

Assessment of systemic right ventricular function using tissue Doppler imaging in children with hypoplastic left heart syndrome after Fontan operation – preliminary results

Ocena funkcji systemowej prawej komory z wykorzystaniem tkankowej echokardiografii dopplerowskiej u dzieci z zespołem niedorozwoju lewego serca po operacji metodą Fontana – wyniki wstępne

Justyna Topolska-Kusiak, Anna Mazurek-Kula, Katarzyna Szaflik, Jadwiga Anna Moll

Cardiology Department, Polish Mother's Memorial Hospital Research Institute, Lodz, Poland

Abstract

Introduction. Difficulties in the echocardiographic assessment of single ventricle function, particularly with right ventricular morphology, prompt to use different available echocardiographic techniques. Echocardiographic evaluation of the degree of hemodynamic disturbances affecting systemic ventricular function not only allows better investigation of the cardiovascular system but also helps determine prognostic factors to guide further therapeutic decisions. The role of tissue Doppler imaging (TDI) in paediatric patients with univentricular heart has been highlighted but only few studies evaluated the utility of this method in the evaluation of systemic ventricle systolic and diastolic function after the Fontan procedure. The aim of the study was to assess the relationship between conventional echocardiographic and TDI parameters in the evaluation of the performance of a functional single right ventricle in children with hypoplastic left heart syndrome (HLHS) after the Fontan procedure.

Material and methods. A total of 34 patients with HLHS after staged surgical treatment culminating in the Fontan procedure underwent evaluation, including medical interview, physical examination, electrocardiography, and transthoracic echocardiography in standard views using M-mode, two-dimensional imaging, continuous and pulsed wave Doppler, colour Doppler, and TDI. The effect of demographic and perioperative factors on selected parameters of the echocardiographic evaluation of systemic ventricular function was analysed. In addition, we evaluated relations between conventional echocardiographic and TDI parameters in the evaluation of single right ventricular function in children after Fontan procedure.

Results. Statistical analysis showed no significant correlation between TDI parameters of systolic and diastolic function (E' , E'/A') and standard echocardiographic indices (E , A , E/A). Likewise, no significant correlation was found between the myocardial performance index (MPI) obtained from TDI and conventional MPI. A significant correlation was found between the E/E' ratio and MPI.

Conclusions. No significant correlation found in children after Fontan procedure between diastolic function parameters and right ventricular MPI measured using TDI and conventional echocardiographic parameters indicates that TDI is a technique complementary to conventional echocardiography in the evaluation of single right ventricle function in children. In addition, TDI does not depend on preload, and thus it can be speculated that this technique may identify ventricular dysfunction (mostly diastolic) at a stage when conventional echocardiographic parameters are still normal. Further studies in a larger number of patients are needed to support these conclusions.

Key words: functionally univentricular heart, functionally single ventricle, Fontan procedure, congenital heart disease, tissue Doppler imaging, echocardiography

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Introduction

Congenital heart disease collectively labelled as functionally single ventricle or functionally univentricular heart is a group of most complex congenital heart defects. Their common feature is the presence of a dominant ventricle which supplies both pulmonary and systemic circulation, while the other ventricle is much less developed, often rudimentary, or even absent [1]. Single ventricle defects account for 7.7–7.8% of all congenital heart disease and are lethal without appropriate treatment. The most common form of a functionally univentricular heart is hypoplastic left heart syndrome (HLHS). Treatment outcomes in children with functionally univentricular heart have significantly improved with advances in cardiac surgery, anaesthesiology, intensive care and paediatric cardiology, particularly over the last 25 years. Patients with single ventricle undergo multi-stage cardiac surgical treatment, with the Norwood procedure or hybrid approach (cardiac surgery combined with interventional cardiology techniques) being the first treatment step. A bidirectional Glenn procedure is the second step, and the final step is the Fontan procedure, resulting in the single ventricle serving as the systemic ventricle only, while the systemic venous return is directed to the pulmonary circulation. This non-physiological hemodynamic scenario relieves the single functioning ventricle but also contributes to the development of irreversible changes in the cardiovascular system, leading to multiple complications. The rates of Fontan circulation-related complications increase with time and include systemic ventricular dysfunction, protein-losing enteropathy, plastic bronchitis, progressive atrioventricular valve insufficiency, cardiac arrhythmia, and thromboembolic complications. Systemic ventricular dysfunction begins as diastolic dysfunction and may be easily missed in the early stage [2, 3]. Magnetic resonance imaging is the gold standard for the evaluation of the single ventricle function. However, it is expensive, time-consuming, requires patient cooperation and is not widely available in outpatient settings. Echocardiography remains the most widely available, non-invasive, and reproducible diagnostic tool [4]. Echocardiographic evaluation of the single ventricle function, particularly with the right ventricular morphology (e.g., in HLHS), continues to be a challenge for cardiologists due to its specific anatomic features which cannot be described with a simple geometric model [5, 6]. Thus, it is particularly important to use different available echocardiographic techniques for the systematic evaluation of patients with functionally univentricular heart. These techniques not only allow better investigation of the cardiovascular system but also help determine prognostic factors to guide patient management. Evaluation of the single ventricle includes conventional echocardiographic parameters such as the

