



Biomarkers and Thrombosis

By: Saanvi Tatipalli, Arav Bongirwar, and The GTF Group

Abstract



- A biomarker is a biological molecule found in blood, body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition.



- Biomarkers such as D-dimer, P-selectin, cardiac enzymes (CPK, MB, troponin, and CRP) have been used to see how well the body responds to a treatment for a disease or condition.



- Several of these biomarkers also have significant links with COVID-19.

Introduction

- As discussed in the abstract, a biomarker is a biological molecule found in blood, body fluids, or tissues used as a sign of a normal or abnormal process, of a condition, or of a disease.
- A biomarker may be used to see how well the body responds to a treatment for a disease or condition.
- Through our research, we identified a few of these markers and researched if there is a link to thrombosis, and we found that thrombosis is, indeed, linked to several biomarkers.

Outline

1. D-dimer
2. P-selectin
3. Cardiac enzymes
 - 3.1. **C**reatinine **P**hospho**K**inase (CPK)
 - 3.2. Myoglobin (MB)
 - 3.3. Troponin
 - 3.4. **C**-Reactive **P**rotein (CRP)
4. Additionally, we conducted research on their relationship to COVID-19



D-Dimer

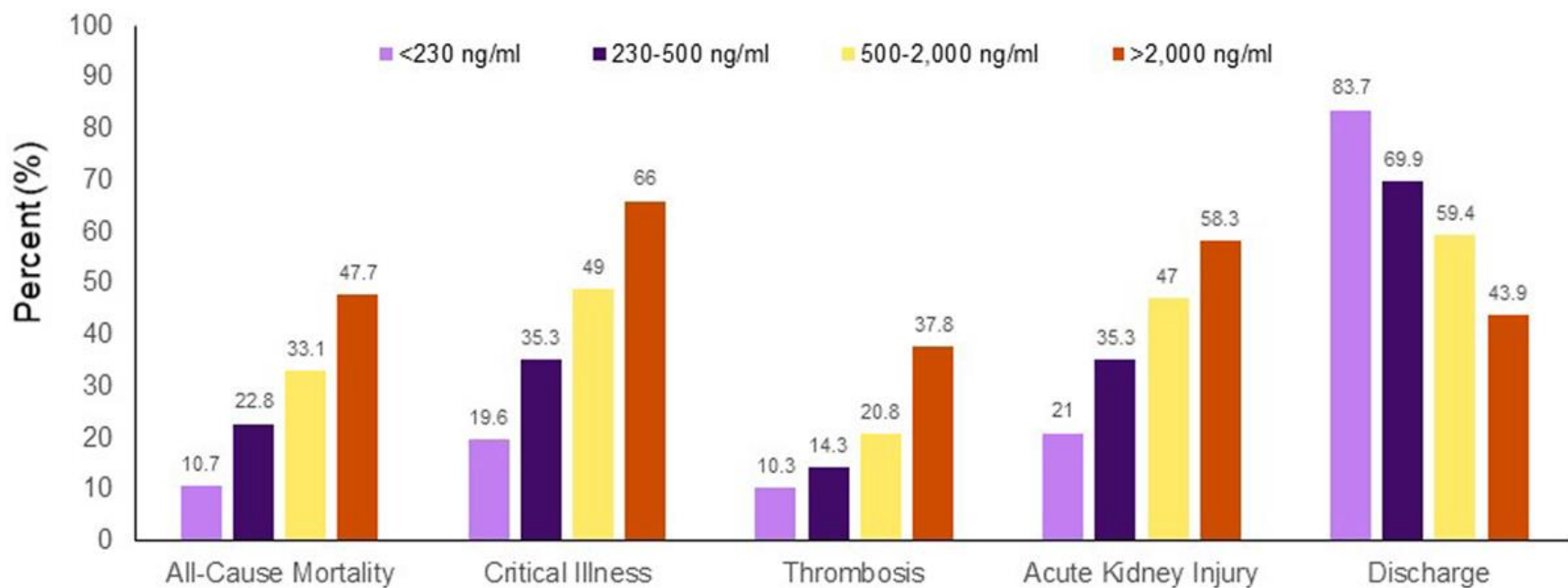
D-Dimer

What is D-Dimer?

