IS FETAL ECHO USEFULL IN AN INAVSIVE THERAPY IN CHEST ANOMALIES?

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PRENAT CARDIO. 2013, DEC;3(4):15-22
DOI 10.12847/12133

Abstract

The aim of this study was to check whether echocardiography is useful in patients with thoracic anomalies undergoing an invasive therapy in utero.

Material and Methods: Retrospective analysis of 42 pregnant women and their fetuses (2003 - 2012), which, due to the chest anomalies had genetic ultrasound and ECHO and then were subjected to an invasive intrauterine therapy.

Results: The mean maternal age was 30.2 years, there were 18 high risk pregnancies and 24 low-risk pregnancies, the average gestational age at diagnosis was 28.2 wks (17-38), the average week of delivery was 35 wks (24-41), the average birth weight was 2700g (700 - 4050g). The average number of fetuses with chest anomalies undergoing therapy in utero in our center was 4.2 per year. The most common anomaly was hydrothorax, then CALM and DH and one case of AS. Anomalies coexisted with generalized edema, ascites and/or polyhydramnios. Most often shunts and/or decompression of pleural fluid and / or abdominal cavity were performed. Structural heart defects occurred in 6 fetuses and functional anomalies in echocardiography were recorded in 29 fetuses (73%).

Selected group of 19 fetuses had echocardiography before and after surgery. In 14 fetuses hemodynamic improvement was observed and in 5 patients fetal functional changes have persisted. The time from the last treatment to the delivery averaged was 40,2 days (2 to 140).

The follow-up was analyzed in a group of 37 fetuses: there were 2 intrauterine deaths, 11 deaths after delivery and 24 infants were discharged home. Mean hospitalization duration of the live-born infants was 23.7 days (1 -70). Hospitalization of 14 neonates with hemodynamic improvement after surgery was 25.5 days and in a group of five fetuses with no improvement after surgery, was mean 45.6 days.

Conclusions: The number of fetuses undergoing an invasive therapy due to anomalies of the chest during 2003-2012 remained at a similar level (an average of approximately 4 patients per year). Thoracic defects were often accompanied by functional anomalies in the circulatory system. Majority (73%) of fetuses had shown a significant improvement in cardiac efficiency after an invasive treatment. In the group of fetuses in which the interventional procedure has improved cardiovascular hemodynamics, average duration of hospitalization was shorter as compared to the group without haemodynamic improvement (25,5 days versus 45,6), however there was no statistically significant difference.

Key words: *monitoring, prenatal echocardiography, invasive therapy, fetal chest*

INTRODUCTION

These days in utero therapy in chest anomalies is an accepted approach. In specialized centers , dealing with fetal anomalies on a daily basis, echocardiography is a routine examination.

Despite this, there are no original papers, which would describe the usefulness of prenatal echocardiography in monitoring of such cases.

This paper is an attempt of a new approach to cooperation between the prenatal surgery and the use of echocardiographyin selected patologies of fetal chest.

How to cite this article:
Pietrzyk I, Moczulska H, Słodki M, Szaflik K, Respondek-Liberska M.
"Is fetal echo usefull in an inavsive therapy in chest anomalies?".
Prenat Cardio. 2013, Dec;3(4):15-22

MATERIAL AND METHODS

We performed a retrospective analysis of the data collected in documentation of examinated featuses, which were diagnosed (genetic ultrasound + echo examination) due to chest anomalies in Polish Mother's Memorial Hospital Research Institute, and then treated with in utero therapy in the Department of Gynecology, Reproduction and Fetal therapy (head of the department: prof Krzysztof Szaflik). Also the data from discharge cards of the neonates were analyzed (Head of the Department of Neonatogy prof

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Submitted: 2015-09-22; accepted: 2015-09-27

Ewa Gulczyńska, head of the Department of Intensive Therapy and Congenital Malformation of the Newborns and Infants prof. Iwona Maroszyńska). The material for analysis contained 42 cases of fetuses, in which invasive intrauterine treatment had been introduced (2003-2012).

