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INSIDE

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Maybe Atkins Was Right

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

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Dr. Phillips serves on the speakers bureau for PotomaCME.

Synopsis: *Compared with a low-fat diet, low-glycemic index and very low-carbohydrate diets resulted in higher resting and total energy expenditure (thus more calories burned) during the weight loss maintenance phase after a low-calorie diet.*

Source: Ebbeling CB, et al. Effects of dietary composition on energy expenditure during weight loss maintenance. *JAMA* 2012;307:2627-2634.

This study of 21 young adults included run-in and test phases. The run-in phase included collection of baseline data, calorie restriction to achieve a 12.5% decrease in body weight, and determination of energy (calorie) requirements necessary to maintain weight at the reduced level. During the test phase, the investigators used a three-way crossover design to evaluate test diets (low-fat, low-glycemic index, and very low-carbohydrate) in random order; thus, every subject experienced each of the three diets.

The run-in (weight loss) diet was consistent with the Acceptable Macronutrient Distribution Range specified by the Institute of Medicine.[1] The low-fat diet was designed to reflect current conventional recommendations to reduce dietary fat, emphasize whole grain products, and include a variety of vegetables and fruits.[2] The low-glycemic index diet replaced some grain products and starchy vegetables with sources of healthful fat and low-glycemic index vegetables, legumes, and fruits. The low-fat and low-glycemic index diets had similar protein and fiber contents. The very low-carbohydrate diet was modeled on the Atkins diet and had severe restriction of carbohydrates. Participants took supplemental fiber with the very low-carbohydrate diet and also took multivitamins and mineral supplements throughout.

Measurements included resting energy expenditure (REE), total en-

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ergy expenditue (TEE) as well as leptin, thyroid stimulating hormone, triiodothyronine, free urinary cortisol, insulin sensitivity, high-density lipoprotein (HDL) cholesterol, total cholesterol, triglycerides, plasminogen activator inhibitor 1 activity, C-reactive protein (CRP), blood pressure, participant ratings of hunger and well-being, and physical activity.

Although the investigators enrolled 32 participants, only 21 finished the study. This final cohort included 13 men who had a mean body mass index (BMI) of 34.4 kg/m^2 and a mean age of 30 years. During the run-in (diet) phase, participants lost a mean of 31.5 pounds (14.3 kg), corresponding to 13.6% of baseline body weight. This phase included 12 weeks of weight loss and 4 weeks of weight stabilization. Percentage body fat decreased from a mean of 33.6% at baseline to 29.1% after weight loss. Mean calorie intake during the test diet phase was 2626 kcal/d.

The participants then underwent 12 weeks of weight maintenance, spending 4 weeks on each of the diets (low-fat, low-carbohydrate, low-glycemic index). As predicted, calories burned were reduced overall for all dietary conditions, a usual response to weight loss.[3] But calories burned during weight-loss maintenance differed significantly among the three diets. The decrease in REE from pre-weight-loss levels was greatest for the low-fat diet (mean, -205 kcal/d), intermediate with the low-glycemic index diet (-166 kcal/d), and least for the very low-carbohydrate diet (-138 kcal/d; overall $P = 0.03$). In other words, people who ate the low carbohydrate/high fat (Atkins-like) diet burned more calories during the weight-maintenance phase than those in the other two groups. There was a similar pattern in TEE.

Serum leptin was highest with the low-fat diet, intermediate with the low-glycemic index diet, and lowest with the very low-carbohydrate diet. Cortisol excretion was highest for the very low-carbohydrate diet. Indexes of peripheral ($P = 0.02$) and hepatic ($P = 0.03$) insulin sensitivity were lowest with the low-fat diet. Measures of lipids were most favorable with the very low-carbohydrate diet and least favorable with the low-fat diet. However, CRP tended to be higher with the very low-carbohydrate diet. Blood pressure did not differ among the three diets. Ratings of subjective hunger and well-being were not different between diets. And actual weight change did not differ among the three diets.

