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ABSTRACT & COMMENTARY

The Pulmonary Embolism Rule-out Criteria in Low-risk Patients

By Michael H. Crawford, MD

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

SYNOPSIS: A cluster randomized trial of the pulmonary embolism rule-out criteria (PERC) compared to usual care for patients estimated to be at low risk of pulmonary embolus (PE) in EDs showed that PERC was non-inferior to usual care at identifying patients who would be free of symptomatic PE at three months, resulting in less use of healthcare resources.

SOURCES: Freund Y, Cachanado M, Aubry A, et al. Effect of the pulmonary embolism rule-out criteria on subsequent thromboembolic events among low-risk emergency department patients: The PROPER randomized clinical trial. *JAMA* 2018;319:559-566.

Kline JA. Utility of a clinical prediction rule to exclude pulmonary embolism among low-risk emergency department patients: Reason to PERC up. *JAMA* 2018;319:551-553.

The pulmonary embolism rule-out criteria (PERC) for use in EDs consists of eight clinical criteria that are used to identify a population at low risk of PE in whom further testing would be associated with an unfavorable risk-benefit ratio. Observational studies have demonstrated its usefulness, but the lack of prospective, randomized trials has hampered its adoption. Thus, investigators from 14 EDs in France conducted a multicenter, non-inferiority, randomized, clinical trial to test the hypothesis that a PERC score of 0 would identify patients in whom the diagnosis of PE can be excluded safely. Patients who presented with new-onset or worsening dyspnea or chest pain and a low clinical gestalt of PE (likelihood < 15%) were included. Patients were excluded if another diagnosis was obvious, if they were in severe distress (e.g., hypotensive), receiving anticoagulants, or had contra-indications to contrast CT of the pulmonary arteries (CTPA).

The PERC criteria were: O_2 saturation < 94%, pulse > 100 bpm, age > 50 years, unilateral leg swelling, hemoptysis, recent trauma or surgery, prior PE or deep venous thrombosis, and estrogen use. Seven

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EDs used PERC, and seven did not. At six months, there was a two-month break. Then, the EDs switched to the opposite strategy. In the PERC groups, if the score was 0, no further testing was conducted. If the PERC was ≥ 1 (maximum of 8), the usual strategy was followed: measuring D-dimer and then CTPA if the D-dimer was positive. In the control group, the usual strategy was applied to all. If CTPA was inconclusive, pulmonary ventilation perfusion (VQ) scanning or lower leg ultrasound was performed. All patients were followed for three months. The primary outcome of the study was the occurrence of a symptomatic thromboembolic event.

After excluding protocol violations, 1,749 patients were included in the per-protocol population (902 controls and 847 PERC). The mean age was 44 years, and 51% were women. In the PERC groups, there were 459 PERC-negative patients. PE was diagnosed in 2.7% of the control patients and 1.5% of the PERC group. The proportion of patients undergoing CTPA was less in the PERC group (13% vs. 23%; $P < 0.001$). ED length of stay also was lower in the PERC group (mean reduction, 36 minutes).

Only one PE was missed by the PERC rule initially, but because of ongoing pain and a positive D-dimer, a CTPA was conducted, which was negative, but a VQ scan showed small defects. There was no difference in mortality at three months. The non-inferiority of PERC was confirmed. The authors concluded that in low-risk ED patients undergoing evaluation for possible PE, randomization to a PERC strategy vs. usual care did not result in an inferior rate of thromboembolic events over three months, confirming that this is a safe strategy in such patients.

■ COMMENTARY

Many believe that with the development of D-dimer and CTPA at the turn of this century, ED patients are over-tested for PE in the United States. Given that CTPA can result in renal injury (14%), a false-positive diagnosis of PE (5%), and possibly later breast cancer in women, various clinical scores were developed to help identify low-risk patients who probably didn't need further testing. The PERC rule has the advantage of first using the clinicians' gestalt that the patient has a < 15% chance of developing a PE. Then, if all eight PERC criteria are negative, the person is at such a low risk of PE that more harm than good is likely to result from further testing.

