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INSIDE

Choosing the right starting dose of warfarin ***page 99***

Prospective study of alcohol consumption and risk of dementia in older adults ***page 100***

Pharmacology Update: *Gefitinib tablets* ***page 101***

Risk Factors in Sleep-Disordered Breathing

ABSTRACT & COMMENTARY

Synopsis: *Over a 5-year period, the incidence of developing sleep-disordered breathing (AHI ≥ 5 events / hr) is about 37%, about 7% per year. With aging, male gender and body mass index (BMI) lose importance as risk factors for obstructive sleep apnea.*

Source: Tischler PV, et al. *JAMA*. 2003;289:2230-2237.

THE PURPOSE OF THE CLEVELAND FAMILY STUDY IS TO DETERmine the incidence, natural history, and risk factors of obstructive sleep apnea (OSA). This report includes longitudinal data for 285 individuals who were considered not to have significant sleep apnea at baseline (apnea plus hypopnea index [AHI] of fewer than 5 events per hour of sleep). At baseline, 72% were women, 21% were black, 16% had cardiovascular disease and/or diabetes, 42% snored, the mean body mass index (BMI) was 27.6 ± 6.4 kg/m^2, and the mean age was 36.8 ± 11.9 years. Extensive medical, demographic, and anthropometric data were gathered; in addition, a limited physical examination and some laboratory testing were performed. Subjects in this report all underwent in-home polysomnography (PSG, a.k.a. "Sleep Studies") on 2 occasions about 5 years apart.

The 5-year incidence of developing sleep-disordered breathing (defined in this study as an AHI of ≥ 5 or more events/hr) was 36.7%. With regard to severity for these incident cases of sleep-disordered breathing (SDB), 20.3% had AHIs of 5-9.9 events/hr, 6.3% had AHIs of 10-15 events/hr, and 10.1% had AHIs of more than 15 events/hr. After ordinal logistic regression to adjust for significant covariants, age, BMI, gender, waist/hip ratio (WHR), and serum cholesterol were significantly associated with the AHI. Variables that were not associated with AHI included self-reported cardiovascular disease, diabetes, family history, race, smoking, alcohol ingestion, or tonsillar size. The association of hypertension with AHI was inconsistent. With aging, the risks for SDB changed. After the age of about 50, male gender was no longer a significant risk factor, and after about age 60, BMI was no longer a significant risk factor.

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COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

These are astonishing findings, any way you look at it. There are several tempering factors (infra vide), but a 5-year incidence of 37% for an AHI that many would consider to be diagnostic of OSA is downright frightening. To put this in context, CMS (Centers for Medicare and Medicaid Services, formerly known as HCFA or Health Care Financing Administration) will pay for continuous positive airway treatment (CPAP) for patients who have an AHI of 5 or more with just about any symptom[1] and for asymptomatic patients who have an AHI of 15 or more (which 10% of this population developed over the course of 5 years). Tischler and colleagues carefully skirt the issue of what constitutes OSA, referring instead to "SDB," or to absolute AHIs. This is smart, given that that they used a nonstandard definition of oxygen desaturation for identifying apneas and hypopneas (this study used an oxygen desaturation of 2.5%, instead of the more standard 4%)[2] and that AHIs must be correlated with symptoms to make a diagnosis. Even so, a 5-year incidence of 10% (2% per year) for an AHI of 15 events per hour of sleep is alarmingly high, given that the risk of cardiovascular disease is correlated with AHI and is certainly significant at AHIs of 15 events per hour of sleep or more.[3]

The classic patient with sleep apnea is a 48-year-old, obese, hypertensive man. This study clearly documents that sleep apnea begins to look different after the age of about 50. Gender and obesity become negligible risk factors after the ages of 50 and 60 years, respectively. This has been reported before.[4] It is likely that older patients with sleep apnea are being overlooked because they don't match the classic stereotype; this is really a disservice to senior citizens, since we know that sleep apnea causes so many of the afflictions of older age, such as hypertension,[5] cardiovascular disease,[3,6] and cognitive decline,[7] and that CPAP can reverse these changes.[8-10]

Some findings of this study contradict earlier reports. This study found no relationship between AHI and self-reported race, cigarette smoking, or alcohol use. These findings are at variance with previous data.[11-13] However, the results of a prospective study of incident data such as this one are more powerful than cross-sectional ones. These issues may remain open questions for now.

