of the technique as only axial velocities can be acquired as well as sensitivity to fetal positions, respiratory and body movements and maternal body mass index especially when calculating the derived modalities. c-TDI equipment is designed for adults (higher myocardial velocities) what may limit an adequate examination of the fetal heart.

We acknowledge the small number of cases included in this series. In conclusion we have shown an altered right ventricular myocardial function in HLHS within different myocardial segments of the right ventricle. The technique may be of value in the prenatal assessment of myocardial function, however its role as a monitoring tool and outcome predictor in fetuses with HLHS needs to be defined in future studies.

References

1. *Natarajan S, Szwast A, Tian Z, McCann M, Soffer D, Rychik J. Right ventricular mechanics in the fetus with hypoplastic left heart syndrome. J Am Soc Echocardiogr 2013; 26: 515 – 520.*

2. *Brooks PA, Khoo NS, Mackie AS, Hornberger LK. Right ventricular function in fetal hypoplastic left heart syndrome. J Am Soc Echocardiogr 2012; 25: 1068 – 1074.*

3. *Szwast A, Tian Z, McCann M , Donaghue D, Rychik J. Right ventricular performance in the fetus with hypoplastic left heart syndrome. Ann Thorac Surg 2009; 87: 1214 – 1219.*

4. *Saini AP, Ural S, Pauliks LB. Quantitation of fetal heart function with tissue Doppler velocity imaging-reference values for color tissue Doppler velocities and comparison with pulsed wave tissue Doppler velocities. Artif Organs 2014; 38: 87 – 91.*

5. *Nii M, Roman KS, Kingdom J, Redington AN, Jaeggi ET. Assessment of the evolution of normal fetal diastolic function during mid and late gestation by spectral Doppler tissue echocardiography. J Am Soc Echocardiogr 2006; 19: 1431 – 1437.*

6. *Paladini D, Lamberti A, Teodoro A, Arienzo M, Tartaglione A, Martinelli P. Tissue Doppler imaging of the fetal heart. Ultrasound Obstet Gynecol 2000; 16: 530–535.*

7. *Bijnens BH, Cikes M, Claus P, Sutherland GR. Velocity and deformation imaging for the assessment of myocardial dysfunction. Eur J Echocardiogr. 2009 Mar;10(2):216-26.*

8. *Bijnens B, Cikesf M, Butakoff C, Sitges M, Crispi F. Myocardial Motion and Deformation: What Does It Tell Us and How Does It Relate to Function? Fetal Diagn Ther 2012;32:5–16.*

9. *Rydman R, Söderberg M, Larsen F, Caidahl K, Alam M: Echocardiographic evaluation of right ventricular function in patients with acute pulmonary embolism: a study using tricuspid annular motion. Echocardiography 2010;27:286–293.*

10. *Chrustowicz A, Gackowski A, El-Massri N, Sadowski J, Piwowarska W: Preoperative right ventricular function in patients with organic mitral regurgitation. Echocardiography 2010;27:282–285.*

11. *Kjaergaard J, Iversen KK, Akkan D, Møller JE, Køber LV, Torp-Pedersen C, Hassager C: Predictors of right ventricular function as measured by tricuspid annular plane systolic excursion in heart failure. Cardiovasc Ultrasound 2009;7:51*

12. *Axt-Fliedner R, Graupner O, Kawecki A, Degenhardt J, Herrmann J, Tenzer A, Doelle A, Willruth A, Steinhard J, Gembruch U, Bahlmann F, Enzensberger C; Fetal Cardiac Imaging Research Group, Germany. Evaluation of right ventricular function in fetuses with hypoplastic left heart syndrome using tissue Doppler techniques. Ultrasound Obstet Gynecol. 2015 Jun;45(6):670-677.*

13. *Graupner O, Enzensberger C, Wieg L, Willruth A, Steinhard J, Gembruch U, Doelle A, Bahlmann F, Kawecki A, Degenhardt J, Wolter A, Herrmann J, Axt-Fliedner R; Fetal Cardiac Imaging Research Group Germany. Evaluation of right ventricular function in fetal hypoplastic left heart syndrome by color tissue Doppler imaging. Ultrasound Obstet Gynecol. 2016 Jun;47(6):732-8.*