Observational studies in the United States and elsewhere have confirmed the utility of the rule, but two retrospective studies in Europe did not. Hence, these investigators from France designed and carried out this real-world randomized, clinical trial of the use of PERC vs. usual care. Both strategies employed D-dimer and CTPA if deemed necessary. The endpoint was symptomatic PE in the three months after the ED visit. In the PERC group, only one clinically apparent PE was missed, albeit a small one only detected by VQ scanning. Thus, the criteria for non-inferiority were met. Since the PERC strategy identified PE in 1.5% of the PERC group and 2.17 of the usual care (control) group, the PERC rule probably missed some small sub-segmental PEs. Whether such small PEs require treatment or not is unresolved. Clearly, no clinically significant PEs were missed by the PERC strategy. Studies have shown that usual care detects PE in 5% of patients, so the rate of 2.7% in the control group is low, which speaks to the value of clinical gestalt for initial screening. If the risk is low, then PERC can be applied. In the United States, most EDs would also perform a D-dimer in almost all patients, but if PERC and D-dimer are negative, CTPA or other imaging tests could be avoided. This strategy was not tested in the French study.

There were limitations to this study. It was not a randomized trial at the patient level, which would have been challenging to conduct, but rather a cluster randomization of EDs. Also, 54 patients were lost to follow-up, which could have influenced the results. No cost data were presented, although there was clearly less testing, shorter ED stays, and fewer hospital admissions in the PERC group. However, a negative PERC could have led to more testing for other conditions. Despite these shortcomings, this trial adds considerable weight to the use of the PERC rule in low-risk patients undergoing evaluation for possible PE. ■

ABSTRACT & COMMENTARY

Chiropractic Spinal Manipulation for Migraine

By Concepta Merry, MB, BCh, BAO, BA

Associate Professor, Global Health, School of Medicine, Trinity College, Dublin

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

SYNOPSIS: Chiropractic spinal manipulation offers no benefit over placebo for migraineurs.

SOURCE: Chaibi A, Benth JŠ, Tuchin PJ, Russell MB. Chiropractic spinal manipulative therapy for migraine: A three-armed, single-blinded, placebo, randomized controlled trial. *Eur J Neurol* 2017;24:143-153.

Manual therapy sometimes is used as migraine prophylaxis in migraineurs who fail pharmacological therapy and also in migraineurs who wish to avoid drug treatment.[1] The rationale for the role of spinal manipulative therapy in migraine is based on research that suggests spinal manipulation may activate neural inhibitory systems at different spinal cord levels.[2]

The field of manual therapy research has been limited by a lack of an acceptable sham procedure to act as a placebo control. Researchers in Norway developed a nontherapeutic chiropractic manipulative therapy involving manipulation in a nonintentional, nondirectional line of the lateral edge of the scapula and/or gluteal region. The aim of this study was twofold: 1) to conduct a prospective three-arm, placebo-controlled study for migraineurs and 2) to assess the efficacy of chiropractic spinal manipulation vs. sham manipulation (placebo) vs. standard of care for migraine prevention.

The eligibility criteria for entry into the study included age between 18 and 70 years and at least one migraine headache per month. Exclusion criteria were any contraindication to spinal manipulative therapy, spinal radiculopathy, pregnancy, depression, or chiropractic spinal manipulation in the previous year. Study participants were allowed to continue and change acute migraine medication at any time during the study.

A total of 104 migraineurs were randomized into three groups: chiropractic spinal manipulative therapy, sham manipulative therapy (placebo), or control (who continued with their usual standard of care). Both the treatment and placebo groups underwent structural and motions assessments prior to and after each intervention. Each intervention lasted for 15 minutes. The chiropractic treatment arm of the study received a specific contact, low-amplitude, short-lever spinal with no adjustment recoil directed to the spinal biomechanical dysfunction (Gonstead method).

The sham manipulation was conducted outside the spinal column without soft tissue pre-tension and with adequate joint slack. The sham manipulation involved low-velocity, non-intentional maneuvers in the direction of the lateral edge of the scapula and/or the gluteal region. The primary endpoint was the number of migraine days per month. A migraine day was defined as a day with a migraine or probable migraine.

