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Ultrasonic Evaluation of Cervical Length in Pregnancies Complicated by Preterm Premature Rupture of the Membranes

ABSTRACT & COMMENTARY

GIRE AND COLLEAGUES RECENTLY PUBLISHED DATA THAT HAVE interesting potential in the management of patients with preterm premature rupture of the membranes (PPROM). Over a 3-year period they assessed cervical lengths through transvaginal ultrasound examinations on admission in more than 100 patients diagnosed with PPROM. Gire et al were interested in determining if cervical length was related to the development of chorioamnionitis in these patients, who, by protocol, were managed expectantly unless there was evidence of infection. Although there was no statistically significant relationship between cervical length and maternal or neonatal sepsis, there was a strong relationship between cervical length and length of latency. Using a receiver operator curve (ROC) Gire et al found, using a 2 cm cutoff, that the average time from admission to delivery was 59 hours when cervical length was below this threshold, compared with 240 hours when cervical length was longer than 2 cm. There was a trend toward a higher rate of chorioamnionitis in multiparas who presented after 28 weeks with longer cervices, but this was not statistically significant (Gire C, et al. *Ultrasound Obstet Gynecol*. 2002;19[6]:565-569).

COMMENT BY JOHN C. HOBBINS, MD

PPROM occurs in about 3% of pregnancies but is responsible for substantial perinatal morbidity secondary to prematurity and/or maternal or neonatal sepsis. In PPROM, a good noninvasive predictor of chorioamnionitis is yet to be found. However, this study helps to distinguish patients who will deliver within a few days of admission from those who will be in the hospital for at least 10 days.

Some have questioned the safety of transvaginal ultrasound examination in premature rupture of the membranes because of the potential to introduce bacteria into the cervix. Upon entering the vagina, the transducer is on course to make contact with the cervix well back in the anterior fornix and far from the exocervix. Also, the

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transducer would add few new bacteria to the already rich microbial environment in the vagina.

Gire et al found that patients who were more than 28 weeks tended to have a greater chance of chorioamnionitis if their cervices were long is intriguing. On one hand, if a patient is developing chorioamnionitis, one might expect the cervix to be soft and well effaced because of the indirect action on the collagen and elastin of the cervix. However, if membranes are ruptured because of intracervical exposure to bacteria alone, then a long cervix might be expected, as long as it is not coupled with ascending infection, which would come later.

For years physicians have been reluctant to send patients home with PPROM because: a) they often go into labor soon after rupture of the membranes; b) of concern that early signs of infection will go unnoticed; and c) of liability if complications occur.

According to the above study, transvaginal ultrasound should be able to predict which patients would be most likely to occupy a bed for at least a week and a half while being exposed to the hospital's own special brand of microbes. Often patients would be far happier in their home environment and it would be substantially less expensive to use some form of home surveillance for the right patient, rather than having her "stew" in the hospital for more than 10 days (costing between $1500 and $2000/day by my most recent calculations).

Obviously many safeguards would have to be set up to make sure that early signs of chorioamnionitis would not be missed, and expeditious transfer to the hospital could be accomplished.

Certainly this study presents food for thought. ■

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Do Women Prefer Female Obstetricians?

ABSTRACT & COMMENTARY

Synopsis: *One third of postpartum women delivered in a tertiary hospital in the Northeast prefer female obstetricians.*

Source: Howell EA, et al. *Obstet Gynecol*. 2002;99: 1031-1039.

In recent years, many medical professionals have come to believe that female patients prefer to see female physicians. As Howell and colleagues point out in their brief review of the literature, there is little literature to review. Most studies have focused on one type of patient (obstetrical, primary care, postmenopausal, or some other group) or a specific type of physician (OB/GYN, or family physician, etc). Howell et al recruited 67 postpartum patients who agreed to undergo an interview. The interview was carried out using a non-standardized instrument. They state that they used open-ended questions. The responses were "collected, transcribed, and printed" and were then analyzed.

Fifty-eight percent of the patients stated that they had no preference for physician gender. Thirty-four percent preferred a female obstetrician. Howell et al state that "a theme emerged" showing that as long as the patient felt a "connection" to their obstetrician, gender did not matter, but only provided vague information supporting this contention.

Howell et al acknowledge that their results differ from 2 other recent studies. They believe that this might be due to the nature of the patient population that they studied.

