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Internal Medicine

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

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ABSTRACT & COMMENTARY

Is Sodium Restriction Detrimental in Chronic Heart Failure?

By Van Selby, MD

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

SYNOPSIS: In an observational study of outpatients with NYHA class II or III heart failure, dietary sodium restriction (< 2500 mg/day) was associated with increased risk of death or heart failure hospitalization.

SOURCE: Doukky R, et al. Impact of dietary sodium restriction on heart failure outcomes. *JACC Heart Fail* 2016 2016;4:24-35.

Dietary sodium restriction is perhaps the most common self-care recommendation patients with chronic heart failure (HF) receive. However, data evaluating the effectiveness of sodium restriction are sparse, and the few studies that do exist have shown conflicting results.

To evaluate the relationship between dietary sodium restriction and clinical outcomes in chronic HF, Doukky et al analyzed data from the HF Adherence and Retention Trial (HART), a multicenter study of 902 patients with New York Heart Association (NYHA) functional class II or III systolic or diastolic HF. Patients were followed for a median of 36 months, and sodium intake was assessed using a food frequency questionnaire. Patients were classified as either sodium restricted (< 2500 mg/d) or unrestricted (≥ 2500 mg/d), and propensity score matching was used to address possible confounders. The primary outcome was the composite of death or HF hospitalization.

Sodium restriction was associated with a significantly higher risk of death or HF hospitalization (42.3% vs 26.2%; hazard ratio [HR], 1.85; $P = 0.004$). The difference was due primarily to higher rates of HF hospitalization (HR, 1.82; $P = 0.015$), although there was also a nonsignificant increase in the rate of death ($P = 0.074$). Subgroup analyses found the increased risk associated with sodium restriction was particularly high in patients not taking angiotensin-converting-enzyme inhibitors or angiotensin

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receptor blockers (HR, 5.78; $P = 0.002$) and patients with milder NYHA class II symptoms (HR, 2.36; $P = 0.003$). Sodium restriction was not associated with any significant effect on quality of life, 6-minute walk distance, or symptom severity. The authors concluded that dietary sodium restriction may have a detrimental effect on outcome in patients with symptomatic chronic HF. They stress that a randomized clinical trial is warranted to resolve the issue.

■ COMMENTARY

Excessive sodium intake is associated with fluid retention, and many episodes of acute decompensated HF are often attributed to "sodium binges" in patients with stable chronic HF. For decades, sodium restriction has been a cornerstone of appropriate HF management, and the benefits of sodium restriction were so obvious that a trial evaluating its effectiveness seemed unnecessary. Current U.S. guidelines recommend patients with symptomatic HF restrict sodium intake to between 2000-3000 mg/day.

More recently, investigators are evaluating the effectiveness of sodium restriction more rigorously, and the results have been mixed. Several small studies have shown a clear benefit, with decreased signs and symptoms of HF as well as improved event-free survival. However, other studies have shown no clear benefit associated with sodium restriction, especially in patients with milder (class I-II) HF. The Doukky study is important for two reasons. First, the patients were recruited from a large, multicenter clinical trial. Second, the study evaluated an objective clinical outcome and found increased adverse outcomes among sodium-restricted patients.

Why would sodium restriction be harmful? Small studies have shown that sodium restriction increases neurohormonal activation by worsening intravascular volume depletion. Sodium restriction may also worsen hemodynamics, with a decrease in cardiac index and increase in systemic vascular resistance. In the Doukky study, patients not receiving angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers showed an especially high risk of adverse events with sodium restriction, suggesting the effect is mediated through neurohormonal pathways. Interestingly, sodium restriction was associated with a greater increase in adverse outcomes among patients with milder, class II symptoms. This is similar to what has been reported in other studies. It is possible that more symptomatic (class III) patients are particularly prone to hypervolemia, and, therefore, sodium restriction is beneficial for preventing worsening fluid overload. Class II patients, on the other hand, experience the detrimental neurohormonal activation from sodium restriction without seeing the benefits related to hypervolemia.

Limitations include the retrospective design, small sample size, and use of a food frequency questionnaire to measure dietary sodium intake. The authors used propensity matching to eliminate confounders, but it is still possible the sodium-restricted patients comprised a sicker group overall. This study offers no information regarding the utility of sodium restriction during hospitalization for acute HF.

