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INSIDE

Prostate-Specific Antigen: To Test and Test and Test Again? Or Should We Test at All?

ABSTRACT & COMMENTARY

Synopsis: *An isolated elevation in PSA level should be confirmed several weeks later before proceeding with further testing, including prostate biopsy.*

Source: Eastham JA, et al. *JAMA*. 2003;289:2695-2700.

Serum prostate-specific antigen (PSA) testing is frequently used in early detection programs for prostate cancer. While PSA testing has resulted in an increase in prostate cancer detection, its routine use has been questioned because of a lack of specificity.

The objective of this study was to determine whether year-to-year fluctuations in PSA levels are due to natural variation and render a single PSA test result unreliable.

The main outcome measure was an abnormal PSA test result based on a PSA level higher than 4 ng/mL; a PSA level higher than 2.5 ng/mL; a PSA level above the age-specific cutoff; a PSA level in the range of 4-10 ng/mL and a free-to-total ratio of less than 0.25 ng/mL; or a PSA velocity higher than 0.75 ng/mL per year.

Prostate biopsy would have been recommended in 207 participants (21%) with a PSA level higher than 4 ng/mL; in 358 (37%) with a level higher than 2.5 ng/mL; in 172 (18%) with a level above the age-specific cutoff; in 190 (20%) with a level between 4 and 10 ng/mL and a free-to-total ratio of less than 0.25 ng/mL; and in 145 (15%) with a velocity higher than 0.75 ng/mL per year.

Among men with an abnormal PSA finding, a high proportion had a normal PSA finding at 1 or more subsequent visits during a 4-year follow-up: 68 (44%) of 154 participants had a PSA level higher than 4 ng/mL; 116 (40%) of 291 had a level higher than 2.5 ng/mL; 64 (55%) of 117 had an elevated level above the age-specific cutoff; and 76 (53%) of 143 had a level between 4 and 10 ng/mL and a free-to-total ratio of less than 0.25 ng/mL.

Eastham and colleagues concluded that an isolated PSA level

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should be confirmed several weeks later before proceeding with further testing, including prostate biopsy.

COMMENT BY RALPH R. HALL, MD, FACP

This information clouds the use of the PSA even further. When I have 2 tests for the same condition, 1 positive and 1 negative, which one do I believe? I usually do a third test hoping to get some consistency in the results. But, how do I interpret the third test result with this information?

Measurement of the serum PSA in combination with the digital rectal examination has been used for the detection of early prostate cancer for more than 10 years. Eastham et al note that at present PSA testing is not recommended as a screening test by the United States Preventative Disease Task Force or by the Canadian Task Force on Preventative Health Care. The National Cancer Institute defines the PSA as a strategy that is under investigation.

If we use the information from this study to reduce the number of costly prostate biopsies, will we raise the cost in terms of morbidity and mortality? We do not have these data; so what do we do? One of my colleagues, an oncologist, advocated watchful waiting until he was diagnosed with prostate cancer after a suspicious rectal examination. His Gleason scores were less than 7. He opted for aggressive therapy for his cancer.

Now we read that prostate cancer might be prevented by using finasteride.[1] This will likely result in our having to evaluate PSA level changes in many patients taking finasteride for prevention. What do we know about PSA levels under these conditions?

Combining the digital rectal examination with 2, and perhaps 3, PSA determinations may still be a reasonable approach until we have better data or better tests. Some physicians will undoubtedly avoid this approach. Patients will have to know and understand the current data and to participate in an active manner in the decisions that are made. The circumstances really haven't changed, have they?

I am reminded of a verse from the *Rubaiyat of Omar Khayyam*:[2]

Myself when young did eagerly frequent
Doctor and saint, and heard great argument
About it and about: but evermore
Came out the same door as in I went. ■

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Should Both Aspirin and Clopidogrel Be Used for the Treatment of Acute Coronary Syndromes?

