AHC Media

Internal Medicine

Evidence-based summaries of the latest research in internal medicine [ALERT]

Vol. 39, Issue 1, January 15, 2017
AHCMedia.com

ABSTRACT & COMMENTARY

Common Triggers of Acute Myocardial Infarction

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, David Geffen School of Medicine at UCLA

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

SYNOPSIS: Physical exertion and anger or emotional upset are common one hour before the onset of symptoms of acute myocardial infarction (AMI). Although either exposure may act alone as the external trigger for AMI, the greatest magnitude of association was seen in those subjects who experienced both physical exertion and anger or emotional upset one hour before the onset of symptoms of AMI.

SOURCE: Smyth A, et al. Physical activity and anger or emotional upset as triggers of acute myocardial infarction. *Circulation* 2016;134:1059-1067.

Cardiovascular disease is the leading cause of death worldwide.[1] More than 90% of the risk of developing an acute myocardial infarction (AMI) has been attributed to long-term exposure to multiple risk factors such as hyperlipidemia, exogenous obesity, and lack of exercise.[2] Published studies have identified potential external triggers for AMI, including anger, emotional upset, and physical exertion.[3,4] The prevalence of potential triggers of AMI also may vary by geographical region in that triggers that have been found to be important in one region or ethnic group may be absent or different in others. The INTERHEART study[20] was a case-control study of first AMIs conducted in 262 centers across 52 countries.[2,5] Highly trained staff performed a standardized physical exam on participants and then administered a carefully structured questionnaire. Participants who had suffered an AMI were questioned carefully about physical activities and episodes of anger or emotional upset in the one hour before the onset of symptoms and during the same hour on the previous day. All collected data were transferred to the Population Health Research Institute at the McMaster University and Hamilton Health Sciences in Hamilton, Ontario, Canada. The authors concluded that physical exertion and anger or emotional upset were common events in the one hour before the onset of symptoms of AMI and that

Financial Disclosure: *Internal Medicine Alert's* Physician Editor Stephen Brunton, MD, is a retained consultant for Abbott Diabetes, Actavis, AstraZeneca, Becton Dickinson, Boehringer Ingelheim, Cempra, Janssen, Lilly, Merck, Novo Nordisk, Sanofi, and Teva; he serves on the speakers bureau of AstraZeneca, Boehringer Ingelheim, Janssen, Lilly, Novo Nordisk, and Teva. Contributing Editor Louis Kuritzky, MD, is a retained consultant for and on the speakers bureau of, Allergan, Daiichi Sankyo, Lilly, and Lundbeck. Peer Reviewer Gerald Roberts, MD, Executive Editor Leslie Coplin, and Assistant Editor Jonathan Springston report no financial relationships relevant to this field of study.

Internal Medicine
Evidence-based summaries of the latest research in internal medicine [ALERT]

Internal Medicine Alert,
ISSN 0195-315X, is published monthly by AHC Media, LLC
One Atlanta Plaza,
950 East Paces Ferry Road NE, Suite 2850
Atlanta, GA 30326.

GST Registration Number: R128870672.
Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to *Internal Medicine Alert*, P.O. Box 550669, Atlanta, GA 30355.

SUBSCRIBER INFORMATION
(800) 688-2421
Customer.Service@AHCMedia.com
AHCMedia.com

Questions & Comments
Please call Assistant Editor Jonathan Springston at (404) 262-5416 or email at jspringston@reliaslearning.com

Subscription Prices
United States:
Print: 1 year with free *AMA PRA Category 1 Credits™*: $349
Add $19.99 for shipping & handling.