Despite these limitations, the Doukky study adds to a growing body of research suggesting dietary sodium restriction may not be beneficial, perhaps even harmful in chronic HF. In response to this increasing evidence, the most recent European guidelines have removed any formal recommendation regarding sodium restriction, and the 2013 American Heart Association/American College of Cardiology guidelines downgraded the strength of their longstanding recommendation regarding dietary sodium restriction from class I (recommended) to class IIa (reasonable). Given the prevalence of chronic HF and the widespread use of recommendations regarding dietary sodium intake, many in the field echo the authors' call for a randomized trial to rigorously evaluate the effectiveness of these recommendations. Until then, there is no clear evidence to support aggressive sodium restriction in chronic HF, especially in patients with mild disease. ■

ABSTRACT & COMMENTARY

Spironolactone for Resistant Hypertension

By Michael 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: A randomized, double-blind, placebo-controlled study in resistant hypertension patients on three drugs, including a diuretic, showed that the addition of spironolactone was superior to doxazosin and bisoprolol for lowering blood pressure and it was well tolerated.

SOURCES: Williams B, et al. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): A randomised, double-blind, crossover trial. *Lancet* 2015;386:2059-2068.

Sternlicht H, Bakris GL. Spironolactone for resistant hypertension-hard to resist? *Lancet* 2015;386:2032-2034.

Resistant hypertension is common, and the choice of additional drug therapy in this condition is not clear. Investigators tested three drug classes as additional therapy beyond the recommended angiotensin-converting-enzyme inhibitor (ACEI)/angiotensin II receptor blocker (ARB), calcium blocker plus diuretic. An alpha-blocker to further reduce peripheral resistance (doxazosin), a beta-blocker to reduce renin (bisoprolol), and additional diuresis with spironolactone were tested in a randomized, double-blind, placebo-controlled, crossover trial. The study included patients on maximally tolerated doses of the recommended three classes of drugs who had a clinical blood pressure (BP) of > 140 mmHg systolic or > 135 for diabetics and average home BP measures > 130 over 4 days (18 measurements). After 1 month of single-blind placebo, patients were rotated through four regimens for 6 weeks at the lower dose and 6 weeks at the higher dose: spironolactone 25-50 mg/day, doxazosin 4-8 mg/day, bisoprolol 5-10 mg/day, and placebo. The primary endpoint was the average of three home systolic BP twice a day for 4 days (24 measurements). Plasma renin was measured at baseline, and serum electrolytes were measured at each visit. Researchers screened 436 patients 18-79 years of age, randomized 335 patients (mean age 61 years), and placed 314 patients in the intention-to-treat analysis. Two hundred thirty patients completed the entire protocol. The average decrease in systolic BP on spironolactone was significantly greater than on placebo (-8.7 mmHg, $P < 0.0001$) and the response to doxazosin (-4.0 mmHg, $P < 0.0001$) and bisoprolol (-4.5 mmHg, $P < 0.0001$). Spironolactone's superiority persisted across all measured renin levels except the very highest, where it was equally as efficacious the other two drugs. Adverse events were not different with the three drugs, and only six patients on spironolactone had a potassium > 6.0 mmol/L on one occasion only (maximum 6.5). The authors concluded that spironolactone was the most efficacious fourth drug for patients with drug-resistant hypertension.

■ COMMENTARY

Resistant hypertension is defined as levels above the patients target on maximally tolerated doses of three drugs, one of which is a diuretic, and afflicts about 10% of treated hypertensives. Current guidelines suggest adding a fourth drug, but do not specify which one. It has been suggested that resistant hypertension is a result of non-compliance, not necessarily with drug therapy but rather lifestyle modifications such as reduced salt intake, alcohol consumption, and weight loss. The most important of these is probably salt intake. In this study, 24-hour urine-sodium excretion on placebo was 8 g. Thus, the concept of additional diuresis has arisen. Some believe that switching to a longer-acting diuretic, such as chlorthalidone or indapamide, works, but this has not been systematically studied. Another concept is that those treated with long-term ACEI/ARB develop aldosterone escape, leading to salt and water retention. Therefore, previous observational studies suggest aldosterone antagonists may be efficacious in resistant hypertension. This study tested this hypothesis and compared spironolactone to two other classes of agents: beta-blocker and alpha-blocker.

In this population of predominantly white subjects, spironolactone was remarkably effective. It was twice as effective as bisoprolol and doxazosin. Also, about 60% achieved target BP (< 135 systolic) on spironolactone vs about 40% on the other two drugs. Although bisoprolol and doxazosin were better than placebo, only spironolactone showed a dose response relationship, suggesting that higher doses, if tolerated, would produce better results. The authors suggested that the use of spironolactone in resistant hypertension may reduce the fuel for non-pharmacologic approaches such as renal denervation. Also, the study raises the question as to whether the earlier use of spironolactone would be beneficial. In the

past, combination pills with hydrochlorothiazide and spironolactone were popular to reduce the incidence of hypokalemia. Perhaps these agents should receive another look in light of these data.