ABSTRACT & COMMENTARY

Synopsis: *Clopidogrel, an alternative antiplatelet agent used in patients with aspirin intolerance, is especially useful in combination with aspirin after coronary stent procedures.*

Source: Jneid H, et al. *Arch Intern Med*. 2003;163:1145-1152.

ACUTE CORONARY SYNDROMES (ACS) (IE, UNSTABLE angina, non-ST and ST segment elevation myocar-

dial infarction, and acute sudden cardiac deaths due to coronary artery disease) are ischemic coronary events caused by the same pathophysiology. Coronary atherosclerosis is the cause of more than 725,000 deaths per year in the United States, and fortunately, this number has been steadily falling due to effective strategies designed to prevent and slow the progression of coronary atherosclerosis including lifestyle modification and pharmacological approaches. Although the lipids play a critical role in atherosclerosis, significant coronary atherosclerosis develops in many people without lipid abnormalities and even continues to progress in people with normal or pharmacologically controlled lipid levels. In addition, coronary arterial inflammation and endothelial dysfunction almost certainly contribute to acute thrombus formation, which appears to be the major mechanism responsible for the onset of ACS.

Jneid and associates critically analyzed the results of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) study[1] and several other antiplatelet trials to provide guidance to the physician regarding the use of aspirin and/or clopidogrel in patients with ACS. Since acute thrombus formation upon a disrupted atherosclerotic plaque appears to be the major mechanism responsible for the onset of ACS, appropriate inhibition of thrombus formation is crucial in the prevention and treatment of ACS. Platelet aggregation leading to acute thrombosis is a complex process and, therefore, multiple therapeutic agents may be required simultaneously to block at least 2 separate pathways in order to prevent thrombus formation. The CURE study was a randomized, double-blind study involving 482 centers from 28 countries enrolling a total of 12,562 patients diagnosed as having ACS without ST segment elevation. Using clopidrogrel plus aspirin reduced the risk of nonfatal myocardial infarctions, strokes, and death by 20 percent. The myocardial infarction risk reduction rate was reduced by 23 percent and multiple other end points (stroke occurrence, cardiovascular death, refractory ischemia, etc) demonstrated lower event rates.

COMMENT BY HAROLD L. KARPMAN, MD, FACC, FACP

Coronary atherosclerotic plaque disruption depends upon both active and passive phenomena.[2] The plaques most vulnerable to fracture and disruption are characterized by having a thin fibrous cap, a large atheromatous core, microphage infiltration, and a scarcity of smooth muscle cells. Although lipids play a critical role in atherogenesis, during the 1990s many studies clearly demonstrated that coronary atherosclerosis develops in many people without lipid abnormalities, may continue to progress in people with pharmacologically controlled lipid profiles, and that other mechanisms such as inflammation and endothelial dysfunction may contribute to the formation of atherosclerotic plaques. Beyond prevention and, certainly of equally importance, once plaque disruption occurs, the magnitude and stability of the thrombus which is formed and regulated by the biochemical composition of the lesion, the degree of injury, numerous local conditions, and the presence or absence of certain systemic factors affecting blood thrombogenicity.

Conventional antiplatelet therapy with aspirin is designed to diminish platelet aggregation, however, aspirin is a relatively weak antiplatelet drug and, in addition, up to 10 percent of patients do not respond to the antiplatelet effects of aspirin.[3] Aspirin works by inhibiting the formation of thromboxane A2, thereby reducing platelet aggregability. Clopidogrel inhibits ADP-induced platelet aggregation and has been demonstrated to produce a significant 8.7 percent risk reduction in the combined end points of myocardial infarction, ischemic stroke, and vascular deaths[4-5] after an average of 1.9 years of follow-up therapy.

