Original Paper

Ultrasound Evaluation of Fetal Biometry and Doppler Parameters in the Third Trimester of Pregnancy Suspected of Intrauterine Growth Restriction

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ABSTRACT: Purpose. The purpose of this study was to investigate fetal biometry and Doppler parameters in the third trimester of pregnancy with suspected restriction of fetal growth as potential predictors of unfavorable neonatal status. Material/Methods. The uterine artery, umbilical and middle cerebral artery, cerebroplacental ratio (CPR), and estimated fetal weight (EFW) were evaluated in a cohort of 126 pregnancies that resulted in the birth of a fetus <10 percentiles (SGA). Results. The demographic data of the studied cases did not show a significant difference between the parameters studied in the two study groups: Late SGA fetuses and Early SGA fetuses. Analyzing fetal biometry we found a significant difference for some parameters in relation to the two study groups. Our study showed that the Early SGA fetuses group had a lower birth weight, a lower gestational age at birth, an increase in the incidence of premature birth with an increase in Doppler abnormal incidence. Conclusions. Ultrasound examination and Doppler monitoring provide a non-invasive repetitive method for supervising fetuses with growth restriction in order to apply an adequate management.

KEYWORDS: intrauterine growth restriction, Doppler, fetal compromise

Introduction

Fetal intrauterine growth restriction (IUGR) is defined as an ultrasonographic estimated fetal weight (EFW) less than the 10th percentile for gestational age, identified as small for gestational age (SGA) fetuses [1,2].

In the Early onset IUGR (<32 weeks of gestation), the clinical standard for SGA fetuses identification is umbilical artery Doppler (UA) and abdominal circumference (AC) <10 percentile [3], and these SGA fetuses are associated with adverse perinatal outcomes [4,5].

Although for a long time, SGA with normal Doppler UA was considered a non-pathological condition, it is now accepted that such fetuses include a fairly high rate of late-onset forms of SGA, leading to an increased risk of adverse perinatal outcome [6,7]. The antenatal identification of the SGA fetus is extremely important for improving the perinatal outcome of pregnancies with risk factors and suspicion of growth restriction.

Doppler velocities of placental circulation improve the diagnosis of growth restriction which is due to placental dysfunction and can be used as a specific clinical tool if a placental insufficiency may lead to IUGR [8].The consensus for defining early and late IUGR was Delphi procedure. For early IUGR (<32 weeks), three parameters were established: abdominal circumference <3rd percentile, estimated fetal weight <3rd percentile and absent end-diastolic flow in the umbilical artery and four more additional parameters: AC or EFW <10th percentile, pulsatility index (PI) >95th percentile in UA or uterine artery (UtA).

For late IUGR (≥32 weeks), two individual parameters (AC or EFW <3rd percentile) and another four additional parameters (EFW or AC <10th percentile, AC or EFW crossing centiles

by >2 quartiles on growth charts and cerebroplacental ratio (CPR) <5th percentile or UA-PI >95th percentile) have been established [9]. However, a lot of SGA children remain unnoticed until birth, even when routine third-trimester ultrasound is performed [10].

Materials and methods

We conducted a prospective study that included a group of 126 patients studied between October 2015 and December 2017. Inclusion criteria were singleton pregnancy with gestational age correctly dated in the first-trimester; fetal biometry with an estimated fetal weight below the10[th] percentile in the third trimester of pregnancy (30.6-32.6 weeks) and at birth; fetus alive at the time of ultrasound examination. Exclusion criteria were multifetal pregnancy, major congenital abnormality or chromosomal abnormality, infection status.

EFW and percentile were calculated by software package using the parameters of fetal biometry. Fetal umbilical artery (UA) and middle cerebral artery (MCA) flow velocity were assessed using color Doppler studies. Uterine artery velocimetry was recorded just cranial of the apparent crossover with the external iliac artery. The cases were organized in two study groups, one group with Late SGA fetuses and one group with Early SGA fetuses. We considered early onset SGA fetuses those who had <32 weeks of gestation, an abdominal circumference <10[th]percentileand umbilical artery Doppler pulsatility index >95[th]percentile.

We defined an adverse perinatal outcome as Apgarscore of <7 at 1 min, admission to NICU, birth weight of <10th percentile at delivery, gestational age of <37 weeks at delivery.

