Tips from Other Journals

Women at Risk of Breast Cancer–Associated Lymphedema Can Safely Lift Weights

Background: Many of the 2.4 million breast cancer survivors in the United States are at risk of breast cancer–associated lymphedema as a result of axillary surgery. One-third of patients require axillary node dissection, which is associated with a 13 to 47 percent risk of lymphedema; even lymphatic-sparing surgery, such as sentinel node biopsy, causes lymphedema in 5 to 7 percent of patients. Arm lymphedema causes swelling and discomfort, impairs arm function, and decreases quality of life. Women at risk often restrict activities with the affected arm and are sometimes instructed not to lift children or other heavy objects. Paradoxically, such protective actions may discourage healthy exercise, leading to deconditioning and increased risk of injury and possibly lymphedema onset. To test the safety of weight-bearing exercise in breast cancer survivors, Schmitz and colleagues conducted the Physical Activity and Lymphedema trial.

The Study: This randomized controlled trial followed a smaller pilot study that did not find any evidence that regular weight lifting precipitated lymphedema. The authors randomized women to two groups: one year of supervised progressive weight lifting versus no intervention. The primary outcomes were the effect of weight lifting on established lymphedema (published previously) and the incidence of lymphedema in the weight-lifting group. Women were included if they had a one- to five-year history of unilateral, nonmetastatic breast cancer with no history or current evidence of lymphedema; a body mass index of 50 kg per m^2 or less; no other medical conditions that would preclude weight-lifting exercise; and no intentional weight loss or participation in a weight-lifting program in the previous year. Participants were placed in two groups of equal size through a computerized program to balance potential confounders at baseline, including age (younger than 54 years versus 54 years and older), number of lymph nodes removed (less than six versus six or more), obesity (body mass index less than 30 versus 30 or more), and history of radiation treatment (yes versus no). Women in the intervention group received a one-year membership to a fitness center near their home. They participated in twice-weekly supervised upper- and lower-body weight lifting for 13 weeks, and then continued with unsupervised progressive weight training twice weekly for the remainder of the year. Those in the control group were asked not to change their baseline activity levels and were offered a one-year gym membership after the study period.

Lymphedema was defined as at least a 5 percent increase in arm swelling and at least a 5 percent interlimb water volume difference. Arm swelling was assessed by water volume displacement at baseline and at 12 months. Fitness trainers or study measurement staff also measured arm volumes monthly. In addition, participants were formally evaluated for lymphedema if they experienced symptoms lasting at least one week.

Results: The study was adequately powered to detect more than a doubling of the background 6 percent rate of incident lymphedema. At 12 months, there was no significant difference between groups in the number of women developing a 5 percent or greater increase in arm volume (17 percent [13 of 75 women] in the control group versus 11 percent [eight of 72 women] in the weight-lifting group). No differences in the number and severity of symptoms were noted. A subgroup analysis of women with five or more lymph nodes removed was also performed. Among these women, the proportion who experienced a 5 percent or more increase in arm volume was significantly lower in the weight-lifting group (7 percent [three of 45] in the weight-lifting group versus 22 percent [11 of 49] in the control group).

Conclusion: Slowly progressive weight lifting does not contribute to lymphedema in breast cancer survivors, and may be beneficial in women who have had five or more lymph nodes removed.

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Source: Schmitz KH, et al. Weight lifting for women at risk for breast cancer–related lymphedema: a randomized trial. *JAMA*. December 22/29, 2010;304(24):2699-2705.

Reducing HIV Transmission via Preexposure Prophylaxis with Antiretroviral Drugs

Background: Postexposure prophylaxis against potential human immunodeficiency virus (HIV) exposure has several limitations. Patients must not only recognize when they have been exposed to HIV, but they must also start therapy within 72 hours. Recently, HIV preexposure prophylaxis has gained increasing interest, particularly after one trial reported a 39 percent reduction in HIV infection rates among women who regularly used tenofovir 1% vaginal gel. The Preexposure Prophylaxis Initiative trial evaluated the safety and effectiveness of a combina- ▶

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tion of antiretroviral drugs for the prevention of HIV transmission.