From a clinical point of view, current evidence strongly supports the use of aspirin combined with clopidogrel for at least 9-12 months in patients presenting with ACS who have been subjected to PCI therapy. Many clinicians favor even longer-term therapy for selected patients based upon a variety of coronary risk factors. The most recent data support the use of low-dose (81 mg daily) aspirin for secondary prevention; however, higher dose (at least 162 and preferably 325 mg) therapy is recommended for the treatment of ACS. Clopidogrel should be used instead of aspirin in the primary prevention of coronary artery disease only in patients who are intolerant or resistant to aspirin. In all likelihood, the aspirin/clopidogrel combination will prove to be the appropriate form of therapy for all patients with ACS and not just patients who are at high risk; however, definitive recommendations must wait the results of the ongoing Clopidogrel for High Atherothrombic Risk and Ischemic Stabilization Management and Avoidance (CHARISMA) trial, which will compare the results of combination therapy vs aspirin alone in both secondary and in high-risk primary prevention. ■

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More Bad News for Folic Acid

ABSTRACT & COMMENTARY

Synopsis: *Folic acid supplementation in stable CAD patients on statins, despite reducing homocysteine levels, does not reduce clinical vascular events or death.*

Source: Liem A, et al. *J Am Coll Cardiol*. 2003;41: 2105-2113.

Elevated homocysteine levels have been associated with atherosclerosis. Folic acid supplementation is a simple, inexpensive way to reduce homocysteine levels, which has become popular for secondary prevention in patients with coronary artery disease (CAD), despite a paucity of long-term clinical trial data. Thus, Liem and colleagues from the Netherlands studied 593 patients with stable CAD on statins who were randomized to open-label folic acid 0.5 mg/d or standard care, which included aggressive pursuit of lipid goals. The primary end point was a composite of death and major vascular events over 24 months. In folic acid-treated patients, homocysteine levels decreased 18% from 12 to 9 mmol/L but didn't change in the control group ($P < .001$). The primary end point was 10% in the folic acid group and the control group (relative risk, 1.05). In a subgroup where it was measured, C-reactive protein levels were unchanged in both groups. Liem et al concluded that over 2 years, folic acid supplementation in stable CAD patients on statins, despite reducing homocysteine levels, does not reduce clinical vascular events or death and that its use should not be encouraged.

COMMENT BY MICHAEL H. CRAWFORD, MD

This study, following on the heals of the recent negative trial in postpercutaneous coronary stenting patients, suggests that we have more to learn about the role of folic acid and homocysteine in CAD. Explanations for the negative results include that in patients on maximum doses of statins at target lipid levels, there may be little to gain with vitamin therapy. Also, some believe that homocysteine is a marker for more diffuse vascular disease and lowering it does little because it is not causative. Support for this latter explanation comes from this study and others, which have noted that homocysteine levels are related to creatinine clearance. Reduced renal function due to vascular disease is a poor prognostic sign and indicates diffuse vascular disease. Thus, homocysteine levels may correlate with the risk of vascular events, but lowering it may not reduce their incidence.

There are several weaknesses of this study that diminish its authority and make us hold off on definitive conclusions until some of the larger, longer trials are completed (NORVIT, VITATOPS, SEARCH). First, based upon previous observational studies in established CAD patients, it was powered for a larger difference in events than has been observed in trials of patients without preexisting vascular disease. Consequently, it may have been underpowered to detect small differences (ie, 15%) in events. Second, the duration of therapy was short (24 months) and the number of patients was relatively small (fewer than 600). Third, about 15% of patients in both groups were already on B vitamin supplementation, which was not discontinued. Finally, the dose of folic acid in this study was low (0.5 mg/d) compared to other studies in which megadoses have been used (5 mg/d). On the other hand, significant reductions in homocysteine levels were observed with this dosage. Interestingly, the Netherlands, where this study was done, does not fortify grain products with folic acid as is done in other industrialized nations. Therefore, lower doses of folic acid may have a more profound effect in this environment. Regardless, Liem et al's admonition that the routine use of folic acid supplementation should be tempered until more trial outcomes are available seems reasonable given the latest study results. ■

Dr. Crawford is Professor of Medicine, Associate Chief of Cardiology for Clinical Programs, University of California, San Francisco.