Take home messages: Sleep apnea is common and becoming more so. Because the "typical" risk factors (obesity, male gender) become much less important in the older patient, we probably are seriously under diagnosing SDB in geriatric patients, and may be missing opportunities to preserve function and quality of life in this age group. ■

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Choosing the Right Starting Dose of Warfarin

ABSTRACT & COMMENTARY

Synopsis: *A warfarin initiation nomogram that uses 10 mg as a starting dose achieves a therapeutic INR more rapidly than one using a 5-mg starting dose.*

Source: Kovacs MJ, et al. *Ann Intern Med*. 2003;138:714-719.

A patient presenting with a deep-vein thrombosis (DVT) or pulmonary embolism (PE) commonly is started on heparin, either regular or low molecular weight, by subcutaneous injection or intravenous administration, usually for 5 days or so. Warfarin is added and the dose adjusted periodically to achieve the desired international normalized ratio (INR). Once achieved, the heparin is stopped, the INR monitored every so often, and the warfarin dose adjusted to keep it in a predetermined therapeutic range. Since heparin is more costly and more difficult to administer, getting to a therapeutic INR quickly has appeal. The issue of what dose of warfarin to start with has been argued for several years. Too high a starting dose could result in overanticoagulation and hemorrhage. Too low a dose could result in a prolonged initiation and extension of the thrombosis. Many physicians prefer the 5-mg starting dose and others the 10-mg dose. A study by Crowther concluded that the 5-mg dose was safer and as swift as the 10-mg dose.[1]

Building on an earlier trial that favored the 10-mg dose,[2] Kovacs and associates conducted a randomized, double-blind, controlled study of 2 warfarin initiation nomograms (5 mg vs 10 mg) in 4 Canadian thrombosis clinics. They randomized 210 consecutive outpatients with either a DVT or a PE. The diagnostic criteria, while not specified, were described as objective. Patients were excluded if their baseline INR > 1.4; if they were thrombocytopenic; if age was < 18 years; if they required hospitalization; if they had received warfarin in the last 2 weeks; or if they were judged to be at high risk for hemorrhage. Nine patients were excluded; the remaining 201 were randomized into 2 groups. There were 104 in the 10-mg dose group and 97 in the 5-mg group. The 2 groups were statistically similar in age (about 55.5 years), proportion with cancer (25% vs 23 %), and weight (about 83.5 kg). There were proportionately more men in the 10-mg group (62.5% vs 48.4%). All patients received at least 5 days of low-molecular-weight heparin). Blood was drawn daily for INR, beginning on day 3. Subsequent doses of warfarin in both nomograms were administered based on the INR values; however, the 10-mg nomogram did not rely on the day 4 value. The patients were followed for 90 days.

Data analysis was by intention to treat. The primary end point was time to a therapeutic INR, which Kovacs et al defined as >1.9. Patients in the 10-mg group were at end point at 4.2 days compared to 5.6 days in the 5-mg group. More patients in the 10-mg group were at end point at day 5 (83% vs 46%). These findings were statistically significant. Three patients in the 10-mg group experienced venous thromboembolism during follow-up. No patients in the 5-mg did, but this difference did not reach statistical significance. One patient in each group had a major bleeding episode, and 1 patient in the 5-mg group died during the study period. Neither of these was statistically significant. In the first 4 weeks, the patients in the 10-mg group had an average of 8.1 INR tests compared to 9.1 in the INR group; this result just barely made statistical significance. Both groups had equivalent numbers of patients who were overanticoagulated during the first 4 weeks. The researchers defined 3 levels of overanticoagulation: INR = 3.0, INR = 4.0, and INR = 5.0. Many patients in both groups were overanticoagulated by the first definition sometime during the first 4 weeks (78% in the 10-mg group vs 87% in the 5-mg group). The percentages for the second and third definitions were 9% vs 11% and 5% vs 6%, respectively.