Online only: 1 year (Single user) with ***free*** *AMA PRA Category 1 Credits™*: $299

Back issues: $21. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. AHC Media designates this enduring material for a maximum of 2 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This Enduring Material activity, *Internal Medicine Alert*, has been reviewed and is acceptable for up to 1.00 Prescribed credit(s) by the American Academy of Family Physicians. Term of approval begins Jan. 1, 2017. Term of approval is for one year from this date. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic Association has approved this continuing education activity for up to 2 AOA Category 2-B credits.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

This CME activity is intended for the internist/family physician. It is in effect for 36 months from the date of the publication.

either exposure could act as an external trigger for AMI. The greatest magnitude of association was seen in those with both physical exertion and anger or emotional upset in the one hour before the onset of AMI symptoms. The authors reported no differences in numbers of events related to geographical area, in whether the subjects did or did not present with a history of previous cardiovascular disease, in subjects who had a history of taking cardiovascular prevention medications, or who possessed a significant number of cardiovascular risk factors.

■ COMMENTARY

The results reported by the INTERHEART investigators certainly confirm previous findings that physical exertion and anger or emotional upset may act as external triggers for AMI.[6-10] Physical exertion and emotional upset both contributed an additive effect, and they have been reported to cause sympathetic activation,[6] catecholamine secretion,[11] and modification of myocardial oxygen demand because of systemic vasoconstriction, increased heart rate, and increased blood pressure.[12-14] In addition, these events actually may precipitate the rupture of an already vulnerable atherosclerotic coronary artery plaque.[15] These findings previously have led to recommendations that the impact of link between triggering events and their pathophysiological consequences may be reduced through the use of aspirin, beta-blockers, statins, or angiotensin-converting enzyme inhibitors.[16] However, the authors of the INTERHEART study found no beneficial modification produced by cardiovascular prevention medication on the prevention of AMI associated with physical exertion or anger or emotional upset. Although regular physical activity is known to play a role in the long-term prevention of cardiovascular disease,[17] vigorous physical exertion definitely may act as a trigger of AMI. Therefore, clinicians should continue recommending regular physical activity while noting that short-term, intense physical activity may carry a risk of triggering AMI. The authors reported that emotional upset and the negative effects of acute emotional disturbance,[9] acute depression,[18] and work-related stress[19] were reported as significant triggers for AMI. Numerous limitations were noted in the design of this study. First, the study was performed only on patients who were hospitalized for their first AMI and did not include non-hospitalized patients with AMI. Next, since many of the conclusions were based on patient recall of intensity of exposure to any triggering events, it must be recognized that a patient's ability to recall timing and intensity of stimuli varies greatly and is open to question.

Since the patients in the INTERHEART study were all hospitalized with their first AMI, the conclusions cannot be applied to the effect of triggering events in a secondary prevention population or in those patients with atypical AMI. Despite the limitations of the study, the results are valuable, and clinicians should consider counseling their patients to avoid any of the triggers outlined above, which could result in an acute AMI. ■

REFERENCES

1. Yusuf S, et al. Global burden of cardiovascular diseases: Part 1: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001;104:2746-2753.
2. Yusuf S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet* 2004;364:937-952.
3. Culic V, et al. Meta-analysis of possible external triggers of acute myocardial infarction. *Int J Cardiol* 2005;99:1-8.
4. Nawrot TS, et al. Public health importance of triggers of myocardial infarction: A comparative risk assessment. *Lancet* 2011;377:732-740.
5. Ounpuu S, et al. INTER-HEART: A global study of risk factors for acute myocardial infarction. *Am Heart J* 2001;141:711-721.
6. Mittleman MA, et al. Triggering of acute myocardial infarction onset by episodes of anger: Determinants of myocardial infarction onset study investigators. *Circulation* 1995;92:1720-1725.
7. Möller J, et al. Do episodes of anger trigger myocardial infarction? A case-crossover analysis in the Stockholm Heart Epidemiology Program (SHEEP). *Psychosom Med* 1999;61:842-849.
8. Strike PC, et al. Triggering of acute coronary syndromes by physical exertion and anger: Clinical and sociodemographic characteristics. *Heart* 2006;92:1035-1040.
9. Lipovetsky N, et al. Emotional events and anger at the workplace as triggers for a first event of the acute coronary syndrome: A case crossover study. *Isr Med Assoc J* 2007;9:310-315.
10. Smith M, Little WC. Potential precipitating factors of the onset of myocardial infarction. *Am J Med Sci* 1992;303:141-144.

