Prepregnancy overweight and gestational diabetes are both risk factors for subsequent development of diabetes and hypertension, but prepregnancy overweight in and of itself is an essential risk factor.

**Objective:** To evaluate the roles of prepregnancy obesity and gestational diabetes mellitus as determinants of risks for subsequent diabetes and hypertension during 20 years of follow-up.

**Design:** Prospective, population-based study.

**Participants:** 9362 women delivering singleton infants between 1985 and 1986.

**Methods:** On 20-year follow-up, registry-based data was used to ascertain diagnoses of diabetes and hypertension. Of participants, 5 study groups were comprised: (1) normal weight women with gestational diabetes, (2) overweight women with gestational diabetes, (3) normal weight women with risk factors for diabetes with normal oral glucose tolerance tests (OGTT), (4) overweight women with risk factors for diabetes with normal OGTT, and (5) women with no risk factors for gestational diabetes.

**Results:** Accumulated incidence of diabetes and hypertension, 20 years post-index delivery, was 1.3% and 7.5%, respectively. Those who were overweight prepregnancy with an abnormal OGTT had the highest risk for subsequent diabetes (25.9%) and for hypertension (44.4%). Prepregnancy overweight with a normal OGTT was associated with higher risk for diabetes and hypertension, and in normal weight women, gestational diabetes indicated risk for subsequent diabetes but not hypertension.

**Conclusions:** Prepregnancy overweight and gestational diabetes are both risk factors for subsequent development of diabetes and hypertension, but prepregnancy overweight in and of itself is an essential risk factor.

**Reviewer’s Comments:** This was a well-designed and well-conducted long-term study on the contribution of prepregnancy overweight and gestational diabetes to the future development of diabetes and hypertension. The combination of the 2 yields astoundingly high risks for later development of diabetes and hypertension, but as this article points out, prepregnancy overweight in and of itself is a significant and important risk factor for 2 important chronic diseases of adulthood. (Reviewer-Berel Held, MD).

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Keywords: Obesity, Diabetes Mellitus, Prepregnancy

Print Tag: Refer to original journal article
Both gestational diabetes and mild impaired glucose intolerance predict a future likelihood of metabolic syndrome in young women.

Objective: To evaluate the relationship between gestational glucose tolerance testing (GTT) results and postpartum risk of metabolic syndrome.

Design: Prospective cohort study.

Participants: 487 pregnant women.

Methods: Participants underwent 3-hour oral GTT during pregnancy and cardiac and metabolic studies 3 months postpartum. On the basis of testing, 3 study groups were identified: (1) those with gestational diabetes mellitus, (2) those with impaired glucose tolerance, and (3) those with normal glucose tolerance testing. Utilizing criteria as defined by the International Diabetes Federation, the American Heart Association, and the National Heart, Lung, and Blood Institute, the presence of metabolic syndrome in these groups of women was ascertained.

Results: Prevalence of metabolic syndrome postpartum was 10% in those with normal glucose tests, 17.6% in those with impaired glucose testing, and 20% in those with overt gestational diabetes mellitus. Both gestational diabetes and impaired glucose testing were independently predictive of postpartum metabolic syndrome.

Conclusions: Both gestational diabetes and mild impaired glucose intolerance predict a future likelihood of metabolic syndrome, as early as 3 months postpartum, suggesting that any gestational dysglycemia may be associated with underlying latent metabolic syndrome.

Reviewer's Comments: Not much for me to add about this paper or the preceding one. The message is clear: any degree of dysglycemia and/or pre-pregnancy obesity confers real risk for future hypertension and diabetes. (Reviewer-Berel Held, MD).

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Keywords: Glucose Intolerance, Metabolic Syndrome, Postpartum

Print Tag: Refer to original journal article
Aspirin Intake Prolongs Survival After Breast Cancer

Aspirin Intake and Survival After Breast Cancer.
Holmes MD, Chen WY, et al:

J Clin Oncol 2010; 28 (March 20): 1467-1472

Aspirin use may decrease recurrence and death in breast cancer patients.

Objective: To determine if aspirin use in women with breast cancer decreases their risk of death from or recurrence of breast cancer.
Design: Prospective, observational study.
Methods: Data were derived from the Nurse's Health Study and participants were studied until death or June 2006. Breast cancer mortality risk was correlated with numbers of days per week of aspirin use, first assessed at least 12 months following diagnosis and updated thereafter.
Results: Of participants, there were 341 breast cancer deaths. Aspirin use was associated in a statistically significant fashion, with decreased risk of breast cancer death. Relative risk for 1, 2 to 5, and 6 to 7 days of aspirin use per week were 1.07, 0.29, and 0.36, respectively. Results were similar for distant recurrence incidence.
Conclusions: Aspirin use was associated with a diminished risk of distant recurrence and breast cancer death.
Reviewer's Comments: This was an observational study from the Nurse's Health Study, statistically documenting a decreased risk of distant recurrence in breast cancer survivors who took aspirin following their diagnosis. The laboratory evidence supporting aspirin's ability to retard breast cancer growth is supported by this clinical study, yet randomized studies must still be performed to validate the effectiveness of aspirin in prolonging survival and decreasing recurrence in breast cancer patients. (Reviewer-Berel Held, MD).

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Keywords: Aspirin, Breast Cancer, Survival

Print Tag: Refer to original journal article
Risk of pregnancy following hysteroscopic sterilization is low and may be reduced further by following protocol, performing a urine pregnancy test prior to the procedure, and in emphasizing patient follow-up visits.

**Background:** Hysteroscopic transcervical sterilization is a popular means of permanent birth control, firmly established in the gynecologist's armamentarium. Worldwide, over 250,000 women have been sterilized by this method during the past 8 to 10 years. Overall incidence of failure is low, however in truth unknown, but probably is in the neighborhood of 1 in 1000.

**Objective:** To analyze 10 unintended pregnancies of 9000 Essure sterilization procedures.

**Design:** Retrospective study.

**Participants:** 10 cases of unintended pregnancies occurring in >9000 women undergoing transcervical sterilization using the Essure system.

**Methods/Results:** Most pregnancies occurred in patients with only one device placement. There were failures to interpret ultrasounds and hCG post surgery, and 1 undetected pre-procedure pregnancy. Of patients, 2 failed to appear for follow-up of the 10 unintended pregnancies.