D-dimer is the degradation protein fragment product of crosslinked (by factor XIII) fibrin. It reflects ongoing activation of the hemostatic system.

- D-dimer is normally undetectable or is detectable at a very low level unless the body is forming and breaking down significant blood clots. The reference concentration of D-dimer is < 250 ng/mL.
- Elevated D-dimer levels reflect ongoing activation of the hemostatic and thrombolytic system, providing clinical utility in the following:
 - Evaluation of thrombus formation
 - Ruling out DVT
 - Monitoring anticoagulation treatment (a decreasing value of D-dimer indicates effective treatment).

Graphical Abstract. Baseline D-dimer and Clinical Outcomes



The background features a light teal gradient with several wavy, layered shapes in various shades of teal. There are also several thin teal circles of different sizes scattered across the page.

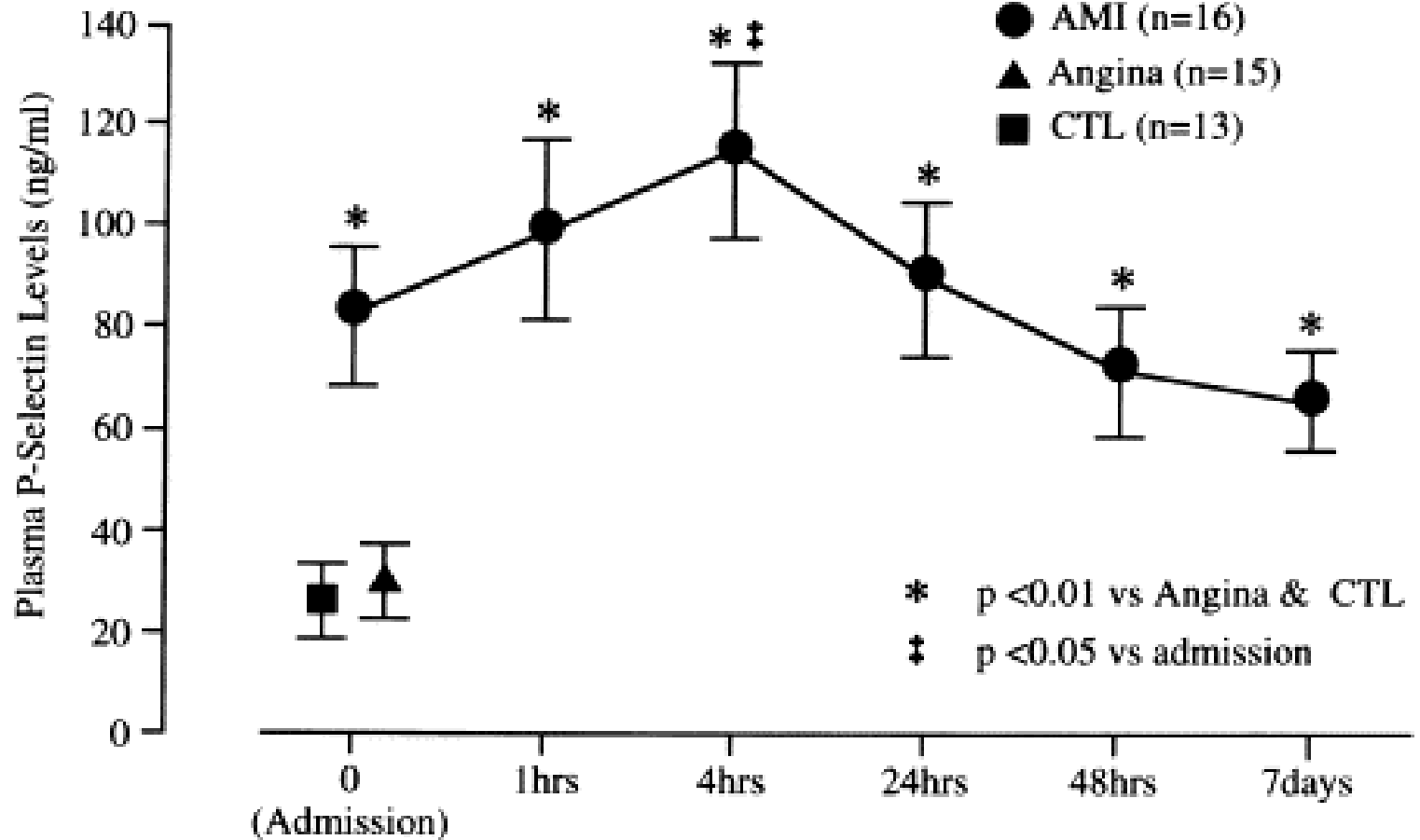
P-Selectin

P-Selectin

What is P-Selectin?

Soluble P-selectin (sPsel) is an important biomarker for DVT patients. P-selectin is a glycoprotein found in platelets which help facilitate their interaction with leukocytes.

- More specifically, it is a cellular adhesion molecule that mediates the interaction of activated endothelial cells or platelets with leukocytes. P-selectin plays a key role in mediating inflammation through promoting adherence of leukocytes to activated platelets and endothelium.
 - This process is one of the initial events in atherosclerosis and restenosis after coronary angioplasty.
- Patients with myocardial infarction often show elevated plasma P-selectin levels, as seen in the next slide.



The background features a light teal gradient with several darker teal wavy shapes and circles of varying sizes scattered across the frame. The text 'Cardiac Enzymes' is centered in a bold, teal serif font.

Cardiac Enzymes

Cardiac Enzymes

- These are the commonly used biomarkers that evaluate a patient's heart health and function and prove to be extremely useful when it comes to diagnosing heart disease.
