

BACKGROUND

There are approximately 10 million cases of VTE worldwide annually. VTE is the leading cause of deaths globally (Figure 1) causing a significant economic burden. It is crucial to have an accurate diagnosis in a timely manner to ensure appropriate treatment. Delayed or misdiagnosis can occur due to the lack of specific signs or symptoms of venous thrombosis. Thrombosis cannot be excluded with history and physical examination alone but requires a combination of blood biomarkers to support diagnosis. A biomarker is a molecule found in blood and a sign of a diseased condition, several have been used in pathophysiology, diagnosis and prognosis of thrombosis. COVID-19 pandemic, a respiratory syndrome caused by SARS-CoV-2 virus, responsible for more than 5.7 million deaths worldwide is found to have some association with high levels of biomarkers D-Dimer and CRP. Elevated D-dimer and CRP levels in COVID-19 patients are known to be associated with higher mortality.

METHODS

Early identification of patients with a high or low risk of any form of VTE is crucial for prompt diagnosis and effective treatment. We reviewed literature to determine the usefulness of some biomarkers that help to identify such patients at an early stage and establish its relationship between a few of the biomarkers and thrombotic events. We have also reviewed literature to demonstrate a prognostic association of D-dimer and CRP levels with COVID-19 associated VTE diagnosis.

RESULTS

D-dimer

- A degradation product of cross-linked fibrin.
- D-dimer level provides a reliable prediction of thromboembolic events allowing early detection of VTE.
- Incorporated into diagnostic algorithms in the management of patients with suspected VTE since D-dimer levels rise during an acute incident of VTE.
- Elevated D-dimer levels are also seen in other conditions making it a non-specific index for DVT.

Troponin

- Contractile proteins present in muscle cells.
- Released into the bloodstream immediately after an MI and remains for a longer duration (Figure 2).

Creatine Phosphokinase (CPK)

- CPK occurs in heart, skeletal and brain muscles.
- CPK-MB indicates myocardial muscle damage, CPK-MM indicates skeletal muscle damage and CPK-BB for brain muscle damage.
- Measurement of CPK activity has been one of the markers of AMI.

Myoglobin

- A protein that assists in oxygen transport and is found in the heart and skeletal muscles.
- Released into the bloodstream upon muscle injury, rises rapidly, peaks in 8 to 10 hours and returns to normality within 24 - 36 hours (Figure 2).

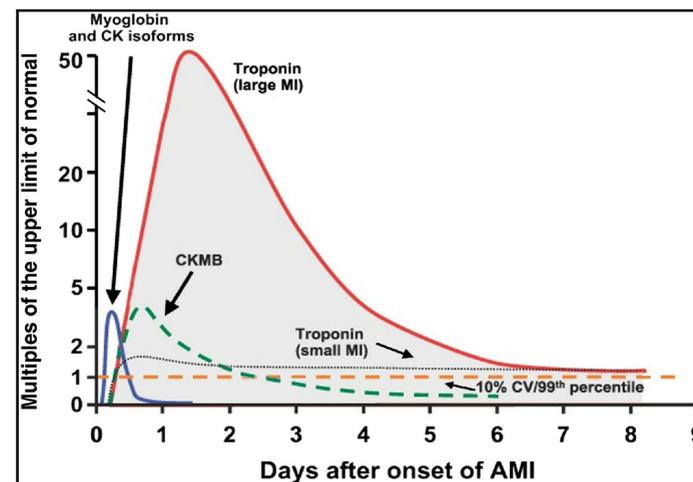


Figure 2: Time course of release of various cardiac biomarkers after acute myocardial infarction (From Anderson et al., 2007)

D-Dimer and COVID-19

- A strong prognostic marker.
- Higher D-dimer and hypercoagulability seen in critically ill COVID-19 patients, presenting more severe hypoxia and lung injury.
- Increased D-dimer and fibrinogen concentrations seen in early stages of the disease.

CRP and COVID-19

- Elevated levels of CRP contributing to COVID-associated hypercoagulability (Figure 3).