**Conclusions:** Risk of pregnancy following hysteroscopic sterilization is low and may be reduced further by following protocol, performing a urine pregnancy test prior to the procedure, and in emphasizing patient follow-up visits. Unilateral device placement in a patient without a history of salpingectomy is ill advised.

**Reviewer's Comments:** This was a good article reviewing a small number of unintended pregnancies following transcervical sterilization procedures in the Netherlands. As with almost every surgical procedure, proper patient selection, proper preoperative evaluation, and adherence to protocol are all keys to minimizing failures and complications. (Reviewer-Berel Held, MD).

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Keywords: Pregnancy, Essure Sterilization

Print Tag: Refer to original journal article
There are limitations to a specific genetic locus being clearly predictive of disease. A self-reported family history of cardiovascular disease is a useful predictor since it reflects interactions of genetic loci and shared environment.

**Objective:** To determine if a genetic risk score developed from a literature-based formulation can be predictive of cardiovascular disease.

**Design:** Prospective cohort study.

**Participants:** 19,333 initially healthy, white women, participating in the Women's Genome Health Study.

**Methods:** The National Human Genome Research Institute has now catalogued 100,000 single nucleotide polymorphisms that are associated with human disease. There have been published associations of certain single nucleotide polymorphisms with cardiovascular disease, including myocardial infarctions, stroke, and coronary disease, variations in lipids, glucose metabolism, and elevated blood pressure. Investigators constructed a genetic risk score using a sum of all cardiovascular risks alleles that have been associated with cardiovascular disease. Incidental myocardial infarctions, stroke, arterial revascularization, and cardiovascular death were the main outcome measures for the study.

**Results:** The genetic risk score was created using the total of 102 single nucleotide polymorphisms that had been associated with cardiovascular disease. Subjects were followed for a median of 12.3 years. During that time, there were 777 cardiovascular disease events, including 199 myocardial infarctions, 203 strokes, 63 cardiovascular deaths, and 312 revascularizations. Genetic risk score had a hazard ratio score of 1.02 per risk allele with a 95% CI of 1.00 to 1.03. This translated to a 3% risk of cardiovascular disease over a 10-year period in the lowest tertile of genetic risk and 3.7% in the highest tertile. However, there was no improvement in either discrimination or classification score for the cardiovascular disease associated with genetic risk score. In multivariable models, self-reported family history remained associated with cardiovascular disease in a statistically significant analysis. Overall predictability of cardiovascular disease was not improved by using genetic score after adjusting for traditional risk factors.

**Conclusions:** There is no significant association with incidence of total cardiovascular disease based on the use of a genetic risk score comprised of 101 single nucleotide polymorphisms.

**Reviewer's Comments:** This study is a testament to the interactivity of genetic markers for disease. There is no doubt that genetic data are important for understanding the biology and the cause of disease, but we have not yet achieved the level of understanding of the interactions of these hundreds of thousands of genetic loci on predicting disease state. (Reviewer-John C. Jennings, MD).
An open wound is fertile ground for bacterial growth. The longer the time a wound is exposed the more opportunity for pathogens to reproduce.

**Objective:** To study the relationship of infectious complications with operative out time.

**Design:** Retrospective database review.

**Participants:** 299,359 operations performed at 173 hospitals.

**Methods:** Investigators used the American College of Surgeons National Surgical Quality Improvement Database to retrospectively study infectious complications as they are related to operative time. Their 30-day postoperative infection complications that were examined during the study included urinary tract infection, pneumonia, sepsis, and septic shock. Investigators then used half hour increments of operative duration to compare with rates of infectious complications. In addition, investigators included the complexity of the surgical case according to work, relative value units, wound class, level of intraoperative transfusion, and length of hospital stay. They also separately analyzed laparoscopic cholecystectomies with low-risk anesthesia classification, since this procedure is usually not prolonged, and has a clean or clean-contaminated wound class.

**Results:** Infectious complication unadjusted rates increased in linear fashion with the duration of operative time with approximately 2.5% increased per half hour. In comparing cases of <1 hour in length, infection complication risks increased, almost doubling at 2.1 to 2.5 hours, with an odds ratio of 1.92, and a 95% CI of 1.82 to 2.03. When comparing laparoscopic cholecystectomy operative times of <0.5 hour to those lasting 1.1 to 1.5 hours, rate of infectious complication doubled from 0.7% to 1.4%. Investigators also found that length of hospital stay increased geometrically with length of operative time at a rate of 6% per half hour.

**Conclusions:** There are increased infectious complications rate and length of hospital stay associated with increased operative time. This linear increase holds after adjustment for procedure and patient risk factors.

**Reviewer’s Comments:** Operative duration indirectly reflects surgical technique, anatomic variations, and complexity of the surgical disease process. Although the data from this study are for general surgical procedures, there is no reason to believe this same relationship of operative duration to infectious complication does not exist with gynecologic surgery. (Reviewer-John C. Jennings, MD).

© 2010, Oakstone Medical Publishing

Keywords: Surgical Operation Duration, Infection Rates

Print Tag: Refer to original journal article
Lactation May Reduce Future Subclinical Cardiovascular Disease

Lactation and Maternal Measures of Subclinical Cardiovascular Disease.
Schwarz EB, McClure CK, et al:

Obstet Gynecol 2010; 115 (January): 41-48

Lactation has been reported to have beneficial effects on blood pressure, risk of developing diabetes, and lipid metabolism; reduced risk of cardiovascular disease may be added to that list.

**Objective:** To study the relationship of subclinical cardiovascular disease with lactation.

**Design:** Cross-sectional analysis of a community-based cohort study.

**Participants:** 297 women with ≥1 live birth.

**Methods:** The Study of Women's Health Across the Nation (SWAN)-Heart Study is a cohort study with enrollment from 1996 to 1997. Included in this study were 3302 women, aged 42 to 52 years with an intact uterus and ≥1 ovary. Of initial participants in this SWAN Study, 608 women (76%), elected to complete the baseline SWAN Heart Examination. Lactation history was assessed at the time of enrollment in the SWAN study. When patients agreed to enroll in the SWAN-Heart Study, calcification of the aorta and coronary arteries was assessed by electron beam tomography. Coronary calcification score was determined from the sum of individual scores of the 4 major epicardial arteries. Demographic data were collected on the interactions of lactation by age, race, and menopausal status and were evaluated in all models. Investigators then used a multivariable, logistic, regression analysis to estimate the relationship of subclinical cardiovascular disease to lactation.

