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ABSTRACT & COMMENTARY

The Effect of Antiviral Drugs on COVID-19 Outcomes and Mortality

By Vibhu Sharma, MD

Associate Professor of Medicine, University of Colorado, Denver

SYNOPSIS: The WHO Solidarity Trial Consortium found remdesivir, hydroxychloroquine, lopinavir, and interferon regimens produced "little or no effect" on relevant outcomes.

SOURCE: WHO Solidarity Trial Consortium; Pan H, Peto R, Henao-Restrepo AM, et al. Repurposed antiviral drugs for COVID-19 — Interim WHO Solidarity Trial Results. *N Engl J Med* 2021;384:497-511.

The Solidarity Trial Consortium sponsored by the World Health Organization randomized inpatients with COVID-19 to one of five drug regimens and the local standard of care: remdesivir (2,750 patients), hydroxychloroquine (954 patients), lopinavir alone (1,411 patients), interferon beta alone (2,063 patients), and lopinavir plus interferon beta (651 patients). The patients were randomized in 405 hospitals and in 30 countries. The trial was open-label, and no placebos were used. The controls were assigned to the local standard of care where the drug that was randomized was available. The only exception was lopinavir plus interferon beta, where the control group was lopinavir alone. Some institutions had multiple drugs available; in these institutions, patients assigned to the control group served as controls for each available drug group. Written informed consent was provided by patients or their designees. National monitors were in place to resolve questions about trial strategy or drug adverse effects. One-third of total patients randomized were younger than age 50 years, and 19% were older than age 70 years. One-third were not receiving any oxygen at the time of study entry, and only 8% were mechanically ventilated; the rest received varying amounts of supplemental oxygen. Overall, 62% were male.

The primary outcome was in-hospital mortality for each intervention/control group, in addition to analyses of in-hospital mortality stratified by age and use of mechanical ventilation. Prespecified secondary outcomes included the need for mechanical ventilation among those not requiring support at the start of randomization, duration of mechanical ventilation, and

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hospital length of stay. All treatments lasted a maximum of 14 days. The results were mostly disappointing, with no drug (or drug combination in the case of lopinavir plus interferon beta) associated with either a reduction in mortality or a favorable outcome regarding secondary outcomes. Importantly, no intervention reduced the need for mechanical ventilation.

■ COMMENTARY

This ambitious worldwide trial failed to demonstrate any mortality reduction of antiviral therapy (remdesivir, lopinavir, or interferon beta) or treatment with drugs repurposed to treat COVID-19 infection (hydroxychloroquine). The lack of benefit was consistent across age groups and disease severity (i.e., including requirements for oxygen, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]). The trial consortium also found no effect on the need for mechanical ventilation among those who were not intubated at randomization. The authors performed a meta-analysis of randomized trials for remdesivir (Solidarity [n = 5,451 randomized] and the Adaptive COVID-19 Treatment Trial, or ACTT-1 [n = 1,062 patients randomized]) and found no mortality benefit. Similarly, meta-analyses for all trials for hydroxychloroquine and lopinavir, including the Solidarity cohort, showed no mortality benefit.

The European Respiratory Society (ERS) recently published guidelines for managing hospitalized adults with COVID-19.[1] The guidelines were developed by a task force using the GRADE methodology (Grading of Recommendations Assessment, Development, and Evaluation), wherein the quality of evidence is rated from very low to high, and recommendations based on the quality of evidence are rated as strong or weak. Regarding drugs evaluated by the Solidarity consortium reviewed here, the ERS recommends not offering remdesivir to hospitalized patients with COVID-19 infection requiring invasive mechanical ventilation (conditional/weak recommendation, moderate quality of evidence), but it makes no recommendations regarding the use of remdesivir in hospitalized patients not requiring invasive mechanical ventilation. The panel recommends against the use of lopinavir for hospitalized patients with COVID-19 (strong recommendation with moderate quality of evidence). The panel also recommends against using interferon beta for inpatients with COVID-19 (weak recommendation based on very low quality evidence).