11. Mittleman MA, Mostofsky E. Physical, psychological and chemical triggers of acute cardiovascular events: Preventative strategies. *Circulation* 2011;124:346-354.
12. Verrier RL, et al. Delayed myocardial ischemia induced by anger. *Circulation* 1987;75:249-254.
13. Boltwood MD, et al. Anger report predicts coronary artery vasomotor response to mental stress in atherosclerotic segments. *Am J Cardiol* 1993;72:1361-1365.
14. Muller JE, et al. Mechanisms precipitating acute cardiac events: Review and recommendations of an NHLBI workshop. National Heart, Lung, and Blood Institute: Mechanisms precipitating acute cardiac events participants. *Circulation* 1989;79:733-743.
15. Braunwald E. Unstable angina: An etiologic approach to management. *Circulation* 1998;98:2219-2222.
16. Tofler GH, Muller JE. Triggering of acute cardiovascular disease and potential preventive strategies. *Circulation* 2006;114:1863-1872.
17. Thompson PD, et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: A statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003;107:3109-3116.
18. Steptoe A, et al. Acute depressed mood as a trigger of acute coronary syndromes. *Biol Psychiatry* 2006;60:837-842.
19. Möller J, et al. Work related stressful life events and the risk of myocardial infarction: Case-control and case-crossover analyses within the Stockholm Heart Epidemiology Programme (SHEEP). *J Epidemiol Community Health* 2005;59:23-30.
20. Smyth A, et al. Physical activity and anger or emotional upset as triggers of acute myocardial infarction. *Circulation* 2016;134:1059-1067.

ABSTRACT & COMMENTARY

White-coat Hypertension: Does It Predict Cardiovascular Disease?

By Michael H. Crawford, MD

Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco

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

SYNOPSIS: Patients presenting with white-coat hypertension were selected from a large, multicenter ambulatory blood pressure outcome study and compared to matched control subjects. Investigators found that the risk of cardiovascular events over a 10-year follow-up was similar between the two groups.

SOURCES: Franklin SS, et al. The cardiovascular risk of white-coat hypertension. *J Am Coll Cardiol* 2016;68:2033-2043.

Mancia G, Grassi G. The heterogeneous nature of white-coat hypertension. *J Am Coll Cardiol* 2016;68:2044-2046.

The association of white-coat hypertension with cardiovascular risk is unclear. Thus, investigators from the International Database on Ambulatory Blood Pressure in relation to the Cardiovascular Outcome compared daytime ambulatory blood pressure monitoring with conventional blood pressure measurements in 653 untreated subjects with white-coat hypertension and 653 control subjects. The study subjects were from 11 randomly recruited population cohorts with validated outcome data, which totaled 12,752 subjects. Ambulatory hypertension was defined as daytime levels of > 135/85 mmHg, and white-coat hypertension was defined as > 140 mmHg at the office visit with normal daytime ambulatory blood pressure. The controls were age- and cardiovascular risk-matched. The prevalence of white-coat hypertension among those normotensive on ambulatory daytime blood pressure was 11%. The white-coat subjects tended to be older, male, and to have higher cardiovascular risk. All subjects were categorized as either low risk (up to two risk factors, not including age or hypertension) or high risk (three or more risk factors, diabetes, or prior cardiovascular events). During a median follow-up of 10.5 years, 70 white-coat subjects and 48 normotensives experienced a cardiovascular event. In low-risk subjects, there was no significant increase in events in the white-coat subjects compared to the normotensive group (494 in each group; hazard ratio [HR], 1.06; 95% confidence interval [CI], 0.66-1.72; $P = 0.80$), whereas in the high-risk subjects (159 in each group) the white-coat subjects experienced more events (HR, 2.06; 95% CI, 1.10-3.84; $P = 0.023$). However, in subjects < 60 years of age, white-coat hypertension did not increase cardiovascular events in either risk group. The authors concluded that the risk of cardiovascular events in white-coat hypertension subjects is comparable to age and risk-adjusted normotensive controls.

