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Multivitamin Use, Folate, and Colon Cancer in Women in the Nurses' Health Study

ABSTRACT & COMMENTARY

Synopsis: *Women who used multivitamins for more than 15 years showed a significant reduction in rates of colorectal cancer. Dietary sources of folate may be less effective in reducing the risk of colon cancer because the folate in multivitamins is more bioavailable than that in foods.*

Source: Giovannucci E, et al. *Ann Intern Med* 1998;129:517-524.

This study asks about determinants of colon cancer. The data are the dietary reports from a cohort of the Nurses' Health Study. This subgroup was composed of 88,756 women followed since 1976. In 1980, Giovannucci and colleagues started tracking dietary habits at two-year intervals using a semiquantitative food-frequency questionnaire. Subjects also provided information about vitamin use, hormone use, smoking, physical activity, aspirin use, colonoscopy or sigmoidoscopy, and parental history of colorectal cancer. After controlling for an array of potentially confounding factors, Giovannucci et al found that those women who used multivitamins for more than 15 years showed a significant reduction in rates of colorectal cancer. Folate from dietary sources alone was related to a modest reduction in risk, whereas the benefits of long-term multivitamin use were seen at all levels of dietary intake.

COMMENT BY ELIZABETH MORRISON, MD, MSED

We already know that all American women of reproductive age should be taking supplementary folate because it prevents neural tube defects in their offspring.[1] Data from the Nurses' Health Study, published in the *JAMA* last year,[2] indicate that women who take multivitamin supplements with folate may decrease their risk of coronary artery disease by up to 25%. Now, we have compelling evidence of yet another benefit of multivitamin supplements and folic acid for women—reducing the risk for colon cancer.

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Giovannucci et al skillfully handled possible confounders. Women who take multivitamin and folate supplements are likely to pursue other "health-seeking behaviors" such as low-fat and high-fiber diets. Giovannucci et al searched for confounding ties between these behaviors and colon cancer risk but found none that altered the substantial relationship between folate, multivitamins, and colon cancer.

It is interesting that even high intake of dietary folate did not seem to decrease colon cancer risk, while folate and multivitamins in supplement form did. Giovannucci et al point out that dietary folate is not as bioavailable as folate supplements, which may account for this difference. One also wonders why no benefit resulted when women took the supplements for less than 15 years. Could other dosages or forms of these nutrients provide more rapid or more powerful benefits?

Giovannucci et al discuss the study's main flaw—its inability to separate the effects of folate from the multivitamins in the supplements. It is certainly possible that unknown nutrients in the multivitamin supplements, and not the folate, are ultimately responsible for the reduced risk of colon cancer. Clearly, we need to see data from a randomized, controlled trial, preferably one that separately analyzes folate and other nutrients contained in multivitamin supplements. Since such data will not be available any time soon, if ever, this study's meticulous analysis provides useful interim findings. I will add this study to my repertoire as I encourage women to pursue "health-seeking behaviors" that include daily folate-containing multivitamin supplements.

COMMENT BY SARAH L. BERGA, MD

Now we have folate and its sources to consider when advising women about the chemoprevention of aging. Folate might well be nominated as the vitamin of the year. Not only does its intake reduce the risk of neural tube defects in pregnant women, but its use also has been touted as a way to diminish the risk of cardiovascular disease due to elevated homocysteine levels. Why might folate be so important? As Giovannucci et al point out, folate is essential for regenerating methionine, the methyl donor for DNA methylation. Also, it is needed for producing purines and pyrimidines for DNA synthesis. Inadequate availability of folate may contribute to aberrations in DNA methylation and may lead to abnormalities in DNA synthesis and repair. Hypomethylation of DNA is reported to be one of the earliest events in colon carcinogenesis. It is estimated that 88% of the population has folate intake of less than 400 g/d, the amount currently recommended and generally contained in multivitamin preparations. While foods naturally high in folate contain important micronutrients and the goal of obtaining most nutrients from food should not be abandoned, multivitamin use or increased intake of fortified foods is recommended to ensure adequate folate status. ❖

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Late-Breaking Lipid Trials

CONFERENCE COVERAGE

Synopsis: *Several studies were recently reported that should influence clinical practice.*

Source: American Heart Association Annual Scientific Sessions, November 8-11, 1998, Dallas, TX.