RESULTS

Average age of the gravidas was 30.2 yrs (min 24, max 39). 24 patients (57%) were described as 'low-risk' prenancies, whilst 18 patients (43%) were 'high-risk'- due to past medical history, age > 35yrs or previous miscarriages. Mean gestational age at the time of diagnosis was 28.2 wks according to LMP and 28 wks according to biometry (min. 17 wks, max 38 wks). Average gestational age at the moment of delivery was 35 wks (min. 24 wks, max 41 wks). Average body weight of the neonate was 2700g (min. 700g, max 4050g). In the analyzed group 20 neonates were female and 17 were male.

The incidence of specific chest anomalies in analyzed cases in 2003-2012 is presented in Graph 1. Most anomalies was reported in 2011 (n=11), least in 2004 (n=1). Average number of fetuses with chest anomalies, undergoing in utero therapy, was 4.2 per year.

In the analyzed material the most common chest anomaly, in which intrauterine therapy was performed, was hydrothorax: n=24, which was 30% of all extracardiac anomalies. Next in frequency were: cycstic adenomatoid lung malfromation (CALM) n=13 (16%), diaphragmatic hernia (DH) n=5 (6%) and aortic stenosis (n=1) (intrauterine therapy was performed in Warsaw, but the patient had been diagnosed in our Center and then postnatally treated in Lodz). Those deffects were accompanied by generalized edema (n=14, 18%), ascites (n=5, 11%), polihydramnion (n=14, 18%) (Diagram 2 and 3).

The most common procedure were shunt implantation and fluid decompression from pleural cavity and/or abdomen. (Diagram 4).

Most of the procedures were performed in ICZMP, in the Department of Gynecology, Reproduction and Fetal therapy, 3 procedures were performed outside of the Insitute- 2 in Belgium (trachea occlusion), 1 in Warsaw (baloon valvuloplasty performed by the team of prof. Joanna Szymkiewicz-Dangel).

Heart anomalies were diagnosed in 6 fetuses (n=6, 14%), 36 featuses (86%) had normal heart anatomy. Types of hearts anomalies in 6 fetuses were summarized in Table 1.

Functional changes were registered in ECHO examination of 29 fetuses (69%), in 13 featuses (31%) changes were not observed.

In the group with functional changes in ECHO examination, following anomalies were observed: disproportion of the heart cavities (n=12, 29%), tricuspid regurgitation (n=11, 27%), heart muscle hypertrophy (n=9, 22%), bright spot (n=5, 12%), cardiomegaly (n=3, 7%) and arrythmia (n=1, 3%) (Diagram 6).

In the analyzed material (n=42), 27 (64%) fetuses had ECHO examinations before and after the procedure. The rest of the fetuses (n=15, 36%) had only one ECHO examination: only before or only after the intrauterine procedure.

In the group with two ECHO examinations (n=27), in 19 fetuses heaemodynamic changes were observed. Dynamics of the functional changes was analyzed: in 14 featuses after the intrauterine procedure improvement of the heamodynamical status was observed, in 5 fetuses functional changes have not subsided. Functional changes in those fetuses are summarized in Table 2 and Diagram 7.

In the group of 14 fetuses with improvement of heamodynamic function after intrauterine procedure, in 3 fetuses occurred death, 10 neonates were discharge from the hospital, in 1 case we were not able to acquire any follow-up information.

In the group of 15 fetuses, which had only one ECHO examination before or after in utero therapy, functional changes were observed in the examination in 10 featuses, in 5 featuses changes were not observed. In the group with observed functional changes, in 2 fetuses occurred death, 5 neonates were discharged from the hospital, in 3 cases we were not able to acquire any information about the follow up.

In the whole group n=42 fetuses, karyotype analysis was performed in 13 fetuses (31%), in 6 cases it was a normal female karyotype, in 6 cases- normal male karyotype, 1 abnormal karyotype 47,XY.