A recent randomized, controlled trial compared tocilizumab (a monoclonal antibody against the interleukin-6 receptor) to placebo in patients admitted to a hospital with COVID-19 and evidence of a hyperinflammatory state (at least one of the following: D-dimer level higher than 1,000 ng/milliliter, ferritin level higher than 500 ng/milliliter, C-reactive protein [CRP] level higher than 50 mg/liter, or a lactate dehydrogenase [LDH] level higher than 250 U/liter).[2] The authors found no benefit regarding preventing intubation or death among inpatients with COVID-19, albeit with wide confidence intervals for efficacy, implying the "possibility of some benefit or harm."

A recent propensity-matched analysis assessing the effect of tocilizumab on outcomes in COVID-19 critical illness revealed a mortality benefit among those who received tocilizumab vs. those who did not.[3] Accordingly, the ERS guidelines suggest "offering interleukin-6 receptor antagonist monoclonal antibody therapy to hospitalized patients with COVID-19 requiring oxygen or invasive ventilatory support" (weak recommendation/low quality of evidence). Therefore, tocilizumab may be considered for inpatients with COVID-19 infection requiring oxygen or undergoing noninvasive mechanical ventilation who worsen while on dexamethasone after 48 hours AND are receiving high-flow nasal cannula oxygen at > 30 L/minute and FiO_2 > 0.4 with CRP ≥ 75 mg/L per institutional guidelines.

Among inpatients who are mechanically ventilated or undergoing ECMO, tocilizumab may be considered as adjunctive therapy to dexamethasone for patients without improvement or with worsening respiratory function within 24 hours and accompanying worsening inflammatory markers. Typically, clinicians dose tocilizumab at 8 mg/kg (single intravenous dose) rounded to 400 mg (40 kg to 65 kg of body weight), 600 mg (66 kg to 90 kg of body weight), and 800 mg (> 90 kg of body weight). Considered contraindications to using tocilizumab are hospitalization longer

than four days; duration of mechanical ventilation > 24 hours; active tuberculosis; pregnancy or breast-feeding; and suspected or confirmed viral, fungal, or bacterial infection other than SARS-CoV-2.

Results of the ACTT-2 trial were reported recently.[4] Baricitinib is an oral Janus kinase 1 (JAK-1) and JAK-2 inhibitor. Researchers hypothesized the drug would modulate the immune response to the virus by inhibiting the signaling pathway of cytokines that are upregulated in COVID-19 infection. Baricitinib and remdesivir were compared to remdesivir alone. Hospitalized adults with COVID-19 infection receiving either high-flow oxygen or noninvasive ventilation were randomized. "Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status." There was no difference regarding 28-day mortality rates. A minimal incremental benefit of baricitinib alone over dexamethasone alone is likely. Institution-specific guidelines may recommend the combination in the defined population studied in the trial. Anti-spike neutralizing monoclonal antibodies have been approved for use in outpatients with COVID-19 infection, but none have been approved for hospitalized patients with more severe disease. The landscape of drug therapy for severe COVID-19 infection has evolved since the start of the pandemic. Unfortunately, only a single therapy (dexamethasone) has clearly been shown to affect mortality in these cases. Multiple clinical trials are ongoing. ■

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ABSTRACT & COMMENTARY

Air Filters and Asthma

By Darren Wong, MD, and Nancy J. Selfridge, MD

Dr. Wong is a Clinical Skills Facilitator, Ross University School of Medicine, Barbados, West Indies.
Dr. Selfridge is Professor, Clinical Foundations Department, Ross University School of Medicine, Barbados, West Indies.

SYNOPSIS: Children with asthma showed improved small airway mechanics following indoor filtration of particulates (2.5 μm and greater) using high-efficiency particulate air filtration devices.

SOURCE: Xiaoxing C, Li Z, Teng Y, et al. Association between bedroom particulate matter filtration and changes in airway pathophysiology in children with asthma. *JAMA Pediatr* 2020;174:533-542.