AVERT: Atorvastatin vs. Revascularization

This multicenter, nine-country study was designed to investigate the potential of aggressive, lipid-lowering strategy with atorvastatin vs. angioplas-

ty in stable patients with CAD with few symptoms and single- or double-vessel disease with preserved left ventricular function. Mean LDL cholesterol was 140; patients had to be able to complete a four-minute exercise test without ischemia. Three hundred forty-one subjects were randomized to receive 80 mg of atorvastatin daily or the scheduled angioplasty that triggered the enrollment process. Follow-up was approximately 18 months. The primary end point was any major ischemic event, including death, nonfatal infarction, stroke, revascularization, or hospitalization for unstable angina. Secondary end points included the time to the first ischemic event as well as safety parameters. Because of the concern that the patient cohort treated with atorvastatin alone might have threatening episodes of ischemia, two interim analyses were scheduled. The patients were evenly matched; approximately 90% were male, with a mean age of 58; more than 50% had single-vessel disease, and 44% had two-vessel disease. The LAD was involved in more than one-third. More than 40% of these subjects had a prior infarction. Patients had angina class 1 or 2. Baseline LDL cholesterol was 140 mg/dL. The angioplasty group received the usual medical care, and at the end of the study, their LDL cholesterol had fallen by 18% to 119 mg/dL. The high dose of atorvastatin resulted in a 46% drop in LDL cholesterol, to a mean of 77 mg/dL. Atorvastatin subjects had less angina and experienced a 36% reduction in the combination of cardiovascular events (nonfatal myocardial infarction, revascularization, hospitalization for angina), compared with individuals treated with angioplasty and usual care. The actual overall event was 13% in the atorvastatin cohort and 21% in the angioplasty cohort (P = 0.048). The time to the first ischemic event was shorter in the angioplasty cohort than in the statin group, with major curve separation beginning at approximately 6-7 months (P = 0.027); the combined end point was relatively low overall—approximately 2% per year. Both angioplasty and coronary bypass surgery were decreased by lipid lowering, as was hospitalization for unstable angina; 87% of these individuals did not suffer an event by 18 months. Safety monitoring revealed a 2.4% incidence of increased liver enzymes. No patient had other adverse reactions and there were no elevations of creatine kinase.

COMMENT BY JONATHAN ABRAMS, MD

This long-awaited study, although modest in patient size, strongly suggests that aggressive lipid lowering in patients with stable CAD is beneficial and may avert or delay revascularization procedures. This is consistent with plaque stabilization and improvement in coronary endothelial function, as well as slowing of progression of coronary atherosclerosis. None of these putative mechanisms can be assessed in this trial. The LDL target achieved is the lowest in any reported statin trial to date; the potency of atorvastatin allows this to occur, and the final mean LDL cholesterol of 77 mg/dL appears to put downward pressure on what is the optimal target LDL for patients with vascular disease. The recently post-CABG trial also achieved an LDL cholesterol level of substantially less than 100, and demonstrated a significant reduction in saphenous vein graph disease. Thus, it appears that a statin should be part of the therapy of most or perhaps all patients with CAD, with a target LDL cholesterol of less than 100 mg/dL. Whether the trial would have been less positive if the achieved LDL-C was 10 or 20 mg/dL higher can only be resolved by subsequent studies. At this time, it does appear reasonable to include as state-of-the-art medical therapy a statin, along with aspirin and anti-anginal drugs. AVERT results support an extremely aggressive approach to cholesterol lowering in patients with established coronary disease, and raise the possibility that such therapy may truly alter the natural history of coronary disease, and potentially decrease the need for revascularization while stabilizing coronary atherosclerosis to prevent acute ischemic events.

