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INSIDE

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An Addition to the Neurological Examination?

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

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Dr. Phillips is a consultant to Cephalon and Ventus and serves on the speakers bureaus of Cephalon and Boehringer Ingelheim.

***Synopsis**: When an older patient lies obliquely (at an angle) when asked to lie on a bed, he or she may be developing dementia.*

Source: Kraft P, et al. Lying obliquely — a clinical sign of cognitive impairment: Cross sectional observational study. *BMJ* 2009;339:b5273.

OVER A PERIOD OF ABOUT A YEAR, THESE GERMAN NEUROLOGISTS asked inpatients who were age 60 or older to lie down on an examination bed. They photographed the position of the patients in the bed, and calculated the body axis angle as the angle between the patient's body axis and the longitudinal axis of the bed. To define which body axis angles are perceived as oblique, they showed photographs of a man positioned in bed at 14 different angles to 23 neurologists, and asked them to classify the orientation of the body axis as either "reasonably straight" or "oblique." The smallest angle that was identified by 90% of the neurologists was considered the angle for obliqueness in this study; this turned out to be 7°.

To evaluate cognition, the investigators performed cognitive testing (the Mini-Mental State Examination [MMSE], the DemTect, and the clock drawing test) on the same day as the calculation of the angle of the body in the bed. They defined dementia as a MMSE score < 24 or a DemTect score < 9. They defined mild cognitive impairment as a MMSE score between 24 and 26 or a DemTect score between 9 and 12. Results of the clock drawing test were considered abnormal when the score was < 5 on a scale of 1-6.

They were able to include 109 patients in this study. After assuming their initial position (which was photographed), all patients were

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eventually able to achieve a straight orientation of the body axis when asked to do so (so they weren't impaired in their physical ability to get straight in the bed). There wasn't any difference in the angle of obliqueness, regardless of the side the patients approached the bed. The absolute value of the angle of the body axis orientation for all patients ranged from 0° to 23° with a median of 3°.

Of 109 patients who completed all the testing in the protocol, 24 had MMSE scores suggesting mild cognitive impairment, and 8 had scores below the dementia cut-off. For the DemTect test, cognitive impairment was suggested in 34 patients, with 11 of them having scores indicating dementia. Cognitive impairment was suggested in 33 patients by the clock drawing test.

Patients who positioned their body at an oblique angle (≥ 7°) from the longitudinal axis of the bed often had cognitive impairment. Larger angles were associated with greater severity of cognitive impairment on all three cognitive test scores. Linear regression analysis showed that the degree of variation of the photographed body position from the axis of the bed correlated significantly with all three neuropsychological tests, even after controlling for age. Indeed, the body axis angles of patients reaching dementia scores were significantly larger than those with normal scores. Relationships persisted after re-analysis excluding those 4 patients who were noted to be wearing shoes when they lay down.

Use of assuming an oblique angle (≥ 7°) as a screen for dementia had a specificity of more than 80% in predicting impaired cognition in all tests, with sensitivities between 27% and 50%. The authors conclude, "… lying down obliquely may be regarded as a simple clinical sign ('oblique sign'), which may prompt further formal assessment."

■ COMMENTARY

Dementia is a scary thing for doctors and their patients, and we are often asked to assess our older patients' cognitive function. Formal testing is expensive and sometimes not very accessible, and even simple screens (such as those used in this study) are time-consuming. This paper offers a simple screen that can be included as part of the physical examination; this assessment does not require any additional tools or time beyond noticing whether the patient lies down at an angle (≥ 7°) on the examination table. It probably is advisable to ask the patients to remove their shoes before lying down, as the authors note that some patients may be uncomfortable about putting their shoes on the exam table. This technique may be better at suggesting if dementia is present (80% specificity) than at ruling it out (sensitivity below 50%), but it is a starting place in determining whether to proceed with further evaluation.

The authors speculate that since their instructions to the patients did not suggest lying straight, cognitively healthy adults naturally adopt a fairly vertical position when lying down in bed. This is different from the behavior of infants and children, and could have the ecological advantage of preventing falling out of bed. They also note that the inability to detect the orientation of an object in relation to others has been observed in Alzheimer's disease,[1] suggesting that impaired spatial relationships may be part of dementia. Further, impaired perception of the upright position may be related to falls in older people,[2] so impaired position sense may be a poor prognostic sign in general.

