MORBIDLY ADHERENT PLACENTA: A PILOT RETROSPECTIVE COHORT STUDY

VERSION 2.0
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STUDY PURPOSE

Evaluating the predictive ability of subtle ultrasound signs of placenta accreta.

BACKGROUND

Morbidly adherent placenta refers to a group of diagnoses delineating various degrees of invasion of the trophoblast into decidua, myometrium or beyond that include placenta, increta and percreta. This problem leads to major obstetric hemorrhage and an increase in morbidity and mortality for pregnant women. Enhanced ability to diagnose this problem can lead to preparation for major hemorrhage and decrease morbidity and mortality.

There are at least four known "classic" signs of morbidly adherent placenta by ultrasound, as follows. All of these signs have been evaluated only in the presence of placenta previa. Diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) of these signs have not been evaluated when previa is absent.

1. Loss of the hypoechoic myometrium or replacement of the hypoechoic myometrium by tissue with the echo characteristics of placental tissue
2. Large hypoechoic areas anywhere within the body of the placenta
3. Loss of integrity of the hyperechoic line separating the lower uterine segment and the urinary bladder
4. Penetrating maternal blood vessels through the myometrium or into the bladder

Over the past 10-15 years, advances in ultrasound imaging technology have allowed improved ability to detect many differences in tissue planes not possible in the past. The classic signs of morbidly adherent placenta were described 25 years ago, and the search for new diagnostic signs has been mostly limited to Doppler characteristics of the lower anterior uterine segment/ retroplacental area. There is improved imaging now available with endovaginal ultrasound, because the ultrasound probe is placed extremely close to the lower uterine segment. The lower uterine segment is where the problem of morbidly adherent placenta usually occurs.

Morbidly adherent placenta is divided into three categories: accreta (lack of the normal cleavage plane), increta (placenta grown into the myometrium) and percreta (placenta grown through the myometrium). Based on the review of numerous articles over the past 12 years, combined with our recent experience in trying to diagnose morbidly adherent placenta, we believe the above "classic" signs may be diagnostic for increta/percreta, but that there are three more subtle signs of accreta:

1. Small hypoechoic areas adjacent to the lower uterine segment
2. Irregular border of the placenta-uterine interface
3. Color or Power Doppler maternal vessels parallel to the base of the placenta within the myometrium and/or a 3D power Doppler confluent pattern.

Hypothesis

We hypothesize that alone, or in combination, the above three subtle signs are predictive of the occurrence of placenta accreta, and are distinctly different from the diagnosis of increta/percreta.

Specific aims

1. *Primary aim*
   Obtain diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) of the three subtle signs for placenta accreta, alone and in combination.
2. Secondary aims

1. Obtain diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) of the three subtle signs for all morbidly adherent placenta diagnoses, including placenta increta/percreta, alone and in combination
2. To assess the predictive ability of the subtle signs for adverse outcomes of placenta accreta (blood transfusion, hysterectomy).
3. To assess the predictive ability of the three subtle signs for adverse obstetric outcomes in patients without the diagnosis of morbidly adherent placenta.
4. To provide short term outcome data on a modern cohort of women with placenta accreta (not increta or percreta), which has not heretofore been presented.
5. To assess agreement of image reviewers for the presence of subtle signs of placenta accreta.

STUDY DESIGN

We will perform a retrospective cohort analysis of all patients with low-lying placenta or placenta previa at the mid-trimester anatomy scan (gestational age 18w0d to 23w6d) who are evaluated by endovaginal ultrasound in the third trimester.

We will compare three groups:

a. Women with no prior cesarean delivery (multiparas only)
b. Those with cesarean delivery in any prior pregnancy and no placenta previa

c. Those with cesarean delivery in any prior pregnancy and placenta previa in the current pregnancy (cases)

This study design assumes that the exposure (or primary risk factor) is a prior cesarean delivery in any pregnancy, a secondary risk factor is the occurrence of placenta previa (or low lying anterior placenta), and confounding factors are BMI and parity. Diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) of the subtle signs for each group above will be determined.