**Results:** Mothers who breastfed all of their children for ≥3 months had a 17% incidence of coronary artery calcification as compared to 32% in women who had not breastfed. In women who breastfed, aortic calcification occurred at 17% while at 39% for those who had not. Carotid plaque occurred in 10% of women who had breastfed as compared to 18% who had not breastfed. When investigators adjusted for other measures, such as socioeconomic status, lifestyle, and family history, those women who had not breastfed remained more likely to have aortic calcifications with an odds ratio (OR) of 3.85 and more likely to have coronary artery calcification with an OR of 2.78 as compared to women who had consistently breastfed. When investigators adjusted for traditional cardiovascular risk factors and body mass index, mothers who had not breast fed remained more likely to have aortic calcifications than women who had breast fed with an OR of 5.26.

**Conclusions:** There is an increased risk of vascular change associated with future cardiovascular disease in mothers who do not breast feed as compared to those who do breast feed.

**Reviewer's Comments:** This study includes a racially diverse group of women, and it accounts for other variables. It reaches the conclusion that lactation has apparent preventive implications for future cardiovascular disease. (Reviewer-John C. Jennings, MD).

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Keywords: Breast Feeding, Cardiovascular Disease

Print Tag: Refer to original journal article
Increase in population in the United States and changing demographics will substantially increase the prevalence of pelvic floor disorders.

Objective: To forecast incidence of symptomatic pelvic floor disorders from 2010 to 2050.
Design: Projected prevalence rate study based upon representative samples.
Participants: 1961 non-pregnant women, aged ≥20 years.
Methods: Investigators used the Pelvic Floor Disorders Network data from 2005 to 2006 and coupled this with the U.S. Census Bureau Population Projections to determine future incidence of pelvic floor disorders. The initial cohort evaluated urinary incontinence severity, fecal incontinence severity, flatal incontinence, and pelvic organ prolapse. Census Bureau information projects a total population of 310.2 million in the United States in 2010, and a 439 million population projected in 2050. They used age subgroups of 20 to 39, 40 to 59, 60 to 79, and ≥80 years to determine age-specific population projections based upon known prevalence rates in these age groups.
Results: Between 2010 and 2050, the number of American women with ≥1 pelvic floor disorder will increase from 28.1 million to 43.8 million women. There is a projected 55% increase in urinary incontinence from 18.3 million to 28.4 million over this same period. This study projects an increase of 59% for fecal incontinence, with a number of 10.6 million increasing to 16.8 million during this 40-year period. Pelvic organ prolapse is expected to increase by 46% from 3.3 million to 4.9 million women. In 2050, the highest projected estimates are for 58.2 million women with ≥1 pelvic floor disorder, 41.3 million women with urinary incontinence, 25.3 million with fecal incontinence, and 9.2 million women with pelvic organ prolapse.
Conclusions: Increase in population in the United States and changing demographics will substantially increase the prevalence of pelvic floor disorders.
Reviewer’s Comments: This study has substantial implications for gynecology, in both the number of gynecologic surgeons needed and type of surgical procedures for which they must be trained. (Reviewer-John C. Jennings, MD).

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Keywords: Pelvic Floor Disorders, Prevalence, Forecast

Print Tag: Refer to original journal article
Objective: To determine maternal outcomes in pregnancies complicated by placenta accreta managed conservatively.

Design: Retrospective multi-center cohort study over approximately 15 years.

Participants: 167 patients with placenta accreta, increta, or percreta managed conservatively.

Methods: Conservative management included retention of placenta in situ with no attempt at forcible removal. Primary outcome was preservation of the uterus. Secondary outcomes included a composite of severe maternal morbidities and maternal death. If hemorrhage occurred ≤24 hours after delivery, it was considered primary postpartum hemorrhage. Secondary postpartum hemorrhage occurred >24 hours after delivery. If a hysterectomy occurred ≤24 hours after delivery, it was considered a primary hysterectomy and delayed if it occurred >24 hours after delivery.

Results: Of patients, 74 (44.3%) had antenatal sonographic findings suggestive of placenta accreta. Overall, 113 (69.0%) had planned cesarean sections and 27 (24.0%) had emergency cesarean sections secondary to hemorrhage. Primary postpartum hemorrhage occurred in 51.5%. In 17.4% of these, medical treatment was successful and the remaining 83% were treated with either uterine devascularization or primary hysterectomy. Of patients, 109 devascularization procedures were done in addition to conservative management. Conservative management was successful in 78.4% of cases. Of patients, 18 (10.8%) had primary hysterectomies and another 18 (10.8%) had delayed hysterectomies. Significant maternal morbidity was seen in 10 (6%) cases. There was also 1 maternal death. Follow-up data were available for 116 patients with successful conservative management. In 75%, there was spontaneous resolution of the placenta at a median of 13.5 weeks. It was necessary to remove retained placenta in 29 (25%) cases at a median of 20 weeks after delivery. Placenta percreta was seen in 18 patients with bladder involvement in 8. In 13 of these percreta cases, a uterine devascularization procedure was necessary. In 4, a primary hysterectomy was performed secondary to hemorrhage, and in 10, conservative management was successful.

Conclusions: Use of conservative management for placenta accreta can result in uterine conservation with a low rate of maternal morbidity.

Reviewer’s Comments: In the multiparous patient not desiring a further pregnancy, a cesarean hysterectomy with no attempt at removing the placenta is the best approach for managing placenta accreta. However, in patients wishing to preserve their fertility, conservative management is an option; although, patients should understand that there needs to be strict adherence to a protocol over a long period. Risk for bleeding and infection persists for months. It would also be interesting to determine the effect on fertility that conservative management has. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Maternal Outcome, Conservative Treatment, Placenta Accreta

Print Tag: Refer to original journal article
History of LEEP Does Not Appear to Increase Rate of Preterm Birth

*Loop Electrosurgical Excision Procedure and Risk of Preterm Birth.*

Werner CL, Lo JY, et al:

Obstet Gynecol 2010; 115 (March): 605-608

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Risk of preterm delivery is not significantly increased with a history of a loop electrosurgical excision procedure.