■ COMMENTARY

Anyone can lose 20 pounds. The trick is to keep it off. This study helps us understand why "low-fat" diets might not be the best recommendation for individuals who are struggling to maintain weight after weight loss. In this rigorous trial, a small number of people who had already lost significant weight burned calories at a higher rate when on a low-carbohydrate (high-fat, Atkins-like) diet than on low-fat or low-glycemic diets. They also had greater improvement of most measures of the metabolic syndrome. Further, they experienced changes in leptin that are associated with improved success at weight loss.[4] Opposite changes were observed with the low-fat diet, with the low-glycemic load diet being somewhere in between. The implication is that low-fat diets, which result in greater reduction in calories burned, may increase the likelihood of regaining weight lost in those who are dieting. In their commentary, the authors note that, "The results of our study challenge the notion that a calorie is a calorie from a metabolic perspective."

This article received a lot of attention in the lay press, as Americans — two-thirds of whom are overweight or obese[5] — continually search for secrets to weight loss. But there are several cautions and caveats here. First, there were no differences in actual weight-loss maintenance in the three groups in this short-term (4 weeks on each diet) study. Second, there were two negative outcomes observed during the low-carbohydrate diet: increased urinary cortisol (a hormonal measure of stress) and a tendency for increased CRP. These two factors are associated with increased cardiovascular risk. Because of this, the authors noted, "These findings suggest that a strategy to reduce glycemic load rather than dietary fat may be advantageous for weight-loss maintenance and cardiovascular disease prevention."

It is worth noting that although the investigators enrolled 32 participants, only 21 finished the study, despite the benefits of a well-controlled weight loss program and a financial incentive ($500). Dieting is hard! In fact, only

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one in six overweight or obese adults report ever having maintained weight loss of at least 10% for a year.[5]

So what does this mean for our patients? At the very least, these results challenge the conventional dogma that low-fat diets are the only way to go. As with many other things in medicine, a "one size fits all" approach is unlikely to be effective for everyone. Ongoing work[6] indicates that tailored treatment approaches might improve our rather pathetic attempts to address the chronic illness known as obesity. Patients might need to be encouraged to try different things until they find something that works. ■

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Eyeing Another Risk from Bisphosphonates

ABSTRACT & COMMENTARY

By Rahul Gupta, MD, MPH, FACP

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Dr. Gupta reports no financial relationships relevant to this field of study.

Synopsis: *People using oral bisphosphonates for the first time may be at a higher risk of developing ocular inflammatory adverse events such as scleritis and uveitis.*

Source: Etminan M, et al. Inflammatory ocular adverse events with the use of oral bisphosphonates: A retrospective cohort study. *CMAJ* 2012;184:E431-E434.

BISPHOSPHONATES ARE WIDELY USED FOR THE PREVENTION and treatment of osteoporosis as well as bone loss and skeletal-related complications resulting from malignancy associated with bone metastases. This class of medications was found to be well tolerated and safe during large-scale clinical trials, which led to their approval and their popularity. However, a number of potential adverse effects have been identified and associated with their long-term use. These have included gastrointestinal intolerance, osteonecrosis of the jaw, atypical fractures, oesophageal cancer, atrial fibrillation, and chronic musculoskeletal pain.[1]

Current evidence also suggests that there may be an association between bisphosphonate therapy and ocular adverse effects, but the extent of this risk remains unclear. Bisphosphonates have been reported to cause a variety of ocular side effects, most of which are inflammatory in nature. Uveitis and scleritis are two such ocular inflammatory diseases that are associated with major morbidity and have been linked to oral bisphosphonate use.[2]

