Title: Evaluation of the Clinical Utility of Fetal Echocardiography in Pregnancies Complicated by Preterm Premature Rupture of Membranes

Summary

Premature rupture of membranes (PROM) occurs before the onset of regular labor contractions. If it occurs before the 37th week of pregnancy, it is referred to as preterm prelabor rupture of membranes (pPROM). It complicates approximately 3% of all pregnancies and is a cause of 30% of preterm births. In addition to the consequences of the preterm birth itself, the neonate may develop complications associated with typical pPROM conditions during pregnancy, e.g. oligohydramnios or intrauterine infection.

A reduced amniotic fluid volume leads to increased intrauterine pressure and compression of the fetus's chest, thus limiting the space for lung development. Additionally, it disrupts respiratory movements, which, together with rhythmic contractions of the diaphragm, ensure a balance between the production and removal of alveolar fluid. Depending on the criteria adopted, intrauterine infection complicates 15-48% of pregnancies with pPROM. Proinflammatory cytokines have an impact on both the fetal circulatory system and the development of the respiratory system, e.g. type II pneumocytes via disruption of their maturation and impairment of surfactant production. Consequently, complications affecting the cardiovascular and respiratory systems are observed in this group of patients more frequently, as evidenced in numerous research studies. With the currently available diagnostic methods, it is difficult to predict the risk of complications in the newborn. Everyday practice consists in cardiotocography, ultrasonography, and laboratory tests. There are reports of the potential suitability of fetal echocardiography assessing the function of the cardiovascular and respiratory systems for prediction of the condition of the neonate and the risk of complications. In order to verify the suitability of echocardiographic scans in pregnancies complicated by premature rupture of membranes, the following objectives of the study were formulated:

1. Assessment of changes in peripheral flows and the fetal circulatory system in gestations complicated by premature rupture of membranes
2. Assessment of the difference in echocardiographic parameters between a group of fetuses from pregnancies complicated by premature rupture of membranes and a control group

3. Assessment of changes in the circulatory system in fetuses from pregnancies complicated by pPROM in correlation with the duration of amniotic fluid leakage
4. Assessment of differences in fetal echocardiographic scan results in pregnancies with and without a suspected intrauterine infection
5. Assessment of the use of fetal echocardiographic scans for prediction of complications in the neonate
6. Assessment of the use of four-dimensional (4D) ultrasound to examine the right ventricle function in fetuses from pPROM-complicated pregnancies

The study group consisted of 46 patients with diagnosed premature rupture of membranes (pPROM) hospitalized in the 2nd Department and Clinic of Obstetrics and Gynecology of the Medical University of Warsaw (Duchess Anna Mazowiecka Clinical Hospital) from 01.06.2017 to 24.12.2019. The inclusion criterion in the study was the diagnosis of pPROM before the 34th week of pregnancy based on physical examination, patient history, and additional tests and assays. The exclusion criteria included congenital defects, fetal karyotype abnormalities, and a period of less than 48 hours between the premature rupture of membranes and the delivery. The control group comprised 46 patients with uncomplicated singleton gestations, normal intracardiac anatomy, and normal structure of other organs. The echocardiographic and ultrasound examinations of fetuses were performed using a Philips Epiq 7 device with the following probes: convex with frequencies of 2–9 MHz and sector with frequencies of 1–5 MHz. The analysis of parameters revealed by the various ultrasound, echocardiographic, and Doppler techniques and the analysis of data on the termination of pregnancy, perinatal course, and neonatal complications allowed formulation of the following conclusions:

1. There are no differences in placental flow in gestations complicated by pPROM compared to the control group.
2. Gestations affected by pPROM exhibit a higher prevalence of abnormal flows in uterine arteries in pregnant females.
3. Leakage of amniotic fluid has a negative effect on the circulatory and respiratory systems in fetuses. This is manifested by:
    a. lower CVPS values
    b. enlargement of the heart and its structures

c. impairment of the right ventricle function manifested by an increase in the Tei index, changes in blood flow through the tricuspid valve, and the development of tricuspid regurgitation
d. impairment of the left ventricle function manifested by a reduced left ventricular ejection time and a lower maximum velocity in the aorta

4. Prolonged amniotic fluid leakage has an impact on the deterioration of the right ventricle function.
5. Ultrasound and echocardiographic examinations of the fetus facilitate prediction of the neonatal condition:
   a. The group of neonates with bronchopulmonary dysplasia exhibited a smaller lung volume and a higher Tei index for the right ventricle observed in the fetal examination
   b. The group of neonates with circulatory failure had a higher Tei index for the LV and a lower middle cerebral artery velocity observed in the fetal examination.

6. No parameters in the fetal echocardiographic scans indicated a higher risk of development of intrauterine infection and early-onset infection in the neonate.

7. In fetuses from pregnancies complicated by pPROM, there is no technical possibility of assessment of right ventricle function with the currently available software for the 4D technique.