Case Report – Lessons in Clinical Reasoning

McCall Walker, Karen M. Warburton, Joseph Rencic and Andrew S. Parsons*

Lessons in clinical reasoning – pitfalls, myths, and pearls: a case of chest pain and shortness of breath

https://doi.org/10.1515/dx-2019-0030
Received April 9, 2019; accepted June 10, 2019; previously published online July 20, 2019

Abstract

Background: Defects in human cognition commonly result in clinical reasoning failures that can lead to diagnostic errors. A metacognitive structured reflection on what clinical findings fit and/or do not fit with likely and "can't miss" diagnoses may reduce such errors.
Case presentation: A 57-year-old man was sent to the emergency department from clinic with chest pain, severe shortness of breath, weakness, and cold sweats. Further investigation revealed multiple risk factors for coronary artery disease, sudden onset of exertional dyspnea, and chest pain that incompletely resolved with rest, mild tachycardia and hypoxia, an abnormal electrocardiogram (ECG), elevated serum cardiac biomarkers, and elevated B-type natriuretic peptide (BNP) in the absence of left-sided heart failure. He was treated for acute coronary syndrome (ACS), discharged, and quickly returned with worsening symptoms that eventually led to a diagnosis of submassive pulmonary embolism (PE).
Conclusions: Through integrated commentary on the diagnostic reasoning process from clinical reasoning experts at two institutions, this case underscores the importance of frequent assessment of fit along with explicit explanation of dissonant features in order to avoid premature closure and diagnostic error. A fishbone diagram is provided to visually demonstrate the major factors that contributed to the diagnostic error. A case discussant describes the importance of diagnostic schema as an analytic reasoning strategy to assist in the creation of a differential diagnosis, problem representation to summarize updated findings, a Popperian analytic approach of attempting to falsify less-likely hypotheses, and matching pertinent positives and negatives to previously learned illness scripts. Finally, this case provides clinical teaching points in addition to a pitfall, myth, and pearl specific to premature closure.

Keywords: assessment of fit; clinical reasoning; cognitive dissonance; diagnostic schema; illness script; problem representation; pulmonary embolism.

***Corresponding author: Andrew S. Parsons,** University of Virginia, Department of Medicine, 1215 Lee Street, Charlottesville, VA 22903-1738, USA, Phone: +4236201398, E-mail: ASP5C@hscmail.mcc.virginia.edu
McCall Walker and Karen M. Warburton: University of Virginia, Department of Medicine, Charlottesville, USA, E-mail: MRW4W@virginia.edu (M. Walker); KMW2G@virginia.edu (K. M. Warburton)
Joseph Rencic: Tufts Medical Center, Department of Medicine, Boston, MA, USA, E-mail: jrencic@tuftsmedicalcenter.org

Summary

A 57-year-old man was sent to the emergency department from clinic with chest pain, severe shortness of breath, weakness, and "cold sweats".

The combination of chest pain and severe shortness of breath brings to mind several possibilities. It is reasonable to begin by considering life-threatening diagnoses, including acute coronary syndrome (ACS), pulmonary embolism (PE), aortic dissection, and pneumothorax. We need additional historical details to distinguish between the myriad conditions that can present with chest pain and shortness of breath. The weakness adds an interesting dimension. Patients often present with asthenia when ill, and it will be important to characterize whether this patient's subjective weakness has an objective correlate on physical examination. Finally, the diaphoresis is a nonspecific symptom that does not aid in narrowing the differential diagnosis.

The discussant demonstrates effective use of diagnostic schema in her initial reasoning. Diagnostic schema are problem-specific, analytic reasoning strategies that can serve as powerful mnemonics for differential diagnoses. They can also act as disease checklists; they make clinicians slow down and consciously rule in or out the diseases or disease categories highlighted in the schema. The discussant immediately activates her chest pain, "worst-case scenario" schema.