Statistical analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), together with the XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA) for processing the data.

To test the normality of the data we used the Anderson-Darling test. Because the numerical variables investigated had a normal distribution of data, we were allowed to use parametric statistical tests (e.g. Student's t test) and the results were summarized as mean value±standard deviation. We used the Chi square test ($\chi 2$) to assess early or late SGA influence over the analyzed parameters.

Results

The demographic data of the studied cases did not show a significant difference between the parameters studied in the two study groups: Late SGA fetuses and Early SGA fetuses. We noticed only a higher rate of Early SGA fetuses at nulliparous women (71.42%) than the Late SGA fetuses group at which the nulliparous rate of this category was 58.16%.

Gestational age at delivery was significantly lower, 36.7±0.951 weeks vs. 37.3±1.116 weeks in pregnancy with Early SGA fetuses vs. Late SGA fetuses. Preeclampsia and Pregnancy Induced Hypertension at current pregnancy was more frequent in the Early SGA fetuses group (17.85% and 21.42% respectively) than the Late SGA fetuses group (10.20% and 13.26% respectively). The rest of the studied parameters (maternal age at inclusion, body mass index, smoking status) did not show significant differences in values. Demographic data are presented in Table 1.

Table 1.Demographic data of the studied cases

Parameters	Late SGA fetuses (n=98)	Early SGA fetuses (n=28)	p value (Student/Chi^2)
Maternal age at inclusion in years (M±SD)	28±6.316	26±6.438	0.153
Parity (%)			0.204
Nulliparous	58.16%	71.42%	
1–2	41.83%	28.57%	
Gestational age at delivery in weeks (M±SD)	37.3±1.116	36.7±0.951	**0.007**
Body mass index (M±SD)	24.2±1.999	24±1.551	0.576
Smoking Status (%)	16.32%	17.85%	0.848
Preeclampsia at the current pregnancy (%)	10.20%	17.85%	0.270
Pregnancy Induced Hypertension at the current pregnancy (%)	13.26%	21.42%	0.287

Analyzing fetal biometry we found a significant difference for some parameters in relation to the study groups. Thus, the EFW percentiles at the routine third trimester of pregnancy ultrasound examination in the Early SGA fetuses group were lower than the Late SGA fetuses group (8±1,290 and 10.5±1,621 respectively). This difference was also maintained with respect to the birth weight percentile, all cases being selected taking into account that the birth weight was <10 percentile, remarking a percentile of 8±0.900 in the Early SGA fetuses group versus 9±1.268 in the group Late SGA fetuses. AC percentiles for Late SGA fetuses were 10±5.972 vs. 5±5.487 in the Early SGA fetuses group. In terms of neonatal outcome, we did not notice significant differences between the two study groups, but we noticed an Apgar score of 7 to 1 minute and a higher admission to NICU for the Early SGA fetuses group (57.14%) versus Late SGA fetuses group (29.59%).

Doppler velocimetry was performed on the uterine artery, the umbilical artery, the middle cerebral artery, the presence of an abnormal Doppler being more frequent in the Early SGA fetuses group than the Late SGA fetuses.

We included uterine artery doppler in growth restricted fetus monitoring to detect fetuses at increased risk through the persistence of an early diastolic notch or by increased vascular impedance in the third trimester in the uterine artery. We noticed an increase in Doppler abnormal frequency in cases with Early SGA fetuses (39.28%) vs. only 12.24% in the Late SGA fetuses.

Umbilical artery abnormal Doppler that reflects rising placental vascular resistance was present in a double percentage in the Early SGA fetuses group versus Late SGA fetuses (57.14% versus 27.55%) including cases with Absent / Reversed end diastolic flow.

Doppler abnormalities of middle cerebral arteries were observed in SGA pregnancies, in a higher percentage (57.14%) in early-onset of fetal restriction than in late restriction (19.38%).

Doppler indices like UA-PI >95 percentiles, showed almost equal values, with no significant differences in both study groups.

Because CPR includes data not only on placental status but also on fetal response, it may be more useful in predicting perinatal outcome.

Fetuses with CPR <1 in our study had a lower birth weight, a lower gestational age at birth, an increase in the incidence of premature birth, an increase in poor neonatal outcome, particularly in the group Early SGA fetuses (Fig.1,2).

