

MIDDLE CEREBRAL ARTERY DOPPLER PEAK SYSTOLIC VELOCITY IN THE EVALUATION OF FETAL ANEMIA

INTRODUCTION

In the 1960's the first in-utero therapy for hemolytic disease was described. Despite the availability of prophylaxis, it has been estimated that approximately 3.5 fetuses per 1000 live births are at risk for anemia due to alloimmunization¹.

SONOGRAPHIC EVALUATION OF SIGNIFICANT FETAL ANEMIA

A number of different sonographic parameters have been evaluated in an attempt to predict significant fetal anemia.

The placenta is enlarged in cases of severe Rh hemolytic disease due to villous edema and hyperplasia². While a dilated umbilical vein has been reported as a sonographic sign associated with hydrops, it is not sufficiently sensitive to be used as a marker for severe anemia^{3,4}.

Roberts et al⁵ reported that the length of the right lobe of the liver was greater than the 90th percentile in fetuses with a hemoglobin of ≤ 10 gm/dl (Fig. 1). However, the authors were concerned about the reproducibility of liver lengths between centers. Fetal position also played an important role - the right lobe of the liver must be up to obtain an accurate measurement.



Fig 1. Hepatomegaly. Click for larger image.

Splenomegaly due to increased erythropoiesis, congestion and red cell destruction is also an acknowledged late finding of fetal anemia. In fetuses with severe anemia, the splenic perimeter

measured at the level of the abdominal circumference, has a sensitivity of 63.6%, specificity of 91.7%, and a positive predictive value of 70% (Fig. 2)⁶. Since extramedullary erythropoiesis begins between a hemoglobin of 5 and 7 gm/dl, splenomegaly does not predict mild to moderate anemia. After intravascular transfusion the splenic perimeter decreases in size⁷.



Fig 2. Normal splenic dimensions (markers). Click for larger image.

Prior to the onset of hydrops, the sonographic manifestations of severe anemia are, in order, polyhydramnios, increased placental thickness (Fig. 3), hepatosplenomegaly and ascites (Fig. 4)⁴. Holosystolic tricuspid regurgitation generally precedes the development of ascites and hydrops⁸. Unfortunately, none of these sonographic parameters can distinguish mild from severe anemia. The speed with which anemia develops, as well as the individual fetal response to anemia are additional factors that result in the manifestation of hydrops at variable hemoglobin levels⁹. A fetus may be able to compensate for a gradual onset of anemia with hepatosplenomegaly. However, with a more rapid breakdown of red cells, anemia may occur without hepatosplenomegaly.



Fig 3. Placentomegaly at 30 weeks' gestation due to severe fetal anemia. Polyhydramnios is also present. Click for larger image.



Fig 4. Cardiomegaly due to fetal hydrops. Click for larger image.

Fetal cardiac output increases as a compensatory response to anemia. While the mean cardiac output is increased prior to transfusion, the value is within one standard deviation of a control group¹⁰. Hence, the increase in cardiac output cannot be used to reliably predict the extent of fetal anemia. As the severity of anemia increases, cardiomegaly (Fig. 4) gives rise to mitral and/or tricuspid regurgitation (Fig. 5). Marked hypertrophy of the ventricular chambers will eventually occur. After intravascular transfusion to correct anemia, fetal cardiac output declines. It has been postulated that the increase in blood viscosity with transfusion results in an increase in cardiac afterload. As a result, stroke volume declines and cardiac output falls to the normal range¹¹.