- They are proteins in our bodies that help break down and quicken the pace of vital processes and are important to have.
- Studies have shown a clear connection between cardiac enzymes and thrombosis.
- When there is either a low oxygen supply such as right after an MI, our bodies release proteins that are broken down by these enzymes. Thus, having a high level of these enzymes shows signs of inflammation of the heart tissue.
- A cardiac enzyme marker test is conducted to test the level of this biomarker in our blood when a patient has signs including chest pain, dizziness, and shortness of breath.
- There are many types of enzymes all with different functions, some of which will be covered in the next few slides.

Creatine PhosphoKinase (CPK)

What is CPK?

This is an enzyme in the body, found mainly in the heart, brain, and skeletal muscle.

- When the total CPK level is elevated, it most often indicates an injury or stress the heart, or the brain, or the muscle tissue.
- Total CPK normal range is between 10 to 120 micrograms per liter (mcg/L).
- When a muscle is damaged, CPK leaks into the bloodstream.
- The CPK blood test is used to diagnose heart attacks, DVT, or determine muscle damage.

Creatine PhosphoKinase (CPK) Contd.

- Higher CPK Levels indicate:
 - Brain injury or stroke
 - Convulsions
 - MI
 - Inflammation of the heart muscle (myocarditis)
 - Lung tissue death (pulmonary infarction)
 - Muscular dystrophies

Myoglobin

What is Myoglobin?

MB is a protein found in the skeletal and heart muscle.

- Normal levels for myoglobin vary between patients of different genders.
 - For males, the normal level is anything under 91 ng/mL, and for females, the normal level is anything under 63 ng/mL.
- When the heart or skeletal muscles are injured, the muscle cells release myoglobin into the bloodstream.
- The level of myoglobin in the tissues can rise very quickly with severe muscle damage and could be detected within a few hours following an injury.
- Having elevated levels of myoglobin in the blood usually indicates that a very recent skeletal muscle or heart muscle damage.