**Objective:** To determine if there was a relationship between use of loop electrosurgical excision procedure (LEEP) and subsequent preterm birth.

**Design:** Retrospective study done over 16.5 years.

**Methods:** Records were reviewed identifying patients who had undergone LEEP. These were singleton gestations having LEEP either prior to the index pregnancy or after the index pregnancy. They were compared to a control group of singleton infants delivered in the same time period whose mothers did not have LEEP. There were therefore 3 groups of patients evaluated: (1) those patients having LEEP prior to the index pregnancy, (2) general obstetric population not having LEEP, and (3) those having LEEP after the index pregnancy. Primary outcome evaluated was rate of preterm delivery <37 weeks. These were sub-divided into 2 groups: (1) those ≤33 weeks and (2) those 34 to 36 weeks. Neonatal outcomes were also evaluated.

**Results:** There were 511 patients having LEEP prior to the index pregnancy and 842 having LEEP after the index pregnancy. The comparison group of the general obstetric population included 240,348 women. Rate of preterm birth in the LEEP before pregnancy group for ≤33 weeks was 4% compared to 2% in the general population and 4% for the LEEP after pregnancy group. Preterm birth rate for 34 to 36 weeks gestation was 3% in the LEEP before pregnancy group, 5% in general obstetric population, and 6% in the LEEP after pregnancy group. There was no increase risk of preterm delivery having LEEP either before a pregnancy or after a pregnancy compared to the general population. Neonatal mortality, stillbirth rate, and perinatal mortality were also no different between groups. There was also no difference for the reasons of preterm delivery between groups.

**Conclusions:** LEEP performed either prior to or after an index pregnancy is not associated with an increased risk of preterm delivery.

**Reviewer’s Comments:** It would appear from this study that having LEEP does not increase the risk of preterm delivery. However, there were no data available on the LEEP itself with respect to volume of tissue, size, depth of tissueremoved, or degree of cervical abnormality that prompted LEEP. Other studies have shown both a causative and a non-causative effect for LEEP in preterm delivery. However, LEEP itself may not be the sole reason patients subsequently have preterm delivery. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Loop Electrosurgical Excision Procedure, Preterm Birth

Print Tag: Refer to original journal article
There is an increased risk of developing gestational diabetes if there is excessive weight gain in the first trimester.

**Objective:** To determine if there was an association between weight gain in pregnancy prior to the 50-gram, 1-hour glucose tolerance test (GTT) and the risk of developing gestational diabetes.

**Design:** Retrospective cohort study over 2.5 years.

**Participants:** 341 patients in the gestational diabetes group and 793 controls.

**Methods:** Singleton pregnancies without pre-gestational diabetes or a history of gestational diabetes in a previous pregnancy were eligible. Patients were screened for gestational diabetes using a 1-hour GTT from 24 to 28 weeks gestation. Pre-pregnancy weight and maternal weight at the first prenatal visit and the weight prior to her 50-gram, 1-hour oral GTT were recorded. Rate of weight gain during the first trimester and second trimester was calculated as kilograms per week. Rate of weight gain was determined up to the 1-hr, 50gm GTT. The Institute of Medicine recommendations for weight gain in pregnancy were used to determine if the rate of weight gain exceeded recommendations. Primary outcome evaluated was the development of gestational diabetes according to trimester specific weight gain. A control group of patients not developing gestational diabetes was used for comparison.

**Results:** Mean rate of weight gain was second highest in women with a body mass index (BMI) of 25.0 to 29.9 kg/m² at 0.36 kg/week. There was an increased risk of gestational diabetes development if there was a weight gain of 0.27 to 0.40 kg/week with an odds ratio (OR) of 1.43. If the weight gain was 0.41 to 0.97 kg/week, the risk of developing gestational diabetes also increased with an OR of 1.74. With respect to weight gain in the first trimester, a gain of 0.07 to 0.26 kg/week was associated with an increased OR of 1.04. If the weight gain was in the first trimester was 0.27 to 1.90 kg/week, OR for developing gestational diabetes was 1.82. If the weight gain was below or within the recommendations of the Institute of Medicine, the OR was 1 for developing gestational diabetes; however, if it was above the recommendations, the OR for gestational diabetes was 1.53. Prepregnancy patients overweight with a BMI of 25.0 to 29.9 and gained 0.41 to 0.97 kg/week, OR for developing gestational diabetes was 2.1. In the obese patient, the same weight gain gave them an OR of 1.2 for developing gestational diabetes.

**Conclusions:** There is a relationship between increased weight gain early in pregnancy especially in the first trimester and the risk of developing gestational diabetes.

**Reviewer's Comments:** It appears from this study that weight gain early in pregnancy is associated with an increased risk for developing gestational diabetes. Patients should be counseled on this since this is a modifiable risk factor to help decrease the risk for developing gestational diabetes. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Gestational Weight Gain, Gestational Diabetes Mellitus

Print Tag: Refer to original journal article
Measurement of Ductus Venosus Flow May Help Predict Twin-Twin Transfusion

Matias A, Montenegro N, et al:
Ultrasound Obstet Gynecol 2010; 35 (February): 142-148

There is an increased risk of developing twin-twin transfusion at a monochorionic twin gestation if there is an abnormal ductus venosus flow in at least one twin at 11 to 14 weeks gestation.

**Objective:** To determine if there was an association between assessment of ductus venosus blood flow in combination with measurement of nuchal translucency, crown rump length at 11 to 14 weeks gestation, and the development of twin-twin transfusion syndrome (TTTS) in monochorionic twins.

**Design:** Prospective study over approximately 1 year.

**Participants:** 99 monochorionic diamniotic twin gestations.

**Methods:** At 11 to 14 weeks gestation, each fetus had a measurement of crown rump length, nuchal translucency, and ductus venosus assessment. After 14 weeks, all monochorionic twin gestations were assessed every 2 weeks for signs of TTTS.