COMMENT BY ALLAN J. WILKE, MD

Outpatient treatment of venous thromboembolism is attractive for a variety of reasons, not the least of which are economic and patient satisfaction. These results should only be applied to the outpatient setting; Kovacs et al's previous study[2] suggested that inpatients are more sensitive to warfarin. The main finding of this study is that a nomogram that uses 10 mg of warfarin as its starting dose is safe and results in speedier anticoagulation than a nomogram that uses 5 mg as a starting dose. The finding is statistically significant, but is it clinically significant? From a patient's perspective, one less blood draw and fewer heparin injections would be welcomed. However, a patient with a venous thromboembolism can expect to be treated for 3 months or more, making the reduction in blood draws and heparin injections small

indeed. From the physician's perspective, there may be one less day of laboratory review and decision-making, but, again, in the long run this appears to be a modest improvement. Both nomograms are safe, but not simple, and would require having them in front of you as you make dosing decisions. Ideally, someone will write a program for a handheld computer that would make the decision-making automatic. ■

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Prospective Study of Alcohol Consumption and Risk of Dementia in Older Adults

ABSTRACT & COMMENTARY

Synopsis: *Compared with abstention, consumption of 1-6 drinks weekly of alcoholic beverages was associated with a lower risk of dementia among adults older than 65 years.*

Source: Mukamal KJ, et al. *JAMA*. 2003;289:1405-1413.

ALCOHOL CONSUMPTION IS A COMMON PRACTICE, BUT the notion that drinking alcoholic beverages has health benefits remains controversial. Like drinking, dementia is common among adults older than 65 years and thus, is an important public health concern. Given that there are more than 360,000 new cases of Alzheimer dementia diagnosed annually in the United States, there is a pressing need to identify modifiable factors that may cause or prevent dementia. The present study was undertaken to see if there was a link between alcohol consumption and the risk of dementia. Pre-existing data were conflicting, with some data indicating that alcohol promoted cortical atrophy or cerebral hemorrhage, which would promote dementia. Other data indicated a beneficial effect, possibly because of a reduced risk of cardiovascular disease or increased cerebral circulation. Prior studies also suggested sex-linked differences in the health effects of alcohol consumption.

This was a meticulously conducted, prospective, nested case-control study of 373 persons with incident dementia and 373 controls who were among 5888 adults older than 65 participating in the Cardiovascular Health Study, a prospective, population-based cohort study in 4 US communities. Participants underwent magnetic resonance imaging of the brain and cognitive testing between 1992 and 1994 and were followed until 1999. The ascertainment of dementia was thorough, involving extensive testing done in 4 stages. Alcohol consumption was estimated by questionnaire at 6-month intervals for the course of the study. A number of factors that might modify the association between alcohol consumption and dementia were assessed, including sex, race, age, educational attainment, body mass index, diabetes, income level, physical activity, smoking, depression, use of hormone replacement therapy, cardiovascular disease, stroke, lipoprotein profiles, and apolipoprotein E genotype (ε4 allele).

Of the 373 cases, 258 had Alzheimer disease, 44 had vascular dementia, 54 had combined AD and vascular dementia, and 17 had other kinds of dementia. Age-adjusted rates of dementia were 56 per 1000 among black participants and 36 per 1000 among white subjects. Using the entire cohort, logistic regression models that adjusted for potentially confounding variables indicated that the lowest odds ratio for dementia occurred among those consuming 1-6 drinks per week. The highest odds ratio occurred among those consuming 14 or more alcoholic drinks weekly. Participants who consumed 1-6 drinks weekly had a 54% lower odds of experiencing dementia that those who abstained [OR 0.46; CI, 0.27-0.77]. This same reduction held when AD risk was analyzed separately from all causes of dementia. With increasing alcohol intake, women seemed to fare better than men. For women, the odds ratio fell to 0.23 [CI, 0.09-0.61] for those who drank 7-13 alcohol beverages weekly. For men, the OR increased to 1.42 for those consuming 7-13 drinks weekly. When considering the risk in those who drank more than 14 drinks weekly, for women, the OR remained low at 0.39 while for men it was 2.40. Although Mukamal and colleagues state that the type of alcoholic beverage (wine, beer, liquor) did not change the association, Table 4 in the manuscript showed that among those drinking more than 14 drinks weekly, the OR for wine was 0.62, while it was 1.96 for beer and 1.08 for liquor. Having APOE ε4 further increased the risk of dementia in those drinking more than 14 drinks weekly. These associations were similar in those who met criteria for depression.