■ COMMENTARY

Research on white-coat hypertension has suffered from small numbers of subjects, low cardiovascular event rates, and failure to account for the cardiovascular risk of the subjects. Thus, this study of 11 relatively large databases, which accounts for the subject risk profile and has a median follow-up of 10 years, is of interest. The authors made the following points based on the results: 1) After adjusting for age, the white-coat effect was not influenced by the subjects' cardiovascular risk, or, more precisely, the white-coat effect increased observed events only in older subjects with high cardiovascular risk profiles; 2) In subjects with low risk

profiles or < 60 years of age, the white-coat effect did not increase cardiovascular events, and this represented 86% of the white-coat population in this study; 3) The magnitude of the white-coat effect on blood pressure was not related to the event rate. Also, the authors speculated that in older patients at high risk for cardiovascular events, isolated systolic hypertension may have been missed because they were subject to only one day of ambulatory blood pressure monitoring and two manual blood pressure measurements on the same visit. If this is the case, then white-coat hypertension is entirely benign. Thus, in the older high-risk subjects suffering from white-coat hypertension, more attention should be paid to identifying isolated systolic hypertension and perhaps treating it. Finally, the authors hypothesized that the mechanism of white-coat hypertension is a hyperactive, sympathetic response to perceived stress. If so, one would expect a rise in heart rate as well, but this is not observed in white-coat hypertension. In addition, one would expect the reaction to diminish with age, but the observation is that it is more common among older patients, so the mechanism of this phenomenon is not clear. There are limitations to this study. Despite the large number of total subjects, only 11% presented with white-coat hypertension, and there were a low number of events over a decade of follow-up, which reduces the power of the study. Also, there was considerable heterogeneity between the 11 sites. For example, the incidence of white-coat hypertension ranged from 3-38% of the study population at each site. In addition, there was no information on subsequent anti-hypertensive drug therapy, which could have affected event rates. Finally, there were no data on blood pressure after the baseline visit, so we don't know the natural history of white-coat measurements or whether the development of persistent hypertension occurred in some subjects. The latter has been shown in some prior studies. At this time, we should be reassured that white-coat hypertension is a largely benign phenomenon that should not be overtreated, but in the older subjects at high risk of cardiovascular disease, we need to be sure we aren't missing isolated systolic or masked hypertension. ■

BRIEF REPORT

Migraine and Stroke: Data Are Accumulating

By Matthew E. Fink, MD

Professor and Chairman, Department of Neurology, Weill Cornell Medical College; Neurologist-in-Chief, New York Presbyterian Hospital

Dr. Fink reports he is a retained consultant for Procter & Gamble and Pfizer.

SOURCE: Androulakis XM, et al. Ischemic stroke subtypes and migraine with aura in the ARIC study. *Neurology* 2016;87:2527-2532.

The Atherosclerosis Risk in Communities study (ARIC) is a prospective, longitudinal, community-based cohort study that started in 1993, and followed all vascular events, including stroke, for the subsequent 20 years. At time of enrollment, patients had to be in the age group of 45-64 years, and the mean age of the patients was 59 years at the third clinical visit of follow-up. All strokes are classified as either cardioembolic, lacunar, or thrombotic. Of 12,758 participants, there were 1,622 migraineurs. When compared to non-headache patients, there was a significant association between those patients who had migraine with visual aura and ischemic stroke, with a hazard ratio (HR) = 1.7 (95% confidence interval [CI], 1.2-2.6; P = 0.008). Migraine without visual aura was not significantly associated with ischemic stroke compared to non-headache participants. Among the three stroke types categorized in this study, migraine with visual aura was significantly associated only with cardioembolic stroke (HR, 3.7; 95% CI, 1.6-8.7; P = 0.003). The relationship between migraine and stroke is controversial, and findings vary across different population studies. This study shows a strong association between cardioembolic ischemic stroke and migraine with visual aura, but it does not explain the pathophysiology and mechanism for this association. The authors proposed that migraine may predispose to atrial fibrillation, but this is a purely speculative mechanism. ■

