

Consequences of Medical Overuse

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Case Objectives

- Define overuse and overdiagnosis.
- State how much of all care is estimated to be overuse.
- Describe why the likelihood of disease in a particular patient affects the interpretation of diagnostic test results.
- Discuss approaches to limiting overuse in medical care.
- List domains in medicine where overdiagnosis occurs.

The Case

A 76-year-old woman with history of hypertension, diabetes, and advanced dementia was brought to the emergency department (ED) from a nursing facility with confusion and generalized weakness. Based on her initial evaluation, she was diagnosed with a urinary tract infection and started on antibiotics in the ED. As part of this evaluation, she was found to have a mildly elevated troponin I level (0.10 $\mu\text{g/mL}$; normal is $< 0.07 \mu\text{g/mL}$). Her electrocardiogram (ECG) was unchanged from her baseline and showed no evidence of ischemia. She did not complain of chest pain or shortness of breath.

The hospitalist admitting the patient consulted a cardiologist for evaluation of the elevated troponin levels. The cardiologist recommended starting aspirin, clopidogrel, and heparin for treatment of possible non-ST-elevation myocardial infarction (NSTEMI). The hospitalist wondered if this was overly aggressive treatment for the elevated troponin but followed the specialist's recommendations.

The following day, the patient remained confused. Her troponin level rose to 0.13 $\mu\text{g/mL}$ and was 0.12 $\mu\text{g/mL}$ on repeat. Her ECG continued to show no evidence of myocardial ischemia. At the recommendation of the cardiologist, the aspirin, clopidogrel, and heparin were all continued.

That evening, the patient became acutely confused. A computed tomography scan of the head revealed a large intraparenchymal hemorrhage with midline shift. She was placed on a mechanical ventilator and transferred to the intensive care unit. Given the bleeding, the heparin, aspirin, and clopidogrel were

discontinued. Unfortunately, despite aggressive treatment, she developed evidence of cerebral herniation and became comatose. After discussions with the family, the patient was transitioned to comfort measures and she died a few hours later.

The root cause analysis of this adverse event determined that treatment with three anticoagulants was not clinically indicated as the patient did not have objective evidence of an NSTEMI. The committee believed the overly aggressive treatment had led to the patient's death.

The Commentary

by Daniel J. Morgan, MD, MS, and Andrew Foy, MD

This case represents a common medical scenario. An older woman was transferred from a nursing facility to the hospital with confusion and generalized weakness. For such a patient, polypharmacy, infection, or worsening of her underlying dementia are the most likely causes. She was diagnosed with a urinary tract infection (UTI) on initial evaluation and started on antibiotics. A troponin, ordered as part of the initial evaluation, was found to be above the normal limit and cardiology was consulted.

Before addressing the cardiology aspects of this case, it is worth noting that this patient may have received overly aggressive treatment for the presumed UTI. Specifically, it is possible that she received unnecessary antibiotics for asymptomatic bacteriuria (bacteria in the urine without actual infection of the urinary tract). Weakness and confusion in a patient with advanced dementia are highly nonspecific, and UTI, as a clinical diagnosis, requires symptoms. The patient did not present with any complaints of urinary symptoms or documentation of a fever, abdominal tenderness, or flank pain. (Of course, the dementia may have limited the patient's ability to complain about urinary symptoms.) Urinalysis and urine culture are positive in up to half of all nursing home patients, making asymptomatic bacteriuria the most common reason for overuse of antibiotics in nursing homes.⁽¹⁾ In a different M&M, we could be discussing the common overuse of antibiotics and the known complications including *Clostridium difficile* infection and adverse drug reactions. However, in this commentary, we will consider why this elderly patient received overly aggressive cardiac care and experienced an adverse event.