The Outpatient Bleeding Risk Index

ABSTRACT & COMMENTARY

Synopsis: *The outpatient bleeding risk index is a means of identifying the potential risk of bleeding in patients with deep venous thrombosis and pulmonary embolism.*

Source: Wells P, et al. *Arch Intern Med*. 2003;163:917-920.

Evidence demonstrates that long-term anticoagulation prevents recurrent thrombosis in patients with idiopathic deep venous thrombosis or pulmonary embolism. Recent studies place the risk of recurrent venous thrombosis at 27% per year, whereas the risk of major hemorrhage while on anticoagulation is 3.7% per year.[1]

In 1998, Beyth and colleagues developed a modified

outpatient bleeding risk index and found that rates of major bleeding at 12 months of anticoagulation were 3%, 12%, and 48% for patients considered low, moderate, and high risk respectively.[2] These risk stratifications were based on the original outpatient bleeding risk index by Landefeld[3] which found 5 independent risk factors for major hemorrhage—age older than 65 years, history of gastrointestinal bleeding, history of stroke, serious co-morbid condition, and atrial fibrillation. Patients without any of the aforementioned risk factors were considered low risk, whereas those with 1 or 2 risk factors were placed in the moderate category. High-risk patients were those with 3 or more risk factors.

In this prospective study conducted at the University of Ottawa, 222 patients with diagnosed pulmonary embolism or deep venous thrombosis were observed for an average of 18.5 months. These patients were categorized as low, moderate, or high risk based on the 5 factors published by Landefeld et al. Bleeding events were also recorded with major hemorrhage defined as bleeding that led to the loss of 2 units of blood in a 7-day period or bleeding that was life threatening. All other bleeding episodes were classified as minor.

Within the low-risk group there were 128 patients of which there were 7 minor (5.5%) and zero major hemorrhagic events. Also, 92 patients fell into the moderate risk category of which 5 had minor hemorrhage (5.4%) and 5 had major hemorrhage (5.4%). There were only 2 patients in the high-risk category, 1 of which had a minor bleeding episode (50%), and none suffered a major hemorrhage.

COMMENT BY JONATHAN EDELSON, MD, AND JILL KARPEL, MD

Previous studies reported the average annual frequency of fatal, major, and minor bleeding during warfarin therapy were 0.6%, 3.0%, and 9.6%, respectively.[2-4]

The ability to assess patient risk of bleeding may help to identify which patients need closer monitoring of anticoagulation therapy. In addition, patient risk of bleeding may be weighed against the risk of recurrent thrombotic events. Determining whether an individual patient is at high risk for such complications would be of paramount importance in tailoring treatment strategies for patients with deep venous thrombosis or pulmonary embolism. ■

Dr. Edelson and Dr. Karpel are Pulmonary and Critical Care Fellows at North Shore University Hospital, Manhasset, NY.

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Pharmacology Update

Omalizumab Injection (Xolair)

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

THE FDA HAS APPROVED GENENTECH'S OMALIZUMAB, the first biotechnology drug for the treatment of asthma. Omalizumab is a monoclonal antibody that binds to human immunoglobulin E (IgE), a major mediator of allergy-related asthma. The drug is given by subcutaneous injection every 2 or 4 weeks. It is manufactured by Genentech Inc and is jointly marketed by Genentech and Novartis Pharmaceuticals as Xolair.

Indications

Omalizumab is indicated in adults or adolescents (12 years of age and older) with moderate-to-severe persistent asthma with positive skin test or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled steroids.[1]

Dosage

The recommended dose is 150-375 mg administered subcutaneously every 2 or 4 weeks. Serum total IgE levels before the start of treatment and body weight determine the dose and frequency. Doses greater than 150 mg should be divided among more than one injection site and not more than 150 mg per site.[1]

Xolair is available as a single-use vial designed to deliver 150 mg.