PHARMACOLOGY UPDATE

Insulin Glargine and Lixisenatide Injection (Soliqua)

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

Dr. Elliott is Medical Director, Pharmacy, Northern California Kaiser Permanente, and Assistant Clinical Professor of Medicine, University of California, San Francisco. Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

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

The FDA has approved a fixed-ratio, once-daily, insulin glargine and the glucagon-like peptide-1 (GLP-1) receptor agonist, lixisenatide combination (iGlarLixi) for the treatment of type 2 diabetics. The new combination is marketed as Soliqua.

INDICATIONS

iGlarLixi is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus inadequately controlled on basal insulin (< 60 units/day) or lixisenatide.[1]

DOSAGE

The recommended dose for patients inadequately controlled on < 30 units of basal insulin or on lixisenatide is 15 units of insulin glargine and 5 mcg of lixisenatide administered subcutaneously once daily within the hour prior to the first meal of the day.[1] For those inadequately controlled on 30-60 units of basal insulin, the dose is 30 units of insulin glargine and 10 mcg of lixisenatide. The dosage may be titrated up or down by two to four units every week based on response and until patient achieves desired fasting plasma glucose. The maximum dose is 60 units of insulin glargine and 20 mcg of lixisenatide. iGlarLixi is available as a single-patient use 3 mL pen containing 100 units of insulin glargine and 33 mcg of lixisenatide per mL.

POTENTIAL ADVANTAGES

iGlarLixi provides another option for patients inadequately controlled on basal insulin or lixisenatide. The number of documented hypoglycemic events (FPG < 70 mg/dL) was higher with insulin glargine than iGlarLixi at 3.0 events vs. 4.2 events per patient-year.[3]

POTENTIAL DISADVANTAGES

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been reported with GLP-1 receptor agonists. In clinical trials, the incidence rate for lixisenatide was 21 per 10,000 patient-years compared to 17 for comparators.[1] Diarrhea and nausea were more frequent with iGlarLixi than with insulin glargine. Lixisenatide delays gastric emptying and may reduce the rate of absorption of other drugs.[1] For drugs that should be taken with food, it is recommended that they be taken when lixisenatide is not administered. Antidrug antibodies may develop to glargine and lixisenatide. High levels of antibodies can attenuate the glycemic affect (seen with 2.4% of patients). Antibody-positive patients also are more likely to experience allergic reactions and injection-site reactions.

COMMENTS

The efficacy and safety of iGlarLixi was primarily based on demonstrating superiority to insulin glargine in type 2 diabetic subjects inadequately controlled on basal insulin with or without up to two oral agents.[1,2,3] Subjects had baseline HbA1c of 8.1%. During a run-in period, insulin glargine was introduced and/or titrated, and oral agents other than metformin were discontinued. Subjects were then randomized to iGlarLixi (n = 365) or insulin glargine (n = 365). The primary endpoint was change in HbA1c at week 30. The secondary endpoint was the proportion of responders with HbA1c < 7%. At week 30, iGlarLixi reduced HbA1c to 6.9% compared to 7.5% with a least square mean difference of -0.5 (95% confidence interval, -0.6 to -0.4; $P < 0.0001$). Fifty-five percent of iGlarLixi patients reached HbA1c of 7% compared to 30% for insulin glargine. iGlarLixi produced minimal effect on fasting plasma glucose, since the dose was titrated to fasting plasma levels, but significantly improved postprandial glucose excursion compared to insulin glargine.[3] There is minimal weight reduction with iGlarLixi, as the weight gain caused by insulin glargine is mitigated by weight reduction of lixisenatide.