We must first ask why a troponin level was drawn when the patient had no signs or symptoms of myocardial ischemia. There are several possibilities. One reason is that laboratory tests are sometimes ordered as part of the triage process before the patient is even assessed by a clinician. Another reason is that troponin is often included in routine workups or screening testing in the emergency department (ED). Many providers use it as a differentiating tool, in the absence of an appropriate history and physical, hoping it will provide a diagnosis. The overordering of the troponin test is exacerbated by the fear of missing myocardial infarction (MI) in the ED and the mistaken notion that MI can present with virtually any constellation of symptoms. All of these indications for troponin testing are inappropriate and represent a form of medical overuse.⁽²⁾

Overuse is the provision of care that is more harmful than beneficial and has no benefits or for which a fully informed patient would decide against.⁽³⁾ Overuse includes both overdiagnosis and overtreatment. Over one year of care, most patients will experience overuse, and up to one third of all care appears to represent

overuse.(3,4)

Turning specifically to the troponin, one study reported that of 44,448 ED visits in the United States in 2009 and 2010, troponin was tested in approximately 17% of the visits (representing 28.6 million visits).(2) Among individuals who were subsequently hospitalized, troponin was tested in 47% of patients; it was even tested in 35% of visits *without* MI-related symptoms.(2) Similar results were reported from the United Kingdom.(5) Many patients inappropriately tested for troponin were also inappropriately started on an acute coronary syndrome protocol.(5) In a patient without signs or symptoms of an MI, an elevated troponin is likely due to other factors including myonecrosis from any number of causes, renal failure, or laboratory error.(6) There is limited evidence that a nonspecific elevation in troponin portends a worse prognosis, although the clinical usefulness of this information is uncertain.

In this case, the patient had no signs or symptoms consistent with an MI. (Again, we recognize that the history may have been limited by the dementia, but one would still expect some evidence of chest pain or other relevant symptoms.) The troponin was drawn inappropriately and found to be slightly elevated. We believe that the elevated value should have been ignored, but it wasn't.

The ordering and interpretation of diagnostic tests in everyday medical decision making is seemingly simple, but riddled with error in actual practice. One of the most common errors that can lead to overtreatment is ordering diagnostic tests in patients with a low likelihood of the disease for which the test is being ordered. Such patients are more likely to have false positive than true positive results—even when highly specific tests, like troponin, are used. The pretest probability (i.e., likelihood) that a patient with confusion and weakness, without chest pain or dyspnea, with normal vital signs, and a nonischemic ECG is having an acute MI is essentially zero. Myocardial infarction is a clinical diagnosis—according to the Universal Definition, "the term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia."(7)

This problem with false positive test results can be demonstrated using a simple example. Consider a population of 100 patients whose pretest odds of MI are 0%. The sensitivity of elevated troponin for MI is 100% and specificity is 95%; therefore, the troponin test has a 5% false positive rate. In these 100 patients, there would be 5 positive tests, and in this patient population, all 5 positive tests would be false positives. In this example, since the pretest probability of MI is very low, the positive predictive value of an elevated troponin for MI is 0% despite the high sensitivity and specificity of this test.

In general, physicians perform poorly at such test interpretation. In 1978, Harvard medical students, residents, and attending physicians were asked the following question: "If a test to detect a disease whose prevalence is 1/1000 has a false positive rate of 5%, what is the chance that a person found to have a positive result actually has the disease, assuming you know nothing about the person's symptoms or signs?" The correct answer is approximately 2%. Only 23% answered correctly; 44% believed a positive test meant the disease was 95% likely.(8) Amazingly, this same research study was performed 40 years later, at the same institution, with nearly identical results.(9)

Physicians, like most people, simply aren't good at considering probabilities in their reasoning. For many, it is an unnatural process, and some have speculated that human brains simply aren't adapted for it.(10) Most physicians continue to provide effective and high-quality care by using heuristics. Remembering

common illness scripts is a type of heuristic—for example, remembering the association between long flights and venous thromboembolism or that Lyme disease is associated with tick bites in New England. However, these simple shortcuts can lead to faulty reasoning or conclusions.⁽¹¹⁾ In particular, when illness scripts haven't caught up to newer diagnostic testing modalities, physicians tend to interpret the results too simplistically (e.g., elevated troponin = MI). Because of this, improving medical education, with an emphasis on developing probabilistic reasoning skills, is key to curbing overuse and its attendant consequences.

Other approaches to limiting overuse include audit and feedback and the use of decision support tools. A large pragmatic trial of primary care physicians found that use of accountable justification (providers had to enter free-text justifications for prescribing antibiotics) and peer comparison resulted in lower rates of inappropriate antibiotic prescribing for acute respiratory tract infections.⁽¹²⁾ Using a quasi-experimental study design, Kassakian and colleagues found that red blood cell transfusion rates decreased from 9.4 to 7.8 per 100 patient days after a decision support tool was implemented.⁽¹³⁾

Returning to the case in question, many patients with non-MI-related troponin elevations are misdiagnosed and started on treatment for MI. These treatments are costly, prolong hospital length of stay, and often are continued as an outpatient.⁽⁵⁾ At worst, they can have devastating consequences, as in the patient reported here.