myocardial performance index (MPI) and tricuspid annular plane systolic excursion (TAPSE). MPI is an indicator of global ventricular function independent of its geometry and thus may be used to evaluate function of an irregularly shaped ventricle.

The role of tissue Doppler imaging (TDI) in paediatric patients with univentricular heart has been also highlighted. This technique, first described by Isaaz et al. in 1989, uses pulsed wave Doppler and colour Doppler to measure myocardial motion velocity. It is based on the fact the myocardial wall Doppler signal is characterized by low velocity and high amplitude, in contrast to the signal generated by ultrasound waves reflected from blood flowing through cardiac chambers. With development of Doppler echocardiography, myocardial velocity measurements became widely used for the evaluation of left and right systolic and diastolic function [5, 7, 8].

The aim of the study was to assess the relationship between conventional echocardiographic and TDI parameters in the evaluation of the performance of a functional single right ventricle in children with HLHS after the Fontan procedure.

Material and methods

Study group

We studied children with HLHS who underwent three-stage, palliative cardiac surgical treatment culminating with the Fontan procedure. The first step was the Norwood procedure, the second step involved anastomosing the vena cava superior with a pulmonary artery (bidirectional Glenn procedure), and the third step involved connecting the vena cava inferior with pulmonary arteries (Fontan procedure). Fenestration or a temporary connection between the tunnelled vena cava inferior and the right atrium was performed in high-risk patients. The fenestration was closed by interventional cardiology techniques within 6–12 months after the Fontan procedure. All patients were operated in the Department of Cardiac Surgery at the Polish Mother's Memorial Hospital Research Institute in Lodz, and echocardiographic examinations were performed during scheduled follow-up hospitalizations in the Department of Cardiology at the Polish Mother's Memorial Hospital Research Institute in Lodz.

The exclusion criteria included a functionally single ventricle with non-right ventricular anatomy or double inlet right ventricle, antiarrhythmic treatment, cardiac arrhythmia, an implanted cardiac pacemaker, and operation outside our centre.

Our study was a prospective one. The evaluation included medical interview, physical examination, electrocardiography (ECG), and echocardiography in all children. We used the following echocardiographic techniques: two-dimensional (2D) imaging, pulsed and continuous wave

Doppler, colour Doppler, M-mode imaging, and TDI. We analysed the following variables:

- age, gender, body weight, body surface area;
- age at the time of the Fontan procedure;
- Fontan procedure with or without fenestration;
- right ventricular echocardiographic parameters including MPI, TAPSE, flow through the pulmonary/neoaortic valve and right atrioventricular valve (E/A ratio), systemic (i.e., tricuspid) valve annulus velocity (TrV) by TDI (including S', E', and A' measurements and calculations of TDI MPI and E'/A' and E/E' ratios).

Echocardiographic examination

Echocardiographic examination was performed using a Philips iE33 system with a 5MHz probe, with simultaneous ECG recording. MPI was calculated using the formula $MPI = (a - b)/b$, where a is the time from tricuspid valve closure to tricuspid valve opening as evaluated using a flow velocity spectrum recorded by pulsed wave Doppler in a four-chamber view, with tricuspid flow (A and E waves) recorded by placing the sample volume at the tips of tricuspid valve leaflets, and b is the total duration of flow through the neo-aortic valve, measured by placing the sample volume below the valve in the parasternal short axis view (Figure 1).