VA-HIT Trial

HIT is a VA cooperative trial conducted at 20 centers that asked the question if individuals with low HDL and normal LDL cholesterol would benefit from raising HDL with a fibrate. This ambitious trial enrolled 2531 patients between 1991-1993 who had an HDL of less than 40 mg/dL and an LDL of less than 140, with triglycerides less than 300. Subjects were randomized to gemfibrozil 1200 mg daily in long-acting formulation or placebo. The primary end point was CAD death or nonfatal myocardial infarction. Mean follow-up was seven years. Secondary end points included all-cause of mortality, stroke, revascularization procedures, and nonfatal MI. The male patient cohort was 90% white, with a mean age of 64. Patients were overweight with an increased waist-hip ratio. Twenty percent were smokers, more than 50% had hypertension, and 25% had diabetes. Baseline lipids were: TC 175; LDL-C 111; HDL-C 32; and TG 161. The primary end point of CAD death or nonfatal MI was 21.6% in placebo subjects vs. 17.3% in gemfibrozil patients (RR = 22%, P = 0.006), with similar

results on CAD death and nonfatal MI. Strokes and TIA were decreased. Unstable angina and revascularization were unaffected by therapy. Event curves began to separate by 18-24 months. Treatment lowered TC 28%; HDL increased 7.5%, LDL-C increased 4%, and TG decreased by 25%.

COMMENT BY JONATHAN ABRAMS, MD

Only the Helsinki Heart Study has demonstrated a benefit for HDL-C elevation in patients that had elevated TG, low HDL, and modest elevation of LDL-C. In the HIT population, baseline LDL levels were excellent, yet individuals taking gemfibrozil clearly benefited with respect to cardiac events. Thus, it appears that efforts to increase HDL cholesterol, even in individuals who have no other lipoprotein abnormality, are justified in secondary prevention CAD subjects. The HIT trial confirms the value of gemfibrozil. However, greater HDL elevations can be achieved with niacin, and this is a reasonable alternative for many individuals. Whether other fibrate drugs will have a greater or equivalent effect than gemfibrozil remains to be determined. At the present time, all patients with vascular disease who meet the lipid criteria in VA-HIT should be considered for gemfibrozil treatment. *(Dr. Abrams is Professor of Medicine, Division of Cardiology, University of New Mexico, Albuquerque.)* ❖

E. gingivalis and Periodontal Disease in AIDS

ABSTRACT & COMMENTARY

Synopsis: *Metronidazole is a safe and effective therapy for HIV-infected patients with severe gingival disease.*

Source: Lucht E, et al. *Clin Infect Dis* 1998;27:471-473.

Severe periodontal disease is a frequent occurrence in patients with HIV infection. While earlier studies suggest that many of these patients have significant alterations in their viral and fungal but not their bacterial oral microflora, the possible role of protozoal infection in gingival disease has not been previously explored. Lucht and associates examined the prevalence of various protozoa in salivary and dental plaque specimens in 45 patients with HIV and 15 HIV-negative controls. Periodontal disease was present in 13 of 45 (29%) HIV-positive patients compared with two of 15 (13%) HIV-negative controls.

Entamoeba gingivalis was the only protozoa found in the oral cavities of HIV-infected patients, where it was present in 10 (77%) of those with periodontal disease. Only one of the HIV-negative controls and none of the HIV-positive patients, without evidence of gingivitis, had *E. gingivalis* present in plaque specimens. No other protozoa were identified, including *Cryptosporidium* or *Microsporidium* species, or *Pneumocystis carinii*.

COMMENT BY CAROL A. KEMPER, MD

While good dental cleaning combined with topical solutions of 10% povidone-iodine solution and chlorhexidine mouth rinses are effective for many of these cases, oral metronidazole has been useful in cases of severe acute necrotic gingival disease—which may be, in part, explained by the known susceptibility of *E. gingivalis* to metronidazole. Metronidazole is a safe and effective therapy for HIV-infected patients with severe gingival disease. *(Dr. Kemper is Clinical Assistant Professor of Medicine, Stanford University, Division of Infectious Diseases; Santa Clara Valley Medical Center, San Jose, CA.)* ❖

Pharmacology Update

Tolcapone Tablets (Tasmar-Roche Pharmaceuticals)

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

Author's Note: *Due to recent reports of three deaths (estimated rate of 1 per 20,000) from acute, severe (fulminant) liver failure, the FDA and Hoffmann-La Roche have just issued a warning about the use of this drug. The drug should be reserved for Parkinson patients on levodopa/carbidopa who experience symptom fluctuations and are not responding satisfactorily to or are not appropriate candidates for other adjunctive therapy. The new warning also recommended early discontinuation of the drug (within a 3-week trial period) if no benefit is observed and closer monitoring of liver function test (every 2 weeks) as well as patient self-monitoring signs and symptoms for those remaining on the drug.*