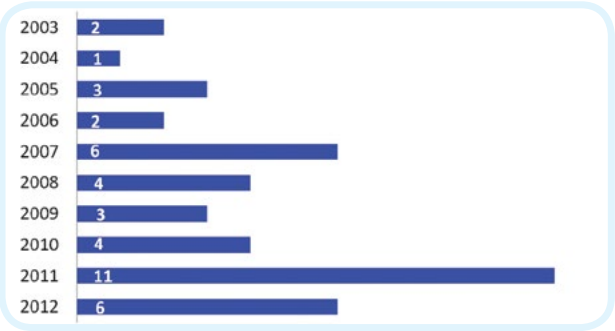


Chart 1. Prevalence of chest anomalies in 42 fetuses in years 2003-2012.

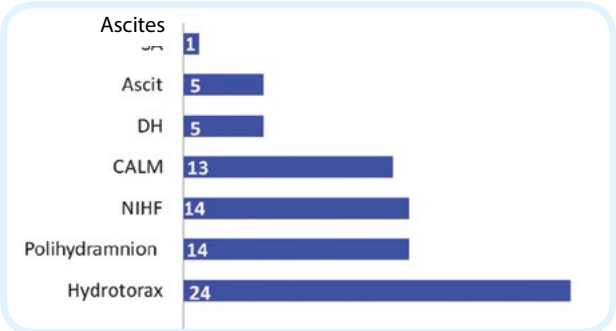


Chart 2. Main diagnoses in 42 fetuses with an invasise therapy due to chest anomalies in our center

Lp	*Cardiac dgn*	ECM	*Delivery*	*Birth weight*	Apgar	*Days after delivery in the hospital*	*Home*	*Death*
1	DORV	*Hydrothorax, lung hypoplazja, hepatomegaly/ hepatitis, hygroma colli, Trisomia 21*	*No info.*					1?
2	Aortic valve stenosis, cardiomegaly, MR, hypertrophy, BS/LV	*Oligohydramnion*	*CC*	3000g	8	53		1
3	CHD – nietypowy przebieg Abnormal dilated IVC	*DH, pyelectasis bil*	*CC*	1815g	1	1		1
4	CHD, hypoplazja aorty CoA?, Dysproportion in 4 chamber view and hypoplastic aortic arch	*Hydrothorax*	*CC*	2580g	8	50	1	
5	CHD - VSD, pulm stenosis, BS, hypertrophy	*Hydrothorax, hygroma coli, IUGR hydronephrosis dex, pyelectasis sin*	*CC*	1680g	3	45	1	
6	CHD- anomalia łuku aorty, zastawki a-v na tym samym poziomie, Dysproportion in 4 chamber view and hypoplastic aortic arch, TR	*Hydrothorax, polihydramnion, skin oedema, sandal gap*	*CC*	2730g	8	13	1	

Table 1.Heart anomalies in group of 6 fetuses out of 42

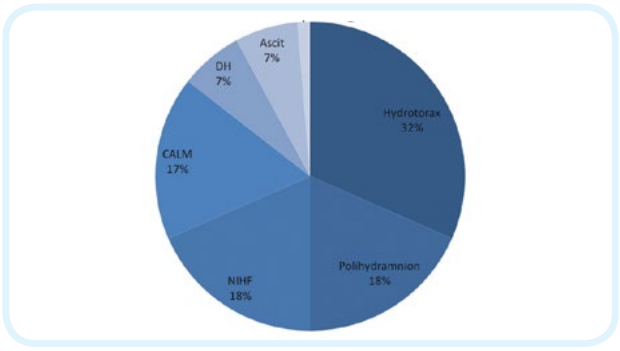


Chart 3. Percetage of main diagnoses in group of 42 fetuses - patients

Information about the deliveries and follow ups were analyzed in 37 fetuses. The biggest group were newborns delivered via C-section (n=24, 65%), vaginal delivery occurred in 12 cases (n=12, 32%), in 1 case forceps delivery was needed. 2 intrauterine deaths occurred, 11 deaths occurred in neonatal period, 24 neonates were discharge home (Diagram 8).

Average time period from the last procedure until the delivery was 40.2 days (min 2 days, max 70 days).

