

Ultrasound in the first trimester of pregnancy

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The Guidelines Project, an initiative of the Brazilian Medical Association, aims to combine information from the medical field in order to standardize producers to assist the reasoning and decision-making of doctors.

The information provided through this project must be assessed and criticized by the physician responsible for the conduct that will be adopted, depending on the conditions and the clinical status of each patient.

INTRODUCTION

Routine ultrasound is established as part of prenatal care and is more frequently used during the second trimester⁽¹⁾. However, in recent years it has been increasingly used during the first trimester, a period that starts from the moment the feasibility of pregnancy is confirmed by verifying the presence of a gestational sac in the uterine cavity with an embryo showing cardiac activity until 13 weeks + 6 days of gestation.

OBJECTIVE

The purpose of this Guideline is to provide recommendations that may assist in the decision-making regarding the use of ultrasound in pregnant patients during the first trimester.

METHODS

The recommendations in this Guideline will be based on a systematic review of the literature guided by questions based on real-life scenarios. We selected four questions considered essential for the formulation of recommendations.

We will consider eligible mainly randomized clinical trials and systematic reviews of randomized clinical trials; however, controlled observational studies, “before and after” studies, and guidelines will also be considered acceptable when intervention studies with these designs are not available. The MEDLINE via PubMed and CENTRAL (Cochrane) databases will be searched using specific search strategies (Table 1).

TABLE 1. SEARCH STRATEGIES USED IN THE MEDLINE AND CENTRAL DATABASES

Database	Strategy
MEDLINE via PubMed	(Pregnancy Trimester, First OR First Trimester OR Phases, Early Placental OR Pregnancy Trimesters, First OR First Pregnancy Trimester OR Pregnancies, First Trimester) AND (Ultrasonography OR Echography OR Ultrasonic Diagnoses).
CENTRAL (Cochrane)	Pregnancy AND first trimester AND (Ultrasonography OR ultrasound)

The search period will comprise from the inception of the database until August 2019, without language restrictions. Three independent researchers (G.R.A., R.S.S., and W.M.B.) will analyze the publications retrieved based on their titles and abstracts. Cases of disagreement will be resolved by consensus. The risk of bias in clinical trials will be assessed using the tool proposed by the Cochrane Collaboration⁽²⁾. Systematic reviews will be assessed using the AMSTAR tool⁽³⁾, and guidelines using the AGREE II instrument⁽⁴⁾.

The evidence was evaluated according to the Oxford classification⁽⁵⁾, which establishes the strength of evidence based on the study design chosen.

Grades for recommendation and levels of evidence:

A: Experimental or observational studies of higher consistency.

B: Experimental or observational studies of lower consistency.

C: Uncontrolled studies/case reports.

D: Opinion deprived of critical evaluation, based on consensus, physiological studies, or animal models.

Conflict of interest

No conflict of interest was declared by the participants in the preparation of this guideline.

What is the goal of first-trimester ultrasound?

In recent years, first-trimester ultrasound has played a crucial role not only for assessing fetal viability and determining the gestational age but also as a screening tool for the identification of chromosomal abnormalities by measuring the thickness of the nuchal translucency (NT)⁽⁶⁾(A). In addition, several studies have demonstrated the capacity of the examination, in the first trimester, to identify more than 80% of the main congenital fetal malformations unrelated to chromosomopathies, with sensitivity between

12.5 and 83.7%^(7,8)(A). It has also been described how some ultrasound markers used for combined testing (such as augmented NT, reverse flow in the ductus venosus, tricuspid regurgitation, absence of internal translucency) can be correlated with the presence of anatomic malformations.

First-trimester ultrasound is used to confirm the feasibility of the gestation, establish the gestational age with accuracy, determine the number of fetuses, and, in the presence of a multiple pregnancy, assess chorionicity and amnionicity. Ultrasound also provides the opportunity to detect severe fetal anomalies and, in health systems that track aneuploidy, it is possible to measure the thickness of the nuchal translucency (NT). It is recognized, however, that many severe malformations can develop later in pregnancy, or may not be detected in this period even with adequate equipment and by experienced professionals⁽⁹⁾(A).

When should first-trimester ultrasound be used?

There is no reason to use first-trimester ultrasound as a routine examination only to confirm pregnancy in the absence of any risk factors. However, when indicated, it must be used between 11 and 13 weeks + 6 days, since it would provide an opportunity to check the objectives presented above, selecting cases that should be referred for invasive examinations (e.g. chorionic villus or amniocentesis biopsy) to obtain diagnostic confirmation by karyotype. Before starting the examination, the physician should inform the pregnant woman and/or couple of the possible benefits and limitations of first-trimester ultrasound⁽⁹⁾(A).

