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Opinion Article

IN PULMONARY EMBOLISM AN INTERPRETATION OF SYSTOLIC BLOOD PRESSURE, TROPONIN (AND OTHER IMPORTANT PARAMETERS) DEPENDS ON THEIR PREVIOUS VALUES AND COMORBIDITIES

Goran Koraćević[1,2], Milan Đorđević[3*]

[1]Department for Cardiovascular Diseases, Clinical Center Niš, Serbia
[2]Faculty of Medicine, University of Niš, Serbia
[3]Emergency Medical Service, Health Center Jagodina, Serbia

Abstract. *We reviewed several important parameters in pulmonary thromboembolism (PTE) and showed how not only absolute values but also relative are relevant in clinical practice. The vast majority of parameters depend both on previous values and co-morbidities; failure to realize this can result in misclassification of a patient and inappropriate treatment. For example, the absolute value of systolic blood pressure (BP) less than 90 mmHg is crucial for urgent treatment (e.g. thrombolysis); obviously, the same admission systolic BP (sBP) of 87 mmHg may not have the same significance if previous usual sBP was also 87 mmHg or it was 220 mmHg. Moreover, cardiac troponin is also very important for the risk stratification; the same troponin concentration ought not to be interpreted equally if it is due to acute pulmonary thromboembolism or if it is chronic and due to e.g. renal failure. The interpretation of important dichotomous parameters (normal or pathologic values) in PTE does depend on previous values (if available) and co-morbidities. This principle should be recognized and used in clinical practice, while risk-stratifying patients.*

Key words: Pulmonary thromboembolism, blood pressure, troponin, right ventricle strain, d-dimer

In addition to the patient's data, medical knowledge, and common sense, at least three aspects are certain for the evaluation of an individual patient: 1) in real life, the situation is far more complex (as opposed to books and guidelines); 2) the result of every single measurement is dynamic (in time), and 3) as a rule, the result of the measurement depends (sometimes dominantly) on the related factors.

Let us start with one of the key measurements in pulmonary thromboembolism (PTE): *the **blood pressure** (BP).* In addition to ongoing/very recent resuscitation, low systolic BP (sBP) (<90 mmHg) -with or without shock- is crucial in PTE to classify the patient as having a high risk with probable consequent administration of a thrombolytic (or proceeding to percutaneous/ surgical intervention) [1]. For the borderline sBP it is difficult to decide if it represents hypotension or not and if PTE is its single cause. Some of the reasons for this difficulty are: sBP is frequently unequal on left versus right arm and it depends on the proper measurement (how adequate dimensions of the cuff are and how tight it is placed, etc.). Moreover, sBP can change e.g. for ± 5 mmHg in a couple of minutes. Additionally, for a patient with PTE with sBP 87 mmHg on presentation, the usual sBP for months before the hospitalization may have been A) 87 mmHg (then 87 mmHg on admission is the patient's typical value, without any BP drop due to PTE) or B) 180 mmHg (then 87 mmHg on admission is approximately half of the usual value; it is likely profound hypotension (possibly PTE-induced) and it raises suspicion on shock) (Figure 1).

Correspondence to: Milan Đorđević
Emergency Medical Service, Health Center Jagodina, Serbia
E-mail: milan_mdj@hotmail.com
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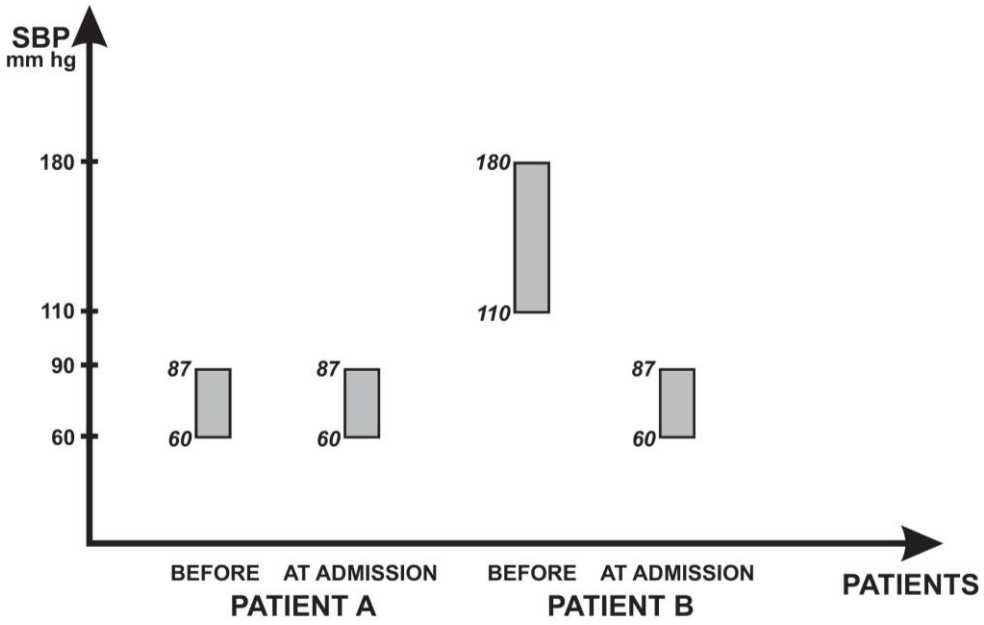