**Results:** Of participants, 12 (12.1%) twin pairs subsequently developed TTTS between 16 to 26 weeks gestation. Normal ductus venosus blood flow was seen in 83 of the twin pairs. Of these pairs, 3 (3.6%) subsequently developed TTTS. There was either absent or reversed A-wave in the ductus venosus flow in 1 of the fetuses in 13 gestations and in both fetuses in 3 gestations. Of these 16 pairs, 9 developed TTTS. Of cases that had abnormal ductus venosus flow in one fetus, 3 showed significant growth discrepancies during the third trimester but did not develop TTTS. With respect to ductus venosus flow, crown rump length, and nuchal translucency, the best predictor of TTTS was ductus venosus flow. Second best predictor was the inter-twin difference of nuchal translucency and least predictive was inter-twin difference of crown rump length. An abnormal ductus venosus flow in at least one fetus was an independent predictor of TTTS. If one fetus had an abnormal ductus venosus blood flow, relative risk of TTTS was 15.5. If there was normal ductus venosus flow in both fetuses, but an inter-twin difference in nuchal translucency ≥0.6mm, no TTTS developed. If the inter-twin difference of the nuchal translucency was <0.6mm but there was abnormal ductus venosus flow in at least one fetus, the relative risk of TTTS was 10. If there was a nuchal translucency ≥0.6mm and abnormal ductus venosus flow, again, in at least one fetus, the relative risk of developing TTTS was 21.0.

**Conclusions:** An abnormal ductus venosus flow in at least one fetus of a monochorionic twin gestation at 11 to 14 weeks gestation increases the risk of developing TTTS. The risk is increased even further if there is an inter-twin difference in the nuchal translucency.

**Reviewer’s Comments:** In diamniotic monochorionic twins, at the 11 to 14 week ultrasound, not only should crown rump length and nuchal translucency be measured, but also ductus venosus assessment. The finding of an abnormal ductus venosus flow as well as an inter-twin difference in nuchal translucency should result in a closer surveillance of these pregnancies because of the increased risk of TTTS. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Screening, Twin-Twin Transfusion Syndrome, Ductus Venosus Blood Flow Assessment

Print Tag: Refer to original journal article
Enlarged yolk sac in early pregnancy has a 3-fold increased risk of first trimester loss.

**Objective:** To describe ultrasonic findings of an enlarged yolk sac and its significance regarding pregnancy outcome.

**Design:** Retrospective study.

**Methods:** Studied were 175 cases, in whom yolk sac diameters could be measured during the first trimester of pregnancy, and whose pregnancies were followed through birth. There were 80 cases in which the mean yolk sac diameter >5 mm, and 95 controls in whom mean yolk sac diameter was 3 to 4 mm. Mean gestational age at time of measurement was similar in both groups, approximately 8 weeks.

**Results:** Those with yolk sac diameter ≥5 mm had an increased risk for first trimester miscarriage compared with controls, 34% versus 14%, respectively. This elevated miscarriage rate, based on yolk size alone was independent of other maternal risk factors such as age, body mass index, underlying medical conditions, and smoking. In those with an enlarged yolk sac, there was a 4-fold increased risk of preterm delivery as well, 23% versus 6%.

**Conclusions:** An enlarged yolk sac diameter ≥5 mm on first trimester ultrasound is associated with an increased risk of first trimester miscarriage and preterm delivery.

**Reviewer’s Comments:** This brief report of a retrospective analysis of yolk sac diameters measured in the first trimester of pregnancy shows a significant increase in first trimester miscarriage and preterm delivery, when the mean diameter ≥5 mm. This is a significant and important finding since the yolk sac is the most prominent structure in the gestational sac during the first 8 weeks of pregnancy. This study needs to be replicated in a prospective fashion to document the significance of the 5-mm cut-off size. (Reviewer-Berel Held, MD).

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Keywords: Yolk Sac Size, Adverse Pregnancy Outcomes, Ultrasound

Print Tag: Refer to original journal article
Placebo medication appears as effective as orally administered indole phytochemicals in the treatment of CIN II and III.

Objective: To test the efficacy of oral diindolylmethane (DIM) in the treatment of CIN II or III lesions.

Design: Randomized clinical trial.

Participants: 60 patients with biopsy-proven CIN II or III who were scheduled for loop electrosurgical excision procedures (LEEPs).

Methods: Patients were randomized to receive DIM orally for 12 weeks or placebo, and then evaluated by Pap smear, human papillomavirus (HPV) testing, colposcopy, biopsy and physical examination every 3 to 4 months for 1 year, to assess this non-surgical treatment for cervical dysplasia. Patients had an average follow-up of 6 months.

Results: No systemic toxicities were observed in the treatment group receiving DIM, a phytochemical plant indole naturally occurring in green vegetables and possessing potential estrogen modulating and anti-neoplastic activities. Half of 47 subjects in the DIM group had improved CIN with a decrease by 1 or 2 grades or a normal result, with median time to improvement of 5 months. Improved pap smear was seen in 49% and colposcopic findings improved in 56%. Results were similar in the placebo group, and at median follow-up time of 6 months, 85% of subjects had not required LEEP procedures based on their most recent clinical findings. There was no statistically significant difference in any outcome between the treated DIM and placebo groups.

Conclusions: A high rate of clinically significant improvement in confirmed CIN II and III lesions occurred over time in both treatment and observation groups in this trial.

Reviewer’s Comments: Sadly for the authors and for the company that manufactures DIM, treatment and placebo groups had identical outcomes. Moral to this story is in HIV-negative women, time alone will have a beneficial effect on CIN lesions. That is not to say that they should not be treated, but they can be followed under ideal circumstances, and the expectation of improvement and in some cases, complete resolution of dysplasia is realistic. (Reviewer-Berel Held, MD).

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Keywords: Non-Surgical, Treatment for CIN

Print Tag: Refer to original journal article
Objective: To devise a nomogram providing accurate estimation of overall survival following primary therapy in women with endometrial cancer.

Design: Statistical study.


Methods: Characteristics associated with overall survival were collected, and for each patient, points were assigned to each of 5 variables; a total score was then calculated. Using multivariable modeling, the association between each predictor and outcome was assessed. Overall 3-year survival probabilities were then determined from the nomogram. The 5 variables assessed were age at diagnosis, status of lymph nodes, stage of disease, grade of disease, and histologic subtypes.

Results: Performance of the nomogram was assessed via statistical calibration and discrimination. The former measured how far predictions were from actual outcomes, while the latter evaluated whether the model is able to discriminate between patients with longer versus shorter survival times. Nomogram graphs are a graphic prediction tool incorporating clinical risk factors providing a simple graphical representation of a statistical model, which generates a numerical probability for a clinical event. This model was internally validated for predicting overall survival after primary treatment.