CLINICAL IMPLICATIONS

iGlarLixi provides a fixed-ratio basal insulin and GLP-1 agonist for patients inadequately controlled on separate agents. Lixisenatide has demonstrated neutrality in terms of cardiovascular events compared to placebo in type 2 diabetics with a recent acute coronary syndrome.[4] The wholesale cost of iGlarLixi is $127 per 3 mL pen. ■

REFERENCES

1. Soliqua Prescribing Information. Sanofi. November 2016.
2. Aroda VR, et al. Efficacy and safety of LixiLan, a titratable fixed-ratio combination of insulin glargine plus lixisenatide in type 2 diabetes inadequately controlled on basal insulin and metformin: The LixiLan-L Randomized Trial. *Diabetes Care* 2016;39: 1972-1980.
3. FDA Briefing Document. Endocrinologic and Metabolic Drugs Advisory Committee Meeting, May 25, 2016. Available at: http://bit.ly/2igCdx8. Accessed Dec. 9, 2016.
4. Pfeffer MA, et al. Lixisenatide in patients with type 2 diabetes and acute coronary syndrome. *N Engl J Med* 2015;373:2247-2257.

Clinical Briefs

By Louis Kuritzky, MD

Topical Agent for Premature Ejaculation

SOURCE: Mark KP, Kerner I. Event-level impact of Promescent on quality of sexual experience in men with subjective premature ejaculation. *Int J Impot Res* 2016;28:216-220.

Premature ejaculation (PE) reportedly is the most common sexual dysfunction in men, even outstripping the prevalence of erectile dysfunction. This may surprise clinicians, since patients do not present often with that complaint, nor is it routine — except when encounters specifically are focused on sexual health — for clinicians to inquire about PE.

Currently, there are no drugs specifically approved for PE; instead, clinical trials documenting the efficacy of selective serotonin reuptake inhibitors (SSRIs) and tramadol for PE have led to their off-label use as often effective treatments.

In this open-label trial in which patients (n = 91) were their own control, investigators invited study subjects who self-designated as PE and fulfilled criteria of a PE diagnostic tool to try topical Promescent (trade name) spray on their penis prior to intercourse. The active ingredient in Promescent is lidocaine.

According to the pre-set parameters of the study, Promescent was efficacious in that it essentially doubled the time to ejaculation; additionally, study subjects believed that the product was easy to use, with minimal interruption of sexual activity.

On the other hand, the latency time (time from intromission until ejaculation) was quite atypical compared to most of the PE trials in the literature. That is, in the Promescent trial, baseline ejaculatory latency time was 6.81 minutes, increasing to 11.16 minutes with treatment.

Previous trials with SSRIs enrolled PE subjects with an ejaculatory latency time of 30 seconds, which would typically increase to three to four minutes with treatment.

In any case, Promescent was effective in prolonging time to ejaculation, and was well tolerated. ■

Are We Using Novel Oral Anticoagulants Wisely?

SOURCE: Barra ME, Fanikos J, Connors JM, et al. Evaluation of dose-reduced direct oral anticoagulant therapy. *Am J Med* 2016;129:1198-1204.

There is little dispute over whether the so-called novel oral anticoagulants (NOACs), currently comprised of apixaban, dabigatran, edoxaban, and rivaroxaban, are as efficacious as warfarin, as well as simpler to use, since food interactions are minimal.

NOACs individually include labeling that calls for potential dose adjustments for chronic kidney disease, low body weight, and interacting substances (agents with p-glycoprotein and/or P450 interactions). Have clinicians performed dose-adjustments appropriately?

Barra et al retrospectively analyzed data from 224 patients who had been prescribed reduced-dose NOACs to determine if the dose reductions had been according to appropriate indications (as per labeling) as well as appropriate in amount of dose reduction.

Less than half the patients who had been prescribed reduced-dose NOACs matched labeling criteria for such dose reduction. It may have been that concern over bleeding risk prompted prescribers to choose dose reduction; however, bleeding rates even within this group of patients receiving reduced-dose NOAC actually were higher than had been seen in clinical trials of NOACs.