Using TDI, tricuspid annulus velocity was measured by placing spectral Doppler volume at the annular attachment to the free myocardial wall. From a recording of cardiac cycle, peak early diastolic velocity (E') and atrial contraction velocity (A') were determined. TDI MPI was calculated using the formula: $TDI MPI = (a - b)/b$ where a is the sum of isovolumic contraction and relaxation times (IVCT and IVRT, respectively), and b is the ejection time (ET) (Figure 2).

TAPSE was measured by M-mode in the four chamber apical view by placing the M-mode interrogation line within the lateral aspect of the tricuspid annulus in the right

ventricular long axis, followed by measurement of the peak annular plane excursion (Figure 3).

Statistical analysis

Statistical analysis was performed using Statistica 5.0 software, with $p < 0.05$ indicating statistical significance. Quantitative data were reported as mean values \pm standard deviation, and categorical data as numbers and percentages. The number of valid measurements, arithmetic mean, minimum and maximum values, and standard deviation were calculated for each variable. Relations between the evaluated variables were assessed using Pearson correlation coefficients, and their significance was tested using Student's t-distribution. Differences between mean values of the evaluated variables in different patient groups were evaluated by the Student t test and non-parametric Mann-Whitney test. Snedecor's F-distribution-based analysis of variance tests were also used to compare mean values of the evaluated variables in different groups.

Preliminary results

We studied 34 children (27 boys and 7 girls) with a functionally single right ventricle. Detailed patient characteristics are shown in Table 1. The mean patient age at the time of the third stage of cardiac surgical treatment, i.e. the Fontan procedure, was 5.21 years. In most children, an extracardiac tunnel was created (32 patients, 94.1%) and fenestration was performed during the surgery (32 patients, 94.1%). Cardiac arrhythmia was not recorded in any children either on ECG or during echocardiographic examination, and first degree atrioventricular block was observed in two patients. Values of the evaluated echocardiographic parameters are shown in Tables 2 and 3.

In our study group, we found significant relations between:

- TAPSE and TDI MPI ($r = -0.45$), TAPSE and S' ($r = 0.40$);

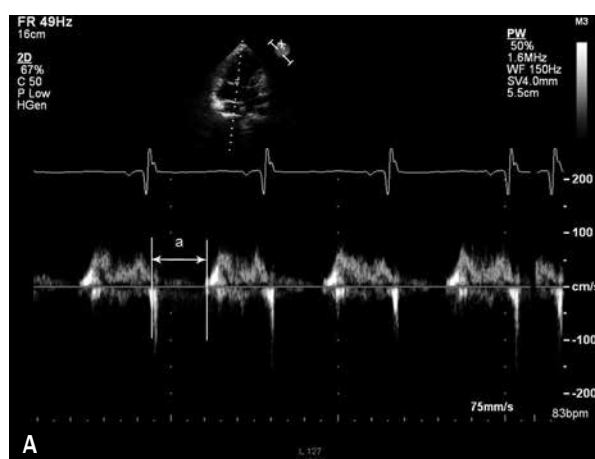


Figure 1A, B. Myocardial performance index – $MPI = (a - b)/b$ (A – PW, 4C; B – PW, 5C).

