

IVF Regimen Linked to Ovarian Cancer Risk

BY JANE SALODOF MACNEIL

SAN ANTONIO — Ovarian stimulation for in vitro fertilization was linked to an increased risk of ovarian cancer 15 years later in a large cohort study that followed thousands of women in the Netherlands.

Compared with a control group of women who had fertility problems but did not undergo in vitro fertilization (IVF), women who underwent IVF had a relative risk of 4.40 for "borderline" (low-malignant-potential) tumors and 1.51 for invasive ovarian cancer. Overall, IVF conferred a relative risk of 2.05 for all ovarian malignancies, Dr. Curt W. Burger reported at the annual meeting of the Society of Gynecologic Oncologists.

Whether borderline tumors eventually become invasive is subject to debate,



Individual risk is 0.45% for the general population vs. 0.71% for women who have undergone IVF.

DR. BURGER

noted Dr. Burger, a gynecologist at Erasmus University Medical Center in Rotterdam, the Netherlands.

"The clinical implications are modest," he said, estimating the cumulative individual risk of developing an ovarian tumor before age 55 years as 0.45% for the general population and 0.71% for women who have undergone IVF.

Dr. Wendy R. Brewster of the University of North Carolina, Chapel Hill, called the results "quite troubling" in a discussion of the study.

"We have to advise our patients that there is some risk of ovarian cancer," Dr. Brewster said. The risk of developing breast cancer may be greater, "but, still, to develop ovarian cancer, your life is much more at risk."

Two earlier reports by Dr. Burger were based on shorter follow-up of women in the current study. At 7.4 years, he reported increased incidence of borderline tumors in subfertile women regardless of whether they had undergone IVF, and said this was not related to IVF.

All 12 IVF centers in the Netherlands participated in the study. The initial cohort comprised 18,970 women who received IVF treatment between 1983 and 1995, and a control group of 7,536 subfertile women who sought help but were not treated with IVF. Agents used were clomiphene (Clomid), clomiphene/human menopausal gonadotrophin, and follicle-stimulating hormone/human menopausal gonadotrophin.

About two-thirds of the women—67% of the total population and 74% of the IVF group—responded to questionnaires on reproductive risk factors between 1997 and 1999. The investigators reviewed their medical records and,

with written permission, followed their cancer diagnoses through linkage with The Netherlands Cancer Registry through 2007.

At a median follow-up of 14.7 years, 61 ovarian cancers were observed in the IVF group and 16 in the control group vs. expectations of 38.4 and 15.6, respectively, in those populations, he said.

Dr. Glenn L. Schattman, chair of the practice committee of the Society for As-

sisted Reproductive Technology, called the study interesting, but noted that "it does not take into account whether the IVF patients were successful in achieving a pregnancy or what their previous pregnancy histories and ovarian cancer risk factors were. It also does not give the dosages of the stimulant drugs they took. It was a retrospective study, and such studies have limitations and are subject to recall bias."

In general, there is evidence that infertile women who achieve pregnancy "reduce their risk of ovarian cancer by that factor alone," said Dr. Schattman, associate professor of ob.gyn. at Weill Cornell Medical College, New York.

In fact, he said, a more comprehensive study that looked at use of specific fertility drugs found no overall increase in ovarian cancer risk (BMJ 2009 Feb. 5 [doi:10.1136/bmj.b249]). ■



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