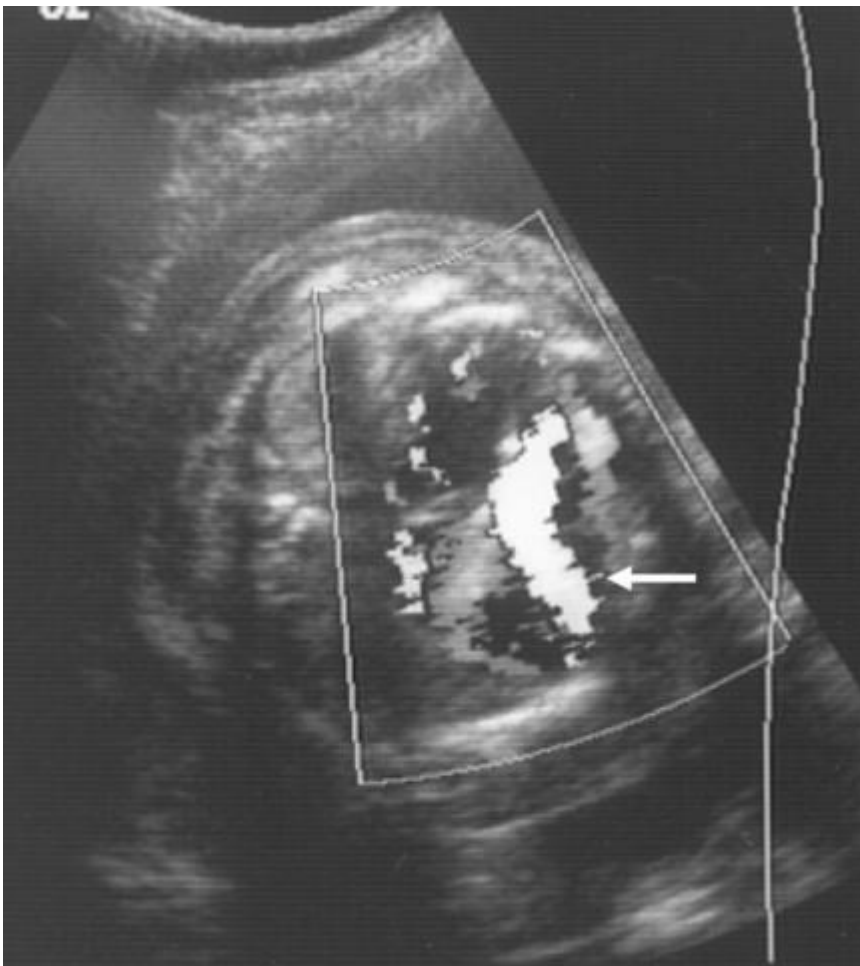


Fig 5. Tricuspid regurgitation (arrow) due to fetal anemia and secondary hydrops. Click for larger image.

RH TITERS AND FETAL TRANSFUSION

The maternal Rh titer is the initial step in the evaluation of an Rh-sensitized patient.

Since there is a variation in results between laboratories, each institution must determine its "critical titer" - the level at which there is a significant risk of hydrops. Liley¹² introduced the spectral analysis of amniotic fluid for bilirubin at 450 nm. His original data divided pregnancies after 27 weeks' gestation into three zones - normal/mild anemia; moderate anemia; and severe anemia. A rising titer that reaches upper zone II or zone III requires percutaneous umbilical blood sampling to accurately determine the fetal hematocrit and possibly perform an intravascular transfusion. Intravascular transfusions are continued up to approximately 35 weeks' gestation¹³.

Ideally, fetal intervention should occur before the onset of hydrops. In a review Schumacher and Moise¹⁴ reported the survival after intravascular transfusion of 75% and 94% for hydropic and non-hydropic fetuses, respectively. As a result, non-invasive methods that predict severe anemia before the onset of hydrops have been sought.

DOPPLER INVESTIGATION IN FETAL ANEMIA

Through the years multiple vessels have been evaluated in an attempt to better predict severe anemia. An increase in blood velocity with fetal anemia has been recorded in the carotid arteries, descending aorta and umbilical vein. Copel et al¹⁵ developed a formula utilizing the peak systolic velocity in the descending aorta that had a 75% efficiency for detecting a fetal hematocrit < 25%. Hydrops does not generally occur until the hematocrit falls below 15%. By setting the formula to detect a hematocrit < 25%, the false positive rate would be increased. In a follow-up prospective study of 13 patients with

severe Rh disease, an angle corrected fetal descending aorta peak velocity did not improve the predictive accuracy of hydrops in the diagnosis of severe anemia¹⁶.

Intracardiac and venous Doppler studies cannot accurately predict anemia⁹. The fetal aorta¹⁶ and splenic artery¹⁷ have also been evaluated with variable success. The use of angle independent indices or measurements that require angle correction are not sufficiently sensitive to detect the velocity changes associated with anemia¹.

MIDDLE CEREBRAL ARTERY

The middle cerebral artery has become the vessel of choice when assessing a fetus for anemia. However, the technique for obtaining the peak systolic velocity in the middle cerebral artery is critical in obtaining reliable results. The fetal vertex is imaged on an axial plane that includes the cavum septum pellucidum and thalami. The transducer is then moved toward the base of the skull until the Circle of Willis is visualized. The angle of vessel insonation should be close to zero and the Doppler gate placed in the center of the vessel immediately above its demarcation from the Circle of Willis (Fig 6)¹⁸. The PSV should not be measured in the distal branches of the middle cerebral artery (Fig 7). The PSV is lower in these vessels than in the main branch of the MCA. The MCA should be zoomed to occupy, at least, 50% of the image (Fig. 8). An angle of insonation of zero degrees insures the most accurate measurement of the PSV¹. The PSV is measured in the MCA closest to the transducer. The fetus should not be active or breathing during the examination. If the MCA is measured with this technique, there is a low intraobserver and interobserver variability in the values obtained¹⁸.

