Antenatal Surveillance in Twin Pregnancies Using the Biophysical Profile

Whitney Booker, MD, Nathan S. Fox, MD, Simi Gupta, MD, Rachel Carroll, MD, Daniel H. Saltzman, MD, Chad K. Klauser, MD, Andrei Rebarber, MD

Objectives—The nonstress test is currently the most widely used modality for antenatal surveillance in twin pregnancies, with a quoted false-positive rate of 11%–12%. Our objective was to report our experience with the sonographic portion of the biophysical profile in twin pregnancies as the primary screening modality.

Methods—Women with twin pregnancies delivered by a single maternal-fetal medicine practice from 2005 to 2013 were included. We excluded monoamniotic twins. Twin pregnancies began weekly sonography for the biophysical profile starting at 32 to 33 weeks, or earlier if indicated. The nonstress test was performed if the sonographic biophysical profile score was less than 8 of 8. We reviewed biophysical profile scores and outcomes for all patients who delivered at 33 weeks or later to assess the false-positive rate for the biophysical profile, as well as the incidence of intrauterine fetal death (IUFD) after initiation of antenatal surveillance.

Results—A total of 539 twin pregnancies were included. The incidence of IUFD per patient was 2 per 539 (0.4%; 95% confidence interval [CI], 0.1%–1.3%), and the incidence of IUFD per fetus was 2 per 1078 (0.19%; 95% CI, 0.05%–0.7%). The overall positive screen rate was 24 per 539 (4.45%; 95% CI, 3.0%–6.5%). The false-positive screen rate, defined as an abnormal biophysical profile that did not diagnose an IUFD or lead to delivery, was 10 per 539 (1.9%; 95% CI, 1.0%–3.4%).

Conclusions—In twin pregnancies the use of the sonographic biophysical profile for routine antenatal surveillance has a low false-positive rate, with a very low incidence of IUFD. The sonographic biophysical profile should be considered as a primary mode for antenatal surveillance in twin pregnancies, with a reflex nonstress test for an abnormal score.

Key Words—antenatal testing; biophysical profile; obstetric ultrasound; twins

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Address correspondence to Andrei Rebarber, MD, Maternal-Fetal Medicine Associates, PLLC, 70 E 90th St, New York, NY 10128 USA.

E-mail: arebarber@mfmnyc.com

Abbreviations

CI, confidence interval; IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction

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The twin birth rate in the United States has increased from 1.89% in 1980 to a reported rate of 3.3% in 2011.[1] In this growing population arises a cohort of pregnancies that are at known increased risk for stillbirth, particularly with advancing gestational age when compared to singletons.[2,3] The increasing incidence of multiple-gestation pregnancies has called for an opportunity to reassess and redefine appropriate and effective antenatal surveillance options in this unique population.

Currently in twin pregnancies, the nonstress test is the most widely published modality for antenatal surveillance. In twins, a reactive nonstress test result is predictive of an uncomplicated perinatal outcome.[4,5] Furthermore, a nonreactive nonstress test result has been associated with increased fetal morbidity and mortality.[6]

However, periods of inactivity and sleep cycles can be confused with fetal compromise, and nonreactive nonstress test results have a false-positive rate as high as 50%, which could lead to unnecessary interventions and premature delivery of otherwise healthy neonates. The nonstress test, particularly in twins, is time-consuming, requires skilled nursing staff, and has the potential for Doppler interface fetal heart rate synchrony, which has been observed as much as 58% of the time.[4] Due to these factors, there is a need to reassess optimal antenatal surveillance in twin pregnancies.

In singleton pregnancies, the biophysical profile has been shown to be a more specific and sensitive marker for fetal well-being than the nonstress test alone.[7] A scarcity of data exists on assessing the utility of the biophysical profile in twin gestations. Lodeiro et al[8] assessed 49 pairs of twins with biophysical profile testing beginning at 26 weeks' gestation; they found the biophysical profile to have sensitivity of 83% for adverse outcomes in this population. This surveillance included the nonstress test portion of the originally described biophysical profile.

In our practice, we have been using the sonographic portion of the biophysical profile as the primary modality for fetal assessment in twin pregnancies, with nonstress test assessment used as a reflex test in the setting of any abnormal sonographic biophysical profile. Our objective was to report our experience with the sonographic biophysical profile for twin pregnancies, assessing the rate of intrauterine fetal death (IUFD) in our population as well as reporting the false-positive rate for the sonographic biophysical profile in this antenatal testing scheme.