The secondary endpoints were migraine duration, intensity, headache index, and medicine consumption. The headache index was defined as mean migraine days per month × mean migraine duration mean intensity (0-10 scale). Medicine consumption was defined as mean doses of paracetamol, ergotamine, paracetamol plus codeine, nonsteroidal anti-inflammatories, or morphinomimetics.

The study took place over 17 months: one month baseline, three months of treatment, and follow-up three, six, and 12 months post-treatment. Migraine days were reduced significantly in all three groups from baseline ($P = 0.001$). Data from the three, six, and 12 months of follow-up showed that the control group returned to baseline but the migraine improvement continued in both the treatment and placebo groups.

A statistically significant reduction from baseline to post-treatment in migraine duration, intensity, and headache index was noted in all three groups and its effect continued throughout the follow-up period. Change in paracetamol consumption was significantly lower in the chiropractic manipulation arm compared to the placebo ($P = 0.04$) or control ($P = 0.03$) arms at 12 months of follow-up. No severe or serious adverse events were reported throughout the study. Side effects were reported more commonly in the chiropractic manipulation arm compared to the placebo arm ($P < 0.001$), with local tenderness the most commonly reported side effect.

The results showed that 80% of the study participants believed they had received the chiropractic spinal manipulation, regardless of the group allocation. The authors concluded that it is possible to conduct a manual randomized, controlled trial with a placebo arm and that the observed effect of the chiropractic manipulation is likely the result of a placebo effect.

■ COMMENTARY

A key strength of the study is that all patients were seen by a neurologist and received a definite diagnosis of migraine. This compares to other migraine studies that recruited people with migraine from advertisements. On the downside, this theoretically limits the applicability of the results to a tertiary referral population.

An Australian randomized, controlled trial in 129 people over six months showed significant improvements in migraine with chiropractic spinal manipulation. Since more than 80% of study participants reported stress as a major factor in their migraines, the authors hypothesized that alleviation of stress was the key mechanism of action at play in this study.[3]

In a study of 218 patients with migraine, researchers compared spinal manipulation, amitriptyline, and spinal manipulation plus amitriptyline for eight weeks. Spinal manipulation was as effective as amitriptyline, and there was no advantage noted for the combination of spinal manipulation plus amitriptyline.[4] Even though Chaibi et al failed to show any benefit of chiropractic manipulative therapy over placebo for migraine, this is a landmark study in many ways. Lack of quality research data always has been a key challenge for integrative health practitioners. The failure of many integrative health modalities to fit neatly into the randomized, controlled trial "box" has been the rate-limiting step for integrative health researchers. Essentially, integrative health researchers have two options: 1) convince the scientific community of the validity of research other than the randomized, controlled trial, or 2) find a way to conform to the randomized, controlled trial. These researchers have achieved the latter, which is the path of least resistance but marks a major milestone in integrative health research methodology. ■

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BRIEF REPORT

Combined Treatments with Medications for Hypertension and Hyperlipidemia Dramatically Reduce the Risk of Stroke

By Matthew E. Fink, MD

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

SOURCE: Bosch J, Lonn E, Zhu J, et al. First stroke reduced 44% by well-tolerated medications. Stroke outcomes from the heart outcomes prevention evaluation 3 study. *Stroke* 2018;49:A104.

Seventy-five percent of strokes are first strokes, and primary prevention by reducing risk factors is crucial for reducing the global burden of stroke. Bosch et al investigated the effectiveness of fixed-dose antihypertensive therapy and statin therapy for primary stroke prevention. They randomized 12,705 participants from 21 countries who demonstrated an intermediate risk of cardiovascular disease in a 2 × 2 factorial design to a fixed-dose candesartan 16 mg plus hydrochlorothiazide 12.5 mg daily vs. placebo, and to rosuvastatin 10 mg daily or placebo. The mean age of the patients was 66 years, 46% were women, and 166 strokes occurred during a median follow-up of 5.6 years. Mean baseline blood pressure was 138/82 mmHg and the blood pressure difference between the treatment groups during follow-up averaged 6.0/3.0 mmHg. During the follow-up period, stroke was reduced by 20% (95% confidence interval [CI], 0.59-1.08; $P = 0.14$) with candesartan/hydrochlorothiazide and 30% (95% CI, 0.5-20.95) with rosuvastatin. In a subgroup analysis, participants in the upper third of systolic blood pressure (> 143.5 mmHg) had stroke reduced by 42% (95% CI, 0.37-0.90; $P < 0.02$). Rosuvastatin reduced all stroke by 30%, but considering hemorrhagic strokes, 15 occurred among those assigned rosuvastatin vs. 12 with rosuvastatin