The day of admission, he was walking up a hill and experienced a non-radiating, dull, substernal chest pain associated with dyspnea, diaphoresis, a "fatigued" fee ling, and a "total body weakness". He went to his truck to rest, which only partially relieved the pain. After several minutes, he tried walking again but the chest pain and dyspnea immediately recurred. This unusual episode worried him so he presented to clinic for evaluation. He recalled intermittent episodes of chest tightness with exertion the previous winter that lasted for seconds and resolved spontaneously. He denied any other prior chest pain or dyspnea, as well as any orthopnea, paroxysmal nocturnal dyspnea, or swelling/pain in his legs. He denied any recent fevers or chills. He had a past medical history of diet/exercise-controlled hypertension and hypercholesterolemia. He took no medications. His past surgical history included bilateral carpal tunnel release. He had no significant family history. He is a never-smoker, drank alcohol socially a few times per year, and denied prior illicit drug use.

The chest pain occurred fairly suddenly in the setting of exertion, and failed to completely resolve with rest. The associated sudden-onset exertional dyspnea remains a prominent feature of the presentation with no preceding history. The weakness is described as a generalized sense of feeling fatigued. The differential diagnosis remains broad, and it is reasonable to begin again with our four "can't miss" diagnoses before considering other, less immediately life-threatening conditions such as pneumonia, obstructive lung disease, pericardial or pleural disease, heart failure, esophageal or mediastinal disease, and anxiety.

We must consider an ACS [comprising ST elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), and unstable angina] which typically occurs following atherosclerotic plaque rupture and resultant thrombus formation, or vasospasm, of the coronary arteries. The patient has risk factors for coronary artery disease, including age, hypertension, and dyslipidemia. ACS-related chest pain often presents with dyspnea, malaise, and diaphoresis, and can be exertional. Pain that lasts for seconds, as described by the patient in the preceding winter, is atypical for ACS. Acute or subacute PE, with its variable and nonspecific presentation, can be an elusive diagnosis and needs to be considered here. We are not given any clear risk factors for PE, such as endothelial injury, hypercoagulability, or immobility, although these are not always immediately obvious on presentation. Chest pain with PE can be acute, dull, substernal, and exertional. PE often causes sudden onset dyspnea, as is described in this case, and may not resolve completely with rest. Acute aortic dissection is a less common, but potentially life-threatening, cause of chest pain that typically occurs in patients older than ours with an antecedent history of hypertension, or in younger patients with history of trauma or collagen disorders, neither of which our patient is known to have. The pain can vary in location and quality but is typically experienced acutely and described as sharp or tearing, sometimes with radiation to the back. Finally, spontaneous pneumothorax seems less likely given the patient's age > 40, the absence of risk factors including smoking, family history, and collagen diseases, and the fact that most patients with pneumothorax present with chest pain at rest.

Initial evaluation of this patient in the emergency department should include an assessment of hemodynamic stability, oxygenation, physical examination, serial electrocardiogram(ECG), troponin measurements, chest radiograph, D-dimer, and toxicology screen.

The discussant again calls upon the "worst-case scenario" diagnostic schema to make sense of the case but now applies her knowledge of illness scripts to narrow the differential diagnosis. Illness scripts are clinicians' idiosyncratic mental representations of diseases and consist of key information such as the base-rates of diseases (i.e. "common things being common") as well as absolute and relative values of clinical and epidemiologic findings in increasing or decreasing the likelihood of a given disease. She demonstrates a Popperian scientific/analytic approach of attempting to "falsify" (i.e. prove unlikely) several hypotheses by illustrating that the patient's presentation fails to match her illness scripts for aortic dissection and pneumothorax [1]. *By eliminating hypotheses, the likelihood of remaining diseases increases.*