Myoglobin Contd.

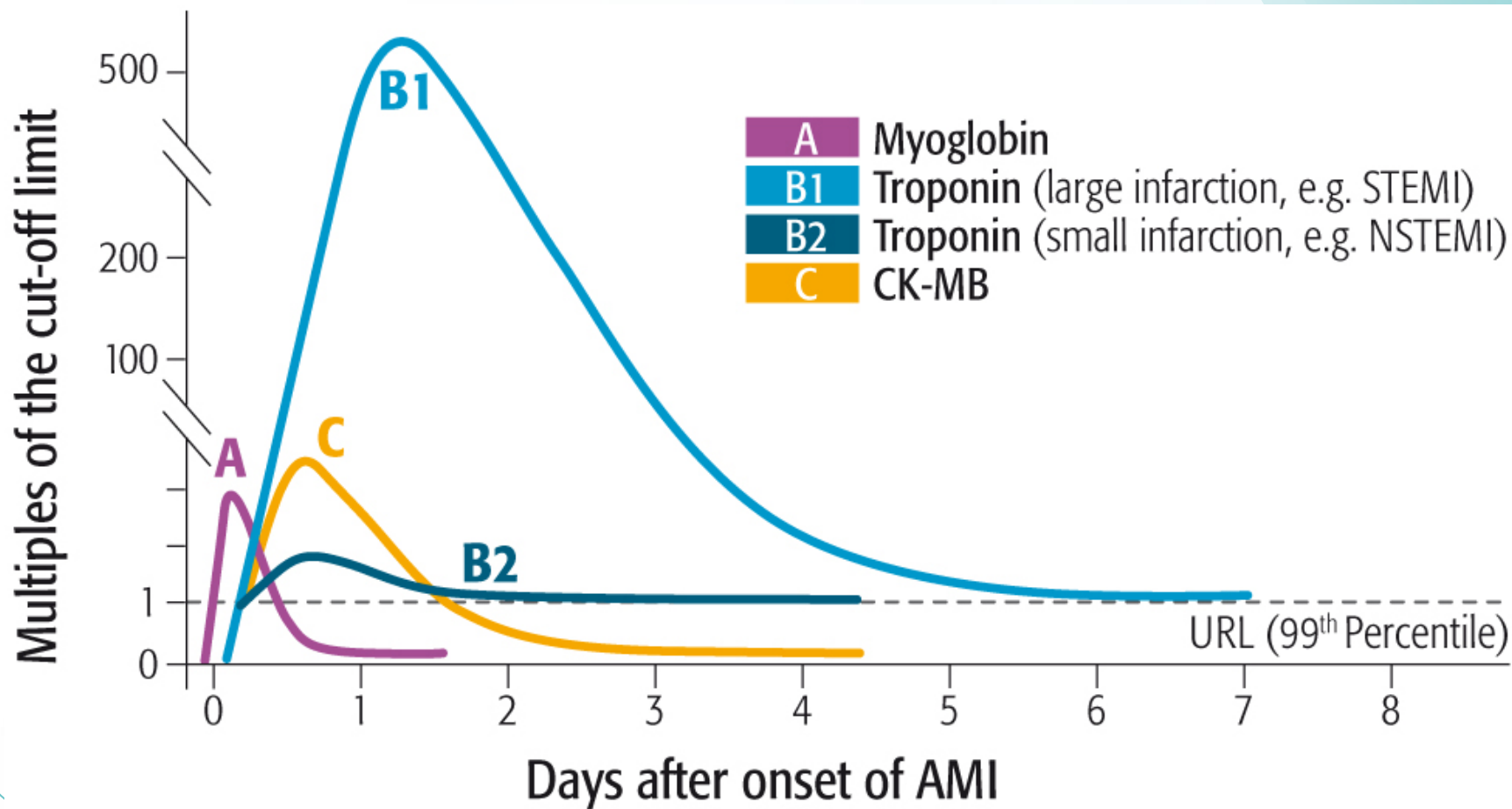
- The following conditions can result in elevated levels of myoglobin in the blood:
 - Accidents that result in muscle trauma
 - Excessive physical activity in untrained people
 - Seizures
 - Surgery
 - Any muscle disease, such as muscular dystrophy
 - Inflammation of skeletal muscles (myositis)
 - Skeletal muscle ischemia
 - Myocardial Infarction

Troponin

What is Troponin?

