16 people (8%). Only about 3% of the general US population exhibits this disorder, according to the study authors, so the finding suggests that caregivers may be more at risk than others of developing this problem. Major depressive disorder affected nine caregivers (4.5%), eight people (4%) exhibited posttraumatic stress disorder, and seven people (3.5%) had generalized anxiety disorder.

The findings are not surprising, said Teschendorf, though the prevalence of panic disorder has not been described before. “Depression is very common,” she explained. “Most caregivers will tell you they’re sad, depressed, grieving. Caregivers are under a lot of stress, particularly when giving care over a long period of time or at the end of life.”

Prigerson and her colleagues said oncologists and other “front-line” providers could be a bridge for caregivers to get the mental health help they need because they interact with caregivers on a regular basis. “Although we recognize that health care providers are under considerable time pressures and are not reimbursed for treating the caregiver, they may be able to ask a few short screening questions to determine whether the caregiver might benefit from a referral to a mental health professional for a more thorough assessment,” Prigerson said. “Discussions with a clinician were the best predictor of whether or not the caregiver accessed mental health treatments, so the oncology team is in the ideal position to initiate such discussions and guide the caregiver toward the appropriate resources to help them deal with the stress of caregiving.”

Teschendorf said another way doctors can help caregivers is by making sure they are comfortable with the tasks they will be asked to perform for the cancer patient. “Part of the stress is caused by having to perform ever more-complicated procedures in the course of caregiving—dealing with feeding tubes, ventilators, IVs,” she explained. “Some doctors don’t ask the caregiver if they know how to do the procedure or are comfortable with it.”

Doctors should be asking these questions, she said, and making referrals to home care agencies in cases where the caregiver may need extra guidance with a particular procedure. Likewise, caregivers need to be assertive about asking for such referrals if they feel insecure about what they must do for their loved one. “One thing caregivers are unaware of is how helpful a home care agency can be,” Teschendorf said. “They can ask for a nurse to come to the home to teach them how to do these things.”

OBESE WOMEN CAN TOLERATE FULL-DOSE CHEMOTHERAPY

Two recent studies suggest that obese women getting adjuvant chemotherapy for breast cancer can not only tolerate full doses of chemotherapy based on body weight, but may even have better outcomes when they receive the weight-appropriate dose. Researchers from the University of Rochester found that overweight and obese women were less likely to be hospitalized for febrile neutropenia than women of normal weight, even when given a full weight-based dose of chemotherapy. A group of international researchers, meanwhile, found that obese breast cancer patients with tumors negative for estrogen receptors (ERs) had worse outcomes when their chemotherapy dose was reduced.

The findings have important implications for treatment because the number of overweight and obese individuals in the United States is rising rapidly, said Jennifer Griggs, MD, MPH, lead author of one of the papers and Associate Professor at the University of Rochester. “There are going to be more of these patients and we need to have standards of care,” she said. “I would go so far as to say that professional guidelines should address dosing.”

In research published in the Archives of Internal Medicine (2005;165:1267–1273), Griggs and her colleagues retrospectively examined dosing practices in 901 US oncology practices that
treated 9,672 women between 1990 and 2001. They found that overweight and obese women were significantly more likely to receive a reduced first dose of chemotherapy than women of normal weight. Just 9% of normal-weight women (body mass index [BMI] 18.5 to 24.9) had a first-cycle dose reduction of 10% or more, compared with 11% of the overweight women (BMI 25 to 29.9), 20% of the obese women (BMI 30 to 34.9), and 37% of the severely obese women (BMI 35 and over).

First-cycle dose reduction varied widely by practice and became less common over time. Dose reductions tend to occur because some doctors are fearful of administering too much of a toxic agent and causing severe side effects, Griggs said.

“We’re treating a person with no measurable disease and our first rule is, ‘Do no harm,’” she said, “so if there’s uncertainty about how to dose patients, you use caution.”

But such an abundance of caution may not be warranted. In Griggs’ study, overweight and obese women were no more likely to require hospitalization for febrile neutropenia than normal weight women, regardless of chemotherapy dose. In fact, severe obesity was associated with a lower risk of hospitalization for this side effect (odds ratio [OR] 0.61, \( P = 0.04 \)). Other factors that reduced hospitalization risk included treatment year 2000 to 2001 (OR 0.55, \( P = 0.03 \)), and use of granulocyte colony-stimulating factor in cycle 1 (OR 0.56, \( P = 0.001 \)). People with comorbidities were more likely to require hospitalization (OR 3.06, \( P = 0.03 \)), as were those who required granulocyte colony-stimulating factor in cycle 4 (OR 3.14, \( P < 0.001 \)).

Griggs and her colleagues did not measure cancer outcomes, although she noted that previous research has found improved disease-free and overall survival when chemotherapy dose is based on actual body weight of heavy patients.

A research letter published subsequent to Griggs’ paper in The Lancet (2005;366:1108–1110) supports that theory. As in Griggs’ study, researchers led by Marco Colleoni, MD, Co-Director of the Division of Medical Oncology of the European Institute of Oncology in Milan, Italy, found that obese breast cancer patients in four clinical trials were significantly more likely to receive a reduced first dose of chemotherapy than normal-weight women (39% vs. 16%, \( P < 0.001 \)), but no more likely to suffer severe toxic effects when they did receive a full weight-based dose (14% vs. 12%, \( P = 0.62 \)). This group also measured survival, however, and found a significant difference based on dose among women with ER-negative tumors.

ER-negative women of all weights had significantly better disease-free survival and overall survival if they received 85% or more of their first-course chemotherapy dose. There was no such effect noted among women with ER-positive tumors. “Our results indicate that for patients with endocrine nonresponsive disease (ER-absent and ER-low tumor), a reduced dose during the first course of chemotherapy is detrimental,” Colleoni and colleagues write.

Griggs agrees. “I think we have enough evidence that dose reduction in anybody is not appropriate and risks outcomes,” she said.

Clifford Hudis, MD, who is Chief of the Breast Cancer Medicine Service at Memorial Sloan-Kettering Cancer Center in New York, also said dose reductions because of body weight should be moving out of common practice. He was not involved in either of the two studies.

“I think these papers are very significant and actually highlight a broader issue,” he said. “The dosing of drugs is weight or [body surface area]-based largely because we can quantify that. But these studies highlight something that goes beyond weight, and that’s that there’s wide individual variability in metabolizing drugs, and getting the right dose across a variety of populations requires more sophistication than we’ve had.”

Hudis said scientists are learning more about specific genes that regulate drug clearance in
the body, as well as genes that predict whether a person will or will not respond to a particular treatment.

“The optimal dose is probably not solely determined by weight, and this is an area that is very actively under study right now,” he said. “We could easily discover that we should be using different doses for lots of patients.”

Hudis said there are some circumstances where reducing dose would be appropriate, such as when a drug causes excessive toxicity, especially when given in a palliative setting. He also suggested that oncologists and their patients discuss this issue. “I think it’s always appropriate for patients to be partners with their doctors. . . they might well want to ask [whether] their doctor is adjusting doses, especially when talking about curable diseases, and if they are. . . why.”

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