This study has several strengths. The authors used average home BP, which is always lower, as their endpoint measure. There was a big placebo effect noted in clinic BP (-10 mmHg) but not with average home BP. The population was relatively large for this type of study and several biochemical measures were taken, which will be reported later.

There are also weaknesses. The trial was of short duration and has no outcome data. The patients were predominantly white and had glomerular filtration rates (GFR) > 45.

There were remarkably few adverse events and they were not different between the three drugs (all < 3%). Hyperkalemia was infrequent and resulted in no serious events. The authors noted that serum sodium decreased 1.2 mmol/L on average, and potassium increased 0.5 mmol/L. Estimated GFR decreased, but no more than you would expect while administering another diuretic. Whether this has long-term consequences is unknown. The authors did not observe gynecomastia, but the length of exposure to spironolactone is probably too short to see this side effect.

The Sternlicht and Bakris editorial concluded that despite the imperfections in this study, using spironolactone for resistant hypertension is "hard to resist." Future studies should clarify general applicability and whether a more aggressive thiazide diuretic approach would be just as effective. ■

BRIEF REPORT

Optimal Antiplatelet Therapy for Secondary Prevention of Ischemic Stroke

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: Kim JT, et al. Different antiplatelet strategies in patients with new ischemic stroke while taking aspirin. *Stroke* 2016;47:128-134.

Patients presenting with acute ischemic stroke are often taking aspirin on a regular basis for prevention of cardiovascular disease. The optimal antiplatelet therapy for secondary prevention has been uncertain in this setting. The authors of this study analyzed 1172 patients in a prospective, multicenter stroke registry database from 14 hospitals in South Korea, selecting patients with acute non-cardioembolic stroke, who were taking aspirin for prevention of cardiovascular disease at the time of onset of stroke. These patients were then divided into three groups, 1) maintaining aspirin monotherapy (MA group = 212), 2) switching aspirin to another antiplatelet agent (SA group = 246), and 3) adding another antiplatelet agent to aspirin (AA group = 714). The patients were then followed for 1 year, using a primary endpoint of a composite of all stroke, myocardial infarction, and vascular death. The results were analyzed in a Cox proportional hazards regression analysis. After 1 year of follow-up, compared to the MA group, there was a reduction in the composite vascular event rate in the SA group (hazard ratio [HR], 0.50; P = 0.03) and in the AA group (HR, 0.40; P < 0.001). This study strongly suggests that compared with maintaining patients on aspirin alone, switching to a different antiplatelet agent, or adding a second antiplatelet agent to aspirin may be better in preventing subsequent vascular events in patients who experienced a new ischemic stroke while taking aspirin. ■

PHARMACOLOGY UPDATE

Patiromer for Oral Suspension (Veltassa)

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 Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

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

A non-absorbed, cation exchange polymer potassium binder has been approved for the treatment of hyperkalemia. The current treatment option is sodium polystyrene sulfonate (SPS), which was approved in 1958. Patiromer is marketed as Veltassa.

INDICATIONS

Patiromer is indicated for the treatment of hyperkalemia.[1]

DOSAGE

The recommended initial dose is 8.4 g (in 3 oz of water) taken once daily with food.[1] The dose may increase by 8.4 g daily as needed at 1-week intervals or longer to obtain desired serum potassium target range. The maximum dose is 25.2 g per day. Patiromer is available as 8.4 g, 16.6 g, and 25.2 g powder packets.

POTENTIAL ADVANTAGES

Patiromer provides an alternative to SPS. It does not exchange potassium for sodium. SPS must be used with caution in patients who cannot tolerate even a small increase in sodium load (e.g., severe congestive heart failure).[2] Cases of colonic necrosis have been reported with SPS.