Troponin is a type of protein found in the muscles of the heart.

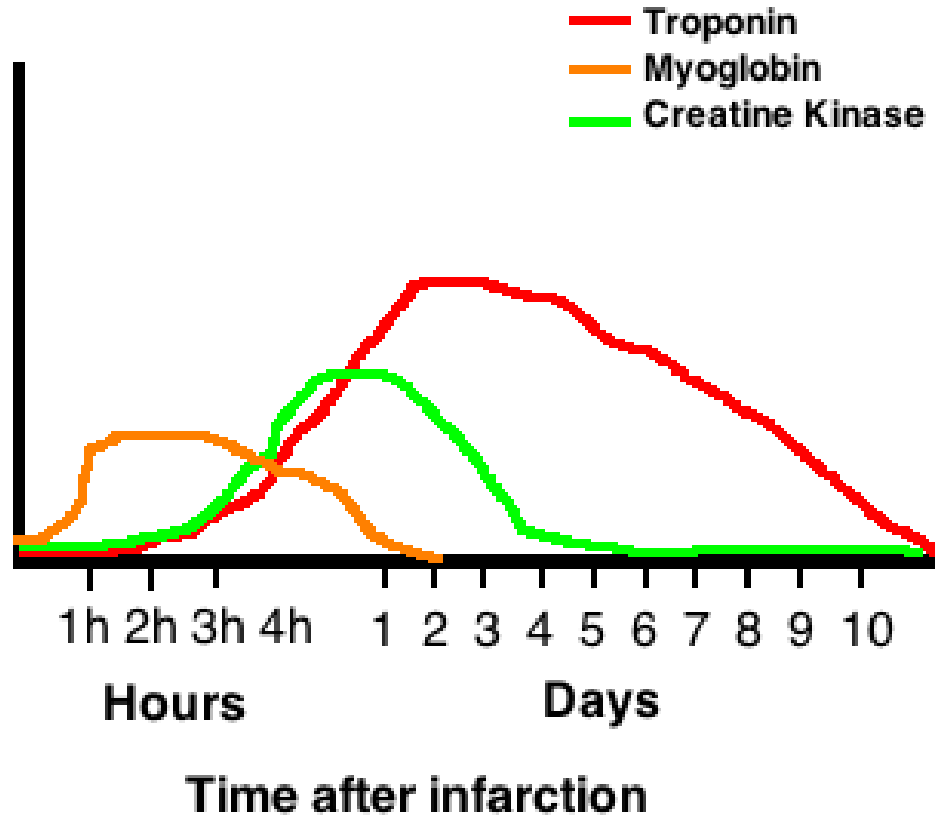
- Troponin is not normally found in the blood.
- When heart muscles become damaged, troponin is sent into the bloodstream.
- As heart damage increases, greater amounts of troponin are released in the blood
- This helps physicians dictate a patient's chance of thrombosis



C-Reactive Protein (CRP)

- CRP levels rise and fall depending on how much inflammation is present.
- If a patient is diagnosed with an infection or has a chronic disease, this test may be used to monitor treatment.
- If CRP levels go down, it's a sign that the treatment for inflammation is working.
- CRP test is used to:
 - Check for inflammation due to an infection
 - Help diagnose a chronic inflammatory disease such as rheumatoid arthritis, or lupus.
 - Determine your risk of heart disease
 - Evaluate your risk of a second heart attack
 - Check for thrombosis
 - Check for signs of COVID-19

Cardiac Biomarkers



The background features a light teal gradient with several large, overlapping, wavy shapes in various shades of teal. Scattered throughout are several thin teal circles of different sizes and a few solid teal circles of varying diameters.