In many environments, from industrial settings to indoor homes, pollution has an elevated amount of particulate matter 2.5 µm or smaller ($PM_{2.5}$). It is widely believed that $PM_{2.5}$ deposits in smaller pulmonary airways leads to asthma exacerbation. Specifically, $PM_{2.5}$ has been associated with increased oxidative stress and pulmonary inflammation. Before this study, there was little conclusive information on whether the reduction of $PM_{2.5}$ exposure improves small airway function in children with asthma.

This randomized, double-blind, crossover study of 43 children with mild to moderate asthma and ages ranging from 5 to 13 years took place over the course of 70 days in Shanghai, China, where the $PM_{2.5}$ used ranged from less than the U.S. National Ambient Air Quality standard (35 µg/m^3) to nearly double this level. $PM_{2.5}$ was measured indoors and outdoors, and filtration of $PM_{2.5}$ occurred in the children's indoor bedrooms with high-efficiency particulate air (HEPA) filtration and activated carbon. The primary outcome of the study examined fractional exhaled nitric oxide (FeNO), while also examining the effects of $PM_{2.5}$ on airway mechanics and function using impulse oscillometry (IOS) and spirometry, respectively. The authors also examined $PM_{2.5}$ filtration on children with various baseline FeNO and eosinophil levels and its subsequent effect on airway physiology.

In comparison to no filtration, true filtration led to a reduction of $PM_{2.5}$ by 79.6% and 63.4% in outdoor and bedroom concentrations, respectively. Furthermore, true filtration showed improved respiratory inflammation (FeNO 24.4%; 95% CI, 11.8%-37.1%), mean peaked expiratory flow (PEF) (1.6%; 95% CI, 0.8% to 2.5%), and airway mechanics (reduction in resistance at 5 Hz [R5] and resistance at 5 Hz to 20 Hz [R5-R20] by 43.5% and 73.1%, respectively). Further analysis showed that for every 10 µg/m^3 reduction in bedroom $PM_{2.5}$ concentration, there was a significant improvement in airway mechanics (reduction in R5 and

R5-R20 by 4.6% and 7.6%, respectively), small airway airflow, and inflammation (6.8% reduction in FeNO). Children with lower baseline FeNO or eosinophil count showed significant improvement in airway mechanics vs. children with higher baseline values. However, airway function did not show significant improvement, since overall small airway function (forced expiratory flow), forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC were not significant.

■ COMMENTARY

This study reinforces the evidence suggesting the negative effects of air pollution on the respiratory system. Prior studies have shown air particulates found in air pollution result in increased oxidative stress and airway inflammation in children with asthma.[1-4] A study conducted in 2015 revealed that for every 10 µg/m^3 increase in $PM_{2.5}$, there was an increased relative risk of 1.021 for asthma-related hospital admission.[5]

The filtration of $PM_{2.5}$ in this study revealed improved airway mechanics and reduction in small airway inflammation. Similar results were seen in other studies.[2,3,6] However, no significant improvement was seen in airway function. This contrasts with a 2008 study that revealed a significant inverse association between $PM_{2.5}$ and FEV1 and FVC in children with and without asthma.[2] The discrepancy may be caused by the duration of the study/sample size or other risk factors that were not accounted for, such as other air pollutants like sulfur dioxide (SO_2) or nitrogen dioxide (NO_2).[4,7,8] A study of children with asthma in inner U.S. cities showed higher five-day average concentrations of NO_2, SO_2, and $PM_{2.5}$ were associated with significantly lower pulmonary function and increased asthma-related missed school days.[4] Other factors that could influence airway mechanics and airway function include urbanization, age, and social economics.[1,6,7] Studies have shown exposure to an increase in air pollution in minority children in the first year of life was associated with an odds ratio of 1.17 for physician-diagnosed asthma.[7] Based on the study, I would agree that additional clinical trials are needed to evaluate whether filtrating $PM_{2.5}$ is an effective tool to improve airway mechanics and prevent/reduce asthma symptoms. However, if financial costs are not an issue, I would suggest households include a HEPA filter to reduce $PM_{2.5}$ levels, since the study reveals significant improvement in airway mechanics and reduction in small airway inflammation. ■

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ABSTRACT & COMMENTARY

Using Procalcitonin to Limit Antibiotic Treatment for Sepsis Reduces Infection-Related Adverse Events

By Samuel Nadler, MD, PhD

Critical Care, Pulmonary Medicine, The Polyclinic Madison Center, Seattle; Clinical Instructor, University of Washington, Seattle

SYNOPSIS: By shortening the duration of antibiotic therapy, a procalcitonin-guided protocol decreased the rate of infection-associated adverse effects, decreased costs, and reduced mortality in patients with sepsis.