■ COMMENT BY SARAH L. BERGA, MD

Alcohol consumption is often considered a taboo subject of discussion, even in physician's offices. But patients need to know which lifestyle factors make a difference. Counseling patients about alcohol consumption is not as straightforward as coun-

seling patients about smoking cessation, because there is less room for dogmatism when it comes to alcohol. As far as I know, there are no known health benefits associated with smoking or using tobacco. In contrast, studies have indicated that light-to-moderate drinking may confer a range of health benefits when compared to abstention. The present study, which has many strengths, suggested that there is a relatively narrow dose range in which alcohol may provide neuroprotection from dementia. Because the dose range for benefit was wider for women than for men and for those who drank wine rather than beer or liquor, one wonders if the different results in men and women are explained by alcohol preferences. Did women drink more wine than men? Did men drink more beer and liquor than women? Mukamal et al did not provide these data nor discuss this aspect. They do caution that the study results should not be interpreted as suggesting an increased intake of alcohol is recommended for women. As I have pointed out in previous reviews on this subject, women are more at risk than men for alcohol-induced myopathy and cardiomyopathy. Also, some have suggested a link between alcohol consumption and breast cancer in women. Women may absorb alcohol more quickly than men and achieve higher blood levels, placing them at increased risk for motor vehicle and other accidents after drinking. Thus, it would be premature on the basis of this study to counsel women that it was safe to drink more than 6 drinks weekly. We want to screen for those who are alcoholics, while reassuring the rest of our patients that "light" drinking might provide health benefits. ■

Dr. Berga is Professor and Director, Division of Reproductive Endocrinology and Infertility, University of Pittsburgh.

Pharmacology Update

Gefitinib Tablets (Iressa—AstraZeneca)

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

THE FDA RECENTLY APPROVED GEFITINIB, AN inhibitor of tyrosine kinase activity of the epidermal growth factor receptor (EGFR), for the treatment of non-small-cell lung cancer (NSCLC). The drug received an accelerated approval, reserved for new drugs for life-threatening conditions. Gefitinib, which is administered orally once a day, is similar to imatinib (Gleevec). Gefitinib is marketed by AstraZeneca as "Iressa."

Indication

Gefitinib is approved as monotherapy for the treatment of patients with locally advanced or metastatic NSCLC after failure of both platinum-based and docetaxel chemotherapies.[1]

Dosage

The recommended dose is 250 mg daily. It may be taken without regard to meals.

Gefitinib is available as 250 mg tablets. A 500-mg dose should be considered in patients with concomitant therapy with a potent inducer of CYP 3A4 (eg, rifampin, phenytoin).

A brief hiatus of up to 14 days, followed by reinstatement, may be considered in patients with poorly tolerated diarrhea or skin reaction.

Potential Advantages

In patients who have failed one or more chemotherapy regimens, gefitinib has been reported to produce objective radiographic response, improvement in disease-related symptoms, and quality of life in patients with NSCLC.[1-3,8]