Fig. 1 SBP systolic blood pressure

Shock is easier to recognize as compared to hypotension, and hypotension itself, even without shock is a marker of high risk in PTE and consecutively it speaks in favour of thrombolytic treatment. What we suggest is what is considered in everyday practice: *to include a relative aspect in the interpretation of the absolute values.*

Similarly, the correct classification of non-high risk PTE patients requires ***troponin***. Troponin is very important, but far from specific for PTE – apart from the crucial cause (acute myocardial infarction), the increased troponin concentration may be a consequence of numerous diseases, such as stroke, subarachnoid hemorrhage, chronic kidney disease, infectious disease, etc [2]. Many of the causes of elevated troponin are chronic, for example, chronic renal failure (CRF) [2,3]. As many as 33–43% of patients with CRF may have increased troponin concentration [4].

If a patient with CRF and chronic troponin elevation experience an acute venous thromboembolism (VTE), his/her troponin elevation may be misinterpreted as a result of this acute VTE event which could lead to misclassification. Therefore, if the cause of increased troponin in a patient with PTE is concomitant chronic heart or renal failure, it may be misleading for a physician to classify the patient as having intermediate-high risk PTE, according to the latest 2019 European Society of Cardiology (ESC) PTE guidelines [1,2]. In order to avoid such fault we may make it more precise by stating: "increased cardiac troponin concentration in plasma, provided it is not due to other causes, such a renal failure". This would be completely in line with the statement about hypotension in the recent ESC guidelines for acute PE, where the experts exclude other prevalent causes of low BP aiming to underline the importance of hypotension which results from PE itself [1].

The similar situation is also true for N terminal-pro brain natriuretic peptide ***(NT-proBNP) / BNP***. Many non-cardiac conditions are capable of increasing their concentrations, such as advancing age, anemia, renal failure, obstructive sleep apnea, severe pneumonia, etc [5]. As with troponin, NT-proBNP / BNP elevation may be due to some of the other mentioned causes and present before the actual VTE event carrying the opportunity to be inadequately interpreted as caused by PTE; such misinterpretation could lead to higher patient's risk perceived by physician. Therefore, abnormalities of numerous parameters, which are used for the risk stratification of PTE, have the additional potential causes and can be chronic. The

interpretation of a few other parameters also depends on previous values and comorbidities. For example, ***heart rate (HR)*** ≥ 110 beats per minute (bpm) is an important part of the original and simplified Pulmonary Embolism Severity Index (PESI) and it carries the most points (+30) following the altered mental status (+60 points) [1]. HR depends on the rhythm: in atrial fibrillation (AF), HR is usually higher. Therefore, it is easier for AF patients to "achieve" the HR ≥ 110 bpm with the same severity of PTE. This is a very good example of the influence of chronic disorder (co-morbidity) upon a parameter used for risk stratification.

Similarly, interpretation of the imaging parameters of the ***right ventricle (RV) strain*** (obtained by echocardiography and/or by computed tomography pulmonary angiography, *CTPA*) is also determined by the previous measures (and is frequently influenced by the co-occurrence of pulmonary and heart disease). ***D-dimer*** may also be increased due to numerous causes, such as bleeding, thrombosis [venous, including VTE and risk factors for it; arterial e.g., AMI, stroke, peripheral artery disease; microvascular thrombosis and intravascular thrombosis (disseminated intravascular coagulation – DIC, thrombosis due to foreign material, such as catheters, pacemakers, artificial valves); aortic dissection, other cardiologic diseases (e.g., AF, left ventricle aneurysm, heart failure, thrombus in the heart) as well as kidney and hepatic diseases and false positives] [6].

