American Journal of Obstetrics and Gynecology (2005) **192**, 199–207

ELSEVIER

AMERICAN JOURNAL of OBSTETRICS and GYNECOLOGY

www.ajog.org

Predicting respiratory distress syndrome using gestational age and fetal lung maturity by fluorescent polarization

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Received for publication December 3, 2003; revised April 7, 2004; accepted April 27, 2004

KEY WORDS
Fetal lung maturity
Quantitative fluorescence polarization-based fetal lung maturity assay
Gestational age
Sensitivity
Specificity

Objective: This study was undertaken to design a predictive model for assessing the risk of developing respiratory distress syndrome (RDS) by using gestational age (GA) and results from a quantitative fluorescence polarization-based fetal lung maturity assay (TDx FLM II).
Study design: The study populations from the 3 largest published studies analyzing the association between TDx-FLM II and the development of RDS were combined for this analysis. A total of 509 patients were included in this study; 57 gave birth to infants who had RDS develop, and 452 gave birth to infants who were unaffected. Logistic regression analysis was used to model the odds of RDS as a function of GA, TDx FLM II ratio, and study site.
Results: The absolute and relative risks of an infant having RDS develop as a function of GA and TDx FLM II were calculated. The odds of RDS decrease 31% for each increasing week of GA and decrease 67% for each 10 mg/g increase in the TDx FLM II ratio. GA-specific TDx FLM II cutoffs are provided for sensitivities between 84% and 100%. The bias-adjusted area under the receiver-operating characteristic curve for the classification of RDS, based on GA and TDx FLM II ratio, was 0.957 with the use of the logistic model.
Conclusion: The incorporation of GA into the evaluation of fetal lung monitoring allows for individualized, GA-specific risk assessment and provides GA-specific cutoffs with increased specificity.

Respiratory distress syndrome (RDS), also referred to as hyaline membrane disease, is associated with insufficient surfactant production by the neonatal lung and is a major cause of death in the newborn infant. In 2000, RDS ranked sixth among leading causes of infant

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doi:10.1016/j.ajog.2004.04.023

deaths, with 999 deaths caused by RDS in the United States.[1] The likelihood of developing RDS decreases with increasing gestational age (GA), as the fetal pulmonary system matures.[2] The ability to predict the risk for RDS before parturition enables physicians to either delay delivery of an immature infant (to administer steroids that hasten fetal lung development) or elect to deliver a preterm infant whose lungs are mature.

The TDx-FLM assay (Abbott Laboratories, Abbott Park, Ill) is a fluorescence polarization assay that rapidly measures a ratio of milligrams of surfactant per gram of albumin in amniotic fluid. In 1995, production of the original TDx FLM assay was discontinued and was replaced with the TDx FLM II assay. As a result of the assay change, the manufacturer's recommended cutoff for maturity changed from 70 mg/g or more to 55 mg/g or more. Studies showed that this cutoff could be lowered further to between 40 and 45 mg/g.[3,4]

Studies that have examined TDx FLM cutoff values have tended to select cutoffs that maximize sensitivity and the predictive value of a mature result to reduce the risk of delivering immature infants. However, the same cutoff is applied to all gestational ages even though it is known that the risk of RDS varies with GA. In 1994, Tanasijevic et al[5] reported a predictive model for the probability of fetal lung maturity that combined GA and the original TDx FLM assay. This approach individualized TDx FLM cutoffs for different GAs and allowed prediction of the probable risk associated with a given TDx result.

The concept of reporting the probability of RDS on the basis of GA and TDx FLM has been revisited several times recently.[6,7] In December 2002, Pinette et al[6] used the probability model of Tanasijevic et al[5] to produce a table giving the risk of RDS as it varies with GA and TDx FLM values. The need for an easy and practical approach to predicting fetal lung maturity was emphasized in an accompanying editorial.[8] Unfortunately, 2 major problems exist with the table that Pinette et al[6] constructed from data from Tanasijevic et al.[5] These problems were highlighted in 2 letters to the editor.[9,10] First, as already discussed, the article by Tanasijevic et al[5] used the original TDx FLM assay that was replaced in 1995 by the TDx FLM II assay. Because the 2 assays have different cutoffs for maturity, the use of the table by Pinette et al[6] will misrepresent the increase in probability of RDS with decreasing TDx FLM II ratio at all GAs. Second, the ability to assess absolute probability (as opposed to relative probability) in such a model is dependent on the prevalence of RDS in the population being tested.

Also in December 2002, Kaplan et al[7] published an article that investigated the risk of RDS as a function of GA and TDx FLM II values. However, they did not report a probability model for calculating the risk of RDS on the basis of GA and TDx FLM II values, but provided estimated probabilities of RDS when GAs were categorized as less than 34, 34 to 36, and more than 36 weeks and TDx FLM II ratios were categorized as less than 20, 21 to 44, and greater than 44 mg/g. This article was also accompanied by an editorial that stressed the need for probability reporting that incorporates test results and GA.[11]

The purpose of this study was to create a model to predict risk of RDS by using the results from the TDx FLM II assay and GA. We have combined the 3 largest published studies using the TDx FLM II assay to produce tables of absolute risk estimates, relative risk (RR) estimates, and GA-stratified TDx FLM II cutoffs. Furthermore, we discuss the merits of RR estimates versus absolute risk estimates when using risk tables in diverse clinical settings. The size and breadth of this study, representing data from 9 different institutions, provides the most accurate assessment of risk to date, and should be applicable across a broad range of clinical settings.

Material and methods

Patients

This was a retrospective cohort study spanning a 5-year period (1995-2000), including women whose physicians ordered a fetal lung maturity analysis by TDx FLM II (Abbott Laboratories, Abbott Park, Ill). The study populations and TDx FLM II results used in this study were taken from 3 previously published reports, here after referred to as: study 1 = Fantz et al[3]; study 2 = McManamon et al[4]; and study 3 = Kaplan et al.[7] The analysis was performed by using the raw data from the 3 studies. Study 1 included 185 patients from Barnes-Jewish Hospital, St. Louis, Mo, during the period 1998 to 2000 and Hennepin County Medical Center in 1998.[3] Study 2 included 94 patients from Mercy Medical Center, Des Moines, Iowa, from 1995 to 1997.[4] Study 3 included 307 patients from Bellevue Hospital, New York, NY; University of North Carolina Hospitals, Chapel Hill, NC; State University of New York, Stony Brook, NY; Tulane University, New Orleans, La; St. Mary's Hospital, Decatur Ill; and The Mary Imogene Bassett Hospital, Cooperstown, Md, during the period 1995 to 1999.[7] All 3 studies were retrospective cohorts using a series of samples (studies 1 and 2 were consecutive, study 3 was nonconsecutive) for which physician-ordered TDx-FLM II results and patient health information for both mother and infant were available. Inclusion criteria in all the studies required that delivery occurred within 72 hours of amniocentesis. Some patients included in the original published studies did not meet criteria for this study and some patients not included in the original studies did meet the criteria for this study.