

## CLINICAL DECISIONS

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# Avoiding Contrast-Enhanced Imaging to Prevent Contrast-Induced Acute Kidney Injury

*This interactive feature addresses the approach to a clinical issue. A case vignette is followed by specific options, neither of which can be considered either correct or incorrect. In short essays, experts in the field then argue for each of the options as assigned. Readers can participate in forming community opinion by choosing one of the options and, if they like, providing their reasons.*

### CASE VIGNETTE

## A Man with a Suspected Pulmonary Embolism

Clement D. Lee, M.D.

A 65-year-old man with type 2 diabetes, class II obesity (body-mass index [BMI, the weight in kilograms divided by the square of the height in meters] >35), coronary artery disease, and chronic kidney disease (estimated glomerular filtration rate [eGFR] of 28 ml per minute per 1.73 m<sup>2</sup> of body-surface area) presents to the emergency department after sudden onset of dyspnea 6 hours earlier that was associated with chest discomfort and slight light-headedness. He has had no recent surgeries or long-distance travel, and he reports no hemoptysis or swelling in his legs or feet.

On physical examination, he is afebrile, with a heart rate of 109 beats per minute, blood pressure of 135/88 mm Hg, and respiratory rate of 22 breaths per minute. His oxygen saturation is 87% while he is breathing ambient air. He appears uncomfortable, but his condition does not appear to be critical. Cardiopulmonary examination is normal. An electrocardiogram shows sinus tachycardia with no ST-wave or T-wave

changes. The D-dimer level is 724 ng per milliliter (reference range, <650, adjusted for age); high-sensitivity troponin I is undetectable. A pulmonary embolism is suspected.

You are the physician evaluating this patient in the emergency department. You would normally recommend computed tomography (CT), preferably with contrast material, to help determine whether a pulmonary embolism is present, but you must decide whether contrast-enhanced CT should be avoided in this patient who has stage 4 chronic kidney disease.

### TREATMENT OPTIONS

Which one of the following approaches would you take? Base your choice on the literature, your own experience, published guidelines, and other information.

1. Recommend performing contrast-enhanced CT.
2. Recommend avoiding contrast-enhanced CT.

To aid in your decision making, we asked two experts in the field to summarize the evidence in favor of approaches assigned by the editors. Given your knowledge of the issue and the points made by the experts, which approach would you choose?

### OPTION 1

## Recommend Performing Contrast-Enhanced CT

Jeremiah Hinson, M.D., Ph.D.

For clinicians working in the emergency department, this vignette describes a familiar scenario. The patient has signs and symptoms of a high-

risk clinical condition that is most rapidly and effectively diagnosed with contrast-enhanced CT, yet he also has advanced chronic kidney disease, a condition that has historically been associated with an increased risk of adverse renal outcomes after administration of contrast material.

In this case, whether clinical judgment or one of several validated clinical prediction rules is

applied, additional diagnostic pursuit of pulmonary embolism is required.<sup>1</sup> Ventilation–perfusion imaging of the lungs is a potential alternative to contrast-enhanced CT, but its availability is variable, and its usefulness is limited in patients with abnormal chest radiographic findings. Even under optimal conditions, the interpretation of ventilation–perfusion imaging is subject to interobserver variability, and findings are often nondiagnostic. Furthermore, in cases in which pulmonary embolism is ruled out, the potential for this method to identify alternative diagnoses, as would be afforded by contrast-enhanced CT, is absent.<sup>2</sup> Venous duplex ultrasonography of the legs and feet could be used to identify deep venous thromboembolism, allowing for initiation of anticoagulation therapy without definitive evidence of pulmonary embolism. However, the availability of radiologists to interpret ultrasound images and clinicians trained for point-of-care ultrasonography is also variable. Furthermore, this patient shows no clinical signs of deep venous thromboembolism, and if the results of the ultrasonography are negative, use of this imaging method would only delay definitive diagnosis and initiation of therapy in this patient who has overt signs of cardiopulmonary compromise. Empirical treatment with systemic anticoagulants is also an option but is not without risk. Up to 2% of patients with venous thromboembolism have a major hemorrhagic episode during the initial treatment period — an unnecessary risk for a patient without confirmed disease.<sup>3</sup> Finally, doing nothing is not an option, since a delay in the diagnosis and treatment of an acute pulmonary embolism would increase this patient’s short-term risk of death and long-term risk of complications.<sup>4</sup>