This study was done in a highly selected population (inpatients age 60 or older with neurological disorders, but no known vascular dementia or dementia associated with hypokinetic movement disorders), and needs to be replicated in a more general population. However, it does suggest a very quick and easy screen that may prompt more specific testing for our older patients who are at risk for dementia. ■

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Continuing Low-dose Aspirin with Peptic Ulcer Bleeding

ABSTRACT & COMMENTARY

By Mary Elina Ferris, MD

Clinical Associate Professor,
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Dr. Ferris reports no financial relationship to this field of study.

Synopsis: *Recurrent peptic ulcer bleeding was increased in patients with known cardiovascular or cerebrovascular disease when daily low-dose aspirin was continued along with proton-pump inhibitors, but overall mortality was significantly less during the 8-week follow-up.*

Source: Sung JJ, et al. Continuation of low-dose aspirin in peptic ulcer bleeding. *Ann Intern Med* 2010;152:1-9.

After successful treatment of acute peptic ulcer bleeding with endoscopic control and intravenous pantoprazole, patients who had previously been taking low-dose aspirin for established cardiovascular or cerebrovascular disease were randomized to either continue it or receive placebo; all continued oral pantoprazole for 8 weeks. The study extended over 3 years, enrolling 156 patients of 246 identified with aspirin-related bleeding in a total of 3412 treated for GI bleeding in a tertiary university endoscopy center.

Recurrent GI bleeding occurred in 10.3% (8 patients) of the aspirin group compared to 5.4% (4 patients) in the placebo group (a 50% increase), although this would have been a smaller increase if 2 additional patients in the placebo group who died from GI bleeding had not been excluded according to the strict study criteria. Transfusion rates were similar between the two groups, suggesting similar severity of bleeding episodes. All-cause mortality at 30 days was lower in the aspirin group at 1.3% compared to 12.9% for the placebo group; mortality from cardiovascular, cerebrovascular, and GI complications was 1.3% for the aspirin group compared to 10.3% for the placebo group. Within the 8-week follow-up,only 1 death occurred in the aspirin group from congestive heart failure; 10 deaths in the placebo group included 5 from cardiovascular events, 3 from GI complications, and 2 from pneumonia.

■ COMMENTARY

Despite the known benefits of prophylactic daily low-dose aspirin in cardiovascular and cerebrovascular disease, it does increase peptic ulcer bleeding, and its use requires a risk/benefit analysis between the different organ systems.[1] When patients develop acute peptic ulcer bleeding and the aspirin is stopped, clinicians are faced with the dilemma of whether to resume the aspirin prophylaxis, and when that should occur.

This small study supports resumption of low-dose aspirin as soon as the cardiovascular risks outweigh the GI risks. An accompanying editorial makes a case for resumption within 7 days of the treated bleeding episode, along with continuation of proton-pump inhibitors for at least 8 weeks, based on the observation that thrombotic events often occur as soon as 7-10 days after aspirin withdrawal.[2] The study was stopped after 8 weeks, and thus did not provide further information beyond that time.

Given the devastating consequences of acute thrombosis to the heart and brain, clinicians are left with limited alternatives to resuming low-dose aspirin even though we know it can cause life-threatening GI hemorrhage. Other antiplatelet agents have not been shown to be any better, and may possibly cause even more bleeding.[3] As always, we need to consider the "whole patient" and not focus on one part of the body while ignoring the other organs, and current information suggests that the risks of bleeding from low-dose aspirin are less than the risks of thrombosis without it. ■

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Get the Lead Out!

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD, MA

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Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *Low-level lead intoxication, known to adversely affect young children's cognitive development and behavior, may also harm young adults.*

Source: Bouchard MF, et al. Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in U.S. young adults. *Arch Gen Psychiatry* 2009; 66:1313-1319.