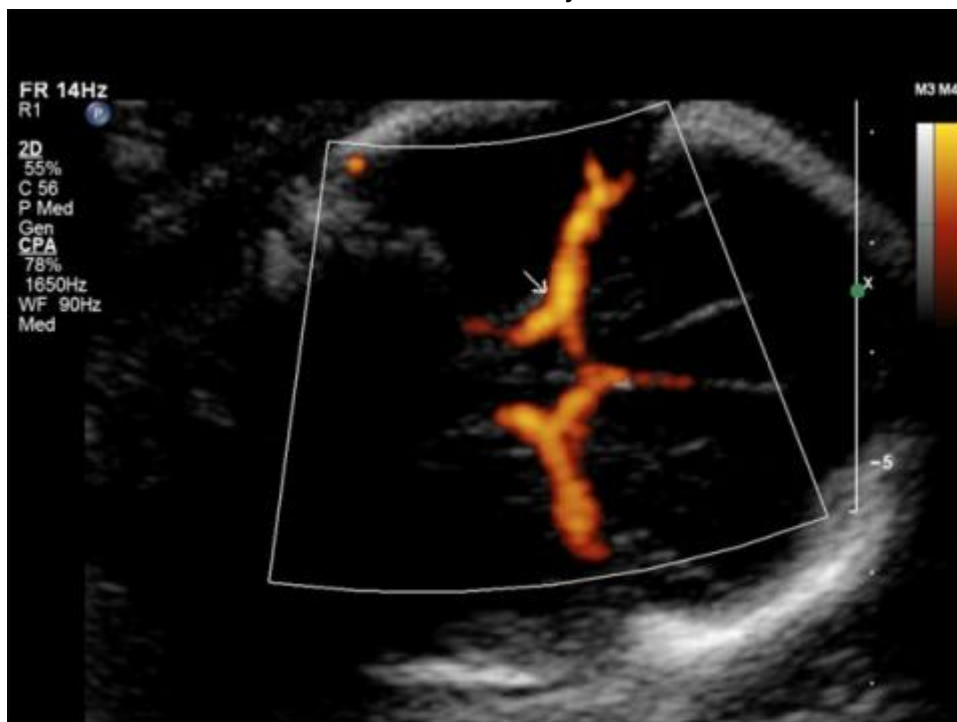


Fig 6. Circle of Willis at 24 weeks' gestation. The appropriate place to measure peak systolic velocity is marked (arrow). [Click for larger image.](#)

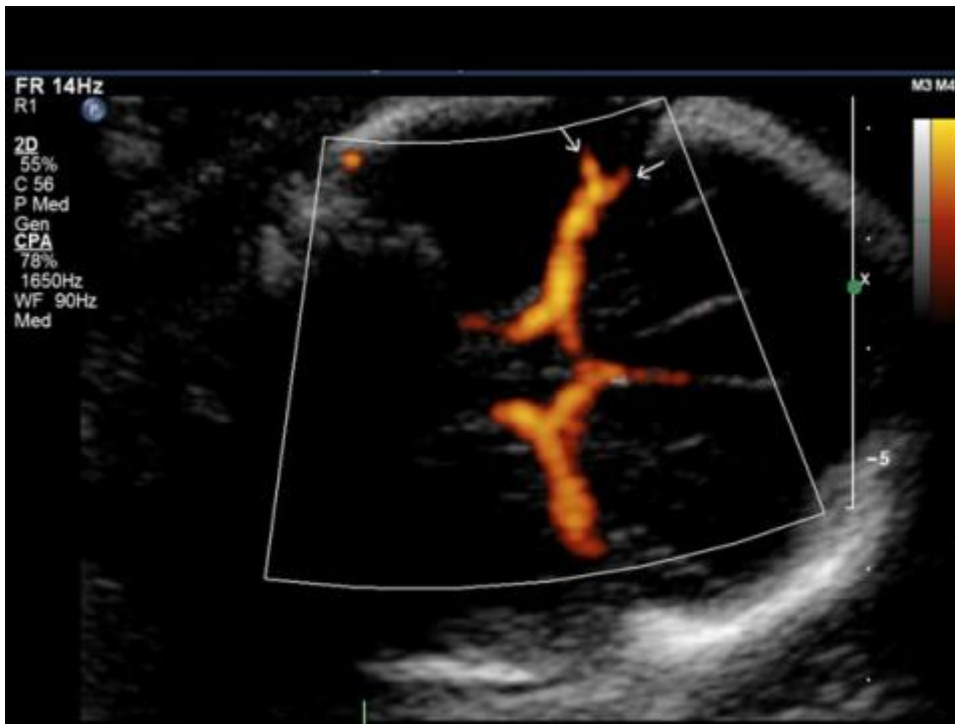


Fig 7. Distal branches (arrows) of the middle cerebral artery. Click for larger image.