Earlier this year, the fda approved the first member of a new class of anti-Parkinson drugs. Tolcapone (Tasmar-Roche) is a potent reversible inhibitor of catechol-O-methyltransferase (COMT), one of the enzymes responsible for metabolizing levodopa in the brain. Levodopa is generally administered with car-

bidopa, an inhibitor of dopadecarboxylase, but, with the use of this agent, COMT becomes the major pathway for the metabolism of levodopa. Inhibition of the COMT metabolic pathway increases levodopa concentrations, permitting higher concentrations of dopamine to reach the brain, where it exerts its therapeutic benefit. Because tolcapone is only a COMT inhibitor, it must be given with levodopa/carbidopa.

Indications

Tolcapone is indicated as an adjunct to levodopa and carbidopa for the treatment of the signs and symptoms of idiopathic Parkinson's disease.

Dosing Information

Tolcapone is available as 100 mg and 200 mg tablets. The initial dose is 100 mg three times a day. A majority of patients will require a decrease in levodopa dose if their daily dose is 600 mg or greater or if the patients have moderate or severe dyskinesia1. After adjustment of the levodopa dose, an increase to 200 mg three times a day is recommended. Further adjustment of levodopa may be required. Data from clinical trials indicate that an average levodopa dose reduction was about 30%.[1]

Tolcapone may be taken with levodopa/carbidopa and may be taken without regard to meals. The first dose of tolcapone each day should be taken with the first dose of levodopa, and the subsequent doses are taken 6-12 hours later. The concomitant administration of tolcapone and selegiline was generally well tolerated during clinical trials. A slightly higher incidence of dyskinesia and sleep disorders was observed.[1]

Patients with moderate hepatic impairment should not have their dose escalated to 200 mg tid.[1]

Potential Advantages

Tolcapone, when administered with levodopa, alone or in combination with carbidopa, increases the systemic bioavailability of levodopa by about twofold. This results mainly from prolonging the elimination half-life of levodopa from 2 hours to 3.5 hours.[1]

Cerebral spinal fluid concentrations of levodopa and total dopamine were increased significantly (about 90%) with tolcapone and levodopa/carbidopa compared to levodopa/carbidopa alone.[2] Tolcapone does not appear to aggravate the amplitude of peak dose dyskinesia.[2] In addition to increasing the bioavailability of levodopa, additional benefit may result from the inhibition of the formation of 3-O-methyldopa. This major metabolite, catalyzed by COMT, may interfere with the activity of levodopa, such as competing with the latter for transport across the blood brain barrier.[1,2]

Potential Disadvantages

In clinical trials, tolcapone increased liver enzymes (ALT or AST) to greater than three times the upper limit of normal in 1% of patients who received 100 mg tid and 3% of patients who received 200 mg tid. The manufacturer recommends that liver enzymes be monitored monthly during the first three months and every six weeks for the next three months.[1] Diarrhea was the most common nondopaminergic side effect leading to discontinuation of the drug. The incidence of diarrhea reported in clinical trials was 16-18% compared to 8% for placebo. Three to four percent of patients developed severe diarrhea. Tolcapone has a short elimination half-life (2-3 h), requiring three times a day dosing.