In the emergency department, he appeared anxious and repeatedly stated "I do not feel well". His initial blood pressure was 147/90, pulse 102, temperature 36.7, oxygen saturation on room air was 92%, and he was breathing 18 times per minute. On exam, jugular venous pressure was not elevated. Precordial auscultation revealed tachycardia with a regular rhythm, a normal S1 and S2, and the absence of murmurs, rubs or gallops. Radial and dorsalis pedis pulses were 2+ bilaterally. Lung exam demonstrated slightly increased work of breathing without accessory muscle use, but was otherwise normal. His abdominal examination was benign. The lower extremities lacked edema. There were no neurologic deficits. The patient became dyspneic after walking only a few steps and had to sit down. A 12-lead ECG showed sinus tachycardia with T wave flattening in leads V2–V4 and occasional premature ventricular contractions.

The subjective perception of anxiety and feeling unwell is nonspecific but is consistent with previously mentioned diagnoses. The patient is not hypotensive but exhibits mild resting tachycardia and hypoxia in the absence of fever. Examination reveals many pertinent negatives, including no signs of right- or left-sided heart failure, pulmonary consolidation or effusion, pericardial or pleural inflammation, valvular heart disease, pulse deficit, peripheral vasoconstriction, or objective neurologic deficits. The ECG is abnormal, but nonspecific, and does not

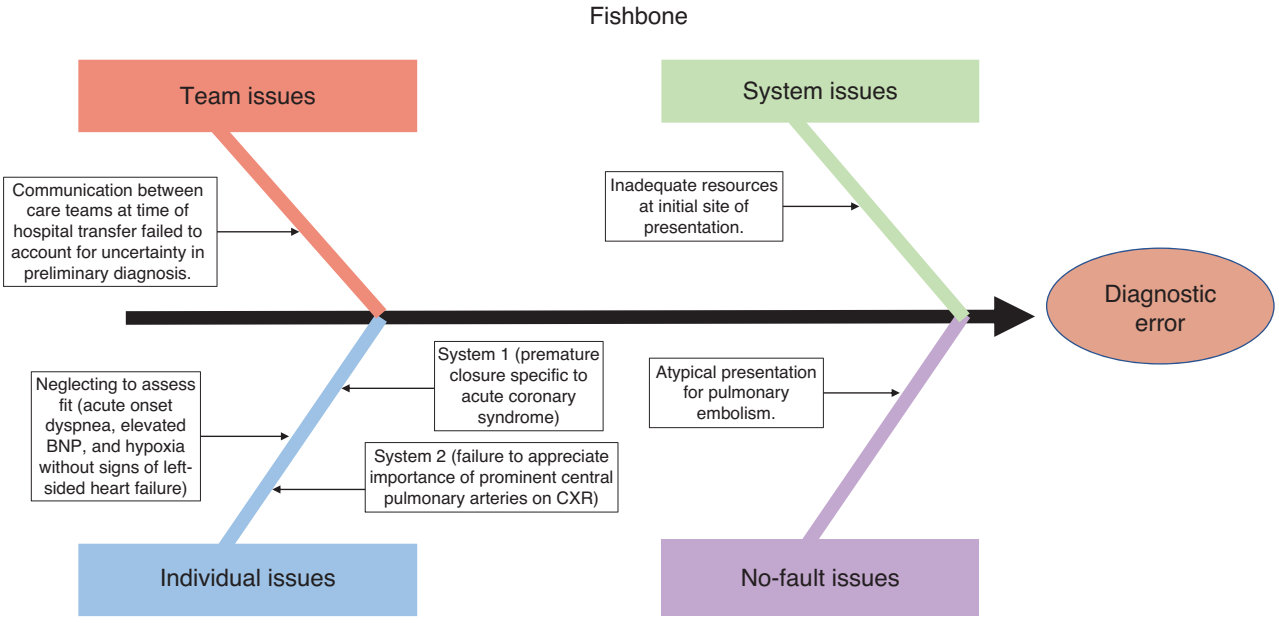

Figure 1: A Fishbone diagram demonstrating the major factors that contributed to the diagnostic error [2].

reveal a STEMI. T wave flattening can be seen in many of the conditions being considered such as NSTEMI or PE.

