Mammography Shown Ineffective in Breast Cancer Improving Survival

Annual mammography failed to reduce mortality due to breast cancer, according to the follow-up data from the Canadian National Breast Screening Study.[1]

"During the 5-year screening period, 666 invasive breast cancers were diagnosed in the mammography arm (n = 44 925 participants) and 524 in the controls (n = 44 910)," Anthony B. Miller, MD, and colleagues said. "Of these, 180 women in the mammography arm and 171 women in the control arm died of breast cancer during the 25-year follow-up period."

The study authors concluded that women aged 40 to 59 who received annual mammography for 5 years had a breast cancer mortality hazard of 1.05 (95% CI, 0.85-1.30) compared with women in the same age group who received physical examination. In a follow-up period (mean 22 years), the group that received mammography had a breast cancer mortality hazard of 0.99 (95% CI, 0.88-1.12) compared with the group that received physical examination.

The study authors noted that after 15 years of follow-up, 106 of the 484 (22%) cancers observed in the mammography arm were attributable to overdiagnosis.

"[These numbers] represent 1 over-diagnosed breast cancer for every 424 women who received mammography in the screening trial," the study authors said.

1. Miller AB, Wall C, Baines CJ, Sun P, To T, Narod SA. Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ*. 2014;348:g366. doi: 10.1136/bmj.g366

Bevacizumab Delivered With Chemotherapy Increases Cervical Cancer Survival

Patients with advanced cervical cancer who received bevacizumab (Avastin, Genentech) in addition to chemotherapy gained nearly 4 months of life, according to a report published in *The New England Journal of Medicine*.[1]

Krishnansu Tewari, MD, and colleagues found that the median overall survival for patients receiving chemotherapy with bevacizumab was 17 months. Overall survival in patients who received chemotherapy with placebo was 13.3 months.

The randomized trial involved 452 patients. Each group received chemotherapy in similar regimens. The group that received combination therapy received chemotherapy with bevacizumab. The monotherapy group received chemotherapy with placebo.

The hazard ratio for death was 0.71 (95% CI, 0.54-0.95) in favor of combination therapy. The response rate for the combination therapy group was 48% and the response rate for the monotherapy group was 36% (P = .008).

Combination therapy was associated with greater toxicity in patients: 29% of patients using combination therapy had grade 2+ hypertension events, and 2% of patients using monotherapy had such events. Concerning thromboembolic events, 8% of combination therapy patients experienced grade 3+ thromboembolic events and 1% of patients receiving monotherapy had such events. Grade 3+ gastrointestinal fistulas occurred in 3% of combination therapy patients; no patients in the monotherapy group had grade 3+ gastrointestinal fistulas.

1. Tewari KS, Will MW, Long HJ III, et. al. Improved survival with bevacizumab in advanced cervical cancer. *N Engl J Med*. 2014;370(8):734-743.

Prescription Testosterone Associated with Increased Risk of Myocardial Infarction in Men

Prescription testosterone increased the rate of myocardial infarction (MI) in men over 65 and men under 65 with a history of heart disease, William D. Finkle and colleagues reported in a study published in *PLoS One*.[1]

The study followed 55 593 men in a health database who received prescriptions for testosterone therapy. It compared the rate of MI during the 1-year period prior to prescription and the 90-day period following prescription. Men over age 65 years who received a prescription for testosterone therapy had a 2-fold increase in MI rate (post/pre ratio rate 2.19) regardless of cardiovascular disease history. Men under 65 with a history of heart disease had a nearly 3-fold increase (post/pre ratio rate 2.90) in MI incidence. The researchers reported no excess risk of MI in men under 65 without a history of heart disease (post/pre ratio rate 1.17).

The study also examined MI incidence rate in 167 279 men who received prescription for phosphodiesterase type 5 inhibitors (sildenafil or tadalafil). The study found no increase in MI among men 65 or older, men under 65 with a history of heart disease, or men under 65 without a history of heart disease (overall post/pre rate ratio 1.08).

"Our findings are consistent with a recent meta-analysis of placebo-controlled randomized trials of testosterone therapy lasting 12 or more weeks among mainly older men," the study authors wrote. "Taken together, the evidence supports an association between testosterone therapy and risk of serious, adverse cardiovascular-related events–including non-fatal myocardial infarction–in men."