Comments

Levodopa has been a therapeutic mainstay of Parkinson's disease treatment for decades. As the disease progresses, levodopa tends to lose its effectiveness, usually manifested by a shortening in the duration of therapeutic effect. Patients experience an end-of-dose deterioration or a "wearing-off" phenomenon. They fluctuate between states of mobility (&on8) and disability (&off8) periods. This phenomenon is generally characterized by sensory, psychiatric, and autonomic as well as motor fluctuations. Paresthesia, pain, tachycardia, sweating, constipation, belching, and shortness of breath also occur during "off" periods.[4] The addition of tolcapone reduces "wearing-off" phenomenon by increasing "on-time" and reducing "off-time." This was shown in several double-blind, placebo-controlled, parallel, 6-13-week trials involving a total of 568 patients who were experiencing end-of-dose "wearing-off" fluctuations.[3,11,12] Tolcapone at a dose of 200 mg tid produced a decline in mean percentage of "off" of 16% or a decrease of about 1.5 hours (40%) based on investigator's 10-hour evaluation of off time.[3] Based on patients' diaries, 200 mg tid reduced "off-time" by 2.5-3 hours (-37% to 51%) and increased "on-time" by 2.3-2.9 hours (25-32%).[11,12] The total daily dose of levodopa was reduced by an average of 30%.[1] Tolcapone 200 mg tid is generally more effective than 100 mg tid. Maintenance of effectiveness has been reported for up to 52 weeks in one study.[11] Tolcapone also appears to benefit patients who were receiving levodopa but have yet to develop motor fluctuations.[5] Patients treated with tolcapone (100-200 mg tid) showed improved daily living activities and motor function as assessed by Parkinson's disease rat-

ing scale scores. Clinical study results suggest that approximately 70-80% of patients respond to tolcapone.[1]

Diarrhea is the most common nondopaminergic side effect leading to discontinuation of the drug, and patients should be monitored for occasional elevation of liver enzymes. The effect of tolcapone on the pharmacokinetics of drugs metabolized by COMT (e.g., methyldopa, adrenaline, and isoproterenol) has not been adequately studied.[1] Caution should be exercised when these drugs are coadministered with tolcapone. A dose reduction should be considered.[1]

Clinical Implications

Parkinson's disease is a common disease of the elderly, affecting 1.5 million Americans. The prevalence increases significantly with age, with an overall prevalence estimated at 15% for people ages 65-74 and 30% for those people ages 75-84 years.[9] After a long lull, the FDA has recently approved three drugs for this neurodegenerative movement disorder—pramipexole (Mirapex), ropinirole (ReQuip), and tolcapone, the first COMT inhibitor.

Approximately 50% of patients treated with levodopa for longer than 2-5 years develop the "wearing-off" phenomenon. Strategies for managing "wearing-off" phenomenon include adjusting the dose of levodopa (lowering individual doses and shortening the dosage intervals), use of controlled-release formulations alone or in combination with an immediate-release form, or adjunctive therapy with a dopamine agonist.[6] A COMT inhibitor, such as tolcapone, provides an effective alternative. Studies, available in abstract form only, have suggested that tolcapone is as effective as bromocriptine, a dopamine agonist in patients with fluctuating Parkinson's disease.[7,8]

The wholesale cost of tolcapone is between $4.60 and $5 per day. ❖

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9. Bennett DA, et al. *N Engl J Med* 1996;334:71-76.
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11. Rajput AH, et al. *Neurology* 1997;49(4):1066-1071.

CME Questions

4. Which of the following conditions has *not* been linked to inadequate intake of folate?
a. Neural tube defects
b. Osteoporosis
c. Colon cancer
d. Cardiovascular disease associated with elevated homocysteine levels

5. Strategies likely to reduce the risk of colorectal cancer include all of the following *except*:
a. dairy food or calcium supplementation to achieve 1200 mg of calcium daily.
b. smoking cessation.
c. exercise.
d. 5000 mg of vitamin C daily.
e. five servings of fruits and vegetables daily.

6. The aggressive atorvastatin therapy vs. angioplasty trial showed that atorvastatin:
a. increased liver function tests in 24%.
b. increased creatine kinase in 15%.
c. reduced cardiac events by 36%.
d. reduced mortality.

7. The initial dose of tolcapone is:
a. 200 mg daily.
b. 100 mg three times a day.
c. 500 mg twice a day.
d. none of the above.