The discussant focuses on pertinent positives and negatives, attempting to match each finding with previously learned illness scripts. This search for a recognizable pattern is a hallmark of system 1 thinking. Dual process theory describes two systems that account for how a physician thinks when reasoning through a clinical case. System 1 is intuitive, efficient, and based on pattern recognition. System 2 is analytical, deliberate, and time-intensive. In this case, as in reality, the clinician actively toggles back and forth between both systems to promote problem-solving. As new information is obtained, the discussant attempts to update disease probabilities and reprioritize the differential diagnosis (Figure 1).

The white blood cell count was 8600 mm/dL with an unremarkable differential. The hemoglobin was 15.2 g/dL and the platelet count was 215,000 g/dL. The serum sodium was 135 mg/dL, potassium was 4 mg/dL, chloride was 99 mg/dL, and bicarbonate was 21 mg/dL. The blood urea nitrogen was 10 mg/dL and the creatinine was 0.86 mg/dL. Magnesium, calcium, and transaminases were within normal limits. Thyroid-stimulating hormone (TSH) was within the normal limits. B-type natriuretic peptide (BNP) was elevated to 2384 pg/mL and troponin I was elevated to 0.7 ng/mL initially, with subsequent values elevated to 1.12 and 0.64 ng/mL, respectively. Chest radiograph was normal. Neither an arterial blood gas nor a D-dimer was initially obtained.

His vital signs remained stable in the emergency department with a repeat blood pressure of 136/88, pulse of 100, and respiratory rate of 18 with an oxygen saturation of 94% on room air. He remained afebrile. He was given 325 mg of aspirin to chew. One inch of nitroglycerin paste was applied to the patient's chest, but his chest pain had already dissipated. He was admitted to the cardiology floor on telemetry. He was given clopidogrel 600 mg once and started on enoxaparin at 1 mg/kg, metoprolol tartrate 50 mg twice daily, rosuvastatin 20 mg daily, and losartan 25 mg daily. Over subsequent hours, he remained chest pain-free and serial ECGs were unchanged. He was transferred to a quaternary-care hospital with cardiac catheterization capabilities.

To summarize, this is a 57-year-old male with risk factors for coronary artery disease who presents with the sudden onset of exertional dyspnea and chest pain that is incompletely resolved with rest, as well as mild tachycardia and hypoxia, abnormal ECG, elevated serum cardiac biomarkers, and elevated BNP in the absence of signs of left-sided heart failure on examination. The elevation in cardiac biomarkers, in the setting of normal or near-normal kidney function, suggests myocardial injury, either from acute coronary thrombosis or a mismatch between oxygen supply and demand. Fortunately, the degree of biomarker elevation, coupled with the fact that we have already seen the troponin peak, suggests that the myocardial damage is modest. Elevation in BNP, which is specific for ventricular myocardium, can occur in the absence of signs and symptoms of left-sided heart failure and predicts increased risk of death and heart failure. Although the presentation is consistent with acute coronary thrombosis, it is difficult to attribute the hypoxia, in the absence of signs and symptoms of left heart failure or a new right-to-left shunt, to ACS from plaque rupture. Myocardial injury from an oxygen supply and demand mismatch (type 2 NSTEMI), another possibility, can be seen in

many conditions, including shock, coronary vasospasm, aortic dissection, and arrhythmia. The patient's initial management suggests a strong suspicion for ACS. Unfortunately, most scoring systems for ACS, such as the Thrombolysis in Myocardial Infarction (TIMI) risk score, have limited utility here as a diagnostic tool, though they do provide valuable risk stratification. His TIMI risk score suggests that he is at low-intermediate risk of further cardiac events. Given the uncertainty of the underlying diagnosis, it is reasonable to heparinize the patient and treat with antiplatelet therapy as the team did. It is also important to rule out PE, which is a reasonable alternative diagnosis given the hypoxia.