Using data from the National Health and Nutrition Examination Survey (NHANES), these researchers investigated the association between blood lead levels (BLLs) and psychiatric illnesses in young adults with a cross-sectional epidemiological survey. The dataset included 1987 individuals who had been administered the World Health Organization Composite International Diagnostic Interview (CIDI) to identify major depressive disorder (MDD), panic disorder (PD), and generalized anxiety disorder (GAD). The individuals ranged in age from 20 to 39 years and 55% were female. NHANES is designed to be a national sample and the race/ethnicity composition of this sample reflects that of the country. MDD was diagnosed in 134 respondents (7%), PD in 44 (2%), and GAD in 47 (2%). Some respondents had more than one diagnosis. The mean BLL was 1.61 µg/dL and ranged from 0.3 to 37.3 µg/dL. Levels were higher in men, older individuals, Mexican Americans, less well-educated, and smokers. When the blood levels were divided into quintiles, after appropriate adjustment, odds ratios (OR) for MDD and PD, but not for GAD, were greater with increasing BLL concentrations. The OR for MDD, comparing the lowest quintile with the highest quintile, was 2.32 (confidence interval [CI], 1.13-4.75) and for PD was 4.94 (CI, 1.32-18.48). Since smoking cigarettes is associated with higher blood lead levels and with psychiatric disorders, the investigators repeated the analysis after excluding smokers. The results were essentially unchanged: MDD 2.92 (CI, 1.24-6.92) and PD 9.57 (CI, 1.28-71.43).

■ COMMENTARY

Since a randomized controlled study exposing individuals to lead is highly unlikely, this study may be the best we can do until larger studies replicate it. I mention size, because it is one of the weaknesses of this study. In the analysis of PD, for example, after excluding smokers, only 14 of 1359 persons were so afflicted, and this is reflected in the wide confidence interval. As with all studies of this sort, causation is not established. On the other hand, accepting reverse causation means explaining why young adults with MDD or PD go out of their way to intoxicate themselves with lead. One plausible explanation goes like this: Persons with psychiatric conditions tend to smoke cigarettes more than folks without those problems. Tobacco can be contaminated with lead. Hence, significantly depressed or panicky persons are accidentally intoxicating themselves. Refuting this argument is the finding that the results hold even when smokers are excluded.

I think it helps to put this article into the context of lead poisoning, also known as plumbism. Reviewing quickly, lead poisoning has been recognized since at least the second century BCE.[1] Acute poisoning results in abdominal pain and a host of other gastrointestinal side effects, paresthesias, hemoglobinuria, and muscle weakness. Chronic poisoning can include other neurological symptoms, such as memory loss and depression. Adults historically have developed lead poisoning from occupational exposure, although there are other sources, such as spiking wine with lead acetate to sweeten it. Children, by contrast, are usually the victims of environmental pollution. Physicians of my generation will remember the initial efforts to rid our country of sources of lead, including the removal of tetraethyl lead as a gasoline additive and banning lead-based house paints. This has not eliminated the danger worldwide, as developing countries still use leaded gasoline and children are still sickened by lead in ceramic glazes and lead-containing "traditional" medicines,[2] by living near lead smelters, or by exposure to lead dust introduced by parents who work at smelters or lead-acid battery plants.[3] As late as 2007, toys imported from China were found to have unacceptably high concentrations of lead in their paint.[4]

Ingested lead appears in blood, tissue, and bone, where its half-life is measured in years. BLLs do not correlate to total body lead burden. In children, BLLs < 10 µg/dL are associated with decreased cognitive function, developmental delays, and behavior problems,[5] and Medicaid mandates screening of children with 10 µg/dL as the cutoff.[6] Although we have made progress in reducing elevated BLLs in children, in 2004, 1.4% of screened children still had BLLs > 10 µg/dL.[7] Consider now that the mean BLL in these young adults was 1.61 µg/dL and, in the highest quintile, the low end of BLLs was only 2.11 µg/dL. In the NHANES 1999-2002, the mean BLL in adults was 1.64 µg/dL.[8] In a recently published study, kidney function was reduced in adolescents with BLLs < 10 µg/dL.[9]

If lead at these levels can affect children and adolescents, is it too great a leap to assume that very low BLLs can cause MDD and PD in adults? Now what? Do you screen all your depressed patients for elevated BLLs? If you find an elevated BLL, do you recommend chelation, even though there is no evidence for efficacy of lead chelation, except in moderate and severe intoxication?[10] I believe that, for now, learning what, if any, exposure all of your patients have to lead is best, along with reducing individual exposure and advocating for reduction of lead

environmental pollution. There may be no "safe" level of lead exposure. ■

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Effects of High- vs Low-dose ARBs on Outcomes in Patients with CHF

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, UCLA School of Medicine

Dr. Karpman reports no financial relationship to this field of study.

