

## No. of Small Antral Follicles Can Predict IVF Pregnancy

BY PATRICE WENDLING

HAMBURG, GERMANY — The presence of small antral follicles measuring 2.1-4.0 mm predicted pregnancy and ovarian response in a prospective cohort of 142 women who underwent in vitro fertilization.

The study took advantage of a novel software program called sonography-based automated volume count (SonoAVC) that can automatically identify and measure the dimensions of hypoechogenic areas such as ovarian follicles observed on 3-D ultrasonography. In this instance, the program was used to calculate the

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number of antral follicles measuring 9 mm or less in diameter in the early follicular phase (days 2-5) in subfertile women (aged 40 years or less) who were due to undergo their first cycle of assisted reproductive technology.

In all, 73 viable pregnancies were confirmed on ultrasound 7 weeks following embryo transfer.

Women who conceived had significantly more antral follicles measuring 2.1-4.0 mm than did those who had unsuccessful treatment, Nick Raine-Fenning, Ph.D., and his colleagues reported at the World Congress on Ultrasound in Obstetrics and Gynecology. There were no significant differences among women with antral follicles measuring 4.1-6.0 mm, 6.1-8.0 mm, or 8.1-9.0 mm.

On multiple logistic regression analysis, the number of antral follicles measuring 2.1-4.0 mm was a significant independent predictor of pregnancy (odds ratio, 1.23), said Dr. Raine-Fenning of the University of Nottingham (England). The total number of antral follicles and younger age also were significant predictors, while other antral follicle subgroups and type of treatment were not.

"These early results are encouraging, as

very few studies have shown a link [between the number of these small follicles and] eventual pregnancy outcome," they said.

Larger follicles are more likely to be atretic and of poorer quality, while smaller antral follicles relate more closely to serum levels of anti-Müllerian hormone and may better reflect the quality of the oocyte, Dr. Raine-Fenning said in an interview.

Current tests of ovarian reserve are considered quantitative, in that they give an idea of how many oocytes one can expect during in vitro fertilization (IVF) treatment, but are not qualitative, as they cannot predict pregnancy, he noted.

Among women who conceived in the current study versus those who did not, there were more mature oocytes (10.73 vs. 9.04), fertilized oocytes (7.26 vs. 5.81), and cleaved embryos (6.89 vs. 5.53). The number of small antral follicles 2.1-4.0 mm in size was a significant predictor for all three of these secondary outcomes both in univariate and multivariate analyses, Dr. Raine-Fenning reported.

Earlier this year, the investigators reported that SonoAVC identified a comparable number of follicles to real-time 2-D ultrasound in a preliminary study of 72 women undergoing their first cycle of assisted reproductive technology. Follicle tracking with SonoAVC did not significantly improve the number of mature oocytes retrieved, however, when compared with conventional ultrasound (11.43 vs. 10.70) or clinical pregnancy rates (43% vs. 42%).

The SonoAVC software is available only with a few General Electric ultrasound machines, but the additional cost of the software should be reclaimed in improved efficiency in the IVF unit, Dr. Raine-Fenning said.

He reported no relevant financial conflicts of interest. ■

## Biomarkers Fail to Deliver in Ovarian Cancer Detection

BY PATRICE WENDLING

HAMBURG, GERMANY — The combination of four new serum biomarkers did not improve differentiation of adnexal malignancies from benign disease in a study of 83 women, a finding that differs from those of previous studies.

Median concentrations of osteopontin, insulinlike growth factor (IGF)-II, leptin, and prolactin in preoperative serum samples were not significantly different between women with benign ovarian neoplasm and those with ovarian cancer, Dr. Stefano Guerriero said at the World Congress on Ultrasound in Obstetrics and Gynecology.

Ten women were found to have ovarian cancer, and 73 had benign neoplasm.

The diagnostic performance of the biomarkers was also evaluated using a split-point scoring method in which a score of 1 or lower was required for a benign mass and a score of 2 or more indicated cancer.

With this method, the simultaneous evaluation of the four serum protein markers had a sensitivity of 80% and a specificity of just 10%, he said.