The discussant forms a problem representation, a one-sentence summary that highlights the salient features of the case. An accurate and concise problem representation has three components: demographics, risk factors, and key symptoms and signs modified by semantic qualifiers to more accurately describe the nature of illness. If appropriate, the key signs and symptoms can be combined to describe a syndrome. When appropriately constructed, a problem representation will include discriminating features of the case and exclude non-specific findings in order to reduce cognitive load. It also allows the discussant to translate the patient's language into medical terminology that enables easier access to stored illness scripts. In this case, the discussant's problem representation highlights a prominent feature: significant hypoxia without an obvious cause.

At the quaternary-care hospital, he was continued on aspirin, clopidogrel, enoxaparin, metoprolol, and rosuvastatin. A repeat chest radiograph ordered for persistent exertional dyspnea was notable for mildly prominent hila bilaterally, thought to be due to prominent central pulmonary arteries versus adenopathy. The radiologist recommended a computed tomography scan with intravenous contrast for further clarification of these findings, but it was never completed as it was deemed not clinically indicated. Repeat basic laboratory tests demonstrated no significant changes from previous studies.

The next morning, a left-heart catheterization was performed. He was found to have non-obstructive coronary atherosclerosis with the most severe lesion documented as a 10% mid-right coronary artery lesion. Dual anti-platelet therapy and therapeutic anticoagulation were discontinued.

He subsequently underwent transthoracic echocardiography which demonstrated a normal echocardiogram with an ejection fraction of 60–65% and no wall motion abnormalities. Later that day, he ambulated with nursing through the hospital hallways without chest pain, dyspnea, or hypoxia. He felt well enough to go home, and he was discharged with close follow-up with his primary care physician and cardiology. Discharge diagnosis was "non-STEMI due to either plaque rupture event with resolution or secondary to cardiac dysrhythmia". He was continued on aspirin 81 mg daily, losartan 25 mg daily for mildly elevated blood pressure, and atorvastatin 80 mg daily (switched from rosuvastatin 20 mg daily from the previous hospital). Outpatient Holter monitoring was recommended for further evaluation of a potential cardiac dysrhythmia.

Prior to the left-heart catheterization, the patient undergoes a repeat chest radiograph which is notable for two things: clear lung fields, the most interesting finding, and mildly prominent hila bilaterally. This patient has dyspnea and hypoxia in the setting of what is essentially a clear chest radiograph. If this is a posterior-anterior (PA) film, the finding of bilateral hilar prominence is concerning for lymphadenopathy or bilateral enlargement of the pulmonary vessels. Neither of these radiographic findings fit with the diagnosis of ACS in the absence of left heart failure.

After the catheterization, the differential diagnosis remains type I NSTEMI from unstable, non-obstructive plaque, or type II NSTEMI due to coronary vasospasm, arrythmia, or hypoxia, although the latter seems too mild to have caused an NSTEMI. A mild myocarditis also cannot be ruled out, although it seems less likely.

The discharge diagnosis suggests that the NSTEMI may have been caused by arrhythmia. Certainly, sustained arrhythmia can cause demand ischemia and troponin elevation, but he has no structural heart disease or other risk factors, and telemetry demonstrated a normal heart rhythm during his hospitalization. Although we can explain many of his symptoms with an NSTEMI or possibly myocarditis, we still have no explanation for his transient, though significant, hypoxia. A D-dimer would be very helpful in guiding our decision regarding additional imaging of the chest, as was suggested by the radiologist who interpreted the chest radiograph. If the D-dimer is elevated, I would proceed with CT angiogram of the chest to rule out a PE, which would be a good way to tie together the clinical presentation.