placebo. Those assigned to both rosuvastatin and candesartan/hydrochlorothiazide had stroke reduced by 44% (95% CI, 0.36-0.87; *P* = 0.009). There was no difference in the rates of medication discontinuation between the groups that took active drugs compared to placebo-assigned patients. In this real-world study, fixed-dose candesartan/hydrochlorothiazide combined with low-dose rosuvastatin reduced first stroke by 44% in patients at intermediate risk of cardiovascular disease and was well tolerated, with minimum dropout of patients. This approach should be considered more widely in our efforts to reduce the global burden of stroke. ■

ABSTRACT & COMMENTARY

Rapid Screening for Future Risk of Parkinson's Disease Dementia

By Claire Henchcliffe, MD, PhD

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Dr. Henchcliffe reports she is a consultant for ACADIA Pharmaceuticals and US WorldMeds.

SYNOPSIS: The Montreal Parkinson Risk of Dementia Scale provides a simple eight-item screening tool with high predictive value for developing Parkinson's disease dementia.

SOURCE: Dawson BK, Fereshtehnejad SM, Anang JBM, et al. Office-based screening for dementia in Parkinson disease: The Montreal Parkinson Risk of Dementia Scale in four longitudinal cohorts. *JAMA Neurol* 2018; Mar 26. doi:10:1001/jamaneurol.2018.2054. [Epub ahead of print].

The Montreal Parkinson Risk of Dementia Scale (MoPaRDS) was developed based on predictors of developing dementia identified in a prospective study of individuals with Parkinson's disease (PD) in Montreal. The scale comprises eight items: age, sex, falls and/or freezing, bilateral symptom onset, history suggestive of REM sleep behavior disorder (RBD), visual hallucinations, orthostatic hypotension, and mild cognitive impairment. Dawson et al extracted MoPaRDS scores from four independent cohorts combined into three groups for analyses: 1) the original Montreal cohort with established PD (n = 80); 2) a combined group with established PD, comprising individuals recruited from two local PD clinical trials (n = 52) and a cohort from Tottori, Japan (n = 82); and 3) the Parkinson Progression Marker Initiative (PPMI) for individuals with PD diagnosed within two years and not yet taking medications (n = 393). Age at diagnosis was 66.0 ± 8.2 years (original), 68.5 ± 10.1 years (combined), and 61.3 ± 9.8 years (PPMI). All patients were free of dementia at baseline visits, although mild cognitive impairment was identified in 51% and 46.3% in the original and combined cohorts (results imputed for the Tottori cohort), and in 21.6% in PPMI. A greater percentage were < 70 years of age in the PPMI group than in the other groups. Additionally, fewer exhibited features suggestive of RBD, hallucinations, orthostatic hypotension, presence of falls or freezing, or history of bilateral onset in PPMI compared to the other groups. Investigators analyzed MoPaRDS scores using the primary endpoint of dementia status at the subject's last office visit, judged by global cognitive decline to Mini-Mental Status Examination (MMSE) < 26, with impairment in > 1 cognitive domain resulting in significant impairment in activities of daily living (ADL). This endpoint was reached in 11.5% of all individuals (but only 3.3% in PPMI alone) over mean 4.4 ± 1.3 years (range, 1-8 years) follow-up. When stratified by MoPaRDS scores, the annual risk of dementia was 0.6% (score, 0-3), 5.8% (score, 4-5), and 14.9% (score, 6-8). Predictive validity, as examined by receiver operating characteristic (ROC) curves, was 0.879 (95% confidence interval [CI], 0.816-0.942), and the determined optimal cutoff score of at least 4 resulted in a positive predictive value of 43.9% (95% CI, 37.8-50.2) and negative predictive value of 96.7% (95% CI, 95.0-97.9).