Synopsis: *Losartan 150 mg/day reduced left ventricular ejection fraction, intolerance to ACE inhibitors, and the rate of death and/or hospital admission for heart failure in patients with CHF more than did losartan 50 mg/day, thereby demonstrating the potential value of uptitrating ARB doses to confer clinical benefit.*

Source: Konstam MA, et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEALL study). *Lancet* 2009:374:1840-1848.

MULTIPLE CLINICAL TRIALS HAVE REPORTED THAT angiotensin-receptor blockers (ARBs) administered with or without an angiotensin-converting enzyme (ACE) inhibitor effectively increase left ventricular ejection fraction (LVEF) and reduce morbidity and mortality in patients with heart failure (CHF).[1-6] These trials were all performed testing the effects of a single dose of an ARB and therefore did not provide information regarding differences in the outcome effects of various dosing regimens. Incremental losartan doses of up to 150 mg in patients with CHF have demonstrated progressive increases in plasma renin activity and in circulating concentrations of angiotensin II,[7] lending support to the possibility that higher ARB doses may improve clinical benefits through more complete inhibition of angiotensin effects at the angiotensin I receptor and/or increased stimulation of the angiotensin II receptor.[8]

Komstan et al performed the HEALL study, which compared clinical outcomes in patients with severe CHF (New York Heart Association class II-IV who were intolerant to ACE inhibitors and with an LVEF ≤ 40%) and who were randomly assigned either to a high (150 mg) or low (50 mg) daily dose of losartan. The primary endpoints were death and/or hospital admission for CHF. The double-blind trial was undertaken at 255 sites in 30 countries in 3846 patients with CHF. Patients receiving the 150 mg dose demonstrated superior outcomes compared to patients receiving the 50 mg dose with respect to the composite outcome of death and/or hospital admissions for CHF. More patients receiving the 150 mg dose had hyperkalemia, hypotension, and renal impairment than did the patients receiving the 50 mg dose; however, these adverse events only infrequently led to discontinuation of the assigned drug.

■ COMMENTARY

The value of incremental inhibition of the renin-angiotensin system had been previously demonstrated by the results of the CHARM-Added trial,[6] which revealed a 15% reduction in the rate of cardiovascular deaths or heart failure hospital admissions in patients treated with 32 mg of candesartan daily in a population already treated with ACE inhibitors. The HEALL study results suggest that a similar benefit can be achieved by increasing

the dose of a particular agent rather than by adding another class of agents, although additional studies are obviously needed to directly test and solidify the hypothesis that titration of ARB doses to higher levels, unless limited by adverse effects such as hyperkalemia, hypotension, and/ or renal impairment, improves the clinical outcomes in patients with CHF with a reduced LVEF.

In summary, multiple published study results have clearly demonstrated that increased inhibition of the renin-angiotensin system is associated with extremely beneficial clinical results in patients with CHF. However, it is not clear whether greater benefit might be achieved by adding an ACE inhibitor to an ARB compared with simply increasing the dose of an ARB that is being administered without ACE inhibition. Further studies will clarify these issues, but for the time being, clinicians should consider adding an ARB to an ACE inhibitor or increasing the dose of an ARB in those patients with CHF who are not receiving ACE-inhibiting therapy and who are not doing well clinically. ■

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Correction

In the Dec. 15, 2009, clinical brief entitled "The relationship of fasting plasma glucose and A1c to diabetic retinopathy" (page 183), the recommended A1c threshold for the diagnosis of diabetes should have read 6.5% instead of 6.2%.

Pharmacology Update

Tranexamic Acid Tablets (Lysteda™)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Elliott and Chan report no financial relationship to this field of study.

THE FDA HAS APPROVED TRANEXAMIC ACID, AN ANTIFIBrinolytic drug, for the treatment of cyclic heavy menstrual bleeding. The drug was originally approved in 1986 (as Cyclokapron™) for hemophiliac patients undergoing tooth extraction. The new formulation is marketed by Xanodyne Pharmaceuticals as Lysteda™.