COMMENT BY KENNETH L. NOLLER, MD

I chose this paper to review, not because it is a good paper (in fact it really is not) but because it gives me an opportunity to ventilate on a subject that is discussed nearly continuously by OB/GYNs. As Howell et al point out, the published data supporting the fact that women prefer to see women physicians are rather scanty. Nonetheless, anyone who has practiced OB/GYN in the last decade has to be aware that a majority of women calling for first time appointments in gynecology, or as new obstetrical patients with no previous OB/GYN experience, request a female physician. If they are told there is no female physician available, many will accept a male. That does not mean that they had no preference. Indeed, that is the most important problem with this current study. The women were all interviewed postpartum—ie, after they already had a prolonged experience with an obstetrician. Some probably had a female obstetrician providing most of their care, but were delivered by a male, some had prenatal care by a female and delivery by a female, and every variation of the combination of prenatal care/delivery/ and physician gender. Howell et al did not report how many women saw men or women for their prenatal care—only who delivered them.

The authors work at a tertiary care hospital and the women they sampled are a poor representation of the general female population. Likewise, after the stresses of labor and delivery, if everything turned out fine (and the infants born to these mothers had high Apgar scores) they perhaps cared little whether their care provider was male or female. In fact, even those who had chosen a female obstetrician and were delivered by her might have seen a male partner during the postpartum stay, were happy with him and thus would answer the questions as indicating no preference. The bottom line is, the population Howell et al chose to study is so poorly representative of women who are calling to make their first appointment with a gynecologist (the most important statistic) that it is meaningless.

For those of us who are at academic institutions where many medical students must be trained, there is great fear that we may never be able to train male medical students adequately in the proper examination of female patients. When asked if they will allow a male medical student to examine them, the rate of refusal among women is extremely high. The problem occurs in OB/GYN rotations, family medicine, and internal medicine.

This is also a great example of a study where the conclusion placed in the abstract does not at all match the study population. In the conclusion section of the abstract Howell et al state that "a majority of women did not prefer a female obstetrician." That is not consistent with their study population. They should have said: "Immediately postpartum women still hospitalized who delivered at a tertiary care center in the northeastern United States did not prefer a female obstetrician." Even that statement is not completely correct since it also should mention that a majority of the women were white, the majority had 2 children, that a female physician performed the interview, and that the study instrument (questionnaire) had not been standardized. Far too often I see this mistake made. I do know that editors constantly try to shorten manuscripts and that may lead to conclusions that are too brief and not exactly accurate. But it is still the authors' responsibility to make certain that the information is not misleading.

A number of physicians seem to want to believe that the fact that most women would prefer to see a female physician (particularly if a pelvic examination is going to be performed) as something "bad." I think that is terribly unfair. There is nothing good or bad about that fact, and most patients will accept either gender if no one else is available. Additionally, if someone has special expertise in a particular field it matters little whether that physician is male or female, or the gender of the patient. Well-trained, thoughtful, compassionate physicians will always be busy regardless of their specialty or their gender. ■

Oral Contraceptives and the Risk of Breast Cancer

ABSTRACT & COMMENTARY

Synopsis: *Among women 35-64 years of age, current or former use of oral contraceptives was not associated with a significantly increased risk of breast cancer.*

Source: Marchbanks PA, et al. *N Engl J Med*. 2002; 346:2025-2032.

Marchbanks and colleagues report the results of a large population-based, case-control study to determine the risk of breast cancer among former and current users of oral contraceptives (OCs). The study population was formed from 4575 women with invasive breast cancer and 4682 matched controls enrolled from Atlanta, Detroit, Philadelphia, Los Angeles, and Seattle. The Centers for Disease Control and Prevention conducted the data coordination. Con-

trols came from the same geographic location. Participants were interviewed using a standardized questionnaire that included photographs about hormonal medications. Sixty-five percent of the women were white and 35% were black. Marchbanks et al state that examination of multiple aspects of OC use revealed little evidence that OCs increase the risk of breast cancer. In particular, neither dose nor duration was associated with an increased risk. Further, among women 45-64 years of age, the risk of breast cancer was not significantly higher among the women currently using OCs containing a low dose of estrogen than among those who had never used OCs. Fully one third of the cases were postmenopausal (n = 1544).