Average time of the hospital stay for the neonates with two ECHO examinations was 23.4 days, for the neonates without ECHO follow-up was 21 days.

Normal distribution of a continuous variable (length of the hospitalization) had been verified with Shapiro- Wilk test, statistical characteristics presented as a median,interquartile range IQR and range (Min- Max). For an intergroup comparisons of hospitalization length U Mann-Whitney test was used, and for comparisons of distributions of discrete variables and quality- Pearson's chi-square test and Fisher's exact test. Calculations were performed with Statistica 10 software (StatSoft, Tusala OK, USA), as the level of statistical significance taking $p \leq 0.05$.

Taking into account the analysis of all the records, compared groups did not differ significantly in terms of length of hospitalization (Diagram 9), although they differed in terms of the average length of stay at a similar standard deviation (Table 3). No significant intergroup differences were found also after exclusion from the analysis cases followed with death or hospitalization lasting less then one day.

There were no significant intergroup differences in terms of number of deaths (3/13 in the group with improvement vs 3/6 in the group without improvement p=0,257).

DISCUSSION

Literature data that discuss the results of ECHO examinations in fetuses undergoing invasive therapy are a few. Many papers are devoted to analysis of specific cases, but only a few discuss the results of echocardiographical monitoring of fetuses undergoing in utero therapy due to chest anomalies. Literature focuses mainly on monitoring individual fetuses with a selected anomaly. One case involved CALM (1), second increasing hydrothorax (2). Both fetuses were

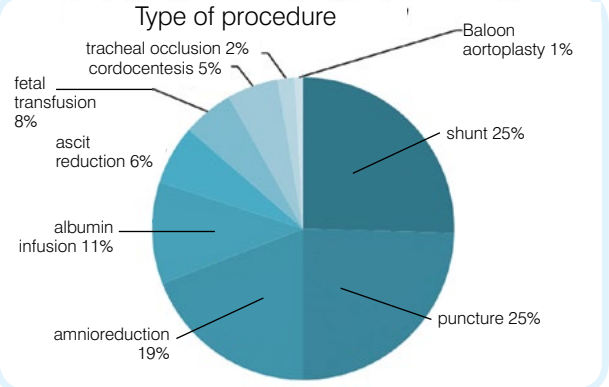


Chart 4. Type of procedures in group of 42 fetuses with chest anomalies, in material from Department for Fetal Malformations Diagnoses and Prevention in years 2003-2012

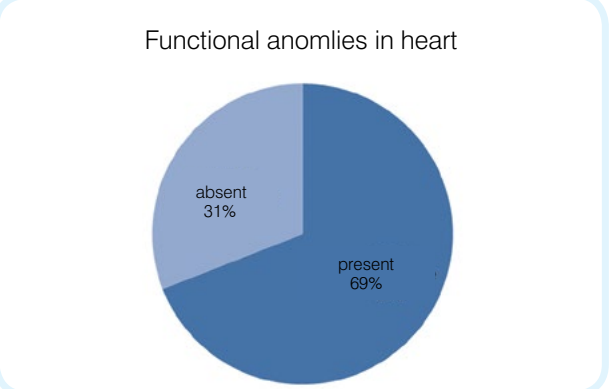


Chart 5. Analysis of functional heart anomalies in echocardiography in 42 fetuses treated due to chest anomalies