Materials and Methods

After Biomedical Research Alliance of New York Institutional Review Board approval was obtained, the charts of all women with twin pregnancies delivered by a single maternal-fetal medicine practice between June 2005 (when our electronic medical record was established) and November 2013 were reviewed. Baseline characteristics and pregnancy outcomes were obtained from our computerized medical record. Monoamniotic twins were excluded.

In our practice, all women with twin pregnancies undergo routine sonographic biophysical profile testing beginning at 32 weeks and then weekly until delivery. As we only perform the sonographic portion of the biophysical profile, the highest score achievable is 8 of 8 points. If clinically appropriate, such as in the setting of intrauterine growth restriction (IUGR), sonographic biophysical profile testing may be initiated earlier than 32 weeks or repeated more frequently than every week. Umbilical artery Doppler testing is not performed routinely but is performed in the setting of IUGR. Estimates of fetal weights are performed every 4 weeks throughout pregnancy in uncomplicated dichorionic twin pregnancies and every 2 weeks in uncomplicated monochorionic twin pregnancies. All women with dichorionic twin pregnancies are delivered at 38 weeks, and those with uncomplicated monochorionic twin pregnancies are delivered at 37 weeks. In the setting of an abnormal sonographic biophysical profile, the woman is sent to labor and delivery for fetal heart rate monitoring, and a possible repeated sonographic biophysical profile, as appropriate. All sonographic examinations are performed by or supervised by maternal-fetal medicine specialists in a single outpatient imaging center. All nonstress tests were reviewed by either maternal-fetal medicine specialists or attending obstetrician-gynecologists.

We reviewed the sonographic biophysical profile results for all women who delivered at 33 weeks or later. We chose this gestational age because all patients who delivered earlier would likely not have initiated biophysical profile testing or would have only undergone biophysical profile testing for major problems, such as early-onset IUGR, twin-twin transfusion, and severe preeclampsia. All biophysical profile results were reviewed, as well as all follow-up testing performed for an abnormal biophysical profile, which was defined as less than 8 of 8. We calculated the rate of IUFD per patient and per fetus, the test-positive rate (defined as the percentage of patients with an abnormal biophysical profile at any time), and the false-positive rate (defined as the percentage of patients with an abnormal biophysical profile that did not diagnose an IUFD or lead to immediate delivery). All results were reported as percentages with 95% confidence intervals (CIs).

Results

Over the course of the study period, there were 552 women with twin pregnancies delivered by our practice at 33 weeks or later. Thirteen women (2.4%) did not undergo outpatient sonographic biophysical profile testing, either due to transfer into our practice right before delivery or due to prolonged hospitalization. Exclusion of these patients left 539 women for analysis. The baseline characteristics and delivery outcomes for these patients are described in Table 1.

There were 2 women with an IUFD over the course of the study period. Therefore, the incidence of IUFD per patient in this population with routine sonographic biophysical profile testing was 2 per 539 (0.4%; 95% CI, 0.1%–1.3%) and the incidence of IUFD per fetus was 2 per

1078 (0.19%; 95% CI, 0.05%–0.7%). One IUFD was an IUFD of twin B at 33 weeks 5 days in a woman with monochorionic twins and a 31% estimated fetal weight discordance (twin B was the smaller twin). This woman had normal biophysical profiles for both twins 6 days before the diagnosis of an IUFD of twin B. There was no oligohydramnios or polyhydramnios during the course of the pregnancy for either twin. The other case in which an IUFD occurred was at 33 weeks 7 days in a woman with dichorionic twins who had a previous diagnosis of IUGR of twin B (estimated fetal weight in the third percentile). The woman had normal biophysical profiles and normal umbilical artery systolic-to-diastolic ratios by Doppler analysis of both twins 6 days before the diagnosis of the IUFD of twin B.