Table 2. Intrauterine ultrasound biometry and Doppler parameters

Parameters	Late SGA fetuses (M±SD) n=98	Early SGA fetuses (M±SD) n=28	p value (Student/ Chi^2)
Fetal biometry			
AC percentile(M±SD)	10±5.972	5±5.487	0.0001
EFW percentile at routine third trimester of pregnancy ultrasound examination (M±SD)	10.5±1.621	8±1.290	<0.0001
Fetal weight at birth in grams	2505±213.337	2282.5±166.028	<0.0001
Fetal birth weight percentile(M±SD)	9±1.268	8±0.900	<0.0001
Neonatal outcome			
1 minute Apgar score (M±SD)	7±1.158	7±0.915	0.962
5 minute Apgar score (M±SD)	8.5±0.894	8±0.886	0.012
Admission to NICU (%)	29.59%	57.14%	0.007
Doppler indices			
UtA-abnormal Doppler	12.24%	39.28%	0.001
MCA-abnormal Doppler ±Absent/Reversed EDF (%)	19.38%	46.42%	0.004
UA-abnormal Doppler ±Absent/Reversed EDF (%)	27.55%	57.14%	0.0035
UA-PI>95 percentile	95±20.564	96±20.061	0.818
CPR <1 (%)	17.34%	42.85%	0.005