In their research, Etminan et al conducted a retrospective cohort study using a comprehensive database consisting of residents of British Columbia. The cohort consisted of all of the 934,147 patients who visited an ophthalmologist from January 2000 to December 2007. There were 10,827 first-time users of bisphosphonates and 923,320 nonusers. All the patients who were first-time users of oral bisphosphonates were followed to the first inflammatory ocular adverse event (either scleritis or uveitis), death, termination of insurance, or the end of the study period. The researchers found that the incidence rate among first-time users was 29/10,000 person-years for uveitis and 63/10,000 person-years for scleritis. In contrast, the incidence among people who did not use oral bisphosphonates was much lower at 20/10,000 person-years for uveitis and 36/10,000 for scleritis. The corresponding numbers needed to harm were 1,100 and 370, respectively. First-time users of bisphosphonates were about 50% more likely than nonusers to develop uveitis and scleritis. First-time users also had significantly elevated risks of both uveitis and scleritis after adjustment for other risk factors (rate ratios, 1.45 and 1.51). These associations persisted in an analysis that took into account propensity scores (rate ratios, 1.50 and 1.53). Additionally, the association for scleritis persisted in a sensitivity analysis in which nonsteroidal anti-inflammatory drug use was added to the definition for scleritis (rate ratio, 1.38). The authors also noted that uveitis and scleritis may be more under-reported than other adverse events that are associated with the chronic use of bisphosphonates, such as atypical fracture and cancer.

■ COMMENTARY

Most of the post-marketing adverse events are initially presented as case reports or observational studies with variable levels of supporting evidence for plausibility and causality. Yet when these reports become public, both patients and physicians may be alarmed out of proportion to the actual effect on a therapeutic regimen. Similarly, several case reports and case series have described a possible relationship between the use of oral bisphosphonates and anterior

uveitis and scleritis.[3] In most circumstances, symptoms occurred within days of starting the oral bisphosphonate therapy and resolved upon stopping the drug. Since case reports and observational studies may not provide the best estimates of the relative risk of adverse events in the exposed population vs placebo, the findings of Etminan et al are significant. Their study found that patients using oral bisphosphonates for the first time may be at higher risk of scleritis and uveitis compared to people with no bisphosphonate use. Release of inflammatory mediators may be a possible mechanism for bisphosphonate-induced inflammatory events, including ocular disease.

In cases of bisphosphonate-induced uveitis and scleritis, early recognition and intervention can potentially reverse these conditions and prevent significant visual morbidity. Since the majority of oral bisphosphonates are prescribed by the primary care physician, it may be worthwhile to note that the risk of inflammatory ocular adverse events, including scleritis and uveitis, is not highlighted in most package inserts included with oral bisphosphonates but only mentioned under post-marketing experience. It is therefore vital that physicians understand this significant and reversible adverse effect and discuss it with patients being initiated on bisphosphonates so that when it does occur, prompt treatment can be sought and a catastrophe averted. ■

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Cardiovascular Dangers of Long-Term Endurance Exercise

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Dr. Scherger reports no financial relationships relevant to this field of study.

Synopsis: *While regular exercise is beneficial to overall health, repeated long-term endurance exercise — such as marathons, ultramarathons, ironman triathlons, and long-distance bicycle racing — may cause myocardial scarring and increase the risk of serious arrythmias, coronary artery calcification, diastolic dysfunction, and large-artery wall stiffening. The cardiovascular benefits of exercise are only seen in regular workouts of up to 1 hour a day.*

Source: O'Keefe JH, et al. Potential adverse cardiovascular effects from excessive endurance exercise. *Mayo Clin Proc* 2012;87:587-595.

THE BENEFITS OF REGULAR EXERCISE ARE WELL KNOWN. PEOple who exercise regularly have a mean life expectancy that is 7 years longer than those who are physically inactive and have lower rates of disabilities.[1,2] Exercise has often been compared with medication, and some have argued that it could be the best medication available for health and longevity. But like any medication, harmful effects may occur from taking too much. There is mounting evidence for such harm from long-term endurance exercise.