Potential Advantages

Omalizumab has been reported in studies to reduce the number of exacerbations, asthma-related emergency room visits, and hospitalizations and to improve asthma symptoms and pulmonary function compared to placebo.[1-3]

Potential Disadvantages

A higher incidence of malignant neoplasms was reported with omalizumab in clinical studies, 20 of 4127 (0.5%) compared to 5 of 2235 (0.2%) for placebo. Rare incidence of anaphylaxis has also been reported. Total serum IgE levels are elevated during omalizumab therapy and for up to 1 year after discontinuation of therapy.

The long-term implications of exposure to omalizumab or elevated total IgE levels after discontinuation of omalizumab is not known. The most common side effect is injection site reactions (eg, bruising, redness, burning, stinging, pain, induration, mass, inflammation) that occurred in 45% of patients and was severe in 12%.[1]

Comments

IgE plays an important role in allergic immune response including bronchial asthma. Omalizumab is a recombinant humanized monoclonal antibody that selectively binds to free human IgE. This reduces binding to various cells such as masts cells, monocytes, eosinophils, and dendrite cells blunting the release of mediators/cytokines.[5] Phase III clinical trials (pooled of 3 studies) in children (n = 334; ages 6-12) and adults (n = 1071) suggest that omalizumab administration reduced unscheduled asthma-related outpatient visits, emergency room visits, and hospitalizations. The rate ratios and 95% CI were 0.60 (0.44-0.81); $P < 0.01$; 0.47 (0.24-1.01); $P = 0.05$, and 0.08 (0.00-0.25); $P < 0.01$, respectively.[2] Omalizumab has also been shown to reduce exacerbations compared to placebo and permitted reduction of the steroid dose.[6] In patients requiring moderate-to-high doses of inhaled corticosteroids, the addition of omalizumab has resulted in an improvement in asthma-related quality of life (QoL) both in a steroid stable and steroid reduction phases.[3,4] The domains of the survey include activities, emotion, symptoms, and environmental exposure. The overall mean change in QoL was 0.90 units in a 32-question 7-point scale vs 0.62 in the steroid-phase ($P \leq 0.001$) and 0.99 vs 0.66 in the steroid-reduction phase ($P \leq 0.001$).[7] A change of 0.5 or greater is considered as clinically meaningful. Omalizumab does not appear to reduce exacerbations in patients who had $FEV_1 > 80\%$ and those who require maintenance with oral steroids.[1] The wholesale cost of omalizumab is $433 per 150-mg vial. Four-week cost ranges from $433 to $2590 depending on pretreatment level of serum IgE and body weight.

Clinical Implications

Omalizumab offers a second-line novel approach to managing asthma patient. Adults and adolescents with moderate-to-severe asthma inadequately controlled on inhaled steroids, with frequent exacerbations, $FEV_1 < 80\%$, not on oral steroid maintenance, and positive skin test to a perennial aeroallergen may be candidates for this expensive biotech drug. ■

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CME Questions

6. Which of the following is *not* one of the 5 predictors of bleeding risk based on the outpatient bleeding risk index?

a. Age older than 65
b. History of stroke
c. History of gastrointestinal bleeding
d. Ventricular fibrillation
e. Co-morbid disease

7. Which of the following statements is correct?

a. According to the National Cancer Institute, the PSA test is considered a strategy still under investigation.
b. The PSA test has a strong specificity for the diagnosis of prostate cancer.
c. Among the men with an abnormal PSA, by any of the criteria used, only 40-55% had abnormal levels on subsequent tests.
d. The investigators recommend that the PSA test should no longer be used.
e. a and c

8. Clinical trial data clearly support which of the following for secondary prevention in CAD?

a. Aspirin
b. Folic acid
c. Vitamin E
d. Fish oil

Answers: 6 (d); 7 (e); 8 (a)

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By Louis Kuritzky, MD

Metformin and Thiazolidinedione Use in Medicare Patients with Heart Failure

With expert guidance encouraging increasingly austere levels of A1C control for diabetics, clinicians have been required to become more sophisticated and diversified in diabetes (DM) pharmacotherapy. Although insulin sensitizers such as metformin (MET) and the thiazolidinediones (TZD) have played a progressively more prominent role in DM control, heart failure (CHF) is a listed precaution for TZDs and contraindication to MET use.