COMMENT BY SARAH L. BERGA, MD

This article could be subtitled "when negative results are positive (good)." This is a large study that was properly conducted, and addressed an important and timely topic. The results are reassuring and certainly welcome. But like most good studies, it raises a number of questions that are outside the immediate focus of the study. One of the most compelling questions from my vantage point is why would OC use *not* raise the risk of breast cancer in older women while HRT use would? This apparent paradox is even more unsettling when one considers that HRT formulations typically contain much smaller amounts of sex steroids and therefore qualify as a lesser exposure in terms of dose. For instance, femHRT contains 5 µg of ethinyl estradiol (EE) while OCs contain between 20-35 µg of EE. There is not a straightforward answer to this question, of course, but there are some candidate explanations that I would like you to consider.

A major difference between HRT and oral contraceptive pills (OCPs) other than dose is that the most commonly used HRT preparation contains a different estrogen type, namely, conjugated equine estrogens (CEE), while all OCP formulations now contain EE. Could it be that the effect of these 2 estrogens, even on a molar basis, upon the breast is not the same? If so, might this be due to the effective half-life of the metabolites? Or is it, as has been hypothesized, due to the high sulfatase of the breast making conjugated estrogens more bioavailable to breast than to other tissues with lesser sulfatase activity? In other words, in giving CEE, are some tissues overdosed relative to others and is this effect not operant for EE? Further, I have worried that to suppress hot flashes, one must give a relatively large dose of CEE because the conjugated moiety cannot transgress the blood-brain barrier. It is only the free fraction that can get into important brain centers. Since giving CEE orally raises SHBG, the free fraction is small. Therefore, to get enough into the brain to quell hot flashes, one must overdose the periphery. The diffusion barrier for EE into the brain might not be the same, although this remains to be shown. Also, since EE is not sulfated in the circulation to the same extent as CEE, the relative exposure of the breast might be lower at a dose that is bioactive for brain or bone.

Another major difference between HRT and OCPs is the progestins used in the most common HRT product and in OCPs. Medroxyprogesterone acetate is a 21-carbon derivative while OCPs contain 19-nortestosterone derivatives. We know little about the differential effects of these progestins upon the breast.

In short, while we try to make sense of an abundance of data on the effects of HRT and OCPs, we must remember not to lump all HRT products together. Perhaps this same argument holds for OCPs, but at least they all contain the same estrogen, even if not in the same dose. The time has come to think critically about how estrogens differ from one another if we are to understand the apparent paradox of the present study. The cartoon that estrogen exposure per se causes breast cancer in a dose- and duration-related manner is outmoded. The present study argues against such a simple conceptualization.

Risk-Reducing Salpingo-oophorectomy in Women with a BRCA1 or BRCA2 Mutation

ABSTRACT & COMMENTARY

Synopsis: *Salpingo-oophorectomy in carriers of BRCA mutations can decrease the risk of breast cancer and BRCA-related gynecologic cancer.*

Source: Kauff ND, et al. *N Engl J Med*. 2002;346: 1609-1615.

KAUFF AND COLLEAGUES CONDUCTED A PROSPECTIVE follow-up study of all women with BRCA1 or BRCA2 mutations identified during a 6-year period at their institution. They compared the effect of risk-reducing salpingo-oophorectomy with that of surveillance for ovarian cancer on the incidence of subsequent breast cancer and BRCA-related gynecologic cancers in women with BRCA mutations. A total of 170 women 35

years of age or older who had not undergone bilateral oophorectomy chose to undergo either surveillance for ovarian cancer or risk-reducing salpingo-oophorectomy. Follow-up involved an annual questionnaire telephone contact, and reviews of medical records. During a mean follow-up of 24.2 months, breast cancer was diagnosed in 3 of the 98 women who chose risk-reducing salpingo-oophorectomy, and peritoneal cancer was diagnosed in 1 woman in this group. Among the 72 women who chose surveillance, breast cancer was diagnosed in 8, ovarian cancer in 4, and peritoneal cancer in 1. The time to breast cancer or BRCA-related gynecologic cancer was longer in the salpingo-oophorectomy group, with a hazard ratio for subsequent breast cancer or BRCA-related gynecologic cancer of 0.25 (95% percent confidence interval, 0.08-0.74). Kauff et al concluded that salpingo-oophorectomy in carriers of BRCA mutations can decrease the risk of breast cancer and BRCA-related gynecologic cancer.