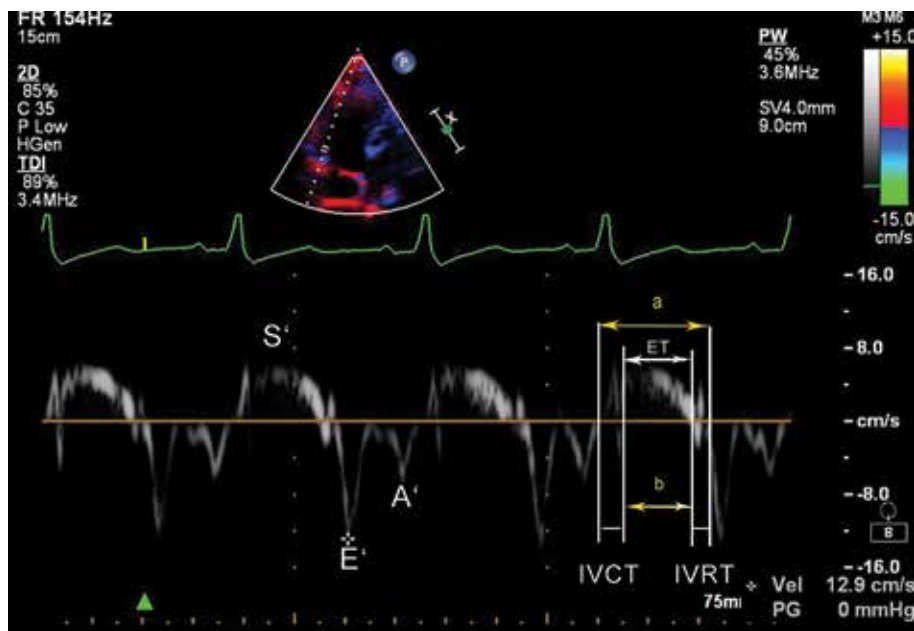


Figure 2. S' – peak tricuspid valve (TrV) annular velocity during systole, E' – tricuspid valve annular velocity in early diastole, A' – tricuspid valve annular velocity during atrial contraction; TDI MPI = (a - b)/b where a is IVCT + IVRT, and b is ET (pulsed wave Doppler, 4-chamber view)

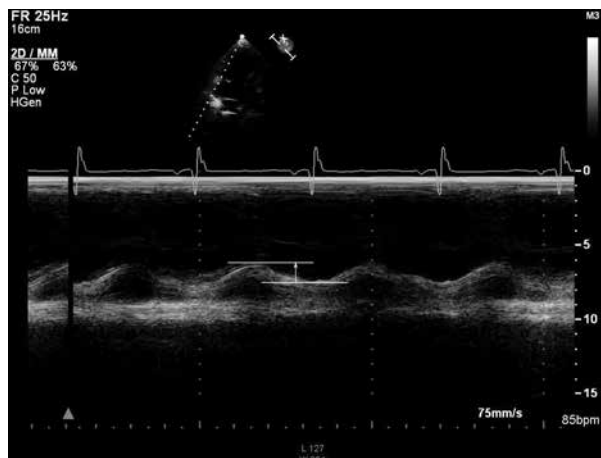


Figure 3. Tricuspid annular plane systolic excursion (TAPSE) (M-mode, 4-chamber view)

- MPI and age at the time of the Fontan procedure ($r = 0.41$), E ($r = 0.54$), and E/E' ratio ($r = 0.46$);
- TDI MPI and TAPSE ($r = -0.45$), age at the time of the Fontan procedure ($r = 0.45$), and the number of years since the Fontan procedure ($r = -0.40$);
- E/E' ratio and MPI ($r = 0.46$);
- E/A and A' ($r = -0.57$) and E/E' ($r = 0.63$);
- S' and TAPSE ($r = 0.40$).

We did not find significant correlations between the E'/A' ratio and other evaluated echocardiographic parameters.

Table 1. Clinical characteristics of the study subjects (quantitative data shown as mean \pm standard deviation, and qualitative data as numbers values and percentages)

Parameter	Value
Age at the time of examination (years)	8.21 \pm 2.45
Boys	27 (79.4%)
Body mass [kg]	23.08 \pm 6.77
Body surface area (BSA) [m ²]	0.88 \pm 0.17
Age at the time of Fontan procedure (years)	5.21 \pm 1.43
Time since the Fontan procedure (years)	2.90 \pm 2.72
Fontan procedure with an intracardiac tunnel	2 (5.9%)
Fontan procedure with an extracardiac tunnel	32 (94.1%)
Fontan procedure with a fenestration	32 (94.1%)
Previous interventional fenestration closure	24 (70.6%)
Fontan procedure without a fenestration	2 (5.9%)

We found a significant difference in the mean TAPSE between patients with present or closed fenestration (14.51 \pm 2.20 vs. 17.58 \pm 3.13, $p < 0.05$), and a significant MPI difference between girls and boys (0.65 \pm 0.19 vs. 0.47 \pm 0.14, $p < 0.05$).