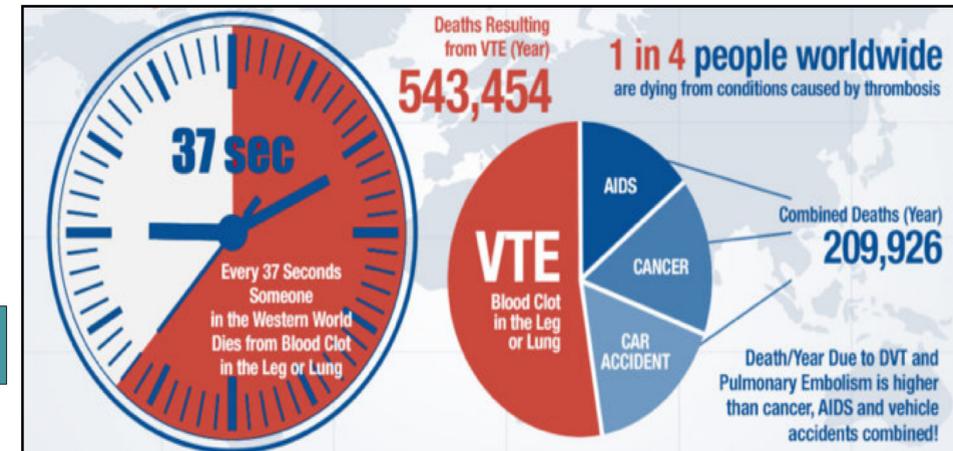


Figure 1: VTE is a major cause of death, imposing a significant global economic burden (From www.worldthrombosisday.org)

P-Selectin (sP-selectin)

- A glycoprotein from the family of cell adhesion molecules, found in the alpha granules of platelets and Weibel-Palade bodies of endothelial cells.
- Platelets are a major source of circulating sP-selectin.
- Patients with myocardial infarction often show elevated sP-selectin levels.
- Elevated sP-selectin levels are a risk factor for VTE with raised levels seen in patients with DVT.

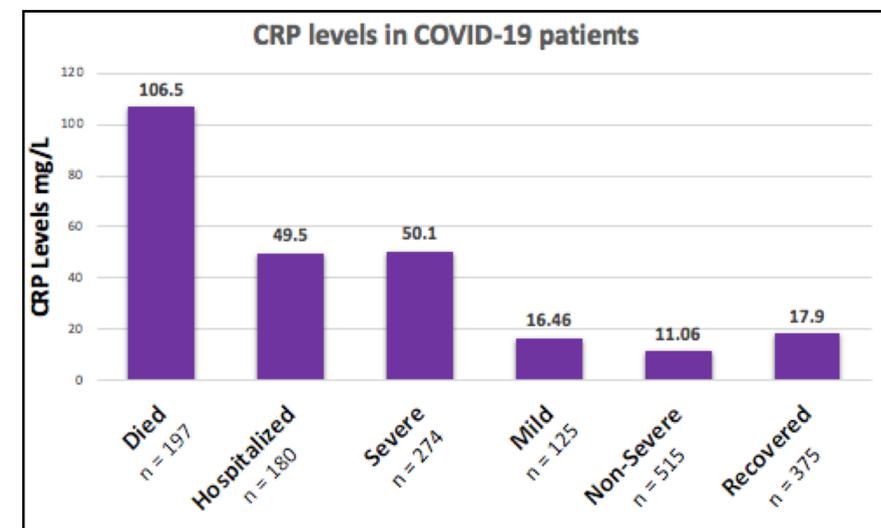


Figure 3: Elevated levels of CRP in different groups of patients with COVID-19 (From Ali 2020)

CONCLUSIONS

Several biomarkers have been used in diagnosis of thrombosis, target, prognosis and monitor appropriate anticoagulation treatments. Our research suggests that thrombosis cannot be excluded with history and physical examination alone and requires a combination of serum biomarkers to support diagnosis. COVID-19 pandemic is shown to have some association with high levels of biomarkers D-Dimer and CRP. Elevated D-dimer and CRP levels in COVID-19 patients are associated with higher mortality. CPK, troponins, and myoglobin are also elevated in COVID-19.

REFERENCES

1. Ali, N.: Elevated level of C-reactive protein may be an early marker to predict risk for severity of COVID-19, *Journal of Medical Virology*, 92 (11), 2409–2411, 2020.
2. Anderson JL; Adams CD; Antman EM; et al: ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction.
3. www.worldthrombosisday.org