14. *Paladini D, Lamberti A, Teodoro A, Arienzo M, Tartaglione A, Martinelli P: Tissue Doppler imaging of the fetal heart. Ultrasound Obstet Gynecol 2000;16:530–535.*

15. *Perles Z, Nir A, Gavri S, Rein AJ: Assessment of fetal myocardial performance using myocardial deformation analysis. Am J Cardiol 2007;99:993–996.*

16. *Tutschek B, Schmidt KG. Sonographic Assessment of Fetal Cardiac Function: Indirect Measurements of Fetal Cardiac Function, Newer Techniques and Clinical Applications. UltraschallinMed2012;33:E16–E24.*

17. *Larsen LU, Petersen OB, Norrild K, Sorensen K, Uldbjerg N, Sloth E. Strain rate derived from color Doppler myocardial imaging for assessment of fetal cardiac function. Ultrasound Obstet Gynecol. 2006 Feb;27(2):210-3.*

18. *Larsen LU, Sloth E, Petersen OB, Pedersen TF, Sorensen K, Uldbjerg N. Systolic myocardial velocity alterations in the growth-restricted fetus with cerebroplacental redistribution. Ultrasound Obstet Gynecol. 2009 Jul;34(1):62-7.*

19. *Di Salvo G, Russo MG, Paladini D, Pacileo G, Felicetti M, Ricci C, Cardaropoli D, Palma M, Caso P, Calabro R. Quantification of regional left and right ventricular longitudinal function in 75 normal fetuses using ultrasound-based strain rate and strain imaging. Ultrasound Med Biol 2005; 31: 1159–1162.*

20. *Ta-Shma A, Perles Z, Gavri S, Golender J, Tarshansky S, Shlichter C, Bar Tov H, Rein AJ. Analysis of segmental and global function of the fetal heart using novel automatic functional imaging. J Am Soc Echocardiogr. 2008 Feb;21(2):146-50.*

21. *López-Candales A, Rajagopalan N, Gulyasy B, Edelman K, Bazaz R. Differential strain and velocity generation along the right ventricular free wall in pulmonary hypertension. Can J Cardiol. 2009 Mar;25(3):e73-7.*

22. *Edvardsen T, Gerber BL, Garot J, Bluemke DA, Lima JA, Smiseth OA. Quantitative assessment of intrinsic regional myocardial deformation by Doppler strain rate echocardiography in humans: Validation against three-dimensional tagged magnetic resonance imaging. Circulation 2002;106:50-6.*

23. *Willruth AM, Geipel AK, Fimmers R, Gembruch UG. Assessment of right ventricular global and regional longitudinal peak systolic strain, strain rate and velocity in healthy fetuses and impact of gestational age using a novel speckle/feature-tracking based algorithm. Ultrasound Obstet Gynecol. 2011 Feb;37(2):143-9.*

Division of work:

Oliver Graupner: Concept/Design, Data analysis/interpretation, Drafting article, Statistics, Data collection, Critical revision of article, Approval of article

Christian Enzensberger: Concept/Design, Data analysis/interpretation, Data collection, Critical revision of article, Approval of article

Larissa Wieg: Data analysis/interpretation, Data collection, Critical revision of article, Approval of article

Aline Wolter: Data analysis/interpretation, Data collection, Critical revision of article, Approval of article

Can Yerebakan: Data analysis/interpretation, Critical revision of article, Approval of article

Markus Khalil: Data analysis/interpretation, Critical revision of article, Approval of article

Roland Axt-Fliedner: Concept/Design, Data analysis/interpretation, Drafting article, Statistics, Data collection, Critical revision of article, Approval of article

Conflict of interest: The authors declare no conflict of interest

Authors do not report any financial or personal links with other persons or organizations, which might affect negatively the content of this publication and/or claim authorship rights to this publication