POTENTIAL DISADVANTAGES

Patiromer binds to many orally administered drugs (e.g., amlodipine, furosemide, levothyroxine). The FDA added a boxed warning to the drug's labeling, recommending a 6-hour window between patiromer administration and any other orally administered medication. It also binds to magnesium, which may lead to hypomagnesemia. It should not be used in patients with severe constipation, bowel obstruction, or impaction, including postoperative bowel motility disorder. Other adverse events include constipation and diarrhea. Hypokalemia occurred in 3% of subjects in the clinical study.[3]

COMMENTS

Hyperkalemia is generally seen in patients with acute or chronic kidney disease or heart failure and on drugs that inhibit the renin-angiotensin-aldosterone system (RAAAS). Elevated potassium levels can lead to conduction abnormalities and potentially fatal cardiac arrhythmias. Patiromer binds to potassium in the lumen of the colon, resulting in potassium excretion in the feces. The efficacy of patiromer was evaluated in a two-part, single-blind, randomized, withdrawal study.[1,3] Those with serum potassium of 5.1 mEq/L to < 5.5 mEq/L started on 8.4 g per day. Those with serum potassium levels of 5.5mEq/L to < 6.5 mEq/L started on 16.8 g per day. The dose was titrated as needed. At week 4, those in the lower potassium group had a reduction of serum potassium of -0.65 mEq/L and those in the higher baseline potassium group -1.23 mEq/L. In the second part of the study, subjects (still receiving RAAS inhibitors) who achieved serum potassium levels of 3.8 mEq/L to < 5.1 mEq/L were randomized to continue patiromer or placebo. At week 4, those on placebo showed an increase of 0.72 mEq/L compared to no change for those randomized to patiromer. Through week 8, 60% on placebo had hyperkalemia recurrence, compared to 15% on patiromer. Six percent of those randomized to patiromer had to discontinue RAAS-inhibitor therapy, compared to 56% for placebo. In a separate study, the effect of patiromer appears to be maintained for 52 weeks.[1,4]

[Patiromer provides a potentially safer alternative and allows patients to continue their renin-angiotensin-aldosterone inhibitors, although the timing of dosing of other medications potentially may be a problem for some patients, many of whom are on multiple drug regimens.]

CLINICAL IMPLICATIONS

Other than discontinuation of RAAS-inhibitors, options for the management of hyperkalemia are limited. SPS can cause serious adverse events and is not ideal for the at-risk population due to the increase in sodium load. Patiromer provides a potentially safer alternative and allows patients to continue their RAAS-inhibitors, although the timing of dosing of other medications potentially may be a problem for some patients, many of whom are on multiple drug regimens. The wholesale cost for patiromer (regardless of strength) is $595 per 30 packets. For Kayexalate, the cost for 30 doses (15 g/dose) is $762. ■

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2. Kayexalate Prescribing Information. Sanofi-Aventis 2009.
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4. Montaperto AG, et al. Patiromer: A clinical review. *Curr Med Res Opin* 2016;32:155-164.

Clinical Briefs

By Louis Kuritzky, MD

Sexual Health Supplement Leads to Priapism

SOURCE: Campanelli M, et al. *Int J Impot Res* 2015;28:39-40.

Were you to plug "*Tribulus terrestris* supplement" into Google, numerous opportunities to purchase OTC supplements, within a wide range of affordability, would appear. It appears tribulus has some effects similar to PDE5 inhibitors (e.g., sildenafil) that would potentially enhance sexual function in males: enhancement of nitric oxide production in the endothelium of the corpora cavernosa, and cavernosal smooth muscle relaxation. Apparently, tribulus — also known as puncture vine or Gokhru — grows well in numerous countries around the world (especially China, India, the southern United States, and Spain), and has long been utilized by herbalists as a primary or contributing ingredient in herbal supplements.

Since OTC supplements lack FDA oversight and regulation, it should not be surprising that unanticipated adversities occur. Such misadventure may be attributed to mislabeled amounts of constituents, adulterants, idiosyncratic reactions, or may represent spontaneous events unrelated to ingestion of the supplements.

Campanelli et al reported a case of a young man with persistent priapism (duration = 72 hours) subsequent to 2 weeks of daily *Tribulus terrestris* supplementation. Invasive treatment (aspiration of corpus cavernosa and creation of a cavernoglandular shunt) was required for resolution, with restoration to nearly complete pre-morbid sexual function at 8 months follow-up. This is not the first reported case of *Tribulus terrestris* associated with priapism. In addition to personal preferences, which often motivate patients to seek non-traditional treatments, the current high cost of FDA-approved pharmacologic treatments may motivate some individuals to seek much less expensive OTC remedies. If clinicians become aware of patient tribulus use, they should caution users about the potential for priapism and encourage patients to seek prompt consultation if a prolonged erection occurs. ■

Eluxadoline for IBS-D

SOURCE: Lembo AJ, et al. *N Engl J Med* 2016;374:242-253.