Potential Disadvantages

Response rates were highly variable—5.1% in males, 17.5% in females, 4.6% in current or previous smokers, 29.4% in nonsmokers, 12.4% in adenocarcinomas, and 5.7% in other NSCLC.[1] The addition of gefitinib to carboplatin and paclitaxel or cisplatin with gemcitabine failed to show any improvement in response rate, survival, or quality of life.[1] Interstitial lung disease has been reported with use of the drug with a reported incidence of 2% in the Japanese postmarketing experience.[4] The incidence ranged from 0.3% to 1% in US studies.[1] Approximately one-third of the cases were fatal. Patients should be monitored for acute onset or worsening of pulmonary symptoms such as dyspnea, cough, or fever. Liver enzymes should be monitored for increases in liver transaminases. Gefitinib is metabolized by CYP 3A4 and can interact with inhibitors or inducers of this isoenzyme. Patients on warfarin should be monitored for possible elevation of the International Normalization Ratio (INR). Antisecretory drugs (histamine-2 receptor antagonists or proton pump inhibitors) may reduce the plasma levels of gefitinib. Other side effects associated

with the 250 mg dose include diarrhea (48%), rash (43%), nausea (18%), and vomiting (12%). The onset of adverse events occurred within the first month.[1]

Comments

Gefitinib is an inhibitor of tyrosine kinase of the epidermal growth factor receptor. Activation of these receptors has been shown to increase angiogenesis, cell proliferation and metastasis and to decrease apoptosis.[2] EGFR with tyrosine kinase activity is generally present in NSCLC specimens and in 25% of tumor specimens have been found to overexpress this activity.[5] Despite this apparent targeted therapy, the mean response rate is somewhat modest. In patients who have received 2 or more chemotherapy regimens (n = 216), the mean radiographic tumor response rate for gefitinib monotherapy (250 mg or 500 mg) was 10.6% (95% CI, 6-16.8%).[1,2,8] Median duration of response was 7 months (range, 4.4-18.6 months). About 40% of patients had symptomatic response, and 29% of patients showed improvement in quality of life. In patients who have failed 1 or 2 regimens (n = 210) the mean response rate was about 19%.[2,3] One hundred and forty patients were assessed for symptom response and quality of life and about 38% and 23% showed improvement, respectively. Overall survival ranged from 6.0 to 7.9 months.[8] The efficacy of 250 mg and 500 mg were similar, but the lower dose is better tolerated. The use of gefitinib as first-line treatment in combination with chemotherapy did not provide any benefit in terms of tumor response, time to progression, or overall survival.[1,6,7] The FDA's Oncology Drugs Advisory committee agreed that tumor response was sufficient for an accelerated approval, but improvement in symptoms or quality of life were not sufficient to support such claims.[9] Gefitinib is generally well tolerated, with infrequent incidences of fatal interstitial lung disease reported. The wholesale cost of gefitinib is $1560 for a month's supply.

Clinical Implications

Gefitinib may provide palliative treatment for patients with advanced disease who have failed both platinium-based and docetaxel chemotherapies. The overall benefit is modest, but variable, as some may gain greater benefit than others. AstraZeneca has agreed to complete 2 ongoing placebo-controlled survival trials in Phase IV.[9] ■

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CME Questions

1. **When comparing the 5-mg and 10-mg warfarin-dosing nomograms:**
   a. patients in the 10-mg group, on average, reached a therapeutic INR 1.4 days sooner than patients in the 5-mg group.
   b. a higher percentage of patients in the 5-mg group were at a therapeutic INR at day 5.
   c. patients in the 5-mg group had fewer INR determinations.
   d. there were more major bleeding episodes in the 10-mg group.
   e. there were more deaths in the 5-mg group.

2. **Which of the following is true about the epidemiology of obstructive sleep apnea?**
   a. Body Mass Index (BMI) is a powerful predictor of the risk of sleep-disordered breathing at all ages.
   b. Gender becomes a negligible risk factor after about the age of 50.
   c. Serum cholesterol values have no association with the risk of sleep apnea.
   d. The incidence of sleep apnea is about 0.5% per year.
   e. Sleep apnea is rare after the age of 50.