A team of authors from several major medical groups and universities reviewed the literature about the potential adverse cardiovascular effects from endurance exercise. They reviewed the mechanisms of harm both acutely and chronically from what they consider excessive endurance exercise. Animal and human studies are reviewed and the results are sobering for any competitive endurance athlete.

Sudden cardiac death (SCD) during endurance exercise gets most of the media attention but remains very rare. There is one SCD per 100,000 participants in a marathon, and this rate has remained stable as the number of participants in America has risen 20-fold in the past 35 years.[3-6] There is one SCD per 40,000 participants in triathlons and the increased risk is due to dangers during the swim portion of the event. SCD during extreme exertion for participants younger than age 30 is most commonly related to genetic causes such as hypertrophic cardiomyopathy, anomalous coronary arteries, dilated cardiomyopathy, and congenital long QT syndrome. SCD during events for participants older than age 30 are due to coronary heart disease and myocardial infarction. However, it is the longer-term effects on the cardiovascular system that are the focus of this review rather than SCD during endurance events.

Repeated intense and sustained exercise may cause patchy myocardial fibrosis, particularly in the atria, interventricular septum, and right ventricle, creating a substrate for atrial and ventricular arrhythmias. These effects have been seen in rats forced to run strenuously and continuously for 60 minutes daily for 16 weeks.[7] In humans, highly trained endurance athletes develop enlarged left and right ventricular volumes, increased left ventricular wall thickness and cardiac mass, and increased left atrial size.[8,9] The cardiac enlargements that develop during prolonged training and competition do not completely regress to normal levels even years after the athlete has retired from competition and heavy exercise training, leaving an at risk condition known as the "athletic heart."[10]

Biomarkers of cardiac stress, such as cardiac troponin, creatine kinase MB, and BNP, increase up to 50% during extreme endurance exercise training. These increases may reflect myocardial cell damage that may lead to scarring

of the muscle. The structural remodeling in the heart after repeated endurance exercise increases the risk in some athletes for atrial fibrillation, ventricular arrthymias, and ultimately right ventricular dysfunction.

Coronary arteries dilate with exercise, but the dilation seen in marathon runners my lead to increased coronary artery calcification and greater atherosclerotic burden.[11]

■ COMMENTARY

I have completed 28 marathons and recently three 50 k (31 mile) ultramarathon trail runs. Like many, I am inspired by the 2009 book *Born to Run* by Christopher McDougall.[12] Needless to say this article and the press it generated caught my attention. This review adds reflection to the recent sudden death of Micah True (Caballo Blanco), the hero in *Born to Run*, at age 58. The human race may have survived for 2 million years because we could run down our food, yet we probably did not have the longevity we expect today.

As physicians, we should caution our patients about the potential dangers of long-term endurance exercise. Everyone will need to balance their own risks and benefits, and competitive endurance athletes will take their chances for harm similar to football, soccer, and boxing, to name a few potentially dangerous sports. As for me, I am happy to limit my miles per week to 20-25 with most workouts being under 1 hour. Even when I run longer, my pace is slow and the stress seems to be more on the musculoskeletal system than the heart. I am always at a pace that allows for conversation. I love how lean and fit this makes me. My son and I are training for a 50-mile run on Catalina Island in January 2013. I am 62 and hope to be here writing these articles for many years to come! ■

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Pharmacology Update

Lorcaserin HCl Tablets (Belviq®)

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

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

THE FDA HAS APPROVED THE FIRST NEW WEIGHT LOSS DRUG in more than a decade. Lorcaserin is a selective agonist of the serotonin 2C receptor (5-HT_{2C}). Activation of this receptor is associated with decreased food intake. In 2010, the FDA advisory panel did not recommend approval due to safety concerns but subsequently decided that the benefits outweigh the risks. This product will be manufactured by Arena Pharmaceuticals and distributed by Eisai Inc. as Belviq.

