Bone Health Advice in Cancer Updated

BY BRUCE JANCIN

SAN ANTONIO — Current American Society of Clinical Oncology guidelines for the maintenance of bone health in breast cancer patients are outdated and do not sufficiently protect against fractures, a prominent European expert asserted at the San Antonio Breast Cancer Symposium.

"Nothing against ASCO, but their guidelines were developed in 2002 and published in 2003. Back then people in the osteoporosis field thought bone mineral density was the main contributor to fracture risk, so the ASCO guidelines restrict bisphosphonate therapy to breast cancer patients with a T score of –2.5 or less.

"The osteoporosis world has turned around since then. We don't treat T scores anymore, we treat absolute fracture risk. We calculate the absolute risk of a hip or spinal fracture in the next 10 years based on the T score and also using clinical risk factors," said Dr. Peyman Hadji, professor of endocrinology and reproductive medicine at Philipps University of Marburg (Germany).

He is lead author of an alternative set of evidence-based guidelines developed by expert panel consensus (Ann. Oncol. 2008;19:1407-16). Those guidelines significantly lower the threshold for bisphosphonate therapy. (See sidebar.)

"In Europe, these guidelines have had a big uptake. They're very easy for gynecologists and oncologists to use. But physicians keep asking me, 'What proportion of breast cancer patients do we have to treat?' Their big fear was they'd have to give [zoledronic acid] to everyone on an aromatase inhibitor. That's why we did this new study," he explained in an interview.

He reported on 402 postmenopausal women with hormone receptor–positive breast cancer on tamoxifen or an aromatase inhibitor. This group of women had a calculated 10-year fracture risk of about 25%.

Yet under the ASCO guidelines (J. Clin. Oncol. 2003;21:4042-57), which recommend antiresorptive therapy in patients with a T score of –2.5 or lower, only 9% of the women would have qualified. In contrast, under the new guidelines, which call for treatment initiation in the presence of two or more risk factors, 29% of patients were bisphosphonate eligible.

To estimate how many fractures would be prevented in postmenopausal women with hormone receptor–positive breast cancer, Dr. Hadji and his coinvestigators turned to the 150,000-woman-strong database for the National Osteoporosis Risk Assessment study.

With use of the ASCO guidelines to initiate bisphosphonate therapy in 9% of patients, only 18% of fractures would be prevented. With the guidelines developed by Dr. Hadji and coworkers, roughly 29% of women would be treated and at least 45% of fractures would be prevented. And that 45% figure is probably an underestimate, since women with breast cancer have a higher fracture risk than do healthy age-matched controls, Dr. Hadji said.

"This again indicates that restricting the risk assessment to bone mineral density is not good enough to identify the women at highest risk of fracture. Until ASCO comes out with new guidelines similar to ours, ours are much superior," he declared.

The guideline-development project was funded by Novartis. Dr. Hadji disclosed that he has received honoraria, unrestricted educational grants, and research funding from Novartis and a dozen other companies. ■

Who Gets a Bisphosphonate?

Recent guidelines recommend that all breast cancer patients on an aromatase inhibitor should receive calcium and vitamin D supplements, and that in addition, bisphosphonate therapy is warranted in those with any two of the following validated fracture risk factors:

- ▶ A T score below –1.5.
- ▶ Age greater than 65 years.
- ▶ History of oral corticosteroid use for longer than 6 months.
- ▶ Body mass index below 20 kg/m^2.
- ▶ Family history of hip fracture.
- ▶ Positive smoking history.
- ▶ Personal history of a fragility fracture after age 50.

Source: Dr. Hadji

IVF Appears to Increase Risk of Ovarian Cancer

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 controls who had fertility problems but did not undergo in vitro fertilization (IVF), women who underwent IVF were more than four times as likely to develop "borderline" tumors and 1.5 times more likely to develop invasive ovarian cancer. Overall, IVF conferred a relative risk of 2.05 for all ovarian malignancies.

The "borderline" tumors, also known as low-malignant-potential tumors, tended to occur earlier than the invasive ovarian cancers—for which an increase in incidence did not become apparent until 15 years after treatment, Dr. Curt W. Burger reported at the Society of Gynecologic Oncologists' annual meeting.

Whether borderline tumors eventually become invasive is subject to debate, 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.

Both Dr. Brewster and Dr. Burger reviewed a long line of studies that failed to prove increased incidence of ovarian cancer after ovarian stimulation. Among the earlier reports were two by Dr. Burger, based on shorter follow-up.

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.

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, he reported 61 ovarian cancers were observed in the IVF group and 16 in the control group versus expectations of 38.4 and 15.6, respectively, in those populations. The standardized incidence ratio (SIR) for the IVF group was 1.59.

In the IVF group the SIR for invasive cancers peaked in the first year, probably because of screening after IVF, and at or after 15 years (3.94 and 3.22, respectively). Borderline tumors also showed a peak the first year, and most were found within 10 years of treatment; between years 5 and 9 after treatment, 12 were found (SIR 2.18).

All told, 55 ovarian cancers (SIR 1.49) were found after the first year in the IVF group: 28 invasive cancers (SIR 1.30) and 27 borderline tumors (SIR 1.76).

Dr. Glenn L. Schattman, chairperson of the Practice Committee of the Society for Assisted Reproductive Technology, affiliate of the American Society for Reproductive Medicine, 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." ■

Prior Breast Ca Warrants MRI Screen

BY PATRICE WENDLING

CHICAGO — Screening by breast magnetic resonance imaging is warranted in women with a personal history of breast cancer, data from a retrospective study of 144 women suggest.

A review of 1,699 breast MRI studies performed at Memorial Sloan-Kettering Cancer Center in New York from 1999 to 2001 yielded 144 women with prior breast cancer who underwent breast MRI screening during that time and had more than 1 year of follow-up.

Biopsies were prompted by MRI screening in 44 women (31%), yielding malignancies in 17 (12%), Dr. Sandra B. Brennan reported at the annual meeting of the Radiological Society of North America. One patient had two metachronous cancers; thus 18 malignancies were found right away (17 cancers and 1 myxoid liposarcoma).

"In and of itself, a history of a prior breast cancer is a strong enough indication for screening MRI," she said.

Of the 17 cancers, 12 (70.6%), were invasive (11 infiltrating ductal carcinoma and 1 invasive lobular carcinoma) and 5 cancers (29.4%) were ductal carcinoma in situ (DCIS). The median histologic size of invasive cancer was 0.8 cm (range, 0.2-4.3 cm).

Prior cancer histology had no significant impact on the cancer detection rate, said Dr. Brennan, a radiologist specializing in breast cancer imaging at Memorial Sloan-Kettering. Prior breast cancer histology was invasive in 126 patients (95 ductal, 26 lobular, 4 mixed lobular and ductal, and 1 unknown) and DCIS in 18 patients.

Of the 17 cancers detected by MRI, 10 were nonpalpable and detected by MRI only, and 7 had correlates on post-MRI mammography, ultrasound (2), or ultrasound, mammography, and physical examination (3).

The 10 cancers detected by MRI only were significantly more likely than the 7 cancers detected by other means to be DCIS (40% vs. 14%) or minimal breast cancer (70% vs. 43%), Dr. Brennan said. Minimal breast cancer was defined as DCIS or node-negative invasive breast cancer less than 1 cm in size.

More than two-thirds of cancers were detected during the first 2 years of screening (35% each in year 1 and in year 2), with two cancers (12%) detected in year 4 and one in each of years 5, 6, and 9.

The median MRI follow-up was 4 years (range, 1-9 years).

The investigators disclosed no conflicts of interest and received no funding for the study. ■