Answers: 1 (a); 2 (b)

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We look forward to hearing from you. ■

By Louis Kuritzky, MD

Rapid Magnetic Resonance Imaging vs Radiographs for Patients with Low Back Pain

The role of radiologic evaluation for acute low back pain (LBP) has been plagued with uncertainty, since as many as one-third of asymptomatic persons examined by MRI have signs consistent with herniated disk, and a substantially greater number manifest disk bulges or degeneration, despite an absence of symptoms. On the other hand, the high sensitivity of MRI might provide an opportunity for early diagnosis of problems that could benefit from prompt intervention. Making the possible use of MRI more attractive has been the recent evolution of rapid MRI, which requires only about 2 minutes of scanner activity.

Jarvik and colleagues compared plain x-rays with rapid MRI in subjects older than age 18 (n = 380) suffering acute LBP. Outcomes included functional disability, pain frequency, days of reduced or lost work, and patient satisfaction with care. Patients were interviewed at 1, 3, 6, 9, and 12 months after randomization.

Study results indicated that rapid MRI did not provide any statistically significant long-term advantage over plain films. Indeed, rapid MRI was associated with more frequent use of specialist consultants and more frequent invasive management techniques. Based upon these data, as well as cost considerations, Jarvik et al suggest that rapid MRI does not offer demonstrable long-term advantage over plain films. ■

Jarvik JG, et al. JAMA. 2003;289: 2810-2818.

Effectiveness of Anticholinergic Drugs Compared with Placebo in the Treatment of Overactive Bladder

Overactive bladder (OAB) comprises a syndrome that may include urgency, urge incontinence, frequency and/or nocturia. Incontinence troubles as many as one-third of all overactive bladder patients, but even symptoms of frequency or nocturia may cause substantial negative effect upon quality of life.

The most commonly offered treatment for OAB is anticholinergic pharmacotherapy, which provides reduction of detrusor muscle contraction through blockade of the parasympathetic (cholinergic) pathway. To date, impact upon detrusor contraction has been afforded at the cost of adverse drug effects such as dry mouth, dry eyes, and constipation. Herbison and associates posited that the efficacy of anticholinergic medications is uncertain and sought to provide further insight by performing a systematic review of anticholinergic drug treatment provided in randomized trials.

On the basis of 32 randomized trials (n = 6800), Herbison et al determined that for persons with incontinence, likelihood of an incontinent episode was reduced approximately once in 48 hours; frequency of urination was reduced by approximately 1 micturition per 24 hours.

Herbison et al observe that improvements in treated patients, despite being statistically significant, are clinically modest compared to placebo. Additionally, they comment that bladder training may provide similar magnitude of benefit. ■

Herbison P, et al. BMJ. 2003;326: 841-844.

A Randomized Trial of a Low Carbohydrate Diet for Obesity

At the current time in America, almost half of women and a substantial minority of men (30%) are dieting to lose weight. Unfortunately, diet interventions have had surprisingly little favorable effect upon the weight of the nation, as manifest by a doubling of the prevalence of obesity in the past 20 years.

Much contention surrounds what is the "best" diet for persons trying to lose weight, and a diversity of suggested methodologies abound. If sales of diet books are in any way indicative of public interest, the Atkins diet (low carbohydrate) has been the most popularly addressed, with a readership 4 times greater than any other diet book. Although popular, no randomized controlled trial of the Atkins diet vs, for instance, a high-carbohydrate, low-fat diet has been performed.

Foster and associates report upon subjects who were randomly assigned to either a low-carbohydrate diet (like Atkins) or a "conventional" diet (low calorie, high carbohydrate, low fat) and followed for 12 months.

Although an early difference in favor of the low carbohydrate diet was evident in the first 3 months, there was no statistically significant difference in weight lost at 12 months. Similarly, there were no significant enduring differences in frequency of urinary ketones, blood pressure, glucose tolerance, or LDL. The low-carbohydrate diet did produce more favorable changes in HDL and triglycerides, but Foster et al question whether even these changes would remain beneficial over the long term, in the face of high fat intake associated with chronic adherence to the Atkins diet. ■

Foster GD, et al. N Engl J Med. 2003;348:2082-2090.