The sensitivity was 68% and specificity 40% with the use of only CA 125, a serum biomarker that is widely used to screen women at increased risk for ovarian cancer and to indicate treatment response in those with ovarian cancer.

Transvaginal ultrasonography showed a sensitivity of 80% but a specificity of 92%, reported Dr. Guerriero and his colleagues at the University of Cagliari (Italy).

"Although previously proposed with encouraging results in the

screening of ovarian cancer, the preliminary evaluation of these new biomarkers does not seem to be useful in the preoperative evaluation of patients with an adnexal mass when compared with CA 125 and transvaginal ultrasonography," he said.

In a 2005 blind, cross-validation study, no single marker could completely distinguish women with ovarian cancer from healthy controls, but the combination of the four proteins achieved a striking 95% sensitivity, specificity, and positive predictive value and a negative predictive value of 94% (Proc. Natl. Acad. Sci. USA 2005;102:7677-82). In a more recent study evaluating an ovarian cancer marker panel that included leptin, prolactin, osteopontin, IGF-II, macrophage migration inhibitory factor, and CA 125, only CA 125, osteopontin, and IGF-II levels differed significantly between ovarian cancer patients and controls with benign ovarian disease (Anticancer Res. 2009;29:573-6).

When asked how the studies' findings could be so different, Dr. Guerriero responded that he did not know, adding that his study took considerable time and money to conduct. "It's incredible to me," he said.

The 10 malignancies in the study included 4 primary invasive tumors (2 stage III and 2 stage IV), 3 borderline tumors, and 3 metastatic cancers (2 breast and 1 stomach). The majority of the benign masses were endometriomas (29), serous masses (15), and dermoid masses (13). The mean age of the cohort was 41 years, and 18% were postmenopausal.

The study was supported by Assessorato Igiene e Sanità, Regione Autonoma della Sardegna. ■

## Hot Flash Frequency May Match Circadian Rhythms

BY DOUG BRUNK

SAN DIEGO — Postmenopausal women with severe vasomotor symptoms show a circadian rhythm of hot flashes that peaks in the late afternoon and early evening hours, results from a small study showed.

"A lot of women complain about frequency of hot flashes at night," Lauren Drogos said in an interview after her poster presentation at the annual meeting of the North American Menopause Society. "But we found that women were having the least frequent amount of hot flashes at night."

For the study, Ms. Drogos and her associates evaluated baseline data from a trial of 29 postmenopausal women who had at least 35 hot flashes per week and were enrolled in a clinical trial comparing the efficacy of hormone therapy,

black cohosh, and red clover for menopausal symptoms and cognition. The women wore ambulatory sternal skin conductance monitors, which

recorded their hot flashes over a 24-hour period. Hot flashes were defined as a greater than 2-micromho increase in skin conductance within 30 seconds. The women also kept a diary of their perceived hot flashes.

In an effort to reduce the interindividual variability in the time of hot flashes for study participants on different sleep/wake schedules, the researchers normalized the data to each woman's wake time.



The mean age of the study participants was 53 years, 61% were African American, 36% were white, and the rest were Asian American.

**Hot flashes were least frequent at night, with the peak occurring from late afternoon to evening hours.**

MS. DROGOS

department of psychology at the University of Illinois at Chicago. "There was a broad peak of hot flash frequency, extending from late afternoon to evening hours, and a nadir that roughly corresponded to the time of the sleep episode," the researchers wrote in their poster.

From a clinical standpoint, Ms. Drogos said, "if you have a highly symptomatic postmenopausal woman, you might want to advise her that her symptoms may peak at this time. If she has something important going on, advise her to plan accordingly by dressing in layers or packing an extra T-shirt in her bag."

The pattern matches "other circadian rhythms that generally follow this rise, such as core body temperature and peaks of cortisol levels," she added.

Ms. Drogos acknowledged certain limitations of the study, including its small sample size and the fact that it focused on highly symptomatic women. "We want to do some follow-up studies, possibly looking at women who have shifted circadian rhythm, such as night shift nurses," she said.

She reported no financial conflicts of interest. ■