Masoudi and colleagues analyzed data obtained from the National Heart Care Project, an initiative to improve quality of care for hospitalized CHF patients. In a sample population (n = 12,505) from 1998-1999, approximately 7% of patients discharged with a diagnosis of CHF received prescription for TZD or MET, despite the precautionary labeling for both. A comparative sample from the same population obtained 2 years later (n = 13,158) indicated that not only had TZD/ MET prescribing not shown greater conformity to existing prescribing recommendations, but rather the number of persons receiving either drug had actually increased to 11% (MET) and 16 % (TZD).

Prescription of MET or TZD to patients with CHF presents a recognized risk. Even if some of the provision of these medications is based upon the belief that the benefits of the medication for DM outweigh the risks for worsening CHF, there likely remain a number of patients who receive inappropriate treatment because of lack of clinician awareness. Masoudi et al endorse enhanced adherence to recommended precautionary guidance for patients with CHF and DM, until studies prove whether such treatment can be safely used. ■

Masoudi FA, et al. JAMA. 2003;290: 81-85.

Alcohol Consumption Patterns and Biologic Markers of Glycemic Control Among 459 Women

Several decades of observational data have indicated that moderate alcohol consumption (ALC) is associated with reduced incidence of cardiovascular end points, particularly stroke and myocardial infarction. The relationship between ALC and glycemic control has been less clearly established. Using the population enrolled in the Nurses Health Study II (n = 116,671), a prospective cohort study, Kroenke and colleagues studied the relationship between ALC and glycemic control in healthy women, specifically excluding individuals who had preexisting cardiovascular or other serious disease. In addition to stratification of drinking behaviors, women were categorized by BMI.

The most common alcoholic beverage chosen in this population was white wine. ALC was found to relate inversely with A1C levels, when adjusted for multiple covariates. There was no difference in the relationship when analyzed for a particular type of alcoholic beverage, nor did it make a difference whether ALC occurred with meals or in other venues. Potential mechanisms for the association of ALC with improved A1C include alcohol-induced increases in insulin binding factors, reduced hepatic gluconeogenesis, and increases in plasma leptin levels, which may decrease appetite for sweets. Kroenke et al conclude that 1-2 drinks on several days per week are associated with favorable effects on glucose homeostasis. ■

Kroenke CH, et al. Diabetes Care. 2003;26:1971-1978.

Azelaic Acid Gel as a New Treatment for Papulopustular Rosacea

Rosacea (ros), although sometimes called "acne rosacea," is unrelated pathophysiologically to acne. The pathology of ROS is characterized by vascular, inflammatory, and tissue proliferative components which results in one or more of flushing, erythema, telangiectasia, inflammatory lesions, edema, localized cutaneous swellings, and ocular symptoms. Currently available treatments for ROS include systemic antibiotics, topical antibiotics, and oral isotretinoin, each of which has its own limitations and adverse effects profile. Initial observations have indicated some potential efficacy of azaleic acid, which is recently available in a gel formulation, for ROS.

This report compared azaleic acid gel (AZA) with vehicle in ROS in 2 separate randomized, controlled trials.

AZA was applied twice daily for 12 weeks, after a suitable washout period from prior treatments. Subjects (n = 664) had moderate ROS (mild and severe patients were excluded). Severity of ROS was stratified a 5-point scale, with 1 including compete remission, and indicating severe disease (and hence a deterioration from baseline). AZA gel provided a statistically significant improvement over vehicle, with approximately half of treated individuals showing disease resolution or marked improvement. In the AZA-treated patients, 38% experienced transient, mild-moderate cutaneous burning, stinging, or itching. Such symptoms were considered severe in < 1%.

AZA gel has been demonstrated to be a safe and effective treatment for ROS. ■

Thiboutot D, et al. J Am Acad Dermatol. 2003;48:836-845.