There were 24 other women with abnormal sonographic biophysical profiles at any time (4.5%; 95% CI, 3.0%–6.7%). Fourteen of these 24 women (58.3%) were delivered because of the abnormal biophysical profiles (7 for oligohydramnios, 4 for a score of 4 of 8, and 3 for a nonreassuing fetal heart rate on a reflex nonstress test). The gestational age distribution of these 14 women was 34 weeks (1 patient), 35 weeks (3 patients), 36 weeks (3 patients), and 37 weeks (7 patients). The other 10 women with abnormal biophysical profiles all had normal follow-up nonstress test results, and none of these women had another abnormal biophysical profile before delivery. Figure 1 summarizes our results as noted above. The overall positive screen rate was 24 per 539 (4.45%; 95% CI, 3.0%–6.5%). The false-positive screen rate, defined as an abnormal biophysical profile that did not diagnose an IUFD or lead to delivery, was 10 per 539 (1.9%; 95% CI, 1.0%–3.4%).

Table 1. Population Characteristics

Characteristic	Value
Patients, n	539
Chorionicity, %	
Dichorionic diamniotic	86.1
Monochorionic diamniotic	13.9
Maternal age, y	34.0 ± 6.6
In vitro fertilization, %	63.3
Maternal prepregnancy body mass index, kg/m^2	23.6 ± 4.6
Obesity, %	9.4
White, %	89.2
Prior IUFD, %	2.2
Müllerian anomaly, %	1.9
Chronic hypertension, %	1.1
Preeclampsia, %	15.6
Pregestational diabetes, %	0.6
Gestational diabetes, %	9.7
Gestational age at delivery, wk	36.6 ± 1.3

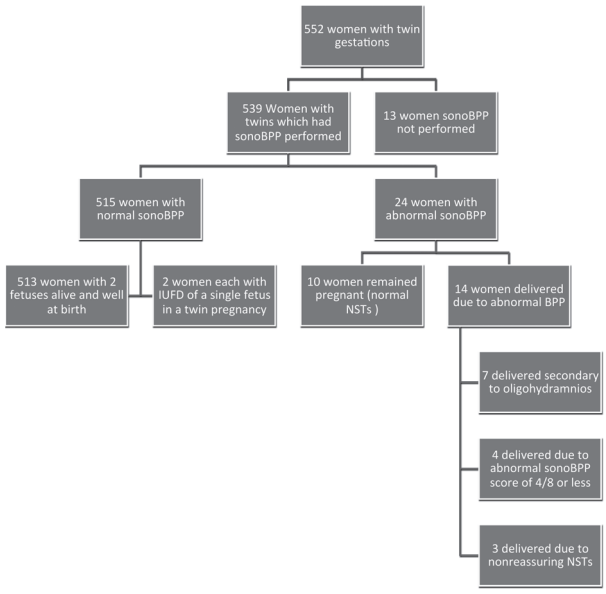
Data are presented as mean ± SD where applicable.

Discussion

The introduction of the biophysical profile in antenatal testing has provided an improved prognostic tool for the reassurance of fetal well-being. A reactive nonstress test result provides reassurance of fetal well-being; however, when abnormal, it has a high false-positive rate of 45% to 75%.[9–11] The fetal heart rate is subject to various dynamic factors, including periodic sleep cycles, medications, and antenatal corticosteroids.[12,13] Further evaluation is needed to differentiate between the hypoxic or acidemic fetus versus the sleeping or medicated fetus.

As early as 1980, Manning et al[14] defined the biophysical profile as a more comprehensive tool for assessing both acute and chronic well-being in a 30-minute assessment comprising the fetal heart rate, fetal movement, fetal tone, fetal respiratory movements, and the amniotic fluid volume. The goal was to assess the fetus for both acute and chronic signs of hypoxia and subsequently decrease associated neonatal morbidity and mortality. This antepartum assessment has since been validated in singleton pregnancies.[15–17]

Figure 1. Summary of results. BPP indicates biophysical profile; and NST, nonstress test.



In an attempt to validate the use of the biophysical profile as a more refined tool in antenatal testing, various components of the biophysical profile have since been studied and found to have different predictive values. Vintzileos et al[7] evaluated 124 nonlaboring singleton gestations who had biophysical profiles before cesarean delivery and correlated the absence of associated biophysical profile components with fetal acidemia. Although fetal breathing alone had low sensitivity, its positive predictive value was 100%. The nonstress test alone had sensitivity and specificity of 100% and 76%, respectively, whereas the combination of the nonstress test and fetal breathing movements had sensitivity and specificity of 100% and 92%. In an additional randomized study published by Manning et al,[18] the authors compared complete biophysical profiles to nonstress tests alone, and the biophysical profiles were found to be more predictive of low Apgar scores than the nonstress tests. In this study, the biophysical profile scoring included the nonstress test as well. A follow-up study by Manning et al[19] assessed 29 fetuses with a biophysical profile score of 0 and found that 14 of these fetuses died, 11 of whom were stillborn and 2 of whom were twins.