Conclusions: This nomogram, based on 5 clinical characteristics, had the ability to predict overall survival with a high concordance probability, and may be useful in assessing patient risks when deciding follow-up strategies.

Reviewer's Comments: This was a purely statistical study of overall survival in 1735 cancer patients treated between 1993 and 2008, whose clinical characteristics were correlated with survival in order to pose a predictive nomogram offering probability of survival. What works for Memorial Hospital presumably could work in other institutions as well, and it is a useful tool for any clinical oncologist. (Reviewer-Berel Held, MD).

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Keywords: Survival, Endometrial Cancer, Nomogram

Print Tag: Refer to original journal article
Objective: To study the relationship and symptoms associated with pelvic prolapse as contributors to urinary incontinence.

Design: Retrospective cohort study based on 2 randomized surgical trials.

Participants: 1252 women participating in 2 randomized urinary incontinence surgical cohorts.

Methods:Investigators used baseline data from the Stress Incontinence Surgical Treatment Efficacy Trial and the Trial of Mid Urethral Slings to relate symptoms of pelvic prolapse to urinary incontinence severity. Participants included 655 women recruited for the Stress Incontinence Surgical Treatment Efficacy Trial and 597 women recruited for the Trial of Mid Urethral Slings. Both studies had eligibility criteria that included both self-reported symptoms and clinical examination measures. Baseline demographic data was collected including age, self-reported race and ethnicity, education, and socioeconomic status. Body mass index was calculated and specific factors related to obstetric and gynecologic history, including the number of vaginal deliveries, prior hysterectomy, and prior urinary incontinence of surgery for pelvic prolapse. Urinary incontinence symptoms were measured using Urogenital Distress Inventory, the Incontinence Impact Questionnaire, and the Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire. Objective measurements included a 24-hour pad test, POP-Q measurements, and bladder volume at the time of the positive stress test. Subjects were grouped according to the stage of pelvic organ prolapse, but data between groups were not pooled. Analysis was then performed to relate prolapse severity with urinary incontinence severity.

Results: Variables including age, nulliparity, prior urinary incontinence surgery, and prior hysterectomy were similar between study samples. Investigators did not find a statistically significant difference between urinary distress inventory scores according to the stage of prolapse in either study population. There were more urinary incontinence symptoms in patients who had prior surgery for pelvic organ prolapse, and these patients were more bothered by their urinary incontinence symptoms regardless of prolapse stage.

Conclusions: Severity of urinary incontinence symptoms in women undergoing surgery for stress urinary incontinence is not consistently associated with prolapse stage. Subjects who have had prior pelvic organ prolapse and urinary incontinence surgery do have worse urinary incontinence severity and bother.

Reviewer's Comments: Degree of prolapse and severity of urinary incontinence can be paradoxical. Sometimes the correction of a severe prolapse will be accompanied by de novo urinary incontinence depending on how anatomic correction affects pressure relationships between the bladder and urethra.

(Rewriter-John C. Jennings, MD).

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Keywords: Pelvic Floor Disorders, Symptoms, Pelvic Prolapse, Urinary Incontinence

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The most common focus of infection in intensive care unit patients is the lungs. *Staphylococcus aureus* is the most common organism isolated but there is an overall predominance of gram-negative organisms.

**Objective:** To study patterns and extent of infection in international intensive care units (ICUs).

**Design:** One day, prospective point prevalence study.

**Participants:** 14,414 ICU patients.

**Methods:** The Extended Prevalence of Infection in Intensive Care Unit Study was selected May 8, 2007, for a point prevalence study >1265 intensive care units in 75 countries. Investigators collected demographic, physiologic, bacteriologic, therapeutic, and outcome data from the patients.

**Results:** 13,796 adult patients were included on the day of study. Of these, 7087 patients (51%) were considered to be infected, and 9084 (71%) were receiving antibiotics. Respiratory infection was identified in 4503 (64%) of infected patients. Cultures were positive in 4947 (70%) of infected patients. Gram-negative organisms were found in 62% of the positive cultures. Gram-positive organisms were found 47% of the cultures and 19% of the cultures fungi were identified. Higher rates of infection were found in patients who had longer ICU stays prior to the study day, and in these patients resistant *Staphylococcus, Acinetobacter, Pseudomonas, and Candida* were present. Patients who were infected as opposed to non-infected patients were twice as likely to die.

**Conclusions:** Risk of infection increases as duration of ICU stay increases. There is also an increased risk of hospital death that is independently associated with infection.

**Reviewer's Comments:** This study has the strength of being international, and it did reveal important differences in outcomes in various parts of the world. However, there are large differences in health care systems and ICU facilities that make comparisons across geographic regions difficult. (Reviewer-John C. Jennings, MD).

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Keywords: Prevalence, Infection, International Intensive Care Units

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Most communication errors in intensive care units occur at night. This observation may be related to work hours and is certainly multi-factorial.

**Objective:** To relate short-term outcomes in surgical intensive care units (ICUs) with patterns of physician/patient care communications.

**Design:** Prospective observational trial.

**Participants:** Patients hospitalized >136 consecutive surgical ICU days.

**Methods:** 3 surgical ICUs led by board-certified intensive care physicians were included in this trial. An ICU study day was defined as a 24-hour period covered by a combination of a resident and a fellow in an individual ICU. Investigators divided the study into an observational phase of 68 ICU days, and an interventional phase of 68 ICU days. They prospectively identified four cardio respiratory events, including hypotension, new arrhythmias, tachypnea, and desaturation. For each event, investigators defined short-term outcomes of improved, not improved, or worse. Residents were given a special communication seminar during the interventional phase of the trial, in which the importance of communication is a benchmark for quality of care was stressed and formally addressed.

**Results:** 166 events occurred in the observational stage and 146 events occurred in the interventional stage. Of communication areas in the observational stage, 73% were accounted for by postgraduate 3-year (PGY 3) residents. In the interventional stage, 59% of communication errors were accounted for by PGY 3 residents. Of all communication errors, 77% occurred on the late shift. Cardio-respiratory events were most affected by communication errors, with worse short-term outcomes. Improved short-term outcomes could be significantly predicted by effective communication. In the interventional phase of the study, communication errors were decreased in the late shift by 10%.