Indications

Lorcaserin is indicated for chronic weight management in conjunction with a reduced-calorie diet and increased physical activity in obese adults or overweight adults with at least one comorbidity.[1] Obese is defined as initial body mass index (BMI) of 30 kg/m^2 or greater. Overweight with comorbidity is defined as a BMI of 27 kg/m^2 with hypertension, dyslipidemia, or type 2 diabetes.

Dosage

The recommended dose is 10 mg twice a day without regard to meals.[1] If a 5% weight loss is not achieved by week 12, the drug should be discontinued.

Potential Advantages

Lorcaserin is a selective inhibitor of 5-HT_{2C} with minimal affinity for 5-HT_{2A} and 5-HT_{2B}. Previous nonselective serotonin agonists such as fenfluramine and dexfenfluramine have been associated with cardiac valvulopathy, but current evidence suggests no increased risk with lorcaserin.

Potential Disadvantages

The most common adverse events were headache, dizziness, fatigue, and nausea.[1] Hypoglycemia has been reported with type 2 diabetic subjects. Less frequent or even rare but potentially serious adverse events include serotonin syndrome or neuroleptic malignant syndrome-like reaction and pulmonary hypertension.[1]

Comments

The safety and efficacy of lorcaserin was studied in three randomized, double-blind, placebo-controlled trials of 52 to 104 weeks duration.[1-4] Study 1 (BLOOM) randomized 3182 obese or overweight adults to lorcaserin 10 mg twice daily or placebo for 1 year and follow-up to 2 years.[2] Study 2 (BLOSSOM) randomized 4008 similarly obese or overweight adults to lorcaserin 10 mg once daily, twice daily, or placebo.[3] Study 3 (BLOOM-DM) randomized 604 adults with type 2 diabetes to lorcaserin 10 mg once daily, twice daily, or placebo.[4] All subjects received nutritional and exercise counseling.

For studies 1 and 2, the mean 12-month weight loss for lorcaserin 10 mg twice daily was 5.8 kg ± 0.1 kg compared to 2.5 ± 0.1 kg for placebo with an adjusted difference of -3.3 kg (95% CI -3.6, -2.9).[1] Forty-seven percent had a 5% or more loss of body weight compared to 22.6% for placebo (adjusted difference of 24.5%) and 22.4% had a ≥ 10% loss of body weight compared to 8.7% for placebo (adjusted difference 13.8%). Weight loss was higher in Caucasians than African Americans or Hispanic patients. Older (> 50 years) subjects lost more weight than younger subjects. In study 1, subjects who completed 1 year of participation continued for another year. The placebo group continued to receive placebo and the lorcaserin group was randomized to placebo or lorcaserin. Weight gain occurred in all groups but ended up below their year 1 baseline weight. At the end of week 104, the weight loss was -2.8 kg for placebo, -3.8 kg for lorcaserin to placebo, and -6.0 kg for lorcaserin.

Lorcaserin showed a small improvement in cardiovascular risk factors (e.g., lipids, fasting insulin) compared to placebo with the waist circumference and triglycerides showing the greatest improvement (-2.5 cm, -4.8%). For type 2 diabetics (study 3), mean weight loss at 1 year was -4.7 kg for lorcasarin 10 mg twice daily compared to -1.6 kg for placebo (adjusted -4.5%). Five percent loss in body weight occurred in 37.5% of subjects taking lorcasarin compared to 16.1% for placebo (adjusted difference of 21.3%). For 10% loss of body weight, the percentages were 16.3%, 4.4%, and 11.9%, respectively. Cardiovascular risk factors also improved in this population compared to placebo, with fasting glucose (-15.5 mg/dL), triglycerides (-5.9%), HDL-cholesterol (+3.6%), and waist circumference (-2.2%) showing the greatest improvements. The rate of echocardiographic valvulopathy was not significantly different between the lorcasarin group and placebo group. Rates were 2.6% vs 2.7% at year 2 in study 1 and 2.0% for each group in study 2. However, in the smaller study (BLOOM-DM) 2.9% (6/256) in the lorcaserin (10 mg twice daily) group and 0.5% (1/252) in the placebo group had new echocardiographic valvulopathy.[4] This did not reach statistical significance (P = 0.122). Lorcaserin is generally well tolerated; 8.6% of subjects prematurely discontinued treatment due to adverse events compared to 6.7% for the placebo-treated subjects.[1]