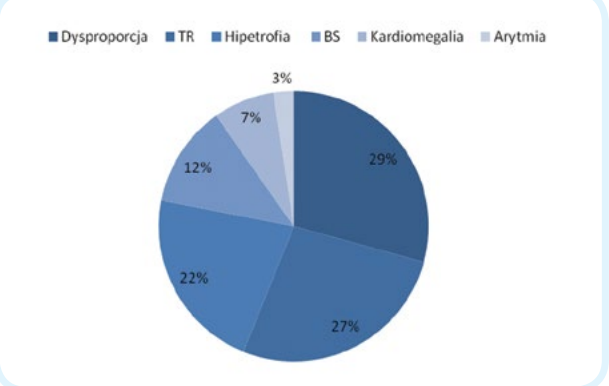
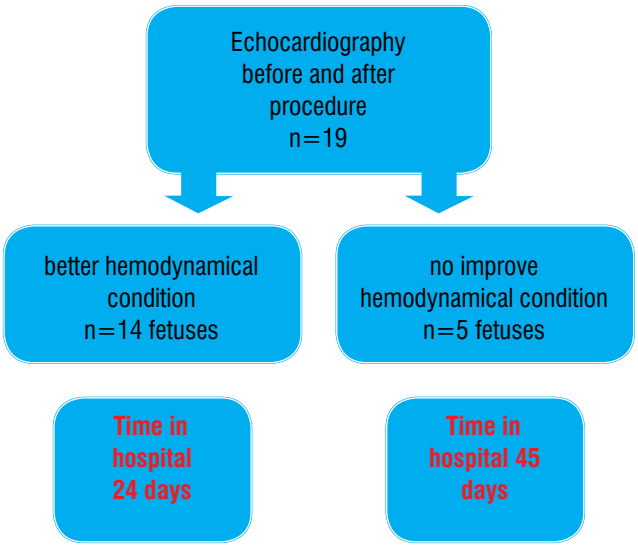


Chart 6. Percentage of functional heart anomalies in echocardiography in 29 fetuses with chest anomalies treated in utero

diagnosed and treated in Department of Diagnoses and Prevention Fetal Malformations , decompression and shunt implantation were performed at the Department of Gynecology, Reproduction and Fetal therapy . Despite steadily increasing number of publications devoted to chest anomalies and in utero therapy (3,4,5,6,7,8,9,10), literature concerning echocardiographical monitoring in intrauterine therapy is still infinitesimal.

That's why this paper is innovatory and doesn't allow us to relate our results to the experiences of other centers (13).

Chart 7. Analysis of the group of 19 fetuses who had echocardiography before and after invasive procedure



Fetal chest anomalies are subject to very high mortality. In many cases, the attempt of intrauterine therapy, which aims to reduce destructive consequences of the defect and improve fetal condition, is the only chance of survival, and whats more- often also a chance for better life quality and fewer complications in postnatal period.

In the above work, 42 cases were analyzed, which have undergone invasive in utero therapy in 2003-2012 due to chest anomalies. In all cases ECHO examination was performed in Department of Diagnoses and Prevention of Fetal Malformations, in accordance with the approved protocol (14). The most common anomalies, due to which invasive therapy was implemented, were hydrothorax (n=24), CALM (n=13), diaphragmatic hernia (n=5) and one case of critical aortic stenosis. The case of aortic stenosis was taken into account in order to present the full spectrum of possible procedures in fetal chest anomalies. It should be emphasized, that lodzian school of prenatal cardiology prefers in such cases intervention at 1st day of postnatal life (or in the 1st hour of postnatal life) rather than baloon valvuloplasty in fetuses.

Also coexisting anomalies were analyzed: generalized edema (n=14), polihydramnion (n=14), peritoneal exudate (n=5). The most common procedure were (ordered according to frequency): shunt implantation: pleuro- amniotic and peritoneal-amniotic, fluid changes decompression. Significant majority of the procedures was performed in Polish Mother's Memorial Hospital Research Institute,

in the Clinic of Gynecology, Reproduction and Fetal therapy by prof. Krzysztof Szaflik. Two treating procedures of tracheal occlusion were performed in Belgium in prof. Deprests clinic. One procedure of a baloon valvuloplasty was performed in Warsaw, by the team of prof. Joanna Szymkiewicz- Dangel, but the directing and monitoring center was Polish Mother's Memorial Hospital Research

Tabela 2. Zestawienie zmian czynnościowych przed i po zabiegu in utero.
Table 2. Functional abnormalities before and after invasive therapy in utero