■ COMMENTARY

Dementia is more common in PD patients than the general population and has a profound effect, not only on the patient's function, quality of life, and life expectancy, but also on the caregiver. It is a common cause of placement in nursing homes, and treatment options are limited. It is critical that we better understand the nature of PD dementia and establish improved counseling and treatment pathways. Several studies have determined various clinical and non-clinical risk factors for PD dementia; for example, greater age, presence of hallucinations, or RBD. The MoPaRDS now may provide a step forward in combining a few easily assessed items. Its strength lies in its ease of administration and the simplicity of the data required to generate a MoPaRDS score. Several items can be simply extracted from the clinical chart, such as age, sex, and whether

symptom onset was bilateral. Others either already may be obtained or could be added easily to a visit at intervals (for example, measuring orthostatic changes or recording items derived from the Movement Disorders Society Unified Parkinson Disease Rating Scale). Therefore, the resulting MoPaRDS score ultimately may be useful for rapid screening of future dementia risk in the clinic. It also is important that in the PPMI cohort, the baseline MoPaRDS score correlated with potential molecular biomarkers previously identified in cerebrospinal fluid: Ab42/tau and tau concentrations. However, it is too early to recommend routine use in the clinic. There was some variability between cohorts in how particular scores were collected, and certain results were imputed. The definition for the primary endpoint may have missed some cases of dementia. Moreover, the scale performed better in men than women, for unclear reasons. Overall, though, the MoPaRDS appears to be a highly promising approach that merits testing in larger cohorts, and once again serves to draw attention to a challenging feature in PD. ■

PHARMACOLOGY UPDATE

Tolvaptan Tablets (JYNARQUE)

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

Dr. Elliott is 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 new indication for tolvaptan as the first treatment in patients with rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). Tolvaptan, an oral selective vasopressin V2-receptor antagonist, was approved in 2009 for the treatment of hypervolemic and euvolemic hyponatremia. The FDA designated the new indication for tolvaptan with a priority review. It is marketed as JYNARQUE.

INDICATIONS

Tolvaptan is indicated to slow kidney function decline in adults at risk of rapidly progressing ADPKD.[1]

DOSAGE

The recommended starting dose is 60 mg daily (45 mg on waking and 15 mg eight hours later).[1] The dose is titrated to 60 mg and 30 mg and 90 mg and 30 mg, with at least one-week intervals between titrations if tolerated. Use with a strong CYP3A inhibitor is contraindicated. The dose should be reduced if used concomitantly with moderate CYP3A inhibitors. Enough water intake is encouraged to avoid thirst or dehydration. Tolvaptan is available as 15 mg, 30 mg, 45 mg, 60 mg, and 90 mg tablets.

POTENTIAL ADVANTAGES

Tolvaptan is the first approved treatment in the United States for rapidly progressing ADPKD.

POTENTIAL DISADVANTAGES

Adverse reactions associated with tolvaptan were related to increased aquaresis.[2] These include thirst, polyuria, and polydipsia. Approximately 15.4% of subjects in the three-year trial discontinued tolvaptan compared to 5% for placebo (8.3% vs. 1.2% because of aquaresis effects).[2] Patients in earlier stages of disease may be more sensitive to aquaretic symptoms.[3] The tolerability appears to stabilize by month four. A higher percentage of subjects on tolvaptan exhibited elevation of liver enzymes. The frequency of ALT elevation at three times the upper limit of normal was 4.9% for tolvaptan compared to 1.1% for placebo.[1] Serious and potentially fatal liver injury has been reported.[1] Monitoring of liver enzymes before and after initiation of treatment is recommended.