8. What is the most common nondopaminergic side effect leading to the discontinuation of tolcapone?
a. Pain
b. Constipation
c. Sweating
d. Diarrhea

9. Strategies for managing the "wearing-off" phenomenon with levodopa include:
a. adjusting the dose of levodopa.
b. use of controlled-release formulations alone or in combination with an immediate-release form.
c. adjunctive therapy with a dopamine agonist.
d. All of the above

Attention CME Subscribers

Due to an American Health Consultants error, a mistake has been made with the CME numbering. The numbering should have started over in your November 1998 issue. In the November 1998 issue, questions 31-32 should be questions 1-2. In the December 1998 issue, question 33 should have been question 3. We regret any confusion this may have caused. ❖

By Louis Kuritzky, MD

Use of Colchicine to Treat Severe Constipation in Developmentally Disabled Patients

The developmentally disabled often suffer some of the worst difficulties with constipation, since they more commonly also experience hypotonia, autonomic dysfunction decreasing bowel motility, physical inactivity, and polypharmacy. Based upon an n = 1 experience with a person suffering chronic constipation refractory to traditional measures, Frame and colleagues successfully managed this patient with colchicine 0.5 mg tid. Following this success, Frame et al performed a prospective, double-blind, crossover study of colchicine vs. placebo for eight weeks in developmentally disabled patients who required three or more laxatives to manage chronic constipation.

As defined by an increased number of bowel movements and/or decreased requirement for laxatives, Frame et al found that eight out of 11 patients were improved while on colchicine, and no clinically important side effects occurred.

Colchicine is known to stimulate gastrointestinal activity through neurogenic stimulation. In these patients, treatment produced an average of 4.27 more bowel movements per patient over eight weeks time.

Colchicine can cause adverse effects, but serious toxicity is rare and usually confined to those with renal or hepatic insufficiency. Frame et al suggest that although colchicine is not suggested as a first-line laxative, persons with refractory constipation to standard methods, as are commonly found among the developmentally disabled or nursing home populations, may merit consideration for this intervention. ❖

Frame PS, et al. J Am Board Fam Pract 1998;11:341-346.

Sinusitis in the Common Cold

Bacterial sinusitis is generally treated with antibiotics. Sinusitis, as determined, may be of diverse origin. During the common cold, if symptoms suggest sinusitis and sinus films are obtained, sinusitis seen on such films might prompt antibiotic use, as differentiation of bacterial from viral sinusitis is difficult. As part of a trial of fluticasone propionate in treatment of the common cold, Puhakka and associates studied sinus radiographs of 197 young healthy adult men and women on days 1, 7, and 21 of a common cold, and followed patients for three weeks clinically beyond that time.

Radiographs showed sinusitis in 14.2% of patients on day 1, 38.8% on day 7, and 11.3% on day 21. Common radiographic findings included mucosal thickening greater than 5 mm, air-fluid levels, and total opacification.

Overall, 57% of study subjects had sinus abnormalities during the first 21 days. All patients made full clinical recoveries, and no patient with radiologic sinusitis was treated for it with antibiotics.

Sinusitis is common, as defined radiographically, during the common cold. Puhakka et al suggest that, with few exceptions, sinus films should not be obtained during the typical evolution of the common cold, as such films lead to unnecessary irradiation, cost, and likelihood of superfluous antibiotic therapy. ❖

Puhakka T, et al. J Allergy Clin Immunol 1998;102:403-408.

Potassium Supplementation on BP in Patients with Essential Hypertension

A variety of diverse pieces of information suggest that potassium (K) status is related to blood pressure (BP). Dietary K intake correlates inversely with BP, and meta-analyses show significant BP reduction with supplementation.

Kawano and colleagues studied, in a randomized crossover design method, 55 hypertensive Japanese men and women given 2500 mg/d K supplementation divided in four doses for four weeks by office BP measurement, home self measurement, and 24-hour ambulatory measurement. Serum K, though not deviating from normal, increased from a mean of 4.15 to 4.42. Similarly, urinary potassium excretion increased from 54 to 96 mmol/d. All BP measurement techniques showed lower BP during K supplementation periods, to a highly statistically significant degree. Overall decreases in BP were modest: home BP decreased 3.6/1.6, 24 hr BP 3.4/1.2, and office BP 2.9/1.3. These changes were consistent whether the patient was receiving pharmacotherapeutic treatment and did not differ by class of antihypertensive agent.

Supplementation of K for hypertensive patients produces small but significant changes in BP. ❖

Kawano Y, et al. Am J Hypertens 1998;11:1141-1146.

Does LBBB Prevent Diagnosis?