COMMENT BY DAVID M. GERSHENSON, MD

We have known for quite some time that women who are carriers of BRCA mutations have up to an 85% lifetime risk of invasive breast cancer and up to a 65% lifetime risk of epithelial ovarian cancer. Options for such women to date include screening—the efficacy of which is in question, particularly for ovarian cancer screening in high-risk women—chemoprevention (ie, oral contraceptives)—and prophylactic surgery. Based on retrospective study data, prophylactic bilateral salpingo-oophorectomy has been recommended for prevention of ovarian and fallopian tube cancer. However, some experts have questioned whether such surgery will prevent primary peritoneal cancer. This is one of the first, if not *the* first, prospective studies evaluating the role of prophylactic surgery in this high-risk cohort. Compared with the surveillance group, there were significantly fewer breast and gynecologic cancers in the prophylactic surgery group. Another study from The Prevention and Observation of Surgical End Points Study Group published in the same issue of the *New England Journal of Medicine* revealed similar findings.[1] The complication rate in the Kauff study was acceptable at 4%. One of the major remaining questions is the role of concomitant hysterectomy and the benefit/risk ratio associated with this procedure. In the interim, female members of high-risk families should be seriously considering enrolling in a comprehensive program to undergo risk assessment and possible genetic counseling and genetic testing. In addition, we need more confirmatory prospective studies to gain important information regarding the relative efficacy of the available risk-reduction strategies. ■

Reference

1. Kauff ND, et al. *N Engl J Med*. 2002;346:1616-1622.

Assessment of Guidelines for Good Practice in Psychosocial Care of Mothers After Stillbirth

ABSTRACT & COMMENTARY

Synopsis: *Patients who saw and held their stillborn babies had the highest rates of depression, anxiety, postpartum stress disorder, and attachment behavior than others who either didn't hold or see their stillborn babies.*

Source: Hughes P, et al. *Lancet*. 2002;360:114-118.

In July 2002, a study appeared in the *Lancet* that challenged the way most providers manage patients who have fetal demises. They identified 60 women who had stillbirths and enrolled another 60 women as matched controls. These women were classified according to whether a) they saw and held their dead infants; b) simply saw the infant; or c) did not see or hold the infant. These patients and the controls, who had live births, were followed into their next healthy pregnancy and at 12 months following their next birth. Hughes and colleagues were interested in assessing the mental status of these patients with regard to depression, anxiety, postpartum stress disorder (PTSD), and attachment behavior toward the next born infant.

The ones who saw and held their babies had the highest rates of depression, anxiety, PTSD, and disorganized attachment behavior than those who saw, but didn't hold their stillborn babies. The ones who did not see their babies had the lowest rates of all of these variables. (*See Table*.)

COMMENT BY JOHN C. HOBBINS, MD

For many years, we have been encouraging mothers to hold their dead babies after birth to "help them grieve" or to "arrive at some form of closure." Some parents have been encouraged to dress these babies, to obtain mementos, and to have a funeral for these babies. Hughes et al did try to evaluate the latter 2 practices and found no difference between groups. However, the numbers of patients precluded a proper evaluation. Nevertheless, their findings regarding seeing and holding their

Table

Patient Reaction Toward Stillborn Births

	Depression	Anxiety	PTSD	Poor Attachment
Saw and held	39%	45%	30%	42%
Saw	21%	31%	14%	42%
Did neither	6%	18%	6%	8%
P =	0.03	0.17	0.13	0.10
Controls	8%	0%	2%	15%

babies was certainly eye opening.

This practice simply evolved over the last few years, not because there were any good data available to back it up, but because it seemed like a rational approach to a very tragic event. I suppose the situation might be likened to a closed casket vs. an open-casket funeral.

Based on the study alone, I am not sure that parents should be discouraged from seeing and holding their babies if they have a strong wish to do so. However, the pendulum certainly should swing away from providers leading patients toward this approach, especially at a time when patients are very vulnerable and primed for any suggestions their providers might have.

I suspect that we will hear more about this topic, as this study should stimulate many others like it. ■

Delivery Outcomes Following Loop Electrosurgical Excision Procedure for Microinvasive Cervical Cancer

ABSTRACT & COMMENTARY

Synopsis: *Most women treated for stage IA1 cervical cancer with loop electroexcision have a normal outcome of pregnancy, if attempted.*

Source: Paraskevaidis E, et al. *Gynecol Oncol*. 2002; 86:10-13.