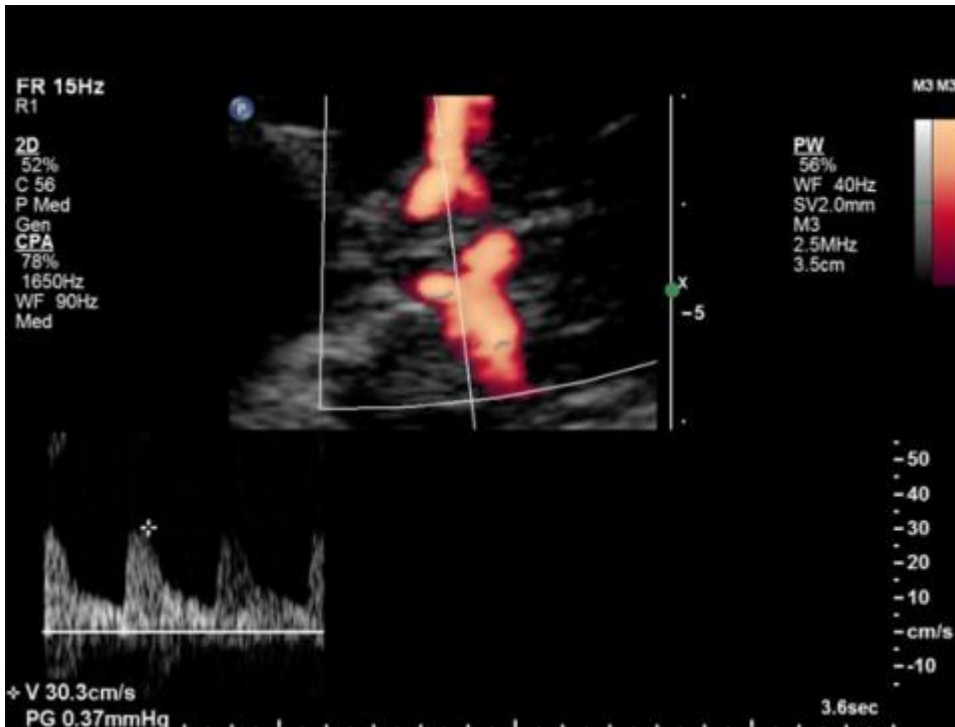


Fig 8. Normal peak systolic velocity (marker) in the middle cerebral artery at 24 weeks' gestation. Click for larger image.

The MCA-PSV may not increase with mild anemia. As the severity of anemia increases, the correlation with MCA-PSV improves. Once the fetal hemoglobin falls to 1-3gm/dl, the velocity in the MCA does not continue to rise¹⁹.

MCA-PSV has also been evaluated with Kell sensitization, in which there is a suppression of erythroid precursor rather than hemolysis. The resulting anemia is accurately reflected in an elevated MCA-PSV²⁰. Anemia secondary to fetal maternal hemorrhage²¹, twin-to-twin transfusion²², and parvo- virus²³ has also been accurately predicted with MCA-PSV. In fetuses with non-immune hydrops, a normal MCA-PSV can be used to exclude anemia as a possible etiology for the sonographic findings⁸.

The use of middle cerebral artery peak systolic velocity has resulted in a 70%¹ to 80%²⁴ reduction in invasive fetal testing (i.e. amniocentesis or percutaneous umbilical blood sampling).

In isoimmunized pregnancies an MCA-PSV of mean plus 1.5 SD detects 96%²⁴ to 100%¹ of severely anemic fetuses with a 12%¹ to 14%²⁴ false positive rate.

MCA-PSV is not performed before 18 weeks' gestation. Prior to this gestational age the reticuloendothelial system is too immature to successfully destroy enough antibody coated erythrocytes to result in significant anemia²⁴.

After the correction of fetal anemia with an intravascular transfusion, the MCA-PSV immediately returns to normal²⁵. Even after two intrauterine transfusions, MCA-PSV remains a reliable test for recurring fetal anemia²⁶.

Healthy fetuses have up to a 10% rise in MCA-PSV during the active state. This increase could contribute to part of the reported false positive rate of MCA-PSV in detecting fetal anemia²⁷.

After 35 weeks' gestation, MCA-PSV is not a reliable predictor of severe anemia²⁸. A physiologic mechanism for this finding has not yet been elucidated.

MCA-PSV has been found to be similar²⁹ or better³⁰ than amniotic fluid OD450 in the prediction of anemia.

CONCLUSIONS

The measurement of MCA-PSV has revolutionized the management of fetuses with suspected anemia. With appropriate training, the accurate measurement of the MCA-PSV can reduce invasive fetal testing for anemia by up to 80%.

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