By Ken Grauer, MD

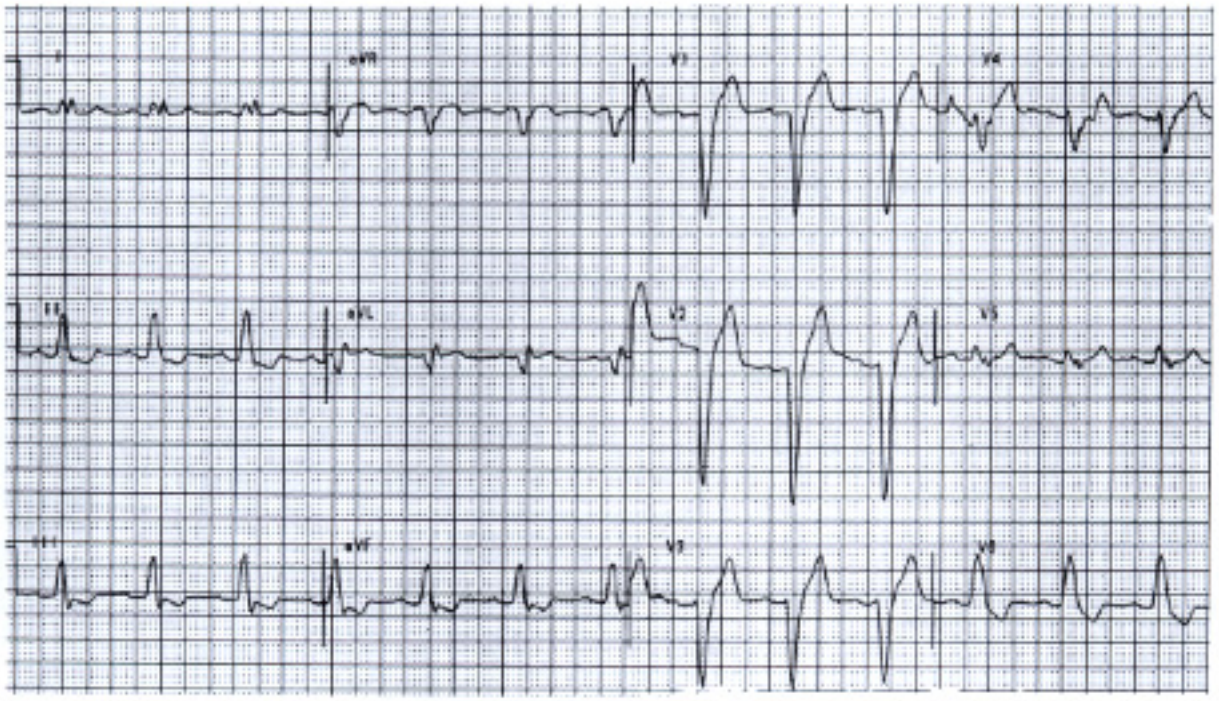

Figure. ECG obtained from a 69-year-old man with known LBBB. Can anything else be said about this tracing?

Clinical Scenario: The ECG shown in the figure was obtained from a 69-year-old man who was known to have complete left bundle branch block (LBBB). Is it possible to draw any other conclusions from evaluation of his ECG?

Interpretation: The rhythm is sinus at a rate of 80 beats/min. As noted above, the patient has complete LBBB. Despite opinion to the contrary, myocardial infarction can sometimes be diagnosed despite the presence of complete LBBB. Prior infarction is suggested in the above tracing by the presence of the wide and deep Q wave in lead aVL, late notching of the upslope of the S wave in two or more mid-precordial leads (in this case, leads V_4 and V_5), and primary ST-T wave changes (unexpected ST segment elevation in lead aVL, and the presence of an upright T wave in leads I and aVL). Q waves should not normally be present in lateral leads with typical LBBB. ST segments and T waves are normally directed opposite to the last QRS deflection in the three key leads (I, V_1, V_6) with typical bundle branch block. Thus, although one often will not be able to comment on the likelihood of past or present infarction in the setting of LBBB, the tracing shown here illustrates an example in which acute infarction should nevertheless be strongly suspected.

Suggested Reading

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In Future Issues:

***Bordetella Pertussis* and *Bordetella Parapertussis* Infections**
Chiropractic Benefit Challenged