As highlighted previously, the discussant created a concise and accurate problem representation in hopes of prompting relevant illness scripts. This is necessarily followed by an assessment of fit and coherence, checking each key feature of the case against the chosen script or scripts. The discussant's thought process illustrates the concept of cognitive dissonance, the uncomfortable feeling that arises when one or more pieces of information does not fit with the preferred illness script for a given clinical presentation. The most dissonant finding in this case is the significant hypoxia in the setting of a clear chest radiograph. Neglecting to assess fit can lead to premature closure – a type of cognitive error in which one does not consider alternative diagnoses once a preliminary diagnosis is made. Finally, the discussant proposes a new diagnostic test (D-dimer) in hopes of resolving this discord.

The day after discharge, the patient developed recurrent chest pain, shortness of breath, and diaphoresis as he was walking around his house. He again presented to an outside facility for these symptoms and was noted on arrival to have a new 4-L oxygen requirement to

keep his oxygen saturations above 90%. A repeat transthoracic echocardiogram was ordered at that time which revealed right heart strain with a dilated right ventricular cavity. He subsequently underwent computed tomography scan with intravenous contrast of the chest which revealed a "saddle" PE. Based on the evidence of right heart strain and lack of hemodynamic compromise, he was diagnosed with a submassive PE, was immediately started on therapeutic enoxaparin, and transferred to the same quaternary-care center for catheter-directed thrombolysis of his PE. Upon arrival, he underwent catheter-directed thrombolysis with tissue plasminogen activator. He was transitioned from therapeutic enoxaparin to apixaban for lifelong anticoagulation in the setting of his unprovoked deep venous thrombosis and life-threatening PE. He was transferred from the medical intensive care unit to the general medicine floor and was discharged the following day in stable condition.

The diagnosis of PE is now unifying in the sense that it explains the mildly prominent hila with clear lung fields seen on chest X-ray, troponin and BNP elevation, significant hypoxia, and non-specific ECG changes.

The fact that the patient was discharged and re-presented with similar symptoms highlights the complexity of this case from a clinical reasoning standpoint. Namely, the patient presented with some findings atypical of PE. This case underscores the importance of frequent assessment of fit along with explicit explanation of dissonant features in order to avoid premature closure and diagnostic error. A structured way to do this in clinical practice is to perform a diagnostic time out – a forced pause in the diagnostic process to ask what key data do not fit with the diagnosis such as hypoxia in the setting of a clear chest radiograph in this case and to generate an alternative diagnosis/es if unable to determine an explanation.

Clinical teaching points

1. Non-pleuritic chest pain occurs in only 17% of patients diagnosed with PE [3]. Additional atypical symptoms of PE include syncope (10%), abdominal pain (6.7%), and seizure (rare) [4, 5]. Shortness of breath, tachypnea, and oxygen desaturation are typical, occurring in roughly 92% of patients diagnosed with PEs [6].
2. The modified Wells Rule and the Pulmonary Embolism Rule-out Criteria (PERC) are validated methods to help stratify patients into a low-risk category or to help rule out the diagnosis. However, these scoring systems should be used cautiously in atypical presentations of PE, when PE is not the primary diagnosis, or if there is already a moderate-to-high suspicion for PE [7, 8].
3. Biomarkers such as troponin, D-dimer, and BNP are commonly elevated in PE and can be misleading. In two studies, the sensitivity and specificity of an elevated troponin I in patients with PE were 50.7% and 88.3%, respectively [9], and 99.5% and 41%, respectively, for D-dimer [10]. Elevated BNP has been identified as a predictor of adverse outcomes in patients diagnosed with PE, with a pro-BNP cut-off value of 600 pg mL^{-1} corresponding to a sensitivity of 86% and a specificity of 50% for PE-related death or complication [11].

Pitfall: "Confirmation bias is a commonly committed cognitive error in which the clinician searches for supportive information in preference to conflicting information when making a decision in a manner that confirms preexisting hypotheses [12]".

