Obesity May Degrade Chemotherapy's Efficacy

BY JANE SALODOF MacNEIL
Senior Editor

San Diego — Obese women may be shortchanged on chemotherapy but do not appear to have worse outcomes with cancer surgery, compared with patients of normal weight, and might do well with robotic-assisted surgery.

These findings, from three separate studies presented at the annual meeting of the Society of Gynecologic Oncologists, address a concern that is growing with the nation's waistline: Does obesity hamper the delivery of standard cancer treatments?

Reviewing a clinical trial conducted by the Gynecologic Oncology Group (GOG), Dr. Jason D. Wright reported that obese ovarian cancer patients had considerably less toxicity than did women of lesser weight and may have received a substandard dose of carboplatin.

His review focused on use of the Jelliffe formula to assess renal function when calculating the carboplatin dosage. The Jelliffe formula does not consider weight and, therefore, can lead to calculations that are significantly different from those reached with the Cockcroft-Gault formula, a similar common assessment method that does take weight into account.

Before reviewing clinical trial GOG 158, Dr. Wright, of the department of ob.gyn at Columbia University, New York, and his colleagues compared the formulas' effects on dosing a hypothetical 60-year-old woman, 5 feet 5 inches tall, with a serum creatinine level of 0.9 mg/dL, who was to receive carboplatin at a dosage that would result in a concentration over time of 7.5 mg/mL per minute. If she weighed 140 pounds, she received 0.7% less carboplatin with the Jelliffe formula. The difference increased with increases in weight, reaching 24% at 200 pounds and 37% at 250 pounds.

In the GOG 158 trial, 387 women received carboplatin and paclitaxel for optimally cytoreduced epithelial ovarian cancer. About half (194) had a body mass index (kg/m^2) lower than 25. The rest were either overweight (122 patients, of whom 32% had a BMI of 25-29.9) or obese (71 patients, of whom 18% had a BMI of 30 or greater).

Whereas platelet count decreased 61% in normal-weight women, Dr. Wright's group found that it fell only 50% among the overweight women and only 25% in those who were obese. Relative changes in hemoglobin and hematocrit also differed significantly with weight.

When the investigators reviewed grade 3 and 4 toxicities, they found only 27% of obese women had thrombocytopenia, compared with 49.5% of women with normal weight and 32% of the overweight women. The obese women were significantly less likely to have leukopenia and granulocytopenia—and also significantly less likely to have dose reductions or dose delays. Only neurologic toxicity was more common in obese patients.

Although a trend toward decreased progression-free survival in obese patients did not reach statistical significance, Dr. Wright noted that the trial did not have sufficient power to find this difference. Overall survival was comparable for all three weight groups.

"You've opened Pandora's box here," Dr. Linda Van Le, professor of ob.gyn. at the University of North Carolina at Chapel Hill, told him in a discussion of the study. "If the dose method is inaccurate, what is the best formula, and should we switch? The ramifications of this are huge."

In an interview after the talk, Dr. Wright said the Jelliffe formula is used in all GOG trials as well as by many gynecologic oncologists in their practices, but other fields of oncology tend to use the Cockcroft-Gault formula.

Concern that a high BMI could increase the risk of death after radical abdominal hysterectomy for cervical cancer led Dr. Meredith P. Crisp to review records of 332 stage IB and IIA patients who underwent the procedure between 1990 and 2003 at the University of Miami. "With any surgery, you need optimal visualization, and radical hysterectomy is certainly no exception to this rule," said Dr. Crisp, of the university. "We can use [devices for positioning patients]. Despite many of these devices, we still have problems with visualization in the obese population."

Dr. Crisp and her colleagues found BMI data for 281 patients. Of these, 10 (4%) were underweight (BMI less than 18.5); 110 (39%) were normal weight; 105 (37%) were overweight; and 56 (20%) were obese. She reported that the only significant dif-

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Consider Vaginal Route in Ca With Comorbidities

BY MICHELE G. SULLIVAN
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HOT SPRINGS, VA. — Total vaginal hysterectomy may be an appropriate therapy for patients with endometrial cancers whose medical comorbidities put them at increased risk of complications with standard surgery, Dr. Susan Smith said at the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists.

She presented a retrospective review of 63 patients who underwent vaginal hysterectomy for proven or presumed endometrial cancer. Their average age was 62 years; 70% were obese, with an average weight of 235 pounds. Most (80%) had at least two comorbidities that put them at increased risk of intra- or postoperative complications, including hypertension (75%), cardiovascular disease (40%), diabetes (40%), or pulmonary disease (27%), as well as obesity. About half of the group had three or more coexisting factors, said Dr. Smith of the University of South Florida, Tampa.

The average operating time was 119 minutes, with an average blood loss of 330 cc. Only two patients (3%) had to be converted to a laparotomy during the surgery.

There were no perioperative deaths, and more than half of the patients (57%) had no postoperative complications. The most common complications were fever (16%), blood transfusion (11%), and prolonged hospital stay (6%). Fewer than 5% of patients had a postoperative infection (cuff cellulitis, pneumonia, or urinary tract infection).

Follow-up ranging from 6 months to 7 years was available for 44% of the patients. None of these had any evidence of disease at their last visit, but five had needed adjuvant therapy.

"More patients did need additional therapy, but their records were not available for review in this study," Dr. Smith said.

"Careful screening and a frank, informed discussion of this nontraditional approach and its implications" are necessary before proceeding with this treatment track, she said.

A hysterectomy by laparotomy is the preferred method of treating endometrial cancer in women who have a good surgical risk-benefit ratio, Dr. Matthew Burrell, a gynecologic oncologist from Atlanta, noted in discussing the report. ■

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ference in outcomes was that obese women lost more blood: The amount reached 1,000 cc or more in 52% of obese women, compared with only 35% of overweight women and 38% of normal-weight women. Surgical-margin measures, surgical complications, and operating times were not significantly different. "Radical hysterectomy is an appropriate and safe therapy for overweight and obese patients with cervical cancer," Dr. Crisp concluded.

Dr. Diane C. Bodurka praised the investigators for adding to the literature on an important issue that gynecologic oncologists face in their practices, but questioned whether the study had an inherent selection bias. "It is a logical assumption that the healthier obese women were offered radical hysterectomy, which could likely bias the results," said Dr. Bodurka of the University of Texas M.D. Anderson Cancer Center, Houston. "It is difficult for me to accept the generalization that radical hysterectomy is an appropriate therapy for obese women."

Dr. Crisp responded that she would not eliminate a patient for radical hysterectomy solely because of obesity. Because such patients are at greater risk of comorbidity, she said that diabetes, cardiac disease, and pulmonary disease should be assessed to make sure the patient is an appropriate candidate for surgery.

Robotic surgery may expand the surgical options for women with cervical cancer, Dr. Aaron Shafer reported in the third study. Dr. Shafer, of the University of North Carolina at Chapel Hill, compared outcomes for 31 women who had robotic type III radical hysterectomies to the experience of 48 case controls who underwent open procedures at that institution. The groups included 13 and 11 obese patients, respectively. Of the robotic group, 15% were morbidly obese.

Dr. Shafer reported that the robotic group had significantly less mean blood loss (119 mL vs. 562 mL), greater lymph node yield on average (38.4 vs. 22.3), and shorter median hospital stays (1 vs. 3.5 days). ■