The Study: A total of 2,499 men who have sex with men were randomized to receive once-daily dosing of placebo or 200-mg emtricitabine/300-mg tenofovir (Truvada). Eligible patients were initially HIV-negative but had evidence of high behavioral risk for HIV. Patients were followed every four weeks for up to 2.8 years (median follow-up period of 1.2 years). At every visit, patients received risk-reduction counseling, HIV testing, and diagnosis and treatment of symptomatic sexually transmitted infections. Exclusion criteria included elevations in hepatic enzyme levels and renal insufficiency.

Results: A total of 100 patients were diagnosed with new HIV infection during the study, with significantly fewer cases occurring in the drug treatment group than in the placebo group (36 versus 64, respectively; 44 percent relative risk reduction). The greatest benefit in preventing HIV transmission was noted in patients who previously had unprotected receptive anal intercourse (58 percent effective) compared with those who had not. Level of protection was not significantly different with regard to circumcision status, alcohol use, or age. There was no statistical difference between groups regarding elevation in serum creatinine levels. The treatment group reported more cases of nausea than the placebo group (22 versus 10 events, respectively; $P = .04$) and unintentional weight loss of 5 percent or more (34 versus 19 events, respectively; $P = .04$). Both groups were similar with respect to sexual practices and incidence of other sexually transmitted infections during the study. Self-reported high-risk behaviors decreased after study enrollment and remained lower than baseline throughout the study.

Conclusion: A once-daily oral combination of antiretroviral drugs helped protect against subsequent HIV infection in men who have sex with men. The authors caution that the optimal regimen for preexposure prophylaxis has not been established, and that the data in this study cannot necessarily be applied to other populations.

KENNETH T. MOON, MD

Source: Grant RM, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med.* December 30, 2010;363(27):2587-2599.

Outcomes of First-Generation Drug-Eluting Stents in Large Coronary Artery Repair

Background: Drug-eluting stents are thought to be more effective than bare-metal stents for small coronary arteries (less than 3.0 mm in diameter). However, it is unclear which type of stent is more effective for large-vessel stenting. Compared with bare-metal stents, first-generation drug-eluting stents (e.g., stents that release paclitaxel or sirolimus) have lower restenosis rates, but an increased risk of late stent thrombosis, which in turn may be associated with death from cardiac causes or nonfatal myocardial infarction. Kaiser and colleagues conducted a large, prospective, randomized, multicenter trial to evaluate the effectiveness of first-generation drug-eluting stents and bare-metal stents placed in large coronary arteries.

The Study: The authors randomly assigned 2,314 patients with acute or chronic coronary disease requiring stenting to receive bare-metal stents (n = 765), first-generation drug-eluting stents containing sirolimus (n = 775), or second-generation drug-eluting stents containing everolimus (n = 774). Patients were eligible if they required stents 3.0 mm or larger in diameter. All patients received aspirin in a daily dosage of 75 to 100 mg indefinitely and clopidogrel (Plavix) in a daily dosage of 75 mg for one year. The primary end point was death from cardiac causes or nonfatal myocardial infarction at two years.

Results: Two-thirds of patients presented with acute coronary syndromes, and one-half of those had myocardial infarction with ST-segment elevation. At two years, no significant differences were seen between groups with regard to the composite primary outcome of nonfatal myocardial infarction or death from cardiac causes, or when these factors were studied separately. The need for revascularization unrelated to myocardial infarction was significantly greater with bare-metal stents than with either drug-eluting stent group (8.9 percent for bare-metal, 3.7 percent for sirolimus, and 3.1 percent for everolimus), although rates with both drug-eluting stent groups were similar. No differences in thrombosis rates were noted between groups.

Conclusion: In patients who required large-vessel coronary artery stenting, no increased mortality risk was noted among those who received first- or second-generation drug-eluting stents compared with bare-metal stents. Both drug-eluting stent groups showed a reduced rate of target vessel revascularization compared with bare-metal stents; however, the risk of clinically relevant restenosis is lower among patients requiring only large-vessel stents than in those requiring small-vessel stents. Also, a nonsignificant reduction in death from cardiac causes or nonfatal myocardial infarction was noted in the drug-eluting stent groups.

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Source: Kaiser C, et al.; BASKET–PROVE Study Group. Drug-eluting versus bare-metal stents in large coronary arteries. *N Engl J Med.* December 9, 2010;363(24):2310-2319. ■