Myth: "Knowing about biases will help prevent the next one [13]". Kahneman has pointed out that, as part of our intuition, cognitive biases are so ingrained that we cannot train ourselves to act otherwise [14]. But, this is somewhat controversial as knowing about cognitive biases may help you, or others, recognize instances where biased cognition has come into play in time to intervene and make a better decision. There are also many interventions that could improve diagnosis (teamwork, reflection, using decision support) that are based on the premise that our intuitive decisions can be improved by invoking "System 2" and input from others.

Pearl: "Diagnostic timeouts are forced pauses in the diagnostic process that allow for metacognition ('thinking about one's own thinking')". A metacognitive structured reflection on what clinical findings fit and/or do not fit with likely and "can't miss" diagnoses may reduce diagnostic error by revealing findings that decrease the likelihood of the working diagnosis leading to further diagnostic evaluation [15].

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.
Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.
Ethical approval/informed consent: Not applicable.

References

1. Popper K. The Logic of Scientific Discovery. Print. Abingdon-on-Thames, 1934 in German, 1959 in English. 513 pages.
2. Reilly JB, Myers JS, Salvador D, Trowbridge RL. Use of a novel, modified fishbone diagram to analyze diagnostic errors. Diagnosis. 2014;1:167–71
3. Stein PD, Beemath A, Matta F, Weg JG, Yusen RD, Hales CA, et al. Clinical characteristics of patients with acute pulmonary embolism. Am J Med 2007;120:871–9.
4. Gantner J, Keffeler JE, Derr C. Pulmonary embolism: an abdominal pain masquerader. J Emerg Trauma Shock 2013;6:280–2.
5. Altınsoy B, Erboy F, Tanrıverdi H, Uygur F, Örnek T, Atalay F, et al. Syncope as a presentation of acute pulmonary embolism. Ther Clin Risk Manag 2016;12:1023–8.
6. Majidi A, Mahmoodi S, Baratloo A, Mirbaha S. Atypical presentation of massive pulmonary embolism: a case report. Emergency 2014;2:46–7.
7. Douma RA, Gibson NS, Gerdes VE, Büller HR, Wells PS, Perrier A, et al. Validity and clinical utility of the simplified Wells rule for assessing clinical probability for the exclusion of pulmonary embolism. Thromb Haemost 2009;101:197–200.
8. Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. J Thromb Haemost 2004;2:1247–55.
9. Kilinc G, Dogan OT, Berk S, Epozturk K, Ozsahin SL, Akkurt I. Significance of serum cardiac troponin I levels in pulmonary embolism. J Thorac Dis 2012;4:588–93.
10. Perrier A, Desmarais S, Goehring C, de Moerloose P, Morabia A, Unger PF, et al. D-dimer testing for suspected pulmonary embolism in outpatients. Am J Respir Crit Care Med 1997;156(2 Pt 1):492–6.
11. Lankeit M, Jiménez D, Kostrubiec M, Dellas C, Kuhnert K, Hasenfuß G, et al. Validation of N-terminal pro-brain natriuretic peptide cut-off values for risk stratification of pulmonary embolism. Eur Respir J 2014;43:1669–77.
12. Schulz-Hardt S, Frey D, Lüthgens C, Moscovici S. Biased information search in group decision making. J Pers Soc Psychol 2000;78:655–69.
13. Norman GR, Monteiro SD, Sherbino J, Ilgen JS, Schmidt HG, Mamede S. The causes of errors in clinical reasoning: cognitive biases, knowledge deficits, and dual process thinking. Acad Med 2017;92:23–30.
14. Kahneman D, Tversky A. On the reality of cognitive illusions. Psychol Rev 1996;103:582–91.
15. Mamede S, Schmidt HG, Rikers RM, Custers EJ, Splinter TA, van Saase JL. Conscious thought beats deliberation without attention in diagnostic decision-making: at least when you are an expert. Psychol Res 2010;74:586–92.