

Using a uniform definition for growth restricted fetuses

Once a woman gets pregnant, the fetus develops and grows through exchange of oxygen and nutrients between the mother and fetus in the placenta. Each fetus has its own growth potential. Therefore, some fetuses are smaller than others. When a fetus is small this can result from a lack of oxygen and nutrients, but this is not always the case. However, the smaller the fetus is the higher the risk of adverse outcomes. It is important to identify these fetuses so that necessary care can be provided. Also, it is important to identify the fetuses who are small and healthy (meeting their own growth potential), so that no unnecessary and potentially harmful interventions are installed. Since the fetus is in the womb, it is difficult to accurately measure the size of the fetus. Besides that, adequate size is not a perfect indicator of fetal growth and thus wellbeing as size is static (measures past growth at a certain point in time but does not indicate speed) and growth is dynamic. Therefore we need tools to estimate whether a fetus is well (grown).



Fig. 1. Schematic representation of the possible overlap between FGR and SGA and between AGA and LGA.

FGR (Fetal Growth Restriction): the fetus does not meet its own growth potential due to placental insufficiency.

SGA (Small for Gestational Age): the fetus is 'small' compared to the reference population.

AGA (Appropriate for Gestational Age): the fetus' size is 'normal' compared to the reference population.

LGA (Large for Gestational Age): the fetus is 'large' compared to the reference population.

Currently, estimating the size of the fetus is performed by ultrasound. The measured values are

plotted on a growth chart wherein the growth lines indicate the mean size of fetuses from the reference population. As soon the fetus' size is plotted beneath the 10%, the fetus is often diagnosed as being 'too small'. It is however possible that its size increased sufficiently compared to the previous measurement. Conversely, if the fetus' size is measured above the 10% but hardly increased or did not increase at all for an unknown period, the size can still be plotted within the normal range. This baby is probably too small for its own growth potential and may suffer from a lack of oxygen and nutrients, but will not get the medical attention it needs as it remains unnoticed. Therefore the use of a cut off at 10% reference population is not adequate for determination of the individual fetus wellbeing.

Concluding: measuring the size of the fetus alone is not sufficient to determine fetal wellbeing or placental function, and therefore we need to find a way to assess the actual function of the placenta. To assess the function of the placenta, the blood flow in both the placenta and the head of the fetus can be measured. Furthermore, there are markers in the blood of the mother that can indicate the function of the placenta. If we use these measurements too, we do not only rely on the size of the fetus, let alone we use a single cut-off for being abnormal or normal. Analyzing data of large cohorts may improve possibilities to identify the fetuses who suffer from a lack of nutrition and oxygen due to placental insufficiency. Then, also fetuses that have a seemingly normal size but who are exposed to a placenta that does not function well, can be identified.

The lack of a uniform way to diagnose fetuses who are *too small* for their potential causes inconsistency worldwide. A uniform definition helps to improve diagnosing the fetuses at risk. Furthermore, studies can be compared with each other which will eventually result in better care of these fetuses. To achieve such a uniform definition, in lack of a better measurement or instrument, consensus definition can be achieved by a panel of experts. Recently, some important definitions for growth restriction have been developed by our group. We now have to implement these definitions in standard medical care and test them for their accuracy.

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