What is the safety of Doppler ultrasonography in the 1st trimester?

For safety reasons, the use of Doppler is not indicated during a routine examination. Doppler ultrasound is associated with higher energy production and, consequently, greater potential biological effect, particularly when applied to a small region of interest^(10,11)(A).

Doppler examinations should be used in the first trimester only if clinically indicated⁽⁹⁾(A). The main reason for defending the *use of Doppler with caution* at the beginning of pregnancy is not because we know that it causes damage, but because we do not know if it is safe and the first quarter is a particularly vulnerable period of fetal life.

What is the value of Doppler ultrasonography in the 1st trimester in predicting and identifying preeclampsia (PE)?

The efforts to effectively predict PE in the first trimester of pregnancy is motivated by the desire to identify women who are at high risk of developing PE to ensure that the necessary precautions can be taken early to improve placentation and, thus, prevent or at least reduce the frequency of its occurrence. In addition, the identification of a group “at-risk” will allow tailored pre-natal monitoring to anticipate and recognize the onset of clinical syndrome and manage it immediately.

The increase in perception of the pathophysiology of PE is reflected in the current screening strategies, which are based on the history, demographic data, biomarkers (including blood pressure), and uterine artery Doppler.

Considering that the *ultrasound screening* for PE should not be removed from the general concept of prenatal care, professionals who carry out this screening should have up-to-date knowledge about the proven risk factors for PE and seek to identify them during the screening.

A *global risk assessment for PE should cover four broad areas*⁽¹²⁾ (A), including:

- Personal risk profile (including age, ethnicity, parity, smoking, obstetric and medical history, and method of conception);
- Metabolic risk profile [including body mass index (BMI) and history of diabetes];
- Cardiovascular risk profile (including existing cardiovascular conditions and measurement of the mean arterial pressure);
- Placental risk profile (including uterine artery Doppler and maternal serum biomarkers).

The use of ultrasound as a tool for screening/predicting PE is based on the fact that the faulty placentation results in an incomplete transformation of the spiral arteries. Villous and vascular histopathological lesions of the placenta are four to seven times more common in pregnancies with PE than in pregnancies without PE⁽¹³⁾ (A) and are associated with greater resistance to blood flow in the uterine artery⁽¹⁴⁾ (A). The measurement of impedance (or resistance) to the flow in the uterine arteries by Doppler assessment makes the incomplete transformation of spiral arteries quantifiable.

Combined screening [including maternal factors, mean maternal arterial pressure (MAP), uterine artery Doppler, and serum level of placental growth factor (PLGF- an angiogenic protein produced by the

placenta, whose synthesis is decreased in women with a high risk of pre-eclampsia] at 11-13 weeks seems to be the most effective screening model for identifying women at risk of PE⁽¹⁵⁾ (A).

When it is not possible to measure the PLGF and/or UTPI (uterine artery pulsatility index), the initial screening test should be a combination of maternal risk factors with maternal risk with MAP, and not only maternal risk factors⁽¹⁵⁾ (A). The risk calculator is available for free at: <https://fetalmedicine.org/research/assess/preeclampsia/First>

Measurement of biochemical markers: for screening in the first trimester, the best biochemical marker is the PLGF. Plasma A protein associated with pregnancy (PAPP-A), with results commonly expressed in multiples of the median (MoMs), is useful if measurements of PLGF and UTPI are not available.

Recommendations

For ultrasound in the first trimester of pregnancy:

- There is no reason for using it as a routine examination only to confirm pregnancy, in the absence of any risk factors. (A)
- When indicated, it must be used between 11 weeks and 13 weeks + 6 days. (A)
- It is a screening tool to identify chromosomal anomalies.
- It identifies over 80% of the main fetal malformations unrelated to chromosomopathies, with sensitivity between 12.5 and 83.7%. (A)
- Some ultrasound markers used for combined testing can be correlated with the presence of anatomic malformations. (A)
- Many severe malformations can develop later in pregnancy or may not be detected during this period by US. (A)

For Doppler ultrasound in the first trimester of pregnancy:

For safety reasons, it is not indicated during a routine examination. (A)

Combined screening including maternal factors, mean maternal arterial pressure, uterine artery Doppler, and serum level of placental growth factor at 11-13 weeks seems to be the most effective screening model for identifying women at risk of PE. (A)

When it is not possible to measure the PLGF (best biochemical marker) and/or UTPI, the initial screening test for PE should be a combination of maternal risk factors with MAP and not only maternal risk factors. (A)

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