Clinical Implications

Lorcaserin is the first weight-loss drug to be approved in more than a decade. The weight loss achieved is rather modest (3.3 kg compared to control at 1 year and an absolute difference of 25% with a 5% loss of body weight). The effectiveness appears to be similar to that reported in placebo-controlled trials with orlistat (120 mg three times daily).[5] The FDA Guidance for Industry: Developing Products for Weight Management indicates that the primary efficacy endpoint should show a statistical difference of 5% or at least 35% and approximately double the proportion of subjects in the drug group achieve a loss of 5% or greater in baseline body weight compared to the control group. Lorcaserin met the second criteria but not the first. The long-term safety of lorcaserin remains to be determined. The drug manufacturer will be required to conduct postmarketing studies, including long-term assessment of risks for adverse cardiovascular events. ■

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CME Questions

1. **Regarding weight maintenance after weight loss:**
   a. a calorie is a calorie.
   b. low-fat diets may be most effective.
   c. resting energy expenditure (calories burned) usually goes up.
   d. low carbohydrate diets may be most effective.

2. **In the study by Etminan et al, first-time users of bisphosphonates were about what percent more likely than nonusers to develop uveitis and scleritis?**
   a. 10%
   b. 25%
   c. 40%
   d. 50%

3. **All of the following have been seen in the hearts of long-term endurance athletes *except*:**
   a. enlargement of the right ventricle.
   b. increased calcification of the coronary arteries.
   c. increased rate of atrial fibrillation.
   d. increased rate of sudden death during events.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is an advisor for Endo, Kowa, Pricara, and Takeda.

Another Look at Bleeding Risk from Aspirin

Source: De Berardis G, et al. *JAMA* 2012;307:2286-2294.

The role of aspirin (ASA) for primary prevention of cardiovascular (CV) events has been a beleaguered topic for more than a decade. Although the risk reduction from ASA for secondary prevention of CV events clearly outweighs the bleeding risk, the balance for primary prevention of CV events is much less weighted toward the benefits side of the equation. Indeed, recent consensus groups have relied on the additional ASA benefits for prevention of colon cancer to make a case that when added to marginal CV event reduction, total risk reduction is sufficiently powerful to give primary prevention the green light.

De Berardis performed an analysis of bleeding risk among adults in Puglia, Italy, during the 2003-2008 interval. To qualify as a bleeding event, the study subject had to be hospitalized for either a gastrointestinal or intracerebral bleeding episode. A direct comparison between adults who received new prescriptions for low-dose (≤ 300 mg/d) ASA (n = 186,425) and matched controls who had not been prescribed ASA (n = 186,425) was done. A second question was whether the effects of ASA were different in diabetics than in others.

In the population as a whole (on ASA and control), diabetics had a higher risk of bleeding than non-diabetics, independent of ASA. Given that two recent randomized, controlled trials of ASA in diabetics have failed to show a CV benefit, the apparently inherently increased risk for bleeding in diabetics is concerning. ■

Can Aspirin Prevent Recurrence of Thromboembolism?

Source: Becattini C, et al. *N Engl J Med* 2012;366:1959-1967.

Current recommendations for management of proximal deep venous thrombosis or pulmonary embolus suggest a minimum of 6 months treatment with a vitamin K antagonist (warfarin). Although more prolonged use of warfarin does continue to reduce the risk of recurrent DVT, the cost, inconvenience, and bleeding risk of long-term warfarin is substantial. Since as many as 20% of persons with an unprovoked thromboembolic event will suffer a recurrence within 2 years of warfarin discontinuation, well-tolerated agents to reduce this risk would be very welcome.