AC: abdominal circumference; EFW: estimated fetal weight; NICU: neonatal intensive care unit; EDF: end diastolic flow; MCA: middle cerebral artery; UA: umbilical artery; PI: pulsatility index; CPR: cerebro-placental ratio
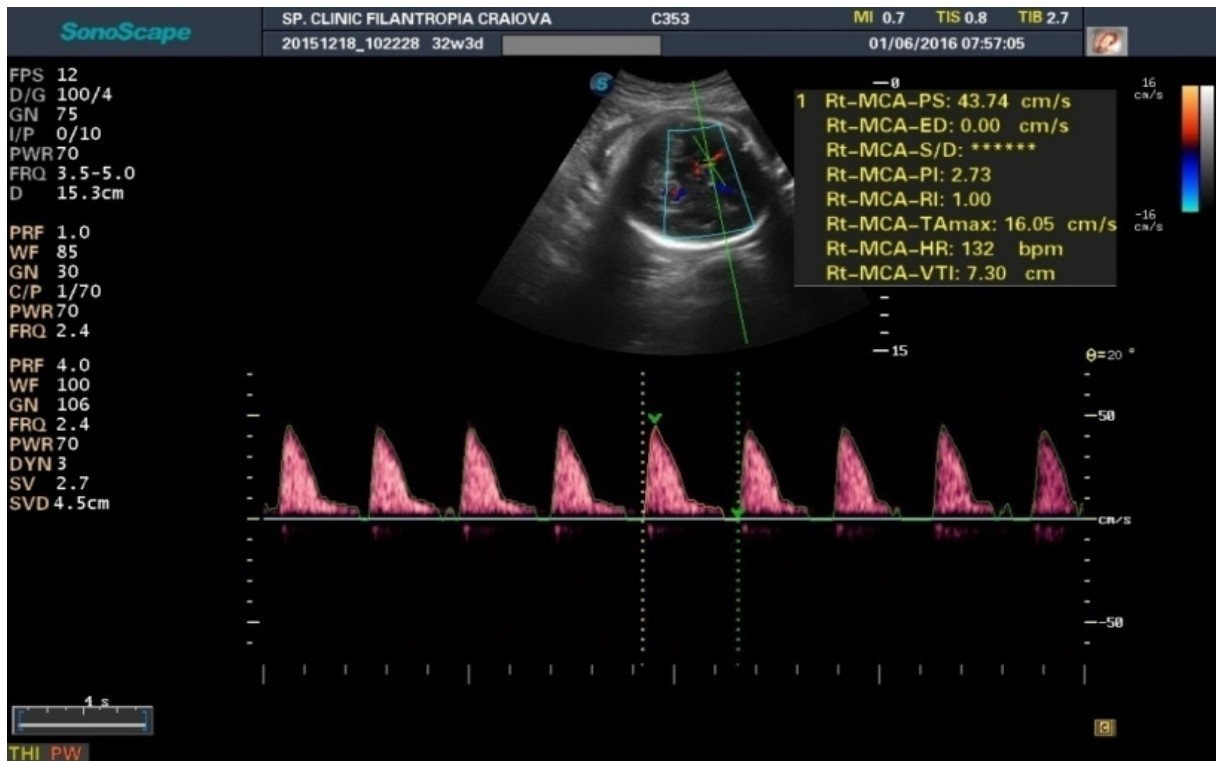
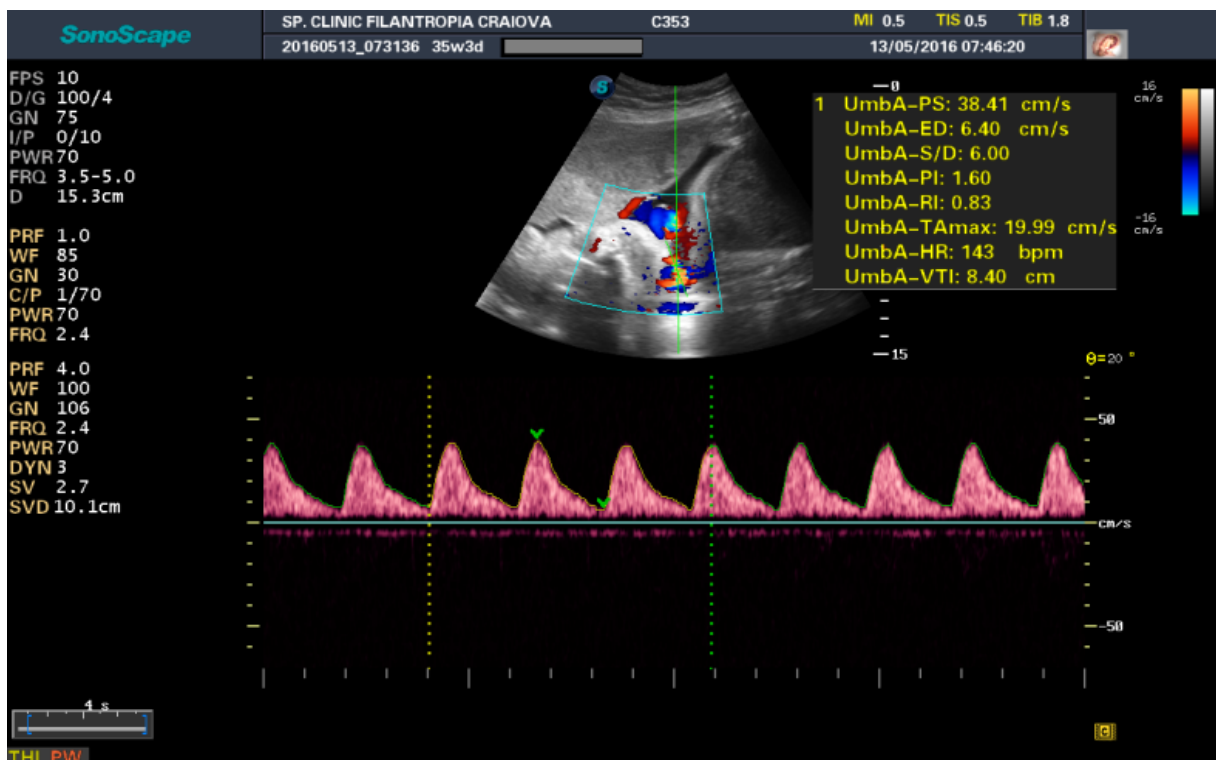***Fig.1. MCA-PI=2.73> 95 percentile; absent end diastolic flow; MCA-RI=1; CPR>5 percentile; SGA<3 percentile***

Fig.2. UA-PI=1.60 >95percentile; UA-RI=0.83 >95 percentile; CPR <5percentile; SGA=6 percentile

Discussion

Intrauterine growth restriction is associated with increased risk of perinatal and long-term mortality and morbidity compared to newborns with normal growth.

Fetal growth restriction remains a challenge in clinical practice worldwide, and the different etiopathogenesis of early and late forms of fetal growth restriction, with sometimes different evolution of perinatal outcomes, further complicates its management [11].