The burden of suffering sustained by persons with diarrhea-predominant irritable bowel syndrome (IBS-D) is substantial, and clinicians often underestimate the condition. While OTC remedies (e.g., loperamide, fiber) may provide some relief for IBS-D, residual symptoms continue to plague most patients.

Eluxadoline is a recently FDA-approved pharmacologic treatment for IBS-D. Mu-receptors are prominently active in the GI system, as evidenced by the commonplace development and persistence of constipation in patients using opioid analgesics. The primary mechanism of eluxadoline is peripheral (i.e., not in the CNS) mu-receptor mediated reduction in colonic visceral hypersensitivity. At the same time, an additional mechanism of eluxadoline — delta-receptor antagonism — appears to reduce the degree of constipation typically induced by pure mu-receptor agonists. Lembo et al reported results from placebo-controlled trials of eluxadoline in IBS-D (n = 2427). The primary outcome was the number of patients who experienced decreased abdominal pain as well as improved stool consistency for at least half the days throughout the studies (one study lasted 12 weeks, the other lasted 26 weeks). Eluxadoline demonstrated a modest but statistically significant greater ability to reach the primary endpoint and was generally well tolerated. Cases of pancreatitis occurred during eluxadoline treatment, but not during placebo treatment. Because these cases occurred in post-cholecystectomy patients or in persons who used excessive alcohol, until more information is available, clinicians would be wise to avoid eluxadoline in these populations. ■

New Orthostatic Hypotension Category

SOURCE: Gorelik O, Cohen N. *J Am Soc Hypertens* 2015;9:985-992.

Traditionally, orthostatic hypotension (OH) is defined as a drop in systolic blood pressure > 20 mmHg or diastolic blood pressure > 10 mmHg (or both) within 3 minutes of standing from a supine position. The consequences of OH include adverse symptoms, such as dizziness or "coat-hanger" headache, as well as serious or even fatal events consequent to falls. Studies on OH measured when patients transfer from supine to the seated position are infrequent; Gorelik and Cohen reviewed data from 17 different studies to elucidate the literature on seated postural hypotension (SOH).

Similar to OH, the prevalence of SOH increases with age and is more frequent among patients ingesting antihypertensive medications. Probably because of the lack of a firmly established definition of SOH, measurement methods varied among studies, such that changes in blood pressure were measured within as little as 1 minute to as long as 5 minutes or even longer after changing from the supine to seated posture; most data employed the standard blood pressure change (> 20/10 mmHg) to define SOH. Symptoms evoked among patients with SOH were essentially the same as those observed in patients with "typical" OH. Some experts have advised routinely measuring orthostatic blood pressure in patients with underlying neurologic disorders, such as Parkinson's disease, in which OH prevalence is distinctly higher. Measurement of postural changes in blood pressure from supine to seated may be helpful to sort out symptoms such as dizziness or falls, especially in older patients. ■

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CME QUESTIONS

1. **Recent studies suggest that dietary sodium restriction in chronic systolic heart failure patients may be:**
   a. of no benefit (neutral).
   b. harmful.
   c. beneficial.
   d. substituted for diuretics.

2. **The best fourth drug for hypertension resistant to three drugs including a diuretic is:**
   a. bisoprolol.
   b. doxazosin.
   c. spironolactone.
   d. minoxidil.

3. **After suffering from an ischemic stroke while taking aspirin, the best secondary prevention for cardiovascular disease would be the addition of a second antiplatelet agent.**
   a. True
   b. False

We Need Your Help!

The editors of *Internal Medicine Alert* are planning topics for 2016 issues and would like your feedback. Please help us by answering these three questions at the following link: https://www.surveymonkey.com/r/IMASurvey2016. Thank you!

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]

Heartburn Drugs Tied to Dementia Risk?

Smartphone Applications for Healthcare

Warfarin Bridging

Internal Medicine [ALERT]