Becattini et al randomized patients (n = 402) who had sustained unprovoked thromboembolism and completed a standard therapeutic course of warfarin (6-18 months) to either 100 mg/d ASA or placebo. Study participants were followed for 2 years, looking at the incidence of new thromboembolism (primary efficacy outcome) and major bleeding events (primary safety outcome).

Risk of thromboembolism was reduced by 42% in the ASA group compared to placebo (6.6% vs 11.2% new events/yr). Major bleeding was uncommon and not different between the groups (one event each group).

At the conclusion of an approved course of warfarin post-pulmonary embolus, clinicians and patients are presented with the difficult choice of whether to continue warfarin long-term. These results are encouraging that low-dose ASA has a meaningful potential role in long-term secondary prevention of thromboembolism, especially when warfarin continuation is not a desirable option. ■

A New Approach to Tinnitus

Source: Cima RFF, et al. *Lancet* 2012; 379:1951-1959.

I was surprised to learn that as many as 21% of adults will develop tinnitus (TIN) during their lifetime, as stated by Cima et al in the introduction to this clinical trial. Persons who develop TIN can experience a major decrement in quality of life. Despite thorough investigation, it is uncommon to find a correctible cause for TIN, which often persists indefinitely. Sufferers are left with sound-based therapies (e.g., a "masking" sound or neutral sound that distracts from the annoyance of the TIN sound) or cognitive behavioral treatment. Clinical trials to support either of these modalities are thus far somewhat insufficient.

Cima et al randomized TIN patients in the Netherlands to usual care vs specialized care (intervention). Components of specialized care included 8 weeks of intensive audiological diagnostics, audiological rehabilitation sessions, and individual cognitive behavioral therapy, followed by 12 weeks of group cognitive behavioral therapy.

At 12 months, the intervention group enjoyed a significant improvement in quality of life compared to usual care. TIN can create TIN-related catastrophic thinking; this aspect of the disorder was also improved to a greater degree with the specialized care. The authors note that efficacy was not altered by TIN severity; hence, all TIN sufferers might benefit from consideration of this methodology. ■

CME/CNE 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.

Would You Clear for Surgery?

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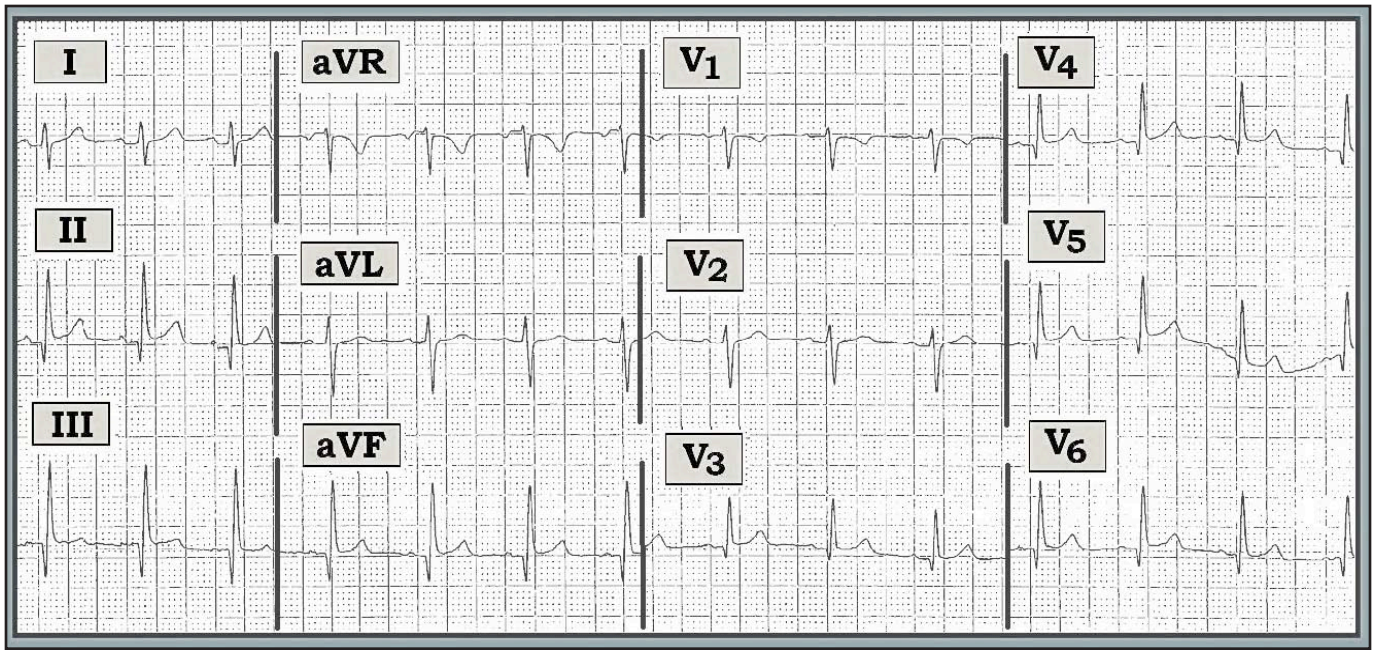