The distinction between misdiagnosis and overdiagnosis depends on the definition of the condition under consideration. *Overdiagnosis* refers to the diagnosis of a medical condition that would not harm the patient if left undetected. Cancer is a histopathologic diagnosis with a spectrum of manifestations, including being asymptomatic. Thus, it is particularly susceptible to overdiagnosis since it may grow slowly, not at all, or even regress.⁽¹⁴⁾ Overdiagnosis may occur in breast cancer, lung cancer, and prostate cancer, to name a few.⁽¹⁴⁾ Detection and treatment of these cancers, which in most cases are found incidentally or as part of screening protocols, are unlikely to benefit the patient and may be harmful owing to unnecessary therapy.

There are multiple examples of overdiagnosis in the field of cardiovascular medicine. The detection of incidental coronary artery disease (CAD) in patients without functional myocardial ischemia is one example.⁽¹⁵⁾ Despite the fact that atherosclerosis and its correlates, like coronary artery calcium, may be associated with an increased risk of cardiac events, knowing this information does not lead to management changes that improve patient outcomes.⁽¹⁶⁾

In one randomized trial, nearly 70% of diabetic patients without symptoms who underwent screening with coronary computed tomography angiography were found to have at least mild CAD. Management changes were made based on these results.⁽¹⁶⁾ Despite this, there was no difference in the composite primary endpoint of mortality, nonfatal MI, or unstable angina over 4 years of follow-up compared to standard care.⁽¹⁶⁾

Anticoagulants are a dangerous form of therapy. One study found that major bleeding developed in 61 of 1011 patients (6%) started on anticoagulant therapy before hospital discharge.⁽¹⁷⁾ The risk of bleeding is greater in a population of patients, like the one in this case, who are older, frail, and also being treated with dual antiplatelet therapy.⁽¹⁸⁾ Thus, starting a patient on this combination of medicines is not a trivial decision and can have disastrous consequences.

Overuse often results from a cascade of events. Here we see how one inappropriately ordered test led to a chain of overuse. As discussed, troponin was ordered unnecessarily, the result was mildly abnormal and misinterpreted. This was followed by several more unnecessary troponins. It also led to an unnecessary cardiology consult. The patient was then started on a combination of dual antiplatelet and anticoagulation therapy, which was also unnecessary and led to her death.

Had this catastrophic outcome not occurred, the patient would have likely undergone one or more unnecessary cardiology tests—echocardiography, stress test, perhaps even cardiac catheterization. And maybe one or more of these tests would have detected an incidental abnormality, which would have led to more testing and treatment. For example, a stress test may have been abnormal or her cardiac catheterization may have demonstrated obstructive CAD. Given her age, this would not be a surprising finding. But it would have represented further overdiagnosis, and she may have received a stent and been started on more medications for secondary prevention.

We don't know exactly what would have happened to this patient if she was admitted to the hospital and treated in a conservative fashion. The patient might have received hydration and physical therapy, and perhaps the providers could have removed any unnecessary medications. There is a great deal of uncertainty in clinical medicine with frail patients near the end of life.⁽¹⁹⁾ She likely would have returned to her nursing home with a diagnosis of worsening dementia and potentially with greater clarity on the part of her family regarding the need to articulate her goals of care. This case of patient death due to overly aggressive care should be as salient to providers as those cases where a patient was saved through medical care.

Take-Home Points

- In patients whose pretest probability of a disease is low, a positive test result for that disease is likely to be a false positive.
- Troponin testing should be reserved for patients with signs and symptoms consistent with myocardial ischemia.
- In patients *without* signs or symptoms of myocardial ischemia, an abnormal troponin does not diagnose acute myocardial infarction.
- Anticoagulation is a dangerous form of therapy and should be used only when the chance of benefit outweighs the chance of harm.
- Overuse is common and physicians should be on the lookout for it in their practice.
- Decreasing the amount of overuse will require better education of clinicians in probabilistic thinking and the use of computerized and other types of decision support tools.

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