How dose adjustment based on clinician judgment, as opposed to specific FDA labeling, will affect long-term outcomes remains to be determined. ■

Lung Cancer Screening at a VA Medical Center

SOURCE: Okereke IC, Bates MF, Jankowich MD, et al. Effects of implementation of lung cancer screening at one Veterans Affairs medical center. *Chest* 2016;150:1023-1029.

Thanks to favorable results from a very large clinical trial of low-dose CT lung cancer screening (n > 53,000) that showed not only a reduction in lung cancer mortality but also all-cause mortality, it is incumbent on clinicians to offer screening to appropriately selected patients.

Experience at a VA medical center in Providence, RI, appears to favorably reflect some of the track record of the aforementioned National Lung Screening Trial.

When Okereke et al compared identification of lung nodules in a pre-screening period (2011-2013) to the 2013-2014 screening interval, they noted a distinct "downgrading" of lung cancer staging achieved through screening; that is, prior to screening, 37% of lung cancers were early stage (Stage I or Stage II). During the screening interval, 60% of identified lung cancers were early stage.

The prevalence of smoking usually is higher in VA medical center settings than the general public. Lung cancer screening in this population assists in identifying lung cancer at an earlier, more survivable stage. ■

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:
1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right, or log on to **AHCMedia.com** and click on My Account. First-time users will have to register on the site using the eight-digit subscriber number printed on their mailing label, invoice, or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After completing the test, a credit letter will be emailed to you instantly.
5. Twice yearly after the test, your browser will be directed to an activity evaluation form, which must be completed to receive your credit letter.

CME QUESTIONS

1. **Physical exertion and anger or emotional upset are:**

   a. triggers for a first acute myocardial infarction in the United States only.

   b. not triggers for a first acute myocardial infarction.

   c. triggers associated with first acute myocardial infarction in all regions of the world, in both men and women and in all age groups.

   d. triggers for a first acute myocardial infarction in men only.

2. **A large observational study of white-coat hypertension showed:**

   a. it occurs in about 10% of those with normal ambulatory blood pressure.

   b. it is associated with a higher risk of cardiovascular events.

   c. it predicts cardiovascular risk in those < 60 years of age.

   d. the magnitude of the effect is correlated to the degree of cardiovascular risk.

3. **Common migraine is a risk factor for ischemic stroke.**

   a. True

   b. False

CME 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.

[IN FUTURE ISSUES]

Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease

New Opioid Analgesic Use and the Risk of Injurious Single-Vehicle Crashes in Drivers 50-80 Years of Age

Treating Delirium Among Patients in Palliative Care

Internal Medicine [ALERT]