Early-onset and late-onset IUGR represents two distinct clinical entities of placental dysfunction with a different clinical evolution. Early-onset IUGR is associated with high impedance of placental perfusion, resulting in increased blood flow umbilical artery resistance [12].

Late-onset IUGR is more frequent but with less severe manifestations. UA Doppler may be normal, but fetuses may respond to hypoxia through decreased middle cerebral artery (MCA) impedance [13].

Uteroplacental Doppler is the most important predictor of clinical deterioration and an indicator of poor neonatal outcome. Umbilical artery Doppler is the only method that can appreciate diagnosis and prognostic information for the management of IUGR. This because it is considered that increased UA Doppler PI can help detect restricted fetuses, either alone or in combination with CPR. Also, the presence of absent or reverse end-diastolic flow correlates with fetal compromise. Cerebral vasodilatation, a marker of hypoxia, is visualized as a reduction in MCA-PI, a rather late manifestation [14].

Some research recommends the use of an AC <10 percentile as predictor for small fetuses for gestational age, being associated to poor neonatal outcomes. But, in the absence of growth restriction, a small AC is not associated with adverse neonatal outcomes [15].

In our study, we found a significant difference between the two study groups, CA 5±5.487 of the Early SGA fetuses group being associated with an increased incidence of premature birth and lower fetal birth weight percentiles. In SGA fetuses, Doppler indices from fetal circulation can detect fetal compromises, birth weight and can predict poor outcomes in Apgar score, admission to NICU [16]. Cruz-Martinez et al suggest that UtA Doppler abnormalities in pregnancies diagnosed with SGA could anticipate early brain-sparing phenomenon. They found that when abnormal UtA Doppler exists, brain redistribution may occur 2 weeks earlier in approximately 63% of cases [17]. The abnormal Doppler of UtA was associated, in our study, with a deterioration of SGA fetuses, especially in Early SGA fetuses group.

In restricted fetuses, velocity is characterized by increased flux resistance in the umbilical artery (PI increase) and may develop a decrease in MCA-PI, which is characteristic of the brain-sparing phenomenon. These two Doppler parameters (increased UA-PI and reduced MCA-PI) can be combined in CPR, which can be lowered in SGA [18].

Our study showed that a CPR <1 was found at 42.85% in the Early SGA fetuses group and in 17.34% in the Late SGA fetuses group. Although late IUGR seems to have a more benign prognosis compared to early IUGR, however, an acute fetal compromise may occur at the end of pregnancy, because there are no observable late-stage signs as in early IUGR. This may be explained by the fact that in these situations there are several causes involved: the restricted fetus has a low tolerance to hypoxia, even if it is near the term, the contractions that may occur increase hypoxia and sometimes also occurs rapid deterioration of placental function [14].

Eixarch et al. showed that SGA fetuses with redistribution of cerebral blood flow show, in a high proportion of cases, a neurological development deficit at the age of two years with communication problems [19].

Thus parent counseling for future pregnancies, development of ultrasound diagnosis and IUGR risk assessment is very important for couples [20].

Abnormal Doppler velocimetry of uterine, middle cerebral artery and umbilical arteries was correlated with SGA newborns, premature birth, Apgar score and admission to NICU. It seems that the three arteries UtA, MCA and UA have the ability to detect fetuses at perinatal outcome risk.

Conclusion

Ultrasound examination and Doppler monitoring provide a non-invasive repetitive method for supervising fetuses with growth restriction in order to apply an adequate management.