1. Finkle WD, Greenland S, Ridgeway GK, et. al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS One*. 2014:9(1);e85805. doi:10.1371/journal.pone.0085805

US Food and Drug Administration Approves Sleep Drug for Blind Patients

The US Food and Drug Administration (FDA) approved tasimelteon (Hetlioz, Vanda Pharmaceuticals) for completely blind individuals with non-24-hour sleep-wake disorder, also known as non-24.[1] Tasimelteon is the first drug approved by the FDA for treatment of non-24.

Non-24 is a disease that affects people whose complete blindness precludes them from perceiving any light, thus preventing their body from adjusting to normal circadian rhythms. People with non-24 may have difficulty falling asleep or staying asleep, may require frequent naps, or may develop non-nocturnal sleeping habits.

Tasimelteon was tested in 2 clinical trials with 104 participants, all of whom were completely blind and diagnosed with non-24. The trails' results showed significant improvement in sleep patterns for patients treated with tasimelteon vs those treated with a placebo pill.

The FDA estimates that there may be up to 100 000 people in the US with non-24. The drug, which the FDA approved at the end of January, underwent an expedited review process.

1. FDA approves Hetlioz: first treatment for non-24 hour sleep-wake disorder in blind individuals [press release]. Washington, DC; January 31, 2014.

Exposure to Pesticide Linked with Alzheimer Disease Risk

Elevated levels of dichlorodiphenyldichloroethylene (DDE), the main metabolite of dichlorodiphenyltrichloroethane (DDT), were found in 86 individuals diagnosed with Alzheimer disease (AD), Jason R. Richardson, PhD, of Rutgers Robert Wood Johnson Medical School, and colleagues reported.[1] In a study published in *JAMA Neurology*, the study authors found that 86 individuals diagnosed with AD had a mean DDE level of 2.64 ng/mg in serum (SEM 0.35). Researchers measured DDE levels in 79 controls and found a mean DDE level of 0.69 ng/mg (SEM 0.1; $P < .001$), meaning that those diagnosed with AD had DDE levels nearly 4 times higher than those who were not diagnosed with AD.

Participants in the highest tertile of DDE levels were 4 times more likely to be diagnosed with AD than those in the lowest tertile (odds ratio 4.18, 95% CI, 2.54-5.82).

The researchers reported that exposing human neuroblastoma cells to DDT or DDE led to increased levels of amyloid precursor protein, which creates beta amyloid, a substance found on the brains of AD patients.

1. Richardson JR, Roy A, Shalat SL, et. al. Elevated serum pesticide levels and risk for Alzheimer disease [published online ahead of print, January 27, 2014]. *JAMA Neurol*. doi: 10.1001/jamaneurol.2013.6030.

Bevacizumab Ineffective in Improving Survival Rates in Glioblastoma

Adding bevacizumab to radiation therapy and temozolomide did not affect overall survival rates when used as first-line therapy for glioblastoma, according to a study published in *The New England Journal of Medicine*.[1] The study found a 4-month improvement in progression-free survival (PFS).

Olivier Chinot, MD, and colleagues found that patients treated with bevacizumab had a median PFS of 10.6 months, vs 6.2 months for patients receiving placebo ($P < .001$). After mean 14 months follow-up, overall survival was nearly identical: 16.8 months for the bevacizumab group and 16.7 months for the placebo group.

Bevacizumab, which is approved for second-line therapy, is not part of the standard of care for patients with glioblastoma. Standard of care consists of chemoradiation with temozolonide. ■

1. Chinot OL, Wick W, Mason W, et. al. Bevacizumab plus radiotherapy-temozolomide for newly diagnosed glioblastoma. *N Engl J Med*. 2014;370(8):709-722.

David S. Boyer, MD, is a Clinical Professor of Ophthalmology at the University of Southern California Keck School of Medicine, Department of Ophthalmology, in Los Angeles. Dr. Boyer is a Retina Today *Editorial Board member. He may be reached at +1 310 854 6201; or via email at vitdoc@aol.com.*