Indications

Tranexamic acid is indicated for the treatment of cyclic heavy menstrual bleeding.[1]

Dosage

The recommended dose is 1300 mg (two 650 mg tablets) three times a day for a maximum of 5 days with each monthly menstruation.[1] The dose should be reduced due to renal dysfunction utilizing serum creatinine concentration as an indicator. The dose is 1300 mg twice a day for SCr > 1.4 mg/dL to 2.8 mg/dL; 1300 mg once daily for SCr > 2.8 mg/dL to 5.7 mg/dL; and 650 mg once daily for SCr > 5.7 mg/dL.

Potential Advantages

Tranexamic acid treatment resulted in a 38%-39% reduction in menstrual blood loss compared to 5%-12% for placebo.[1] It is more effective than intranasal desmopressin (DDAVP) in patients with menorrhagia with abnormal laboratory hemostasis.[2]

Potential Disadvantages

Tranexamic acid may be associated with an increased risk of venous thromboembolism and the risk is

enhanced with use of oral contraceptives.[1,3] Adverse events include headache, sinus and nasal symptoms, back pain, abdominal pain, musculoskeletal pain, joint pain, muscle cramp, migraine, anemia, and fatigue. Tranexamic acid may also cause visual or ocular adverse events, cerebral edema, and cerebral infarction.[1]

Comments

Tranexamic acid is a synthetic lysine derivative that reversibly blocks the lysine binding site on plasminogen. This prevents the activated form of plasminogen (plasmin) from binding to the lysine residue on fibrin, inhibiting its degradation. Women with menorrhagia may have higher fibrinolytic activity in utero than women with normal menstrual blood loss.[4] The efficacy and safety of tranexamic acid in the treatment of heavy menstrual bleeding was shown in one 3-cycle treatment and 6-cycle treatment, randomized, double-blind, placebo-controlled study.[1] Study participants were age 18-49 years, with an average BMI of 32 kg/m^2, history of heavy menstrual bleeding of approximately 10 years, and an average menstrual blood loss of 80 mL or greater. Those randomized to tranexamic acid 3900 mg/day (n = 112) had a 39% reduction in menstrual blood flow compared to 5% for those randomized to placebo (n = 67). Similar results were reported for the 6-cycle study (n = 187), 38% vs 12%. In patients (n = 116) with menorrhagia and abnormal laboratory hemostasis (e.g., abnormal platelet aggregation or subnormal level of coagulation factors), tranexamic acid (4 g/day for the first 5 days) was significantly more effective than intranasal DDAVP (300 µg on days 2 and 3 of menstrual bleeding). It is also more effective than mefenamic acid and flurbiprofen.[4] Tranexamic acid appears to be well tolerated.

Clinical Implications

Menorrhagia is believed to affect 5%-30% of women of reproductive age.[5,6] Menorrhagia is a common reason for hysterectomies. A sizable number of these women may have an underlying hemostatic defect (e.g., von Willebrand's disease, platelet defects).[7,8] A smaller number may have coagulation deficiencies or defect in fibrinolysis. Tranexamic acid provides a new therapeutic option for this condition. Mechanistically, tranexamic acid may benefit those with defect in fibrinolysis. It appears to be more effective than NSAIDs or DDAVP. ■

CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

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CME Questions

3. **Early dementia may be suspected when a patient who is asked to lie on an examination table:**
   a. lies obliquely (at an angle).
   b. lies straight vertically.
   c. gets on the table from the right side.
   d. cannot lie down without a pillow.

4. **Recent studies suggest that continuing low-dose aspirin along with proton-pump inhibitors after acute peptic ulcer bleeding will cause which of the following?**
   a. Decreased recurrent GI bleeding and decreased overall mortality
   b. Decreased recurrent GI bleeding and increased overall mortality
   c. Increased recurrent GI bleeding and increased overall mortality
   d. Increased recurrent GI bleeding and decreased overall mortality
   e. None of the above

Answers: 3. a, 4. d.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville
Dr. Kuritzky is a consultant for Sucampo Pharmaceuticals, Takeda, Boehringer Ingelheim; and is a consultant and on the speaker's bureau for Novo Nordisk, Lilly, Daiichi Sankyo, Forest Pharmaceuticals, Cephalon, Novartis, and Sanofi Aventis.

Oxygen therapy for cluster headache

Source: Cohen A, et al. High flow oxygen for treatment of cluster headache. *JAMA* 2009;302:2451-2457.