**Conclusions:** Communication errors occur frequently during the late shift in surgical ICUs. Short-term outcomes are significantly associated with communication errors.

**Reviewer's Comments:** Surgical ICUs can be very busy places where critical observations can be overlooked. This study suggests that observations are made but sometimes not effectively communicated. (Reviewer-John C. Jennings, MD).

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Keywords: Communication, Surgical Intensive Care Unit

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Atypical glandular cells either of endocervical origin or endometrial origin should be evaluated in the same manner.

**Objective:** To study the relationships of the combination of atypical glandular cells on cytologic examination along with human papillomavirus (HPV) testing as a predictor of reproductive organ specific cancer risks.  
**Design:** Retrospective cohort study with cross-sectional analysis.  
**Participants:** 1422 women with high-risk HPV testing and atypical glandular cytology.  
**Methods:** Atypical glandular cell interpretation of cytologic specimens from a single institution was reviewed. Of 2596 cytologic specimens, 1422 had high-risk HPV testing and were included in the study, along with histology results. Investigators grouped cytologic specimens according to interpretation of atypical glandular cells as being unqualified endocervical cells or endometrial cells, respectively. They calculated risks for cervical intraepithelial neoplasia grade II or more severe and for endometrial cancer as it related to atypical glandular cell cytology and HPV DNA high-risk testing.  
**Results:** Investigators identified 238 women with atypical glandular cell cytology, who were diagnosed with CIN II or worse, endometrial cancer, or other cancers. Women who were aged ≥50 years, who were high-risk HPV negative, with atypical glandular cell cytology had a 10.5% risk for endometrial cancer with a 95% CI of 7.7% to 13.8%. Of women in this same age group, who were high-risk HPV positive, there was a 10.4% risk of cervical cancer, and a 0% risk of endometrial cancer.  
**Conclusions:** It is possible to distinguish between the risk of endometrial cancer and cervical cancer using high-risk HPV testing in women who have atypical glandular cell cytology. This observation is particularly true in women who are aged ≥50 years.  
**Reviewer's Comments:** The relationship of high-risk HPV with cervical cancer is well established. This study simply states that women aged ≥50 years who have atypical cell cytology and are HPV negative are unlikely to have cervical cancer, but have a significant probability of endometrial cancer. (Reviewer-John C. Jennings, MD).
There is both a low sensitivity and low positive predictive value in pregnant patients having only a family history of venous thromboembolism and being subsequently identified as a factor V Leiden mutation carrier.

Objective: To determine if there was an association between a family history of venous thromboembolism and the presence of a factor V Leiden mutation in pregnant women who have no history of venous thromboembolism.

Design: Retrospective study of prospectively collected data.

Methods: Data were collected regarding the presence of factor V Leiden and thromboembolic events during pregnancy. Patients reporting a positive family history of either a first or second degree relative that had a venous thromboembolism were evaluated for the presence of factor V Leiden mutation. The utility of family history to predict factor V Leiden carriage was determined as well as sensitivity, specificity, positive/negative predictive values for use of family history.

Results: 5168 patients had no personal history of venous thromboembolism. All had factor V Leiden mutation analysis available. Of patients, 4756 had no family history while 412 had a positive family history for venous thromboembolism. Of patients with a positive family history of thromboembolism, 23 were carriers of factor V Leiden mutation or 5.6%. Of 23 patients that were carriers for factor V Leiden mutation, none developed a venous thromboembolism. Of patients with a negative family history of venous thromboembolism, 2.5% were carriers of factor V Leiden. In patients with a first degree relative having a history of venous thromboembolism, sensitivity for being a factor V Leiden carrier was 6.4%, specificity 96.6%, positive predictive value 5%, and negative predictive value of 97.4%. In those with either a first or second degree relative, sensitivity was 16.4%, specificity 92.3%, positive predictive value 5.6%, and negative predictive value 97.5%. Positive predictive value was similar whether it was a first or second degree relative having a venous thromboembolism.

Conclusions: Although there is an increase in carrier status of factor V Leiden mutation in pregnant patients having no history of venous thromboembolism with either a first or second degree relative having a venous thromboembolism, there continues to be a both a low sensitivity and positive predictive value.

Reviewer’s Comments: Although there is an association between a carrier status for factor V Leiden mutation and a positive family history, the authors believe that it is not significant enough to recommend screening for factor V Leiden mutation. However, in patients with a negative family history, carrier status for factor V Leiden mutation was found in 2.7% compared to 5.6% in those with the family history, approximately a 2-fold increase. If one encounters a patient during pregnancy who gives a family history of venous thromboembolism, it still seems prudent to identify the relative and to do an appropriate evaluation for the specific thrombophilia. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Family History, Venous Thromboembolism, Factor V Leiden Carriers, Pregnancy

Print Tag: Refer to original journal article
There is actually a decreased rate of hypertensive disorders in pregnancy for patients who have undergone a chorionic villus sampling.

**Objective:** To determine if there was any relationship between patients undergoing chorionic villus sampling (CVS) and subsequently developing hypertensive disorders in pregnancy.

**Design:** Retrospective study over a 5-year period.

**Participants:** 5232 patients in the CVS group and 4136 controls.

**Methods:** Patients having undergone CVS were identified. All patients underwent CVS at 10 to 13 and 6/7 weeks gestation. Primary outcome evaluated included rate of hypertensive disorders in pregnancy including both gestational hypertension, preeclampsia, and hemolysis, elevated liver enzymes and low platelet count (HeLLP) syndrome. Only singleton pregnancies with normal karyotypes were included in the CVS group. A control group who did not have CVS were also included for comparison.

**Results:** When considering all hypertensive disorders, they were seen in 2.6% of the CVS group and 6.8% of controls. Gestational hypertension occurred in 1.1% of the CVS group and in 2% of controls. Mild preeclampsia occurred in 1.5% of the CVS group and in 3.9% of controls. Severe preeclampsia occurred in 0.2% of the CVS group compared to 1% of the control group. HeLLP syndrome was seen in 0.08% of the CVS group compared to 0.30% in the control group. Overall, hypertensive disorders were actually less in the CVS group compared to controls after adjusting for confounding factors. When CVS patients were stratified by gestational age at the time of CVS, again the rate of hypertensive disorders was less in the CVS group than in controls.