SOURCE: Kyriazopoulou E, Liaskou-Antoniou L, Adamis G, et al. Procalcitonin to reduce long-term infection-associated adverse events in sepsis. A randomized trial. *Am J Respir Crit Care Med* 2021;203:202-210.

Achieving the optimal duration for antimicrobial therapy in sepsis remains a challenge. Published guidelines make recommendations, but the prescribed duration of antibiotics commonly exceeds these recommendations. Creating a biomarker-driven protocol to limit antibiotic exposure could decrease antibiotic exposure and improve outcomes.

The Procalcitonin-Guided Antimicrobial Therapy to Reduce Long-Term Sequelae of Infections (PROGRESS) trial was a multicenter, pragmatic, randomized, controlled trial using procalcitonin-driven protocols to discontinue antibiotics in patients admitted with sepsis. Patients meeting Sepsis-3 definitions were randomized to standard of care (SOC) or procalcitonin (PCT)-driven protocols in which antibiotics were discontinued if PCT levels were reduced by at least 80% from admission or the absolute level was below 0.5 mcg/L at least five days after starting treatment. Patients were excluded if they had indications for prolonged antibiotic therapy, viral or parasitic infections, tuberculosis, cystic fibrosis, HIV, or were pregnant or lactating. Exceptions were allowed for unstable patients with fever and/or shock. The primary outcome was the rate of infection-associated adverse events (IAAEs) within 180 days, including new cases of *Clostridioides difficile*, new multidrug-resistant organisms (MDRO), or death associated with these infections. Secondary outcomes included length of antibiotic therapy, 28-day and 180-day mortality, and cost of hospitalization.

Overall, 266 patients were enrolled, mostly with community-acquired pneumonia (CAP) (43.8%) or healthcare-associated pneumonia (HCAP) (16.8%); other infections included pyelonephritis (37.1%) and bloodstream infections (1.2%). Most commonly, a pathogen was not identified (84%), and empiric antibiotics were prescribed. Using the PCT-driven protocol, the duration of antibiotic therapy was reduced from a median of 10 days to five days ($P < 0.001$). The rate of IAAEs was decreased from 15.3% to 7.2% (odds ratio [OR], 0.43; 95% confidence interval [CI], 0.19-0.99; $P = 0.045$). Hospital mortality improved from 25.2% in the SOC group to 13.6% in the PCT group (OR, 0.47; 95% CI, 0.25-0.89; $P = 0.03$). The cost of hospitalization decreased from €1,183.49 to €956.99 ($P = 0.05$). In a multivariate analysis of patients who developed IAAEs, PCT guidance was protective (hazard ratio [HR], 0.38; 95% CI, 0.17-0.95; $P = 0.01$) while dementia, bacteremia, and intake of a carbapenem increased the risk of IAAEs (HR, 4.3, 2.93, and 2.91, respectively).

■ COMMENTARY

The PROGRESS study adds to a growing body of literature indicating PCT-driven protocols can shorten antibiotic duration and reduce complications from antibiotic use without adversely influencing mortality. A previous meta-analysis of studies that included PCT-driven protocols in sepsis confirmed decreased antimicrobial exposure and suggested improved mortality.[1] However, in many of those studies, the discontinuation of antibiotics was a recommendation, and adherence was highly variable. For example, in the largest of these studies from the Netherlands that included 1,546 patients, there was only 44% adherence.[2] The reason for nonadherence to the recommendation in this study was most commonly "other reasons or not specified" (61.1%) or "physician considers risk of discontinuation of antibiotics too high" (12.7%), rather than more objective findings, such as "patient still has fever" (5.7%) or "patient is not stable" (6.1%). The positive effects of protocolized discontinuation of antibiotics often was attenuated by physician discomfort rather than objective data. In the PROGRESS study, there was high adherence to protocol. Thus, the effect of a PCT-driven protocol might be to enable physicians to use objective data to drive discontinuation of antibiotics.

