encouraging evidence to date that we can prevent this serious side effect of acute hospitalization in elderly patients. As the authors correctly point out, this intervention should be subjected to studies of its effect on morbidity and mortality and its cost-effectiveness before global adoption.

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Disclaimer: This information is the opinion of the authors and should not be construed as official policy of the Department of Defense or the Department of the Navy.

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A Meta-Analysis of the Treatment of Intermittent Claudication

Girolami B, Bernardi E, Prins MH, et al. Treatment of intermittent claudication with physical training, smoking cessation, pentoxifylline, or nafronyl: a meta-analysis. Arch Int Med 1999; 159:337-45.

Clinical question **What are the relative benefits of nonsurgical therapy in the treatment of intermittent claudication?**

Background Intermittent claudication results from atherosclerotic narrowing of peripheral arteries and arterioles that prevents adequate tissue perfusion at the time of heightened tissue demand for oxygen during exercise. Available treatments include nonpharmacologic approaches (smoking cessation, exercise therapy), pharmacologic therapy (pentoxifylline, nafronyl), and surgical revascularization procedures. This meta-analysis reviewed the English language literature to assess the relative effectiveness of nonsurgical therapy in the treatment of intermittent claudication.

Population studied Studies in the analysis included only patients with stage II intermittent claudication (able to walk between 50 and 200 meters before the onset of pain). All studies of special populations (eg, patients with diabetes or hypertension) were excluded.

Study design and validity The authors performed a MEDLINE search of the English language medical literature from 1976 to December 1996 using the key words "atherosclerosis," "arteriosclerosis obliterans," "peripheral vascular disease," and "intermittent claudication." Studies were eligible for inclusion if they evaluated primary treatment of patients with intermittent claudication at stage II of disease and measured any of the following: pain-free and total walking distance or time, ankle-brachial index before or after exercise, rest and peak blood flow, or ankle pressure. Along with studies of restricted populations, those without control groups or comparing one treatment approach with another were excluded. Trials were divided into 4 groups according to treatment. The quality of the study was rated as level 1, 2, or 3. Level 1 indicated at least observer-blinded randomized trials, level 2 unblinded randomized trials, and level 3 nonrandomized controlled trials. No specific mention of the statistical methods used to combine results was given. Data were extracted from the studies by 2 independent observers using a standardized form. Tests of homogeneity revealed no heterogeneity.

Outcomes measured The primary patient-oriented outcomes were individual and pooled means for pain-free and total walking distance or time. Disease-oriented outcomes included the ankle-brachial index before or after exercise, rest and peak blood flow, and ankle pressure. Outcomes were pooled only for data at the end of each study period.

Results Physical training as reported in six level 2 and four level 3 studies resulted in significant increases in pain-free and total walking distances (by 130 meters and 179 meters, respectively) when compared with controls. There was no difference observed in ankle-brachial index at rest or after exercise, or in calf blood flow at rest or after exercise.

Four studies of smoking cessation were included, but none of these studies reported similar outcomes, making summary calculations impossible. Results from individual trials of smoking cessation did not show statistically significant improvements in walking distances, ankle-brachial index, or ankle pressures. One study noted larger numbers of failed revascularization procedures among continuing smokers.

In level 1 trials, pentoxifylline and nafronyl were each found to have a statistically significant but clinically questionable increase in pain-free and total walking distances of between 20 and 60 meters. There were no differences in ankle-brachial indexes. Ankle pressure results were not reported.

Recommendations for clinical practice **Among nonsurgical treatments for claudication, physical training has the greatest potential to increase pain-free and total walking distances (by up to 180 meters among patients with stage II intermittent**

claudication). Patients should be advised to walk as far as their claudication permits, resting until pain subsides, then resume their walking, for a total of 1 hour per day. Pentoxifylline and nafronyl can increase walking distance by up to 60 meters, but their effect is unclear when combined with exercise. Smoking cessation has no clear effect on pain-free or total walking distance, but is associated with fewer failed revascularization procedures and may be associated with slower progression of claudication.

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Bupropion or Patch for Smoking Cessation?

Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. N Eng J Med 1999; 340:685-91.

Clinical question **Is the nicotine patch, bupropion, or concurrent use of both most effective for smoking cessation?**

Background Although millions of people attempt to quit smoking each year, only 6% have long-term success. Both the nicotine patch and bupropion are moderately effective for smoking cessation. This study compares the efficacy of bupropion and the nicotine patch used individually and in combination for smoking cessation.

Population studied The study subjects were 18 years old or older, smoked at least 15 cigarettes per day, weighed more than 100 pounds, and were motivated to quit smoking. They were recruited from media advertisements in Arizona, California, Nebraska, and Wisconsin. Exclusion criteria included serious medical conditions, seizure or dermatologic disorders, major depression, prior use of bupropion, drug or alcohol abuse, and regular use of other tobacco products.

Study design and validity This study was a double-blind placebo-controlled trial sponsored by Glaxo-Wellcome (the makers of bupropion). Subjects were randomized into 1 of 4 groups: (1) bupropion 150 mg orally (once daily for 3 days, then twice daily for 60 days) plus placebo patch; (2) nicotine 21-mg patch for 8 weeks, then 14 mg for 1 week, followed by 7 mg for 1 week, plus placebo pill; (3) bupropion and nicotine patch; or (4) placebo patch and a placebo pill. The target quit date was 8 days after starting bupropion, or the first day of using the patch. Subjects attended weekly 15-minute counseling sessions and were followed up in clinic 4 times to assess smoking status and carbon monoxide levels during the 1-year study period.

Two factors may have enhanced smoking cessation rates. Subjects were volunteers recruited through advertisements and may have been more highly motivated to quit smoking. Their motivation to quit may also have been increased by the use of frequent counseling sessions and carbon monoxide testing to confirm self-reports of smoking cessation. This rigorous surveillance may limit the generalizability of these results.

Outcomes measured The primary outcomes were abstinence rates at 6 and 12 months after starting treatment. Withdrawal symptoms, body weight, and Beck Depression Inventory scores were also measured.

Results Nearly one third of all subjects discontinued treatment or were lost to follow-up. To avoid the error of inflating quit rates in the treatment groups, these dropouts were appropriately classified as smokers. The bupropion and patch combination and bupropion alone demonstrated 12-month quit rates of 35.5% (odds ratio [OR] = 3.0; confidence interval [CI], 1.8 - 4.9) and 30.3% (OR = 2.3; CI, 1.4 - 3.9), respectively. These rates differed significantly from the nicotine patch group (16.4%; OR = 1.1; CI, 0.6 - 1.8), and placebo group (15.6%.) No statistically significant difference was found between the bupropion and patch combination and bupropion alone treatments, or between the nicotine patch and placebo gropups. The 6-month quit rates were comparable with the 12-month results.

Despite an initial rise in withdrawal symptoms in all groups during the first week, all treatment groups had smaller changes in symptoms than did the placebo group throughout the study. There were no differences in either body weight or Beck Depression Inventory scores after 7 weeks. Insomnia was the most common adverse effect reported in the treatment groups. Skin reactions at the patch site were highest in the 2 groups receiving the nicotine patch.

Recommendations for clinical practice **It is clear from this study that using bupropion alone or in combination with the nicotine patch achieves higher smoking cessation rates than using the patch alone or placebo (number needed to treat = ~6). Although adding the patch to bupropion resulted in a slightly higher quit rate, this difference was not significant. The fact that these patients were volunteers and received weekly counseling and carbon monoxide testing may have enhanced these rates. Cessation rates with these therapies may differ in clinical practice.**

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