**Conclusions:** Compared to controls, patients undergoing CVS actually have a decreased rate of hypertensive disorder in pregnancy.

**Reviewer's Comments:** The results from this study do not show an increased risk of developing hypertensive disorder in pregnancy in patients having had a CVS. In fact, in this study, rates were lower than in the control group. However in the control group there was a 2-fold increase in patients with chronic hypertension and a 4-fold increase in insulin dependent diabetes. There have been previous studies showing a relationship between CVS and hypertensive disorders so further studies will be needed before patients can be counseled appropriately regarding a possible additional risk of CVS. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Chorionic Villus Sampling, Hypertensive Disorders, Pregnancy

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Cord Entanglement in Monoamniotic Twins May Not Be Related to Pregnancy Loss

Cord Entanglement and Perinatal Outcome in Monoamniotic Twin Pregnancies.

Dias T, Mahsud-Dornan S, et al:

Ultrasound Obstet Gynecol 2010; 35 (February): 201-204

In monoamniotic twins although cord entanglement is frequent, the majority of perinatal mortality is related to other pregnancy complications besides cord entanglement.

**Objective:** To determine rate of cord entanglement and to assess perinatal outcomes in monoamniotic twins.

**Design:** Prospective observational study over 8 years.

**Participants:** 32 monoamniotic twin gestations.

**Methods:** Patients were typically referred from 11 to 16 weeks gestation for evaluation of possible monoamniocity. If monoamniotic twins were confirmed, serial ultrasounds were done every 4 weeks. B-mode and color Doppler ultrasound were used to assess umbilical cord entanglement. Cesarean delivery was undertaken at approximately 34 weeks gestation. Perinatal outcomes were then determined.

**Results:** Of gestations, 3 were conjoined twins and 7 had twin reversed arterial perfusion (TRAP) syndrome. There was 1 miscarriage and 3 pregnancy terminations secondary to discordant fetal abnormality. There were 18 monoamniotic gestations remaining for evaluation. All monoamniotic gestations were confirmed after delivery by placental pathology. Antenatal cord entanglement was verified by sonographic evaluation in all. This initially was seen from 11 to 16 weeks gestation. Of the 18 monoamniotic twin gestations, there were 34 live births. One pregnancy was complicated by a fetal demise of both twins at 19 weeks gestation. Mean gestational age at time of delivery was 34 weeks with a range of 30 to 37 weeks. There were 2 neonatal deaths, both from neonatal heart issues. After 16 weeks, overall perinatal mortality rate was 11.1% and after 20 weeks, 5.9%.

**Conclusions:** When appropriately sonographically evaluated, umbilical cord entanglement is seen in all monoamniotic twins. In monoamniotic twins, perinatal mortality is frequently the result of conjoined twins, discordancy, anomalies, TRAP syndrome, and spontaneous pregnancy loss <20 weeks gestation. Early delivery of monoamniotic twins that was thought to prevent cord accidents should be reconsidered.

**Reviewer’s Comments:** The authors recommend reevaluating the gestational age for delivery of monoamniotic twins. There have been other studies that have evaluated perinatal loss after 32 or 34 weeks gestation in this group of patients and in some cases, a loss of approximately 6% has been seen. When interpreting perinatal loss it is important to distinguish neonatal versus antenatal loss. Large or multi-centered studies need to be done before a definitive gestational age can be chosen for appropriate delivery of monoamniotic twins. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Cord Entanglement, Perinatal Outcome, Monoamniotic Twin Pregnancies

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Both the rate of successful vaginal delivery after cesarean section and maternal morbidities are similar in those patients having ≥3 previous cesarean sections versus those having 1 previous cesarean section.

**Objective:** To determine risks associated with an attempted vaginal birth after cesarean (VBAC) in patients with ≥3 previous cesarean sections.

**Design:** Retrospective, multi-center cohort study over 4 years.

**Methods:** Patients having ≥3 cesarean sections attempting a vaginal birth were evaluated. Primary outcome was a composite of maternal morbidities including ≥1 of the following: bladder or bowel injury, uterine rupture, or uterine artery laceration. Secondary outcomes were successful VBAC, transfusion, and febrile morbidity.

**Results:** Of 25,005 women that had a previous cesarean section, 860 (3.4%) had ≥3 previous cesarean sections: 748 (87%) had 3 previous cesarean sections, 97 (11%) had 4 previous cesarean sections, 13 (2%) had 5 previous cesarean sections, and 2 (0.2%) had 6 previous cesarean sections. Of these women, 89 had an attempted VBAC while 771 had repeat cesarean sections. When comparing those undergoing a VBAC versus those undergoing a repeat cesarean section, there were no cases of uterine rupture and no differences in morbidities including bladder injury, surgical injury, composite morbidity, use of blood transfusions, or febrile morbidity. Of VBAC patients, 32 (36%) had had a previous vaginal delivery and 91% of these successfully delivered vaginally. This compared to a 74% success rate in those 57 women who attempted a VBAC after having 3 previous cesarean sections but no previous vaginal delivery. When comparing those patients undergoing a VBAC having ≥3 previous cesarean sections to those having 2 previous cesarean sections or 1 previous cesarean section, rate of successful VBAC was 79.8% in the ≥3 previous cesarean section group, 74.6% in the 2 previous cesarean section group, and 75.5% in the 1 previous cesarean section group. There was also no statistical difference with respect to the rate of transfusions or febrile morbidity.

**Conclusions:** Patients having had ≥3 previous cesarean sections attempting a VBAC had similar rates of successful vaginal delivery and maternal morbidity compared to those patients having 1 previous cesarean section attempting VBAC and those undergoing repeat cesarean section.

**Reviewer's Comments:** There does not appear to be any difference either in the rate of success of VBAC in patients having 1, 2, or ≥3 previous cesarean sections. Morbidity also does not appear to be different among groups nor did it differ from those undergoing a repeat cesarean section. Patients having a previous cesarean section and a previous vaginal delivery appear to be the best candidates for an attempted VBAC. (Reviewer-Thomas N. Tabb, MD).

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Keywords: Vaginal birth, cesarean sections, VBAC, multiple cesarean

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