The decrease in antibiotic exposures by PCT-driven protocols changes the duration of treatment to be more guideline-concordant. In the PROGRESS trial, most patients were admitted with CAP/HCAP, and antibiotic duration decreased from 10 to five days. Current American Thoracic Society/Infectious Diseases Society of America guidelines for the treatment of CAP recommend an antibiotic duration of five to seven days.[3] Thus, the effect of the protocol was to drive toward more guideline-concordant care. This could have been accomplished without PCT measurement, and simple adherence with published standards. Again, the effect of a PCT-driven protocol may be to improve the comfort of physicians discontinuing antibiotics to conform with established guidelines. The PROGRESS study demonstrates that a PCT-driven protocol can shorten the duration of antibiotic therapies, decrease adverse effects caused by antibiotics, and improve outcomes for patients with sepsis. ■

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PHARMACOLOGY UPDATE

Aducanumab-avwa Injection (Aduhelm)

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.

The FDA has approved a new, but controversial, treatment for Alzheimer's disease (AD). Aducanumab is a recombinant human, immunoglobulin gamma (IgG1) monoclonal antibody that targets aggregated soluble and insoluble forms of amyloid beta, reducing plaque deposits. This therapeutic approach is in contrast to the currently available drugs for AD with limited benefit: acetylcholinesterase inhibitors, such as donepezil, and N-methyl-D-aspartate antagonists, such as memantine. The FDA approved aducanumab through the accelerated approval pathway based on surrogate markers typically used for anti-cancer drugs. This pathway is intended to provide earlier access to potentially valuable therapies for serious disease with an unmet need.[1] Continued approval may be contingent on verification of clinical benefit in confirmatory trials. The approval ran counter to the recommendation of the agency's Peripheral and Central Nervous System Drugs Advisory Committee, which did not support approval. Aducanumab is distributed as Aduhelm.

INDICATION

Aducanumab can be prescribed to treat AD.[2]

DOSAGE

After an initial titration period (six doses), the recommended maintenance dose is 10 mg/kg (given by IV infusion over approximately one hour) every four weeks and at least 21 days apart.[2] The titrations schedule should be 1 mg/kg for two doses, 3 mg/kg for two doses, 6 mg/kg for two doses, and 10 mg/kg for the seventh dose and beyond. Brain MRI should be performed before initiation of treatment and before doses 7 and 12. If there are 10 or more new microhemorrhages or more than two focal areas of superficial siderosis, treatment may be continued with caution only after clinical evaluation and a follow-up MRI demonstrating radiographic stabilization.[2] Aducanumab is available in 100 mg/mL single-dose vials of 1.7 mL or 3 mL.

POTENTIAL ADVANTAGES

Aducanumab is the first drug that targets brain beta-amyloid that is believed to play a key role in the pathogenesis of AD.

POTENTIAL DISADVANTAGES

Clinical benefit remains to be established. The clearance of amyloid is associated with amyloid-related imaging abnormalities (ARIA), including edema (ARIA-E) and hemosiderin deposition (microhemorrhage and superficial siderosis; ARIA-H).[2] ARIA-E and/or ARIA-H were observed in 41% of aducanumab-treated subjects with a planned dose of 10 mg/kg vs. 10% treated with placebo.[1] Incidence of ARIA-E was higher in those who carry the AD gene (APOE epsilon 4). Most ARIA were observed during titration. ARIA-E tends to resolve over time (week 12 to 20). In clinical trials, permanent discontinuation of the drug was required for radiographically severe ARIA-H and temporary dose suspension for moderate or severe ARIA-E and moderate ARIA-H.[2] The most common symptom observed was headache (13%).[2]