In 1987, Manning et al[20] assessed the modification of the fetal biophysical profile score by selective use of the nonstress test component and found that in measurement of gross and corrected perinatal mortality, the nonstress test did not produce a measurable decrease in test accuracy. This study, in which the nonstress test was used only when 1 or more abnormal sonographic variables were identified, supports our clinical protocol.

A paucity of data exists on the use of these antenatal tests in multiple gestations for attempting to predict neonatal/prenatal outcomes and thus dictate timely delivery for this at-risk population. Lodeiro et al[8] found the biophysical profile to be a reliable tool in the follow-up of a nonreactive nonstress test result in a small cohort of twin gestations. In that prospective study, 49 patients with twin gestation were monitored 1 to 2 times per week using nonstress tests, followed by biophysical profiles for each fetus. Of the 34 fetuses with nonreactive nonstress test results, 28 had biophysical profiles of 8 or greater and had good outcomes. The remaining 6 fetuses with nonreactive nonstress test results had biophysical profiles of less than 8, and all of these resulted in fetal distress; no fetal mortality was encountered in their cohort. The biophysical profile accurately predicted the distressed twin.

Although the above data support our hypothesis, we believe that our study provides substantially improved contemporary clinical data. That small trial was conducted in the early 1980s, it universally applied nonstress tests to the study population, and the expertise in equipment, clinician, and sonographer credentialing has changed and become more standardized over time, allowing for generalizability to current standards of care.

The markedly increased risk of stillbirth in twin gestations compared to singletons appears to be primarily the result of placental abnormalities. A recent series of 1000 consecutive twin pairs of at least 24 weeks' gestation noted that stillbirths occurred in 7 monochorionic diamniotic twin pairs (3.6%) and 9 dichorionic diamniotic pairs (1.1%).[21] We have shown in a large cohort of twin pregnancies that the use of the sonographic biophysical profile resulted in a 0.4% IUFD-per-patient rate and a 0.19% IUFD-per-fetus rate. Additionally, the use of routine testing in this at-risk population resulted in only a 1.9% false-positive rate. Routine antenatal testing in twins has not been proven to be beneficial; however, multiple experts in the field recommend initiation of routine screening at 32 weeks in twins, with the generally quoted prevalence of stillbirth noted to be 1.2%.[21]

Our study demonstrates the diagnostic value of the sonographic biophysical profile and its use in the management of antepartum surveillance of twins. The reflex application of the nonstress test may provide improved sensitivity in equivocal cases, with the sonographic biophysical profile providing the primary screening reassurance. This process is expected to save on cost and time for patients and providers, as the lengthier portion of the testing (as described in prior studies) is generally the nonstress test evaluation, particularly with the difficulty encountered in obtaining accurate and prolonged twin gestation monitoring.

Limitations of this research include the retrospective nature of our study design and a larger portion of twin pregnancies characterized by fertility-assisted treatment and advanced maternal age. Additionally, no long-term follow-up was available to determine the potential impact of transient hypoxemic events as they relate to biophysical profile scores. Substantial advantages include the standardized protocol for testing, which occurred in an American Institute of Ultrasound in Medicine–certified ultrasound unit with maternal-fetal medicine specialists reviewing the findings.

Future studies should attempt to prospectively randomize twin pregnancies to testing with either the nonstress test and a reflex sonographic biophysical profile or a sonographic biophysical profile with a reflex nonstress test (as we have described) to better determine the cost-effectiveness of these approaches. In this article, we offer our experience with routine antenatal surveillance in twin pregnancies using the sonographic biophysical profile and

reflex nonstress test. The most recent recommendations suggest antenatal screening of multiple gestations by using the nonstress test and amniotic fluid index in concordant twins starting at 32 weeks.[22] This approach uses ultrasound equipment and fetal monitoring equipment, in addition to the personnel required to obtain this information with each technology. We propose using the sonographic biophysical profile screening strategy, which may be as effective an approach with lower use of nursing time and equipment resources for determining well-being in multiple gestations.

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