Scenario: The ECG shown above was obtained as part of a routine "pre-op evaluation" for a markedly overweight young adult scheduled for bariatric surgery. The patient was asymptomatic and had no history of cardiac disease. In view of the findings on this "pre-op" ECG, would you "clear" this patient for surgery?

Interpretation: The ECG in the figure shows sinus rhythm at ~ 85/minute. Intervals are normal. The axis is vertical (approximately +90 degrees). There is no chamber enlargement. Remarkable findings reside in assessment of QRST changes. Specifically, Q waves are present in no less than seven leads (II, III, aVF; V3, V4, V5, and V6). Although not overly wide, these Q waves are uncharacteristically deep in the inferior leads for a young adult with no history of cardiac disease. In addition, ST-segment elevation is seen in each of the leads that manifest Q waves. Clearly, this is not a normal tracing.

This case brings up a number of important issues: 1) Is this young, asymptomatic adult who manifests large Q waves and ST-segment elevation on pre-op ECG having an acute infarction? Given the patient's age, asymptomatic status, and negative cardiac history, this is highly doubtful. Even if the patient were older and having symptoms, features against acute ST-elevation-myocardial-infarction (STEMI) are diffuseness of the changes, lack of reciprocal ST depression, and upward concavity (*"smiley"-configuration*) ST segment morphology with relative QT shortening that is much more suggestive of early repolarization.

The second issue brought up by this tracing involves the size and number of Q waves seen. Many factors in addition to infarction may produce Q waves on ECG. These include normal variants (due to septal depolarization), non-ischemic cardiomyopathy, and prominent septal forces either as a variant pattern or in its extreme as hypertrophic cardiomyopathy (HCM). Recognition of potential ECG manifestations of this latter entity is important because undetected HCM is the most common cause of sudden death during sports activity in previously healthy young athletes.

The final issue relates to preoperative clearance of this patient. As emphasized above, acute infarction is highly unlikely. On the other hand, this preoperative tracing is not normal. Determining the likely cause of the abnormalities seen is essential for optimal management. Pre-operative echocardiography should provide this information. Echocardiogram will rule out HCM and other forms of cardiomyopathy by providing accurate measurement of septal and posterior wall thickness as well as an estimation of left ventricular function. Given this patient's large body habitus, the finding of eccentric hypertrophy (and possibly even right ventricular hypertrophy) would not be surprising. This should not preclude the bariatric surgery that is clearly in the best interest of this patient. ■