A 3-Beat Run in Lead V_1

By Ken Grauer, MD

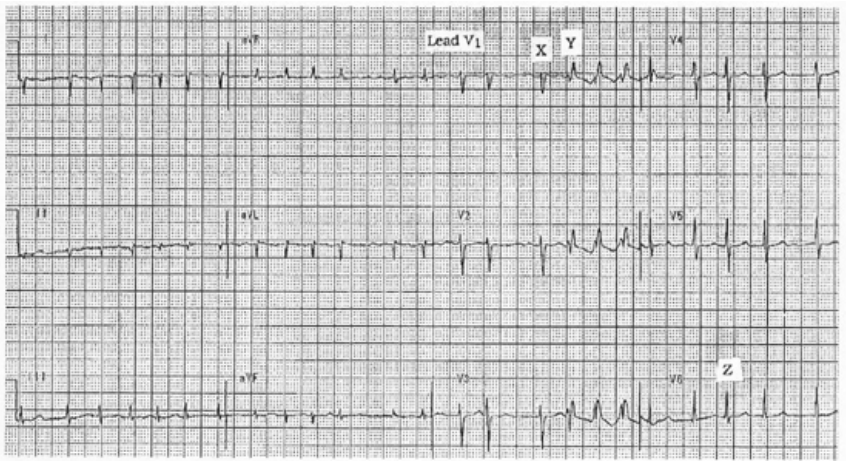

Figure. 12-lead ECG obtained from a 57-year-old woman with palpitations. Note the 3-beat run in lead V_1.

Clinical Scenario: The ECG in the Figure was obtained from a 57-year-old woman with palpitations. Is there a short run of VT (ventricular tachycardia) in lead V_1? What else may be wrong with the tracing?

Interpretation: The rhythm is rapid and irregularly irregular. The absence of P waves defines this as atrial fibrillation with a rapid ventricular response. Three abnormal looking beats are consecutively seen in lead V_1 (beginning with beat Y). Although at first glance one might be tempted interpret this 3-beat run as a salvo of ventricular tachycardia, it is much more likely that these 3 beats are supraventricular in etiology and conducted with aberration. Each of these 3 beats manifests an rsR' morphology consistent with a RBBB (right bundle branch block) pattern. Note that the initial direction and magnitude of the small r wave is identical for the three anomalous and the three narrow beats that occur in this lead. This is consistent with the conduction defect that occurs with RBBB, in which the initial vector of left-to-right septal depolarization is unaffected by the conduction disturbance. In further support that these beats are aberrantly conducted is the finding of a "reason" for aberrant conduction: the *coupling* interval of the first anomalous complex (the distance between beat X and beat Y) is short (increased likelihood that there will be relative refractoriness of the ventricular conduction system). In addition, the preceding R-R interval (ie, the R-R interval before beat X) is relatively long. Since the length of the refractory period is determined by the duration of the *preceding* R-R interval, the opportunity for aberrant conduction to occur is enhanced when early occurring beats (such as Y) are preceded by a relatively longer R-R interval. Finally, the complex labeled Z (in lead V_6) manifests a QRS consistent with incomplete RBBB conduction (it is the only complex in lead V_6 with an S wave), thereby providing additional evidence of RBBB-type conduction delay for selected beats on this tracing. While not infallible, the combination of morphologic features described above (that are consistent with a bundle branch block form of conduction delay) occurring in a setting that predisposes to aberrant conduction (ie, rapid atrial fibrillation) strongly suggest that the 3-beat run seen in lead V_1 is not VT. Rate control of this patient's rapid atrial fibrillation will probably result in resolution of anomalous complexes. Otherwise, there is a low-voltage, non-specific ST-T wave abnormalities, and a highly unusual negative complex in lead I. In view of the upright QRS complex in lead aVR, limb lead reversal would not negate our interpretation of the rhythm, nor of the high likelihood for aberrant conduction of the 3-beat run that is seen in the precordial leads. ■

In Future Issues: The Skinny on Low-Fat and Low-Carbohydrate Diets