The pain of cluster headache (CLUS) is among the most severe of any clinical syndrome. The advent of triptans, especially sumatriptan injection, has restructured the landscape of CLUS management, since SQ sumatriptan has been shown to provide effective CLUS pain relief within 15 minutes. Unfortunately, since some patients with CLUS have multiple attacks per day, for multiple days, triptan dosing limitations preclude use in these high-frequency sufferers. Additionally, CLUS patients with CAD are unable to use triptans.

Another first-line CLUS treatment is high-flow oxygen (OXY). Advantageous aspects of oxygen treatment include its low adverse-effect profile, ability to be combined with other treatments, and applicability for multiple attacks within a short time frame. Despite commonplace clinical use, trial data on OXY are quite limited.

Cohen et al performed a randomized placebo-controlled study to compare 100% oxygen vs room air (both delivered at 12 L/min for 15 min). Study participants (n = 109) were followed for 5 years, with instructions to treat at least 4 attacks of CLUS with either OXY or placebo (room air). All subjects received indistinguishable separate tanks of 100% oxygen and room air, and were instructed to alternate tanks for sequential CLUS episodes in their home.

The primary endpoint of the study was percent of individuals pain-free at 15 min. OXY was much superior to air (78% vs 20% pain free). Randomized, placebo-controlled confirmation of our clinical practice supports continued appropriateness of OXY for CLUS. ■

Resistance vs aerobic exercise and COPD

Source: O'Shea S, et al. Progressive resistance exercise improves muscle strength and may improve elements of performance of daily activities for people with COPD. *Chest* 2009;136:1269-1283.

COPD is currently the 4th most common cause of death in the United States. Other than smoking cessation, only oxygen therapy in late-stage disease has been shown to modify disease. Pharmacotherapy provides improvements in symptoms and pulmonary function tests, but has not been shown to alter disease progression.

Physical deconditioning is commonplace in COPD. Indeed, the pathologic phenomenon seen in COPD of dynamic hyperinflation — an even greater diminution in ability to utilize expiratory reserve during exercise than at rest — helps explain why COPD patients may lack enthusiasm for aerobic exercise. Resistance exercise trials indicate that COPD patients can improve muscle strength, but whether such improvements translate into incremental symptomatic benefit or ability to participate in activities of daily living is uncertain.

O'Shea et al performed a meta-analysis of 18 controlled trials employing progressive resistance exercises for COPD patients. The data show some benefits of resistance exercise in ability to rise from a sitting position and climb stairs; however, trials comparing aerobic training vs resistance training indicated more favorable outcomes for activities like cycling, and that resistance training added to aerobic training provides little if any additional benefit. Finally, studies that indicated resistance training benefits for activities of daily living were ranked as having higher risk of bias. More studies specifically addressing the effects of resistance training upon functionality in COPD are needed. ■

Breast cancer outcomes and soy intake

Source: Shu XO, et al. Soy food intake and breast cancer survival. *JAMA* 2009;302:2437-2443.

Estrogen is felt to play a role in the development of breast cancer (BCA), and modulation of estrogen is utilized as a treatment for BCA. Soy foods contain a large amount of phytoestrogens, which impact natural estrogen receptors. Soy components have also been shown to possess anticancer effects. Ultimately, whether dietary soy affects important outcomes like survival or progression of disease among subjects with cancers that may be estrogen-sensitive — like BCA — is critical to ascertain.

Shu et al studied data from the Shanghai Breast Cancer Survival Study, which provides a population of Chinese breast cancer survivors (n = 5042). After approximately 4 years of follow-up, the relationship between soy intake and BCA recurrence, overall mortality, and BCA-related deaths was evaluated. There was a consistent, linear, and inverse relationship between soy intake and mortality and BCA recurrence. When compared with persons in the lowest quartile of soy intake, those in the highest quartile enjoyed a 29% lower relative risk of mortality, and a 32% lower risk of BCA recurrence.

The relationship between soy intake and favorable outcomes was not altered by estrogen receptor-positive or receptor-negative status or tamoxifen use.

Average soy intake in U.S. women (1-6 mg/day) is markedly less than Chinese women (47 mg/d). Whether incremental dietary soy increases in the U.S. population will translate into risk reduction has not been determined. ■