Discussion

The importance of TDI in the evaluation of left and right ventricular systolic and diastolic function in children has increased [9–11]. However, few studies were performed

Table 2. Values of conventional echocardiographic parameters (quantitative data shown as mean \pm standard deviation)

Parameter	Value
TAPSE [mm]	16.85 \pm 3.14
MPI (for TrV)	0.50 \pm 0.17
E [cm/s]	77.82 \pm 20.53
A [cm/s]	63.35 \pm 20.83
E/A	1.26 \pm 0.37

TAPSE – tricuspid annular plane systolic excursion; MPI – myocardial performance index; TrV – tricuspid valve

Table 3. Values of tissue Doppler imaging parameters (quantitative data shown as mean \pm standard deviation)

Parameter	Value
S' [cm/s]	6.48 \pm 1.62
E' [cm/s]	9.89 \pm 2.45
A' [cm/s]	7.4 \pm 2.16
TDI MPI (for TrV)	0.62 \pm 0.12
E'/A'	1.41 \pm 0.43
E/E'	8.39 \pm 3.16

TDI – tissue Doppler imaging; MPI – myocardial performance index; TrV – tricuspid valve

to evaluate utility of TDI for the evaluation of systemic ventricular function in paediatric patients with functionally single ventricle. Available studies indicate significant systolic and diastolic dysfunction of the single ventricle compared to the control group, even if conventional echocardiographic techniques indicate normal ventricular function [12–14].

Systolic and diastolic dysfunction of the systemic ventricle as well as regional wall motion abnormalities may develop in patients with functionally single ventricle following the Fontan procedure. This is related to persisting abnormal filling of the ventricle that was previously volume overloaded. Diastolic dysfunction may be diagnosed based on a restrictive tricuspid inflow pattern identified by conventional echocardiography with calculation of the E/A ratio. However, this approach is not routinely used in children due to its dependence on cardiac preload, and thus on atrial pressure, and also due to possible fusion of E and A waves, such as during tachycardia [15–17]. In contrast to conventional echocardiography, parameters evaluated using TDI (E', A') are not dependent on filling pressures [18]. This may explain the absence of a statistically significant correlation between diastolic dysfunction parameters by TDI (E', E'/A') and conventional echocardiographic parameters (E, A, E/A) that was also found in our study. Similar results were reported by Watanabe et al. [5] who found a statistically significant correlation only in healthy children. In contrast, such a correlation was not found in patients

with congenital heart disease, particularly in those with elevated right ventricular and pulmonary artery pressures. We found a statistically significant relation only between A' and A, and between E/A and E/E' ratios.

In addition, statistical analysis in our study did not show a significant relation between TDI MPI and conventional MPI. However, similarly to the study by Roberson et al. [10], we found slightly higher TDI MPI values compared to conventional MPI. This is due to longer isovolumic contraction and relaxation times measured by TDI, resulting in higher a values in the MPI formula. An advantage of TDI MPI over conventional MPI is related to the fact that intervals are measured during a single cardiac cycle in one echocardiographic view, which eliminates the effect of heart rate variability on the calculated parameters. Harada et al. [16, 17] found that heart rate variability during an echocardiographic examination was greater than 10% in 59% of patients.

Systolic tricuspid annular velocity measured by TDI (S') is considered a good quantitative parameter used to evaluate right ventricular function in adults. Similarly to the study by Koestenberger et al. [19], we found a significant correlation with TAPSE. The latter evaluates systolic function of the inflow part of the right ventricle which remains relatively normal for the longest time in progressive ventricular dysfunction. Following fenestration closure, hemodynamic conditions of the Fontan circulation change, which indirectly affects systemic ventricular function. For this reason, we observed higher TAPSE values in patients with closed fenestration.

The E/E' ratio allows noninvasive assessment of ventricular end-diastolic pressure (VEDP) and evaluation of ventricular diastolic function. According to literature data, E/E' values above 12 may indicate elevated VEDP and impaired diastolic function [20]. In our study, E/E' values ranged from 4.4 to 17.5, and a value above 12 was noted in 14.7% of patients. We also found a positive correlation between the E/E' ratio and MPI.

Limitations of TDI are as follows: this technique reflects motion of only longitudinal and not circular myocardial fibres but this is not a significant limitation in the right ventricle, as its primary function is to move the atrioventricular valve towards the apex, and twisting and rotating motion is of minor importance; no angle correction is used; preload changes resulting from breathing have not been accounted for (to reduce potential bias, we averaged MPI values from three cardiac cycles).