Patients who have one or more of the four classic signs will be analyzed separately. Diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) of the three subtle signs, alone or in combination, will be determined for each of the three groups for the diagnosis of morbidly adherent placenta (combination of accreta, increta and percreta) as well as placenta accreta. These are diagnostic, not screening tests.

INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria

- All pregnant women who had transabdominal or endovaginal ultrasound scans showing low lying placenta or placenta previa in the mid-trimester.

Exclusion criteria

- Placenta previa or low-lying placenta not seen at the mid-trimester scan
- Endovaginal scan not performed
- Nulliparity
- Delivery information not available

One or more of the classic signs of morbidly adherent placenta are present (These cases will be analyzed separately)PROCEDURES

- Qualifying cases will be identified at each participating site.
- Images from participating sites will be sent to a central location.
- Dr. Skupski, Dr Scholl and Dr. Duzyj Buniak will review films, and determine if classic or subtle signs of morbidly adherent placenta are present.
- Reviewers will be blinded to clinical information (i.e., which of the three groups each case falls into).
- Agreement of reviewers will be assessed using the kappa statistic.
- Diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) will be determined for each of the three groups and compared.

CRITERIA FOR SUBJECT SELECTION

- **Age of Subjects**. 18-55

- **Racial and Ethnic Origin.** All comers.

RISK/BENEFIT ASSESSMENT

Risk Category. Minimal Risk. The risk entailed is that of breach of confidentiality of records.
Potential Risk. Risks to subjects are reasonable in relation to the anticipated benefits to society given the retrospective nature of the study.

POTENTIAL BENEFITS TO THE SUBJECTS

There are no anticipated benefits to individual subjects.

PROCESS OF CONSENT

A waiver of consent is requested. This is a retrospective study being performed by chart review.

DATA ANALYSIS AND DATA MONITORING

Diagnostic performance characteristics (sensitivity, specificity, predictive values, likelihood ratios) will be derived from the data obtained and compared between the three groups. Exposure = prior CD, confounding factors = previa, parity, BMI.

All data, including U/S images, will be coded by the site and sent to New York Presbyterian/Queens (NYP/Q) encrypted. The data will be stored and analyzed by Daniel Skupski, MD of NYP/Q and Cande V. Ananth, PhD of Columbia University.

The U/S images will be uploaded and stored by each site into the Trice Imaging Service system, known as Tricefy. Tricefy is a HIPAA compliant cloud based system that will receive and manage the U/S images and makes them accessible to the reviewers. The images will be reviewed securely in Tricefy, by Dr. Skupski and Dr. Scholl at NYP/Q and Dr. Duzyj Buniak at Rutgers, The State University of New Jersey - RWJMS. Drs. Skupski, Scholl and Duzyj Buniak will perform independent assessments for the subtle signs of MAP in preparation for the KAPPA analysis looking at inter-observer correlation.

The data may be shared with the Perinatal Research Consortium (PRC) member sites for future research purposes.

DATA STORAGE & CONFIDENTIALITY

Data will be kept in a password protected computer in a locked room only accessible by study staff.

Lay Summary

The placenta can sometimes not separate from the wall of the uterus after birth of the baby. This is called placenta accreta or morbidly adherent placenta. This can lead to massive bleeding, and possibly blood transfusion, removal of the uterus permanently, or maternal death. Based on our experience and recent articles in the medical literature, we believe some new findings on ultrasound during pregnancy may be able to help us find this problem before birth so we can prepare for when it happens.

We will perform a "look back" at our ultrasound imaging system to look for these new findings in women who have already given birth to find out if they can help us diagnose this problem. These women's records will be reviewed to correlate the new findings on ultrasound and whether these women actually did have the placenta accreta problem. We will develop "diagnostic performance characteristics", which is finding out in several ways how good we can be at finding the accreta problem. Specifically, the sensitivity, specificity, predictive value positive and predictive value negative will be found.

This type of study can help women in the future, but will not help the women whose images and records we are using.