For more than half a century, clinical decision making in similar scenarios has been driven by an outsized fear of contrast-induced acute kidney injury. Contrast-induced acute kidney injury is commonly cited as a leading cause of hospital-acquired acute kidney injury, yet nearly all studies that established this as a clinical entity were performed in the absence of adequate controls and assumed causality from association.<sup>5</sup> Over the past decade, several large and well-controlled observational studies comprising millions of patient encounters have shown that the risk of acute kidney injury attributable to

intravenous contrast media is much lower than previously thought.<sup>6,7</sup>

In 2020, the American College of Radiology and the National Kidney Foundation reviewed the available evidence and issued updated guidance on the use of intravenous iodinated contrast media in patients with preexisting kidney disease.<sup>8</sup> They reported that the risk of contrast-induced acute kidney injury is near zero in patients with an eGFR of 45 ml per minute per 1.73 m<sup>2</sup> or higher and only slightly higher (2% or less) when the eGFR is 30 to 44 ml per minute per 1.73 m<sup>2</sup>. The evidence is less clear for patients with severe kidney disease (eGFR <30 ml per minute per 1.73 m<sup>2</sup>), since no single study has been adequately powered to reliably assess the risk of contrast administration in this population. Indeed, estimates of risk vary substantially in available reports. However, a meta-analysis of data from these studies, which included more than 3500 patients with an eGFR below 30 ml per minute per 1.73 m<sup>2</sup>, showed no independent association between acute kidney injury and administration of contrast material in this group.<sup>7</sup> The American College of Radiology and National Kidney Foundation acknowledged that in patients with stage 4 or 5 chronic kidney disease, there is potential for increased risk of acute kidney injury after administration of contrast material but recommended against withholding contrast required for the evaluation or treatment of a potentially life-threatening diagnosis on the basis of kidney function alone.

For the patient in this vignette, the risk associated with a missed or delayed diagnosis of acute pulmonary embolism far outweighs the potential risk of acute kidney injury that could be associated with contrast-enhanced CT. Guided by evidence and in accordance with consensus recommendations from the American College of Radiology and National Kidney Foundation, I would proceed with contrast-enhanced CT and focus nephroprotective efforts in areas known to affect kidney outcomes: stabilization of hemodynamic status, avoidance of nonessential nephrotoxic medications, and prompt treatment of acute illness.<sup>8</sup>

Disclosure forms provided by the author are available with the full text of this article at [NEJM.org](https://www.nejm.org).

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## OPTION 2

## Recommend Avoiding Contrast-Enhanced CT

Matthew Davenport, M.D.

The patient described in the vignette presents with signs and symptoms that indicate a moderate risk of pulmonary embolism on the basis of Wells' criteria, a tool developed to help clinicians assess the likelihood of a pulmonary embolism.<sup>1</sup> Pulmonary embolism is common and potentially lethal and requires imaging for diagnosis. In patients without a contraindication to iodinated contrast material, the most appropriate test is contrast-enhanced CT angiography of the chest, with an American College of Radiology appropriateness rating of 9 on a scale of 1 to 9.<sup>9</sup> CT angiography provides accurate diagnosis of pulmonary embolism, since it is both highly sensitive and highly specific.<sup>9</sup> In patients with a contraindication to iodinated contrast material, alternative tests include technetium-99m ventilation–perfusion scanning with chest radiography and duplex Doppler ultrasonography of the legs and feet. Although these tests are less accurate than CT angiography, they can meaningfully inform risk assessment and diagnosis, are considered “usually appropriate” by the American College of Radiology, and do not require iodinated contrast material.<sup>9</sup> In deciding which test to perform, the physician should determine whether iodinated contrast material is contraindicated.