Lp.	Anomalia w badaniu echo *Anomaly in fetal ECHO*	Przed zabiegiem *Before an invasive procedure*	Po zabiegu *After an invasive procedure*	Liczba dni hospitalizacji *Days of hospital stay*	Dom / *Home discharge*	Zgon / *Death*	Poprawa / *Improvement*	Brak poprawy *No improvement*
1	*CALM II*	*Dextraposition, HA/CA 0,19*	*Dextraposition, HA/CA 0,29*	33	1		1	
2	*CALM II, lung tumor*	*Sinistroversion, dysproportion, TR, PE, FO obs*	*Sinistroversion, Dysproportion*	35	1		1	
3	*CALM, ascites, lung hypoplazja*	*Dextroposition, Hypertrophy, FO obs*	*Dextroposition*	brak			1	
4	*Hydrothorax, polyhydramion, ascites, skin oedema*	*Premature Atrial Contractions, Hypertrophy*	*No changes*	13	1		1	
5	*CALM I*	*Levoposition, HA/CA 0,17*	*Levoposition, HA/CA 0,23*	7	1		1	
6	*Hydrothorax, NIHF, polyhydramnion*	*TR*	*TR trivial*	62	1		1	
7	*Hydrothorax, ascites, polyhydramnion*	*Hypertrophy, Dysproportion*	*Dysproportion*	1		1	1	
8	*Hydrothorax, NIFH,*	*HA/CA 0,15, Dysproportion*	*HA/CA 0,32*	62	1		1	
9	*CALM I, polyhydramion*	*Dextraposition, TR, MR*	*Dextraposition, TR trivial*	1		1	1	
10	*Hydrothorax, ascites*	*Dextraposition, BS, TR*	*No changes*		1		1	
11	*Hydrothorax, HIHF, skin oedema*	*TR, PE ,*	*TR*	29	1		1	
12	*Hydrothorax, ascites – polyhydramnion, skin oedema*	*TR, Dysproportion*	*No changes*	1		1	1	
13	*CALM II*	*Dextraposition, Dysproportion, Hypertrophy*	*Dextraposition dysproportion*	18	1		1	
14	*CALM I*	*TR, MR, hypertophy, dysproportion, Fo obs*	*TR, hypertrophy, dysproportion*	28	1		1	
15	*Hydrothorax, cystic hygroma*	*Abnormal blood flow in DV and HV echogenic blood in heart chambers, hepatic veins,*	*Abnormal blood flow in DV and HV echogenic blood in heart chambers*	1	1			1
16	*Aortic valve stenosis*	*MR, hypertrophy, BS, TR*	*MR, hypertrophy, BS, TR, cardiomegaly, PE*	53		1		1
17	*DH, polyhydramnion,*	*Dextraposition, Dysproportion,*	*Dextraposition, dysproportion, TR*	57	1			1
18	*CALM I/II*	*Dextraposition, hiperkinesis*	*Dextraposition, hiperkinesis*	27	1			1
19	*Hydrothorax, ascites NIHF*	*NHS*	*Cardiomegaly, MR, TR*	1		1		1
Total:					13	5	14	5