COMMENTS

Tolvaptan has been reported to slow the growth of cysts, kidney volume, renal function decline, and the progression of the disease. Its efficacy was demonstrated in two Phase III, randomized, double-blind, placebo-controlled, clinical trials.[1,2,4] One study included subjects at earlier stages of disease, while the second study included subjects in later stages. The first was a three-year study that included 961 subjects who received tolvaptan and 483 who received placebo. Subjects demonstrated a mean glomerular filtration rate (eGFR) of about 82 mL/min/1.73 m^2, a mean height-adjusted total kidney volume (TKV) of 972 mL, and a mean age of 40 years.[1,2] The primary endpoint was the rate of change of TKV normalized as a percentage. A key secondary composite endpoint was time to ADPKD-related events, including metrics for worsening kidney function, medically significant kidney pain, worsening hypertension, or worsening albumin/creatinine ratio. During the three-year period, TKV increased by 2.8% per year with tolvaptan and 5.5% with placebo. The largest effect was observed in the first year with little effect beyond that.[1] ADPKD-related events decreased by 13.5% (44 vs. 50 events per 100 person-years), with the greatest benefit in worsening

of kidney function (4.7 vs. 7.3). For the one-year study, in subjects with later-stage ADPKD (mean estimated eGFR of 41 mL/min/173 m^2), tolvaptan slowed the change of eGFR from baseline.[1,3] For tolvaptan, change was -2.34 mL/min/1.73 m^2 vs. -3.61 mL/min/1.73 m^2 for placebo (difference of 1.27 mL/min/1.73 m^2; 95% confidence interval, 0.86-1.68; $P < 0.001$). Those < 55 years of age, white, and with baseline eGFR > 45 mL/min/1.73 m^2 tended to accrue greater benefit.

CLINICAL IMPLICATIONS

ADPKD is an inherited disorder caused by mutation in either of the two genes that affect tubular and vascular development in the kidney and other organs, which can lead to slow growth of fluid-filled cysts in the kidney.[5] The disease begins in utero, but cannot be detected for several decades. The uncontrolled growth of cysts leads to obstruction of renal tubules, blood vessels, and lymphatics. This causes fibrosis, kidney enlargement, kidney pain, hypertension, and, ultimately, end-stage failure. It is the fourth leading cause of end-stage failure in the United States.[4] There is no cure or treatment for this condition. Tolvaptan is the first U.S.-approved treatment that is indicated to slow the progression of the disease. The cost for a 28-day supply, regardless of dose, is $13,041.10. It is available only through a restricted distribution program called the JYNARQUE REMS Program. ■

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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.

CME QUESTIONS

1. **Which of the following is *not* included in the pulmonary embolism rule-out criteria?**
   a. Hemoptysis
   b. Age ≥ 50 years
   c. Current oral anticoagulant use
   d. Heart rate ≥ 100 bpm

2. **Combination therapy with antihypertensives and statins is effective in reducing the incidence of a first ischemic stroke.**
   a. True
   b. False

3. **Which of the following risks of developing dementia in Parkinson's disease is not assessed by the Montreal Parkinson Risk of Dementia Scale score?**
   a. Orthostatic hypotension
   b. Age
   c. Cerebrospinal fluid total tau concentration
   d. Bilateral symptom onset

Internal Medicine [ALERT]