Therefore, the vast majority (if not all) parameters in PTE depend both on previous values and comorbidities; failure to realize this can result in misclassification of a patient and inappropriate treatment. Indeed, there is a positive example of "putting in the context" of previous status and comorbidities: it is stated in guidelines that *"*obstructive shock (systolic BP <90 mmHg or vasopressors required to achieve a BP ≥ 90 mmHg *despite an adequate filling status*…)*"* is mandatory for one of the high-risk PTE varieties [1]. It is clearly stated that in a PTE patient hypotension is not always due to PTE only, but it may be a consequence of comorbidities (e.g., presenting with hypovolemia), or result from a combined origin.

Furthermore, for all 6 mentioned clinical scenarios (regarding sBP, HR, RV strain by echocardiography or CTPA, troponin, D-dimer, NT-proBNP / BNP) and in the given positive example (of "putting in the context") it is important to realize another point. An alternative cause (other than PTE) of the abnormal result does not necessarily imply a better outcome. For example, elevated troponin concentration is sometimes due to other diseases (e.g., chronic renal failure), not PTE itself, but irrespectively of the underlying disease, increased troponin value as the rule is a marker of worse outcome [1,7]. Indeed, the presence of the other causes of the pathologic result suggests that PTE itself may not be a single problem and therefore, that other treatments should be used (not only for PTE). For example, if sepsis is diagnosed in addition to PTE, therapy should also include antibiotics together with PTE treatment, and sepsis may be the contributing/main cause of hypotension [1]. Moreover, if one finds bleeding in a patient with PTE and hypotension, it will also influence treatment choices. None of the other examples we described is elaborated or even mentioned in the excellent guidelines on the topic [1].

Therefore, all afore-mentioned 6 parameters are important in PTE, and their abnormalities are clinically relevant whatever the cause is (PTE or another one). Consequently, for proper clinical decisions, it is important to recognize if the change is acute and due to PTE or it is chronic and/or it results from other diseases.

Final Remarks

We do not disagree with guidelines' cutoffs; moreover, recommendations in guidelines ought to be followed, as they are the best we have contemporary for the vast majority of patients. The improvement we suggest is to take into consideration the individual characteristics during the previous period as well as co-morbidities (which influence directly some of the important

parameters for PTE risk stratification). In this way we evaluate not only the absolute value of a parameter but also if it is changed due to PTE itself or due to co-morbidity or if this abnormality is present from an earlier period. Therefore, the suggestion we advocate may serve to improve interpretation of particular parameters' interpretation, which may in turn improve the validity of the whole score and individual risk estimation. In everyday practice we do it often for numerous diseases: for example, we compare previous findings to the actual ones (such as ECG), to understand if there is a change and if it is recent or long-standing one.

The point we make is the importance of relative values in addition to using the absolute values only. There is no reason to waive relative values of important parameters. An illustrative example is low oxygen saturation (SpO_2): if it becomes low (e.g. 88% on room air) at the time of VTE then it is a sign of increased risk, while it may be the average SpO_2 for a patient with Chronic obstructive pulmonary disease who experience an acute subsegmental PTE.

CONCLUSION

The interpretation of important dichotomous parameters (normal or pathologic values) in PTE does depend on previous values (if available) and comorbidities. This principle should be recognized and used in clinical practice, while risk-stratifying patients. Moreover, this obvious principle probably deserves mentioning in the guidelines (having in mind how important they are).

REFERENCES

1. Konstantinides SV, Meyer G, Becattini C, et al. ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020; 41(4):543-603. doi:10.1093/eurheartj/ehz405.
2. Thygesen K, Alpert JS, Jaffe AS, et al. ESC scientific document group. Fourth universal definition of myocardial infarction. Eur Heart J 2019; 40:237-269. doi:10.1093/eurheartj/ehy462.
3. Koracevic G. Simple and practical classification of elevated troponin values. Am J Emerg Med 2008; 26:951-952. doi:10.1016/j.ajem.2008.01.057.
4. Hsu CK, Wu IW, Chen YT, et al. Value of the high-sensitivity troponin T assay for diagnosis of acute myocardial infarction in patients with and without renal insufficiency. Ren Fail. 2020 Nov; 42(1):1142-1151. doi:10.1080/0886022X.2020.1845732.
5. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Failure Society of America. J Card Fail 2017; 23:628-651. doi:10.1016/j.cardfail.2017.04.014.
6. Koracevic G. Pragmatic classification of the causes of high D-dimer. Am J Emerg Med 2009; 27:1016.e5-e7. doi:10.1016/j.ajem.2008.11.017.
7. Koracevic G. Diseases from every organ system can raise cardiac troponin concentration. Resuscitation 2010; 81:128. doi:10.1016/j.resuscitation.2009.09.019.