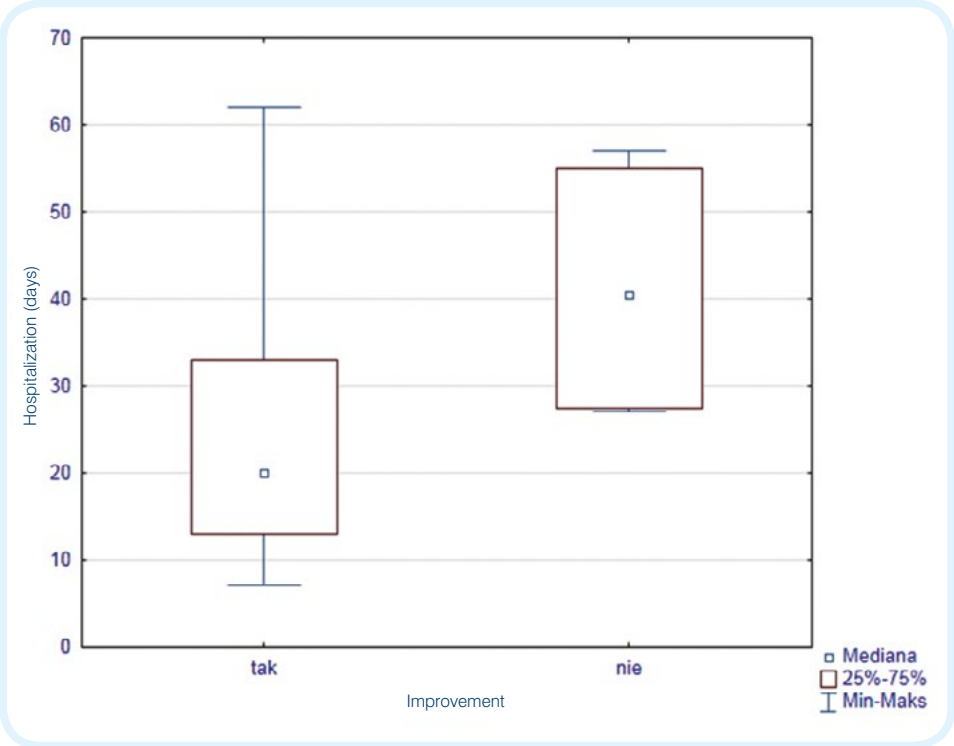


Chart 9. Mean and standard deviation in group of fetuses with haemodynamic improvement after procedure ("tak"= yes; improvement after procedure;"nie" = no; no improvement after procedure)

Institute, implementing under the aegis of Ministry of Health "Program of complex diagnostics and intrauterine therapy in prevention of consequences and complications of malformations and fetal diseases- as an element of improvement of health of fetuses and newborns for years 2009-2013". In the confines of this Program, early diagnostics and implementation of proper therapy were possible in many fetal defects in pregnancies all over Poland. Number of fetuses, which are the topic of this analysis, was 4.2 per year- the most in 2011 (11 patients), the least in 2004 (1 patient).

In the examined group of 42 fetuses, 6 fetuses were diagnosed with a heart anomaly, but relatively simple, not constituting contraindication for in utero therapy due to chest anomaly. In this group of 5 fetuses there were no heart anomalies, which would be considered as most severe or critical. Those were malformations, in which cardiosurgical approach in neonatal period isn't required. In one fetus critical heart malformation was diagnosed, which was life threatening and thus the patient was referred to the center in Warsaw for an attempt of baloon valvuloplasty of the aortic valve. Despite technically successful procedure, despite continuing the pregnancy with pharmacological support, planned delivery in obstetric and cardiological center, despite re-valvuloplasty in the newborn, in this patient symptoms of irreversible pulmonary hypertension occurred, followed by death in 56 day of postnatal life.

In 36 patients heart anatomy was normal, but in ECHO examination functional changes of various intensity were observed. Manifestation of heart failure can be various:from a very subtle symptoms (TR, MR), cardiomegaly or -conversely- small, constricted heart, to even generalized edema. In the examined group of 42 fetuses, functional changes were spotted in 29 fetuses, that accounted for almost 29% of the tested population. The most common was a disproportion of the heart cavities (n=12) and tricuspid regurgitation (n=11), cardiac muscle hypertrophy (n=9), cardiomegaly (n=3), one case of arrythmia, bright spot was observed in 5 fetuses.

Bright spot was included into functional changes, because in some cases regression of the bright spot was observed.

In the subgroup of 19 fetuses with functional changes, there was a group of 10 patients, in which the ECHO examination was performed before and after intrauterine intervention; improvement of cardiovascular status was observed in 14 fetuses (73%).