COMMENTS

The accelerated approval was based on review of the efficacy from two double-blind, randomized, placebo-controlled studies. The diagnosis of AD was based on confirmed presence of amyloid pathology and mild cognitive impairment or mild dementia stage of diseases consistent with stage 3 and 4. Subjects (n = 1,638 in study 1, n = 1,647 in study 2) were randomized to low dose (3 mg/kg or 6 mg/kg for APOE epsilon 4 carriers and noncarriers, respectively), high dose (10 mg/kg), or placebo for 18 months.[2] APOE epsilon 4 carriers were later adjusted to 10 mg/kg. The primary endpoint was change from baseline in Clinical Dementia Rating Sum of Boxes (CDR-SB) score at week 78.[4,5] CDR-SB assesses both cognitive and functional domains of AD disability. Secondary endpoints included change from baseline in Mini-Mental State Examination (MMSE) score, change from baseline in Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), and change from baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory (Mild Cognitive Impairment version) (ADCS-ADL-MCI) score.

Study 1 reached statistical difference for the high dose for all primary and secondary endpoints. However, the *P* values were not statistically controlled for multiple comparison (i.e., less strict statistical threshold). Study 2 did not reach statistical difference for CDR-SB. The FDA supported its case for approval from a subgroup analysis of participants enrolled in a biomarker portion of the study, which showed reduction in amyloid burden detected with PET and reduction of cerebrospinal fluid (CSF) tau proteins (total and phosphorylated) on high-dose aducanumab vs. placebo. Subgroup data at

week 78 represented about 33% and 3.5%, respectively, of those assessed for primary and secondary endpoints at the same time. Significant reductions in amyloid deposits were observed for both subgroup studies (71% and 59%, respectively) for high-dose aducanumab vs. placebo, but significant reductions in CSF tau proteins (16%-23%) were observed only for study 1.

CLINICAL IMPLICATIONS

In recent years, pharmacologic interventions for AD have focused on anti-amyloid agents with the hope of reducing downstream tau pathology and cognitive decline.[3,6] In the two clinical trials, aducanumab met the primary clinical outcome in one of the two studies. However, both studies were terminated based on a futility analysis.[4,5] Ten of 11 members of the FDA's Peripheral and Central Nervous System Drugs Advisory Committee voted against approval, with one abstention.[7] However, the agency decided to grant an accelerated approval based, in large part, on a subgroup analysis of surrogate markers. The agency expects this will result in reduction in clinical decline and that benefit outweighed the risk of the drug. Subsequent to the FDA's decision, three members of the Peripheral and Central Nervous System Drugs Advisory Committee resigned.[7] The estimated cost is $56,000 per patient per year. ■

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CME QUESTIONS

1. **Tocilizumab therapy is contraindicated for:**
   a. worsening hypoxia within 48 hours after dexamethasone therapy.
   b. day 4 of hospitalization.
   c. previously treated tuberculosis.
   d. duration of mechanical ventilation > 24 hours.

2. **Which was the primary outcome when determining the effect of air filters on young asthma patients?**
   a. Fractional exhaled nitric oxide (FeNO)
   b. Peaked expiratory flow (PEF)
   c. Reduction in resistance at 5 Hz (R5)
   d. Resistance at 5 Hz-20 Hz (R5-R20)

3. **The PROGRESS trial showed a procalcitonin-driven protocol can be effective for:**
   a. choosing those patients with sepsis who require antibiotics.
   b. determining which antibiotics work best for patients with sepsis.
   c. reducing the duration of antibiotic therapy for patients with sepsis.
   d. eliminating the adverse effects of antibiotics prescribed for sepsis.

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.