ECG Review

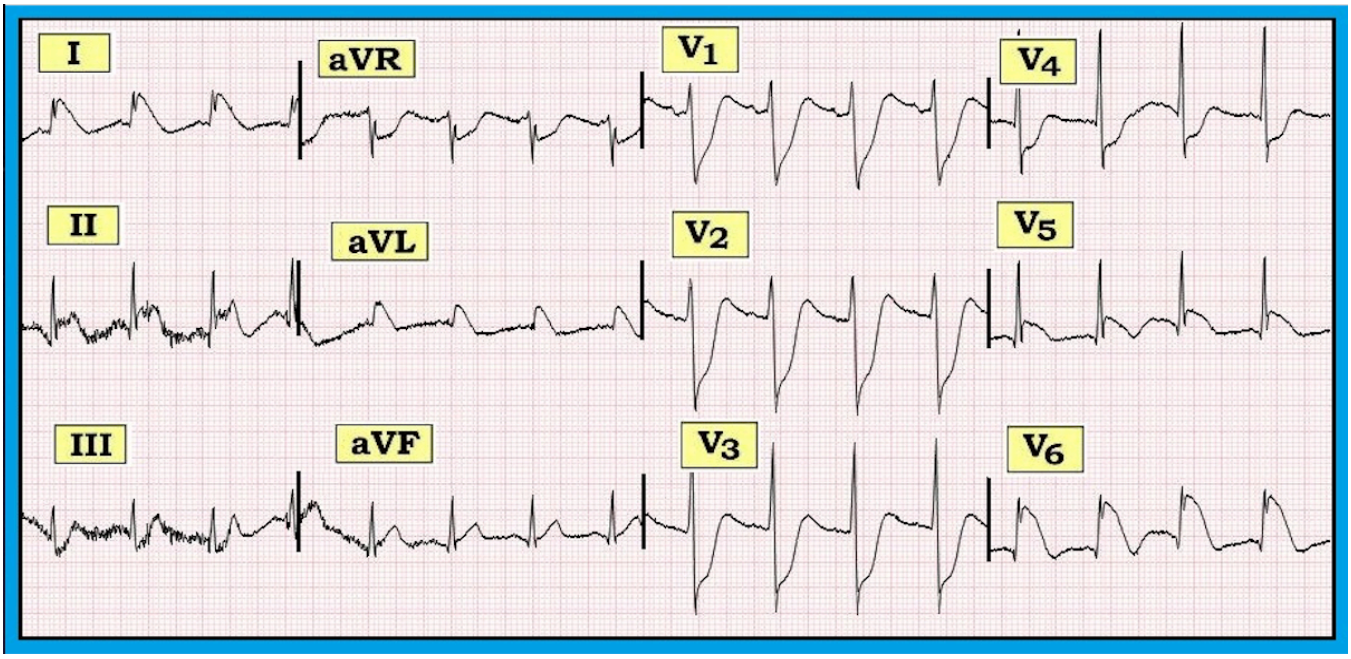
By Ken Grauer, MD

Professor Emeritus in Family Medicine, College of Medicine, University of Florida

Dr. Grauer is the sole proprietor of KG-EKG Press, and publisher of an ECG pocket brain book.

Which Artery is the Culprit?

How would you interpret the 12-lead ECG shown in the figure below? This tracing was obtained from a 51-year-old man with new-onset chest pain. What is the likely "culprit" artery?



Although there is much artifact (especially in leads II and III), this does not prevent appreciation of the obvious abnormalities on this tracing. The rhythm is sinus tachycardia at a rate of just over 100/minute. The PR and QRS intervals are normal; the QT interval appears prolonged. The axis is normal. There is no chamber enlargement. There are small and narrow Q waves in most inferolateral leads. R wave progression is normal, with transition occurring between leads V2 to V3. There are dramatic ST-T wave changes. There is over 10 mm of J-point ST segment depression in several anterior leads. All lateral leads show marked ST segment elevation, which nearly attains 10 mm in lead V6.

There is an obvious acute ST elevation myocardial infarction (STEMI). Localization of ST segment elevation to the lateral leads strongly suggests acute occlusion of the left circumflex (LCx) artery. This is supported by the finding of several millimeters of ST elevation in lead II, but virtually none in leads III and aVF. In contrast, with acute right coronary artery (RCA) occlusion, ST elevation is localized to the inferior leads, with the relative amount of ST elevation typically more in lead III compared to lead II. The dramatic anterior ST depression strongly suggests acute posterior as well as lateral infarction. This distribution of marked and acute inferolateral wall involvement is seen with acute occlusion of a dominant LCx artery.

Fortunately, this large acute STEMI was immediately recognized. Cardiac catheterization with prompt reperfusion of a dominant LCx artery resulted in rapid resolution of virtually all ST-T wave abnormalities. Coupled with no more than minimal troponin elevation and complete resolution of symptoms, it is likely that almost all jeopardized myocardium was salvaged with minimal long-term damage from this acute event. Cardiac catheterization revealed severe underlying multi-vessel coronary disease, which helps account for the extreme amount of ST-T wave deviation seen in this case.

For more about this case, please visit: http://bit.ly/2h6yQHG.