The QRS Complex in Lead V_2

By Ken Grauer, MD

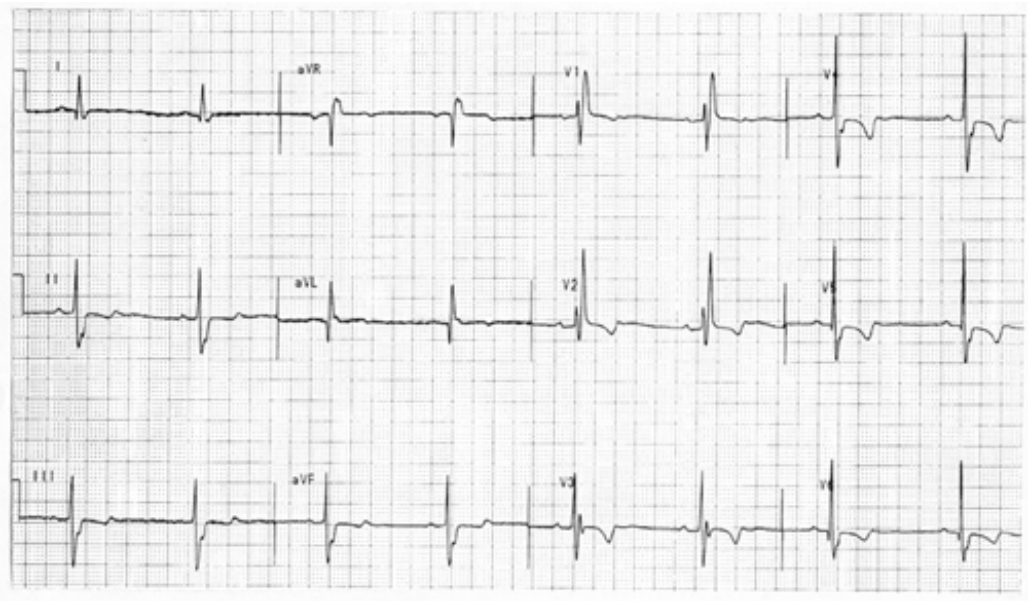

Figure. 12-lead ECG obtained from a 73-year-old man with dyspnea.

Clinical Scenario: The ECG in the Figure was obtained from a 73-year-old man with documented coronary disease and heart failure. He now presents with a 10-day history of dyspnea. How would you interpret his ECG? How does the appearance of the QRS complex in lead V_2 contribute to your answer?

Interpretation: The rhythm is slightly irregular. Although the amplitude of P waves in the limb leads is greatly reduced, the rhythm is probably sinus (suggested by regularly occurring atrial activity in leads V_1, V_2, V_3). The QRS complex is widened. The pattern is most consistent with complete RBBB (right bundle branch block) in view of the widened tall R wave in lead V_1 that occurs in association with wide terminal S waves in lateral leads I and V_6. The atypical feature of this RBBB pattern is the absence of an initial small r wave in lead V_1 (a QR pattern is seen, instead of a more typical rSR' pattern). In view of the fact that a small (but definite) q wave is seen in lead V_2, one should strongly suspect septal infarction as the cause of the initial Q wave in these two precordial leads. Further support of our suspicion that the patient has had an anterolateral infarction is supported by the presence of primary ST-T wave changes in each of the three key leads. Normally the direction of the ST segment and T wave in typical right or left bundle branch block is opposite the direction of the last QRS deflection in each of the 3 key leads (leads I, V_1, and V_6). Thus, the T wave will normally be upright in both leads I and V_6 (opposite the wide terminal S wave in these leads), and the ST segment and T wave are likely to be negative in lead V_1 (opposite the positive R or R' complex). The contrary is true in this case (note especially the hint of ST segment elevation in lead V_1!). In addition, deep symmetric T wave inversion is seen in leads II, aVL, aVF, and V_3 through V_6 of this tracing. The overall ECG picture, in conjunction with the history of heart failure in this 73-year-old man strongly suggest the possibility of recent ischemia and/or infarction superimposed on the underlying pattern of RBBB. Perhaps an "event" (ie, myocardial infarction) and/or ongoing ischemia precipitated this patient's most recent episode of dyspnea? ■

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