Conclusions

No significant correlation found in children after Fontan procedure between diastolic function parameters and right ventricular MPI measured using TDI and conventional

echocardiographic parameters indicates that TDI is a technique complementary to conventional echocardiography in the evaluation of single right ventricle function in children. In addition, TDI does not depend on preload, and thus it can be speculated that this technique may identify ventricular dysfunction (mostly diastolic) at a stage when conventional echocardiographic parameters are still normal. Further studies in a larger number of patients are needed to support these conclusions.

Study limitations

Study limitations included a small patient sample that reduced the power of statistical analysis. The presented results are preliminary findings of our research.

Conflict of interests

None declared.

Streszczenie

Wprowadzenie. Trudności w echokardiograficznej ocenie funkcji pojedynczej komory, zwłaszcza o morfologii prawej komory, skłaniają do wykorzystywania w tym celu różnych dostępnych technik echokardiograficznych. Echokardiograficzna ocena stopnia zaburzeń hemodynamicznych, wpływających na funkcję komory systemowej, umożliwi nie tylko lepszą diagnostykę układu krążenia, ale pomoże także w ustaleniu wskaźników prognostycznych o istotnym znaczeniu w podejmowaniu dalszych decyzji terapeutycznych. Obecnie podkreśla się rolę wykorzystania tkankowej echokardiografii dopplerowskiej (TDI) u pacjentów pediatrycznych z sercem jednokomorowym. Jednak liczba przeprowadzonych dotychczas badań, służących ocenie przydatności tej metody w ocenie funkcji skurczowej i rozkurczowej komory systemowej po operacji metodą Fontana, pozostaje niewielka.

Celem pracy było określenie zależności między parametrami standardowego badania echokardiograficznego a TDI w ocenie funkcji czynnościowo pojedynczej prawej komory u dzieci z zespołem hipoplazji lewego serca (HLHS) po operacji metodą Fontana.

Materiał i metody. Badaniem objęto 34 pacjentów z HLHS po wieloetapowym leczeniu kardiochirurgicznym zakończonym operacją metodą Fontana. U każdego dziecka wykonano badanie podmiotowe i przedmiotowe, elektrokardiograficzne oraz echokardiograficzne w standardowych projekcjach w prezentacji M-mode, 2-D, CW, PW i CD, poszerzone o rejestrację z wykorzystaniem TDI. Analizie poddano wpływ czynników demograficznych i okołooperacyjnych na wybrane parametry echokardiograficznej oceny funkcji komory systemowej oraz określono zależności między parametrami badania echokardiograficznego i TDI w ocenie funkcji czynnościowo pojedynczej prawej komory u dzieci po operacji metodą Fontana.

Wyniki. Analiza statystyczna wykazała brak istotnej statystycznie korelacji między wskaźnikami funkcji rozkurczowej TDI (E' , E'/A') a wskaźnikami klasycznej echokardiografii (E , A , E/A) oraz między wskaźnikiem wydolności mięśnia sercowego (MPI) zmierzonym za pomocą TDI (MPI TDI) a MPI konwencjonalnym. Stwierdzono istnienie korelacji wskaźnika E/E' z MPI.

Wnioski. Brak istotnej korelacji między wskaźnikami funkcji rozkurczowej oraz MPI prawej komory u dzieci po operacji metodą Fontana określonymi za pomocą TDI a wskaźnikami klasycznej echokardiografii świadczy o tym, że TDI jest metodą uzupełniającą klasyczne badanie echokardiograficzne w ocenie zaburzeń funkcji czynnościowo pojedynczej prawej komory u dzieci. W związku z powyższym oraz biorąc pod uwagę brak zależności TDI od obciążenia wstępnego, można spekulować, że technika ta może wskazywać na zaburzenia funkcji komory (głównie rozkurczowej) przy jeszcze prawidłowych parametrach konwencjonalnego badania echokardiograficznego. Poparcie tych wniosków wymaga dalszych badań w większej grupie pacjentów.