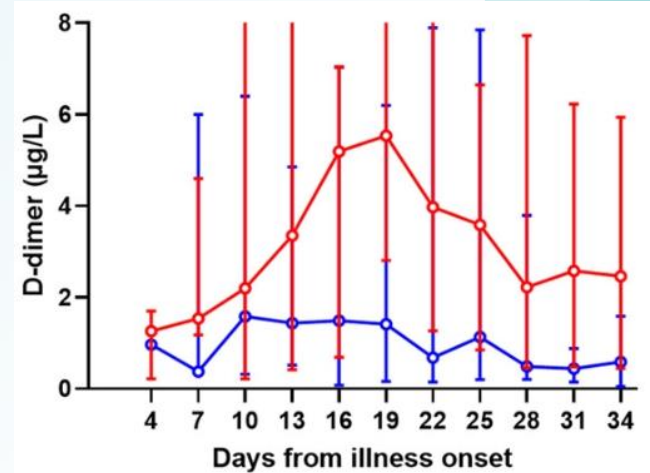
Relationship to COVID-19

C-Reactive Protein (CRP) and its relation to COVID-19

1. A significant increase in CRP is found (20 to 50 mg/L) in patients with COVID-19.
2. Elevated levels of CRP were observed up to 86% in severe COVID-19 patients.
3. Patients with severe disease courses had a far elevated level of CRP than mild or non-severe patients.
4. The level of CRP increases when there's inflammation in the body.

COVID-19, DVT, and D-dimer

- Several studies from Wuhan have shown that elevated D-dimer levels in COVID-19 patients is also associated with higher mortality.
- In one study, patients with COVID-19 without Deep Vein Thrombosis (DVT) expressed in blue lines did not show any changes in the D-dimer levels.
- On the other hand, patients with COVID-19 and DVT exhibited gradually increasing levels of D-dimer until day 19, after which the levels started receding until day 34, however never returning to a normal level.



Key:

Blue- Without DVT

Red- With DVT

Conclusion

- Ultimately, we learned that biomarkers are body molecules which show signs of body processes and indicate a patient's risk of a condition or disease.
- Physicians use biomarkers to understand how well the body is responding to a treatment.
- Through our research, we found that a variety biomarkers are often elevated in the several types of thrombotic conditions
- We also were able to conclude that patients with COVID-19 without Deep Vein Thrombosis (DVT) expressed minimal changes in the D-dimer levels, whereas patients with both showcased gradually increasing levels of D-dimer which seldom returned to normal.

Future Plans

- We look forward to researching the relationship between several other biomarkers and thrombosis in the future, because there are such a wide variety of them we have not yet explored.

Acknowledgements

We want to acknowledge our parents, the Board of GTF, and Dr. Atul Laddu for their mentorship throughout this project.

References

- Logothetis, Constantine; Weppelmann, Thomas; Aryanna MD, Jordan: D-Dimer Testing for the Exclusion of Pulmonary Embolism Among Hospitalized Patients With COVID-19: JAMA Network Open. 2021, 4, 1-4
- Mosevoll, Knut Anders; Lindås, Roald; Wendelbo, Øystein, et al: Systemic levels of the endothelium-derived soluble adhesion molecules endocan and E-selectin in patients with suspected deep vein thrombosis, SpringerPlus, 3: 1-9, 2014
- Ramacciotti, Eduardo; Blackburn, Susan; Hawley, Angela, et al: Evaluation of Soluble P-selectin for the Diagnosis of Deep Venous Thrombosis: Clin Appl Thromb Hemost: 17, 425–431, 2011
- Schutgens, Roger: D-dimer in COVID-19: A Guide With Pitfalls
- Yao, Yumeng; Cao, Jiatian; Wang, Qingqing, et al: D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study: Journal of Intensive Care, 8:49, 2020