Paraskevaidis and colleagues have previously reported that women with FIGO stage IA1 (microinvasive) cancer of the cervix could be treated successfully with loop electroexcision. The women on whom such treatment was performed generally wish to preserve fertility. Paraskevaidis et al now report a series of patients were so treated and who attempted pregnancy.

In the period 1990-1998, 47 women with microinvasive cervical cancer without vascular space involvement were treated with loop electroexcision. Of these, 28 women had at least one pregnancy that progressed beyond 24 weeks gestation and comprise the material for this study. In addition, Paraskevaidis et al performed "a case control study." Each cancer patient was matched to a woman who delivered on her service. Various risk factors and outcome variables were matched.

Because an ultrasound at 12-weeks gestation suggested cervical shortening in 5 cases, cervical cerclage was performed. There were no cerclages among the "controls." The mean gestational age at delivery of the cases was almost 38 weeks compared to 38½ weeks among the "controls." The only variable examined by Paraskevaidis et al that was different was a shorter duration of labor among those who had loop excision.

COMMENT BY KENNETH L. NOLLER, MD

There are many aspects of this study that are unacceptable, and I would not have chosen it for review except for the fact that it demonstrates that women who have had huge loop electroexcision procedures performed (in this case for microinvasive cancer of the cervix) can still become pregnant and, most of the time, deliver at or near term. That is an important fact, though it has been reported before.

The second fact is that women with microinvasive cancer of the cervix without lymphatic or vascular invasion can be treated successfully with loop electroexcision. Paraskevaidis et al and others also have reported before that fact.

On the other hand, this is a terrible example of a "case control" study. In fact, it is almost an excellent example of how not to do a "case control study." There were no sample size calculations performed to assure sufficient power to detect a significant difference between the 2 groups. Thus, the fact that there were few observed differences in obstetrical outcomes between the cases and controls is rather meaningless. Secondly, I believe the choice of cases was totally inappropriate. It would have been much better to match based on maternal age, gravidity, past obstetrical history, and date of conception and then to compare outcomes between the 2 groups. With that type of selection the need for placement of cervical cerclage would have been (most likely) statistically significantly different.

Although not commented on by Paraskevaidis et al (who seem to be more interested in gynecology than obstetrics) the fact that 5 cerclages were placed among a group of 28 women suggest that loop electroexcision does indeed have a pronounced effect on subsequent pregnancy. In addition, though not statis-

tically significantly different (due to the small sample size and lack of power), the cases had shorter mean duration of pregnancy, mean birth weight, precipitous labor, and more admissions of the neonate to the ICU. In general, the women with loop excision did less well than those without. Nonetheless, these women did achieve viable pregnancies, and thus loop excision is certainly a reasonable choice for those women with stage IA1 cervical cancer who wish to maintain fertility. ■

CME Questions

5. **Among a group of women who were treated for stage IA1 cervical cancer by loop electroexcision, Paraskevaidis et al observed which of the following?**
   a. Few women were able to achieve pregnancy successfully.
   b. Cervical cerclage was needed frequently among those who became pregnant.
   c. Loop electroexcision is not recommended for stage IA1 invasive cervical cancer.
   d. All of the above

6. **With regard to the use of oral contraceptives and breast cancer, which statement is true?**
   a. The longer a woman takes oral contraceptives, the higher the risk of breast cancer.
   b. Higher doses of ethinyl estradiol were associated in the present study with an increased risk of breast cancer.
   c. In the present study, there was a significant risk of breast cancer among oral contraceptive users only in women older than 45 years of age.
   d. In the present study, oral contraceptive use was not associated with an increased use of breast cancer except in women who used the pill after age 35.

7. **In the study by Howell et al, postpartum women were asked about their preference of physician gender. What were potential biases in their study?**
   a. The patients were limited to an obstetrical population.
   b. The patients already had an established relationship with a physician.
   c. The study was performed at a tertiary center.

8. **Results from prospective studies are demonstrating that prophylactic salpingo-oophorectomy may:**
   a. decrease the rate of ovarian cancer by increasing the rate of breast cancer.
   b. decrease the rate of both ovarian and breast cancers.
   c. decrease the rate of ovarian cancer and primary peritoneal cancers.
   d. decrease the rate of ovarian cancer but increase the rate of primary peritoneal cancer.
   e. Decrease the rate of breast cancer but have no effect on the rate of ovarian cancer.

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