ECG Review

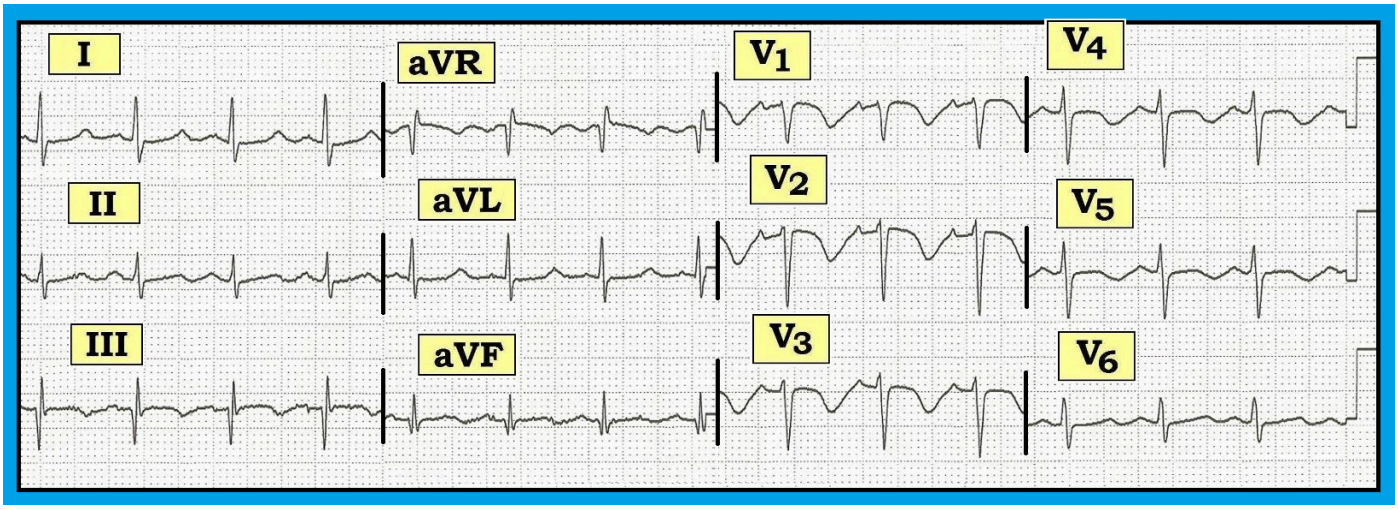
By Ken Grauer, MD

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.

Chest Pain, Dyspnea, and Anterior T Wave Inversion

The ECG in the figure was obtained from a previously healthy 43-year-old woman who presented to the ED with chest pressure and shortness of breath over the past day. She was alert but hypotensive at the time this ECG was recorded. How would you interpret this tracing? What entities should be considered in your differential diagnosis?



This ECG is markedly abnormal. The rhythm is sinus tachycardia at a rate just > 100/minute. The PR and QRS intervals are normal, but the QT interval appears to be markedly prolonged. The axis is normal. There is no chamber enlargement.

When it comes to QRST changes, Q waves are present in leads III and aVF. There is poor R wave progression in the chest leads, with late transition to a predominant R wave not occurring until between lead V5 to V6. But the most remarkable finding is deep symmetric T wave inversion that is most pronounced in leads V1, V2, and V3. Several additional leads show ST segment coving with a lesser degree of T wave inversion.

Clinical correlation is essential for optimal interpretation of this tracing. Deep, symmetric T wave inversion may clearly be a manifestation of ischemia and/or an acute coronary event. Hypertrophic cardiomyopathy (especially when there is apical hypertrophy) is also known to produce deep symmetric T wave inversion in multiple leads. The markedly prolonged QT interval in association with the pronounced ST-T wave changes seen here could be consistent with a central nervous system event such as stroke, intracerebral or subarachnoid bleed, coma, seizure, or trauma. That said, the clinical scenario of hypotension, plus new-onset dyspnea in a previously healthy young adult with this ECG, is most suggestive of acute pulmonary embolism (PE) as the diagnosis. Massive PE was confirmed on further evaluation.

ECG diagnosis of acute PE is difficult because there is no single ECG finding definitive for this diagnosis. Instead, acute PE may be suggested by a combination of supportive ECG findings that occur in a patient with either unexplained dyspnea, syncope, or shock. Although deep symmetric anterior T wave inversion should suggest the possibility of coronary ischemia, this finding is also a manifestation of right ventricular "strain," as is commonly seen in patients with acute hemodynamically significant PE. Other ECG findings consistent with the diagnosis of a large acute PE include sinus tachycardia, the presence of an S1Q3T3 pattern, a positive pointed P wave in leads V2, V3 (a subtle sign of right atrial abnormality), poor R wave progression with persistence of S waves through to lead V6, ST elevation in right-sided lead aVR, and subtle ST segment coving and T wave inversion in leads III and aVF (as may also be seen with right ventricular "strain"). Taken together in the clinical context presented here, the diagnosis of acute hemodynamically significant PE should be presumed until proven otherwise.

Please see http://tinyurl.com/KG-Blog-119 for additional discussion on this case. ■