References

1. American College of Obstetricians and Gynecologists, 2000, Intrauterine growth restriction . Available at: http://www.acog.org
2. Royal College of Obstetricians and Gynaecologists, 2013, minor revisions 2014, 2013, The Investigation and Management of the Small for Gestational Age Fetus. Available at: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg31/
3. ACOG committee opinion. Utility of antepartum umbilical artery Doppler velocimetry in intrauterine growth restriction. Number 188, October 1997 (replaces no. 116, November 1992). Committee on Obstetric Practice. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet, 1997, 59(3):269-270.
4. Figueras F, Eixarch E, Gratacos E., Gardosi J. Predictiveness of antenatal umbilical artery Doppler for adverse pregnancy outcome in small-for-gestational-age babies according to customised birthweight centiles: population-based study. BJOG, 2008, 115(5):590–594.
5. Savchev S, Figueras F, Cruz-Martinez R, Illa M, Botet F, Gratacos E. Estimated weight centile as a predictor of perinatal outcome in small-for-gestational-age pregnancies with normal fetal and maternal Doppler indices. Ultrasound Obstet Gynecol, 2012, 39(3):299-303.
6. McCowan LM, Harding JE, Stewart AW. Umbilical artery Doppler studies in small for gestational age babies reflect disease severity. BJOG, 2000, 107(7): 916–925.
7. Figueras F, Eixarch E, Meler E, Iraola A, Figueras J, Puerto B, Gratacos E. Small-for-gestational-age fetuses with normal umbilical artery Doppler have suboptimal perinatal and neurodevelopmental outcome. Eur J Obstet Gynecol Reprod Biol, 2008, 136(1):34-38.
8. Moldoveanu (Said) AL, Oprescu DN, Catanescu NV, Dragan I, Novac M. The Role of Fetal Doppler Monitoring in Preeclampsia With/without Intrauterine Growth Delay. Conference Proceedings of the 5th Congress Of The Romanian Society Of Ultrasound in Obstetrics and Gynecology, 20-22 April 2017, Tg-Mures, Romania, 401-405
9. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, Silver RM, Wynia K, Ganzevoort W. Consensus definition of fetal growth restriction: a Delphi procedure. Ultrasound Obstet Gynecol, 2016, 48(3):333-339.
10. Figueras F, Gratacós E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther, 2014, 36(2):86-98.
11. Nawathe A, Lees C. Early onset fetal growth restriction. Best Pract Res Clin Obstet Gynaecol, 2017, 38:24-37.
12. Baschat AA. Fetal growth restriction-from observation to intervention. J Perinat Med, 2010, 38:239-46.
13. Flood K, Unterscheider J, Daly S, Geary MP, Kennelly MM, McAuliffe FM, O'Donoghue K, Hunter A, Morrison JJ, Burke G, Dicker P, Tully EC, Malone FD. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO study. Am J Obstet Gynecol, 2014, 211: 288. e1-5.
14. Figueras F, Gratacos E. Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther, 2014, 36(2):86-98.
15. Di Lorenzo G, Monasta L, Ceccarello M, Cecotti V, D'Ottavio G. Third trimester abdominal circumference, estimated fetal weight and uterine artery Doppler for the identification of newborns small and large for gestational age. Eur J Obstet Gynecol Reprod Biol, 2013, 166(2):133-138.
16. Bansal S, Deka D, Dhadwal V, Mahendru R. Doppler changes as the earliest parameter in fetal surveillance to detect fetal compromise in intrauterine growth-restricted fetuses. Srp Arh Celok Lek, 2016, 144(1-2):69-73.
17. Cruz-Martinez R, Savchev S, Cruz-Lemini M, Mendez A, Gratacos E, Figueras F. Clinical utility of third-trimester uterine artery Doppler in the prediction of brain hemodynamic deterioration and adverse perinatal outcome in small-for-gestational-age fetuses. Ultrasound Obstet Gynecol, 2015, 45(3):273-278.
18. Khalil A, Thilaganathan B. Role of uteroplacental and fetal Doppler in identifying fetal growth restriction at term. Best Pract Res Clin Obstet Gynaecol, 2017, 38:38-47.
19. Eixarch E, Meler E, Iraola A, Illa M, Crispi F, Hernandez-Andrade E, Gratacos E, Figueras F. Neurodevelopmental outcome in 2-year-old infants who were small-for-gestational age term fetuses with cerebral blood flow redistribution. Ultrasound Obstet Gynecol, 2008, 32(7): 894-899.
20. Şorop-Florea M, Capitanescu R, Drăguşin RC, Patru CL, Zorila LG, Ciurea R, Marinas C, Tudorache S, Novac M, Dragoescu A, Stoica A, Gheonea M, Coleta E, Stepan A, Simionescu C, Cara M, Cernea N, Iliescu DG. Correlations of the Fetal Anomaly Scan with Fetal Autopsy Results. Conference Proceedings of the 5th Congress Of The Romanian Society Of Ultrasound in Obstetrics and Gynecology, 20-22 April 2017, Tg-Mures, Romania, 242-247.

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