Słowa kluczowe: czynnościowo pojedyncza komora, operacja Fontana, wrodzona wada serca, tkankowa echokardiografia dopplerowska, echokardiografia

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References

1. Sysa A. Pojedyncza komora. In: Kubicka K., Kawalec W. eds. *Kardiologia dziecięca*. Wydawnictwo Lekarskie PZWL, Warszawa 2003: 534–552.
2. Fredenburg T.B., Johnson T.R., Gohen M.D. The Fontan procedure: anatomy, complications and manifestations of failure. *RadioGraphics* 2011; 31: 453–463.
3. Malec E., Januszewska K. Operacja Fontana – gdzie jesteśmy, dokąd zmierzamy? *Kardiochir. Torakochir. Pol.* 2012; 2: 193–198.
4. Wahl A., Praz F., Schwarzmann M. et al. Assessment of right ventricular systolic function: Comparison between cardiac magnetic resonance derived ejection fraction and pulsed-wave tissue Doppler imaging of the tricuspid annulus. *Int. J. Cardiol.* 2011; 151: 58–62.
5. Watanabe M., Ono S., Tomomasa T. et al. Measurement of Tricuspid Annular Diastolic Velocities by Doppler Tissue Imaging to Assess Right Ventricular Function In Patients with Congenital Heart Disease. *Pediatr. Cardiol.* 2003; 24: 463–467.
6. Kapusta L., Thijssen J.M., Cuypers M.H.M. et al. Assessment of myocardial velocities in healthy children using tissue Doppler imaging. *Ultrasound Med. Biol.* 2000; 26: 229–237.
7. Szyszka A., Oko-Sarnowska Z., Siniawski H. et al. Podstawy metody i optymalizacji obrazu. In: Szyszka A., Siniawski H. eds. *Dopler tkankowy – podstawy*. MediPage, Warszawa 2008: 9–19.
8. Correale M., Totaro A., Ieva R. et al. Time intervals and myocardial performance index by tissue Doppler imaging. *Intern. Emerg. Med.* 2011; 6: 393–402.
9. Vitarelli A., Conde Y., Cimino E. et al. Quantitative assessment of systolic and diastolic ventricular function with tissue Doppler imaging after Fontan type of operation. *Int. J. Cardiol.* 2005; 102: 61–69.
10. Roberson D.A., Cui W. Right ventricular Tei index in children: effect of method, age, body surface area, and heart rate. *J. Am. Soc. Echocardiogr.* 2007; 20: 764–770.
11. Liu X.Q., Li W.Z., Wang Y.L., Ai Y. A study on atrioventricular annular movement in healthy children by tissue Doppler imaging. *Zhonghua Er Ke Za Zhi* 2006; 44: 738–742.
12. Cua C.L., Feltes T.F. Echocardiographic evaluation of the single right ventricle in congenital heart disease – results of new techniques. *Circ. J.* 2012; 76: 22–31.
13. Hershenson J.A., Zaidi A.N., Texter K.M. et al. Differences in tissue Doppler imaging between single ventricles after the Fontan operation and normal controls. *Am. J. Cardiol.* 2010; 106: 99–103.
14. Bassareo P.P., Tumbarello R., Piras A., Mercurio G. Evaluation of regional myocardial function by Doppler tissue imaging in univentricular heart after successful Fontan repair. *Echocardiography* 2010; 27: 702–708.
15. Ho C.Y., Solomon S.D. A clinician's guide to tissue Doppler imaging. *Circulation* 2006; 113: e396–e398.
16. Harada K., Orino T., Yasuoka K. et al. Tissue Doppler imaging of left and right ventricles in normal children. *Tohoku J. Exp. Med.* 2000; 191: 21–29.
17. Harada K., Tamura M., Toyono M. et al. Comparison of the right ventricular Tei index by tissue Doppler imaging to that obtained by pulsed Doppler in children without heart disease. *Am. J. Cardiol.* 2002; 90: 566–569.
18. Van der Hulst A.E., Delgado V., Ten Harkel A.D. et al. Tissue Doppler imaging in the left ventricle and right ventricle in healthy children: normal age-related peak systolic velocities, timings, and time differences. *Eur. J. Echocardiogr.* 2011; 12: 953–960.
19. Koestenberger M., Nagel B., Ravekes W. et al. Reference values of tricuspid annular peak systolic velocity in healthy pediatric patients, calculation of z score, and comparison to tricuspid annular plane systolic excursion. *Am. J. Cardiol.* 2012; 109: 116–121.
20. Menon S.C., Gray R., Tani L.Y. Evaluation of ventricular filling pressures and ventricular function by Doppler echocardiography in patients with functional single ventricle: correlation with simultaneous cardiac catheterization. *J. Am. Soc. Echocardiogr.* 2011; 24: 1220–1225.