ECG Review

By Ken Grauer, MD

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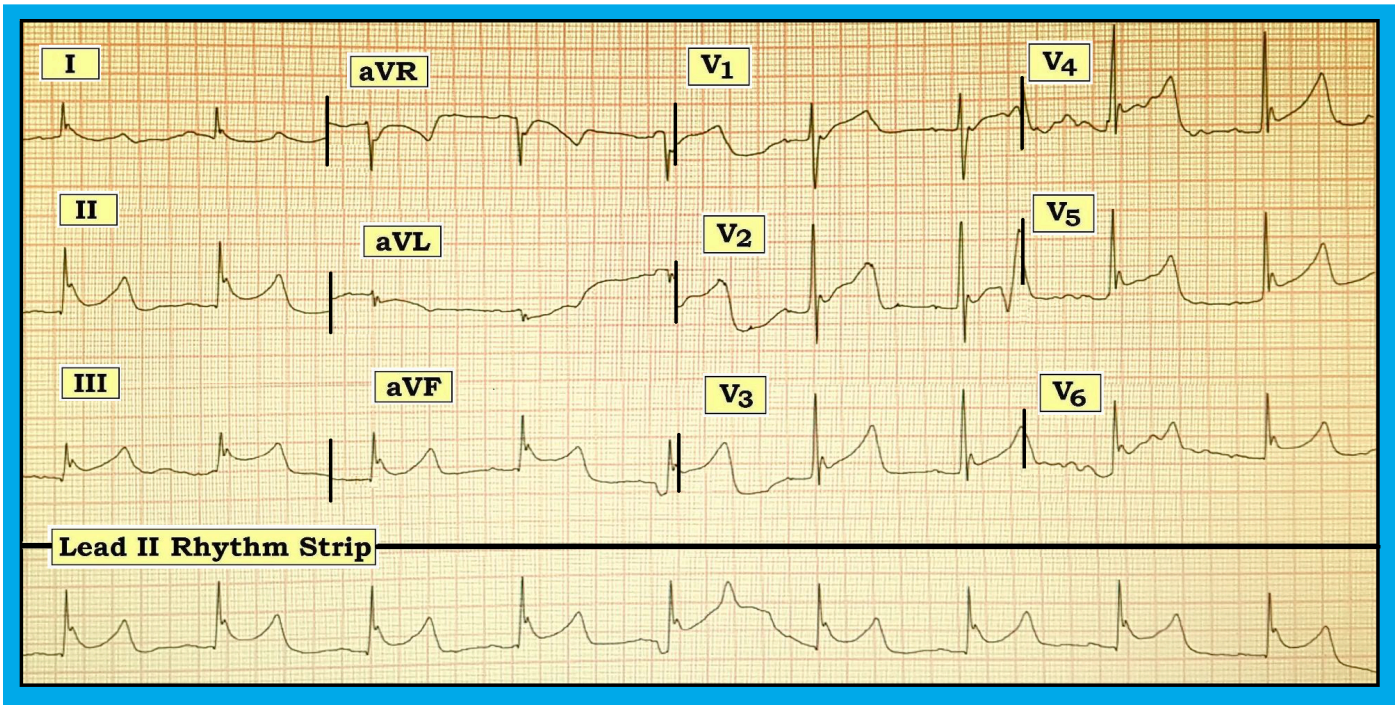
Dr. Grauer reports no financial relationships relevant to this field of study.

Acute Pericarditis or Something Else?

A 28-year-old man was found nearly comatose in front of his house. There was a history of alcohol consumption. The patient was not lucid enough to answer questions. His initial ECG is shown in the figure below. Does this ECG suggest either acute pericarditis or acute infarction? What key piece of information is missing from the history? How would you interpret this tracing?



There is much baseline wandering and significant artifact. Approaching the tracing systematically, we note there appears to be a sinus rhythm at ~55/minute. However, P waves are of such low amplitude in lead II that we cannot rule out the possibility of an ectopic atrial rhythm. The PR interval is normal, and the QRS complex is narrow. However, the QTc interval is prolonged. The axis is normal, and there is no chamber enlargement. There is only one tiny Q wave (in lead II), and transition occurs early (i.e., the R wave already has become taller than the S wave is deep by lead V2).

The J-point elevation, with marked J-point notching at the junction between the end of the QRS complex and the beginning of the ST segment, and the presence of upward-sloping ST segment elevation in multiple leads are remarkable findings on this tracing. J-point elevation with prominent notching at the onset of the ST segment (as is seen in the figure) is designated as an Osborn wave. First described in 1953 by John J. Osborn, the presence of Osborn waves in multiple leads is associated with significant hypothermia (usually indicating a temperature below 32° C = below 89.6° F).

Other commonly associated ECG features with hypothermia include: bradycardia (which may be marked), atrial fibrillation or other arrhythmias, and artifact (from baseline undulations resulting from associated shivering).

The key information missing from the history in this case was the patient's core temperature. Cold exposure plus excess alcohol consumption combined to predispose this patient to developing profound hypothermia, with a nearly comatose state by the time he was finally found. Neither acute pericarditis nor acute infarction were present, and ST segment elevation quickly resolved after the patient's core temperature was corrected.

For more information about and additional discussion on this case, please visit: https://bit.ly/2wORr4M.