Internal Medicine [ALERT]

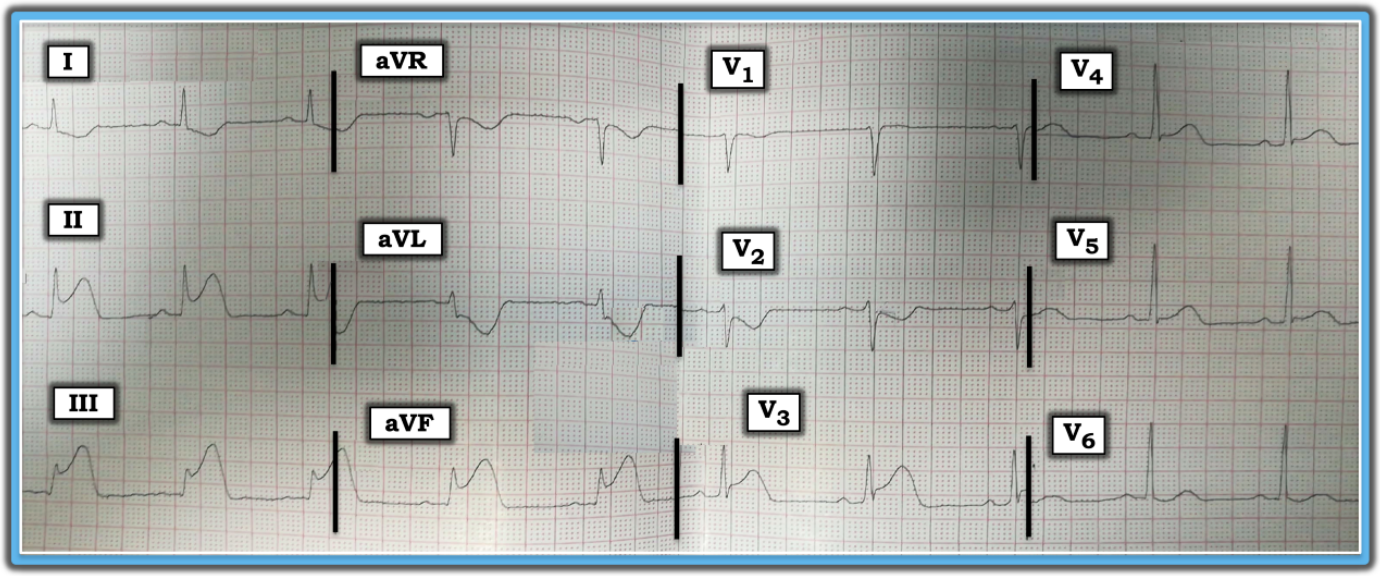
ECG Review

By Ken Grauer, MD

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

Determining the 'Culprit' Artery

How would one interpret the ECG in the figure below, obtained in the ED from a middle-aged man with new chest pain?



Is it possible to predict the "culprit" artery from the 12-leads shown on this tracing, or are additional leads needed? The ECG shows sinus rhythm, with normal intervals and axis and no chamber enlargement. There is dramatic ST-segment elevation in each inferior lead, with equally dramatic reciprocal ST depression in lead aVL (and to a lesser extent in lead I). In a patient with new chest pain, this ECG picture is diagnostic of acute inferior ST-elevation myocardial infarction (MI).

Interpretation of ECG findings in the chest leads is less obvious. Inferior lead ST elevation may be seen with acute occlusion of either the right coronary artery (RCA) or the left circumflex coronary artery (LCx). In either case, there often is associated acute posterior involvement because both vessels also supply the posterior wall of the left ventricle. The finding of ST-T wave depression in lead V2 in the figure strongly suggests there is acute inferior-posterior infarction.

Normally, with acute posterior infarction, ST depression also will be seen in lead V1, as well as in lead V2. The fact the ST-T wave in lead V1 is flat rather than depressed strongly suggests "something else" must be attenuating ST depression that otherwise would be seen as a result of acute posterior MI. This strongly suggests that in addition to acute infarction of the inferior and posterior walls of the left ventricle, there also is acute right ventricular (RV) involvement.

Although ST elevation in right-sided leads is the usual way the diagnosis of acute RV MI is made, right-sided lead V1 occasionally shows either unexpected ST segment flattening or slight ST elevation. Recognition of probable RV involvement localizes the "culprit" artery to the proximal portion of the RCA because the LCx does not supply the right ventricle.

For more information about and further discussion of this case, please visit: https://bit.ly/3dHRIsm.