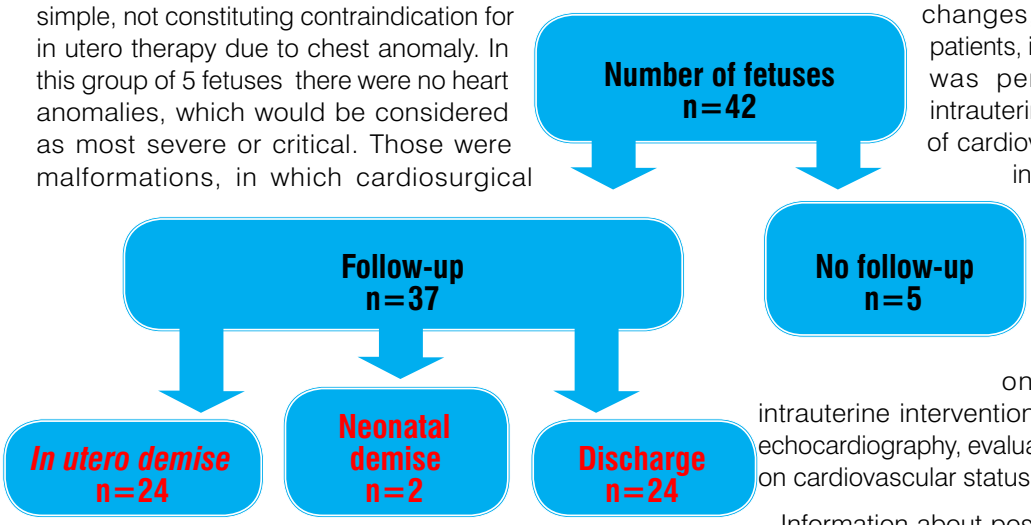


Chart 8. Follow-up of fetuses from study group n=42

The next group of fetuses that presented functional changes was the group of 10 fetuses, in which ECHO examination was performed only once- before or after intrauterine intervention. Because of lack of control echocardiography, evaluation of influence of intervention on cardiovascular status was impossible.

Information about postnatal period was acquired in 37 cases. Newborns were mostly delivered via C-section

Table 3. Comparison of days of hospital stay for newborns with prenatal improvement versus no improvement after an invasive procedure

Days of hospital stay	Nr of cases	Mean	Std	Min-Max	Mediana
Newborns after prenatal improvement in heart evaluation after prenatal invasive procedure	14	24,45	15,629	7-62	20
Newborns after no improvement in heart evaluation after prenatal invasive procedure	5	45,67	16,289	27-57	53

(n=24), in 12 cases vaginal delivery occurred, in 1 case forceps delivery was needed.

In the group of 37 fetuses with known postnatal history, in 13 cases death occurred (2 intrauterine, 11 in neonatal period), 24 newborns were discharged home. Average time of neonatal hospitalization in the group with prenatal hemodynamic improvement was 24.45 days (STD 15.6), median 20. In the group without prenatal improvement it was 45 days (STD 16.2), median 53. Although with statistical tests no difference statistically significant had been noted, those data seems to be interesting for future investigation . Maybe increase number of observations of monitored fetuses, undergoing intrauterine procedures due to chest anomalies, would allow to better objectify the influence of resolving heaemodynamical changes in fetuses on hospitalization length.

Due to the small size of individual groups, we couldn't analyze the influence of drugs taken by gravidas on haemodynamic status of the fetus. It is possible, that observed functional changes can be also a result of drug administration.

Since the duration of a neonatal hospitalization is an important economic indicator, it seems that early introduction of the therapy and documentation of its' effectiveness (hrough improvement of haemodynamic status of the fetus) may be an important prognostic indicator in the future.

Fetal gender was not an important factor in the occurrence of chest anomalies, there was no significant domination of either sex (19 girls and 17 boys).

CONCLUSIONS:

The number of fetuses undergoing invasive intrauterine therapy due to chest anomalies reminded during the period 2003-2012 at a similar level (about 4 cases per year), with a single peak in 2011 (11 cases).

Chest anomalies were often accompanied by functional changes in cardiovascular system, observed in ECHO examination, from singular to plural, while in 73% significant improvement of circulatory status after the intervention.

Most of the patients (64% of newborns) were discharged home and the time of hospitalization after prenatal hemodynamical improvement was two times shorter than in group without this improvement (differences in mean and median were observed, with similar STD, although with no statistical significance).

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Financing: The research was not financed from the external sources
Conflict of interest: The authors declare no conflict of interest and did not receive any remuneration