What is the risk of contrast-induced acute kidney injury in a patient with stage IV or V chronic kidney disease who is undergoing contrast-enhanced CT? In brief, the risk is unknown but has been estimated by the American College of Radiology and National Kidney Foundation to range from 0 to 17%.<sup>8</sup> Historical data on contrast-induced acute kidney injury was confounded by the lack of appropriate controls and conflation of contrast-associated acute kidney injury with contrast-induced acute kidney injury<sup>8</sup>; studies conducted in the past decade have helped clarify the true risk but with limitations. Owing to ethical considerations and sample-size challenges in high-risk cohorts, no randomized trials have directly evaluated the risk of contrast-induced acute kidney injury in patients with

stage IV or V chronic kidney disease. Instead, numerous large, retrospective studies involving hundreds or thousands of high-risk patients who underwent contrast-enhanced CT, including patients in the emergency department, with analyses corrected with propensity-score matching or other advanced controls, have reached conflicting conclusions.<sup>10-12</sup> Some studies have documented a risk of contrast-induced acute kidney injury, with or without a requirement for dialysis, in patients with stage IV or V chronic kidney disease, and others have not. Given such results, the American College of Radiology and National Kidney Foundation have concluded that the risk of contrast-induced acute kidney injury is uncertain in patients with stage IV chronic kidney disease but that the risk cannot be disregarded.<sup>8</sup> Under the principle of beneficence, uncertainty about risk implies that we should proceed as though some risk is present. The certainty regarding risk is more established in patients with an eGFR of 30 to 44 ml per minute per 1.73 m<sup>2</sup> (estimated risk of 0 to 2%) or 45 ml per minute per 1.73 m<sup>2</sup> or higher (estimated risk of approximately 0%).<sup>8</sup> In the scenario presented here, the patient's eGFR is less than 30 ml per minute per 1.73 m<sup>2</sup>, a level for which the risk of contrast-induced acute kidney injury is less certain.

The American College of Radiology and National Kidney Foundation state that contrast-enhanced CT is relatively contraindicated in a patient with stage IV chronic kidney disease; thus, alternative diagnostic approaches are warranted.<sup>8,9</sup>

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1. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med* 2001;135:98-107.
2. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Respir J* 2019;54:1901647.
3. Robertson L, Jones LE. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for the initial treatment of venous thromboembolism. *Cochrane Database Syst Rev* 2017;2(2):CD001100.
4. Mansella G, Keil C, Nickel CH, et al. Delayed diagnosis in

- pulmonary embolism: frequency, patient characteristics, and outcome. *Respiration* 2020;99:589-97.
5. Rao QA, Newhouse JH. Risk of nephropathy after intravenous administration of contrast material: a critical literature analysis. *Radiology* 2006;239:392-7.
  6. Aycock RD, Westafer LM, Boxen JL, Majlesi N, Schoenfeld EM, Bannuru RR. Acute kidney injury after computed tomography: a meta-analysis. *Ann Emerg Med* 2018;71(1):44-53.e4.
  7. Lee Y-C, Hsieh C-C, Chang T-T, Li C-Y. Contrast-induced acute kidney injury among patients with chronic kidney disease undergoing imaging studies: a meta-analysis. *AJR Am J Roentgenol* 2019;213:728-35.
  8. Davenport MS, Perazella MA, Yee J, et al. Use of intravenous iodinated contrast media in patients with kidney disease: consensus statements from the American College of Radiology and the National Kidney Foundation. *Radiology* 2020;294:660-8.
  9. Kirsch J, Brown RKJ, Henry TS, et al. ACR Appropriateness Criteria acute chest pain-suspected pulmonary embolism. *J Am Coll Radiol* 2017;14:5S:S2-S12.
  10. Hinson JS, Ehmman MR, Fine DM, et al. Risk of acute kidney injury after intravenous contrast media administration. *Ann Emerg Med* 2017;69(5):577-586.e4.
  11. Su T-H, Hsieh C-H, Chan Y-L, et al. Intravenous CT contrast media and acute kidney injury: a multicenter emergency department-based study. *Radiology* 2021;301:571-81.
  12. Davenport MS, Khalatbari S, Cohan RH, Dillman JR, Myles JD, Ellis JH. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: risk stratification by using estimated glomerular filtration rate. *Radiology* 2013;268:719-28.
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