



# Biomarkers and Thrombosis

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# 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

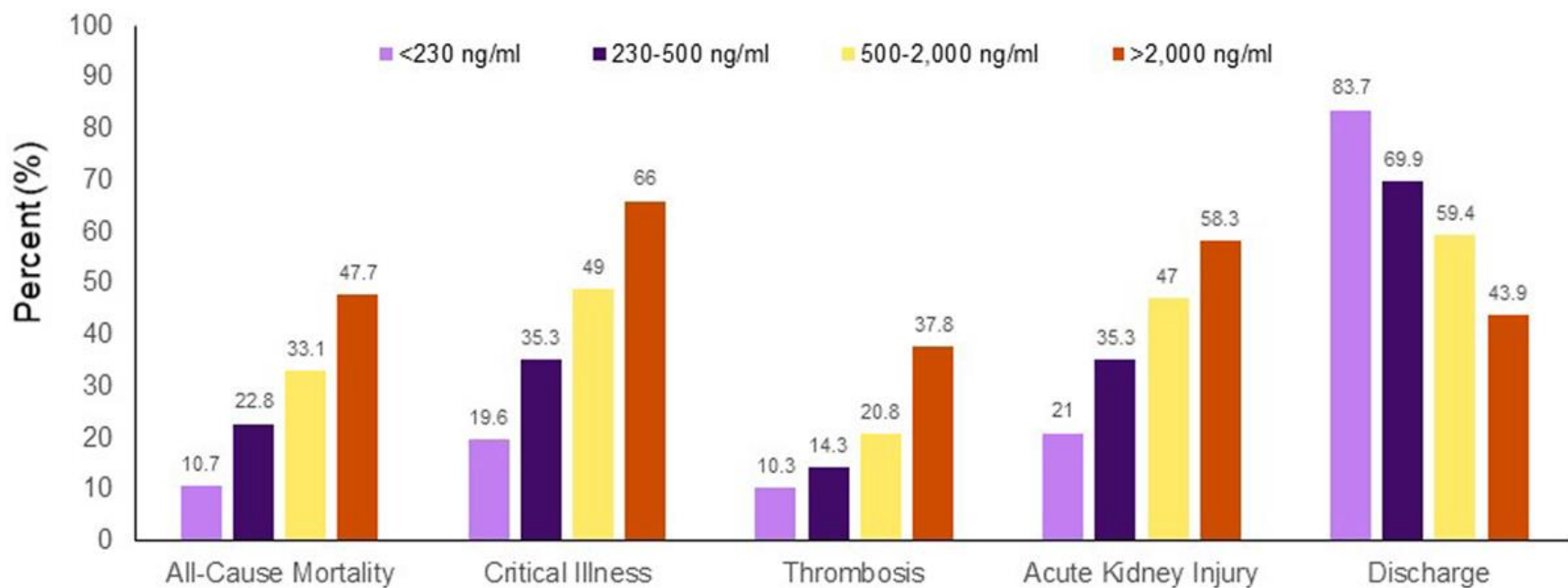
# D-Dimer

## 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





# P-Selectin

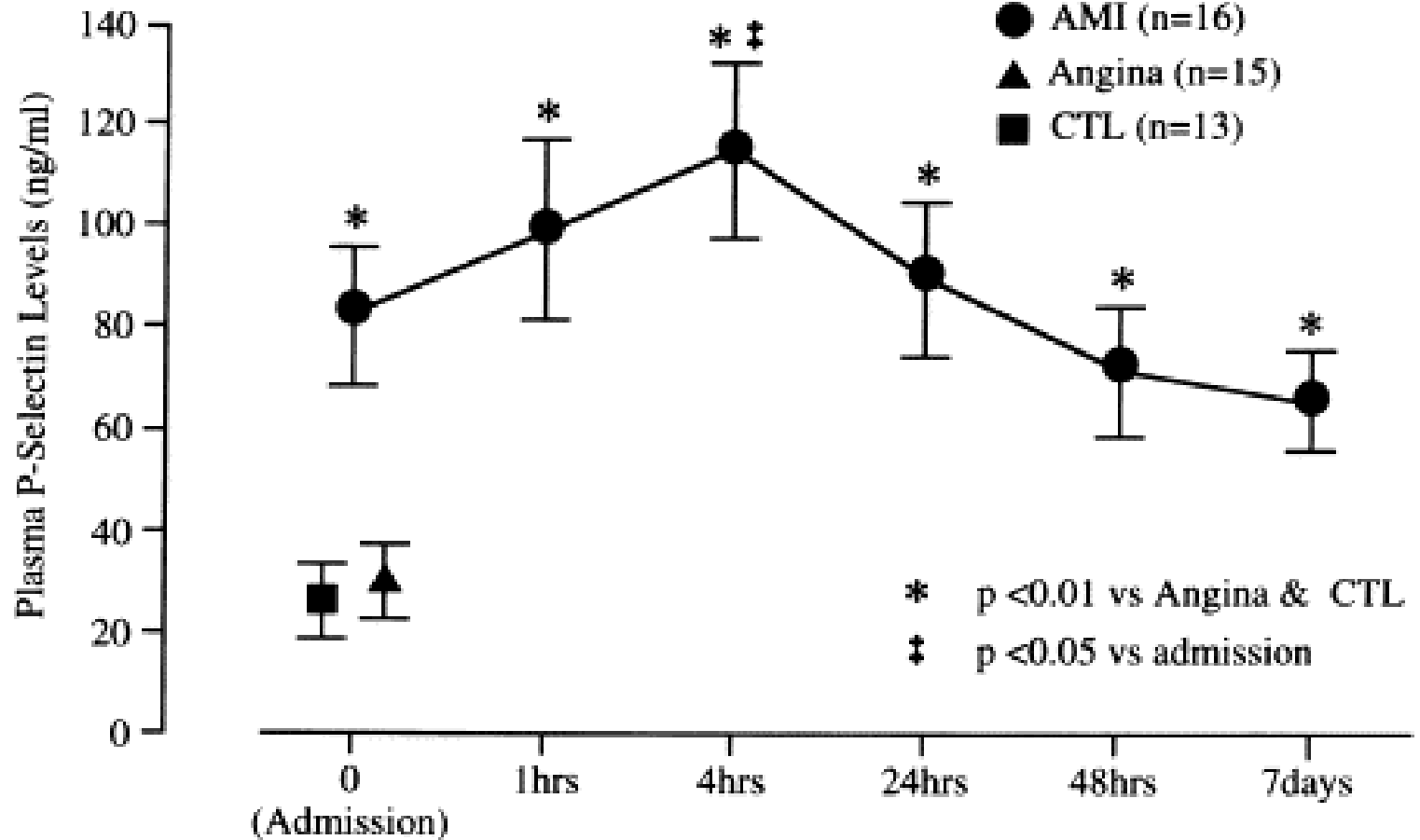


# P-Selectin

## 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.





# 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

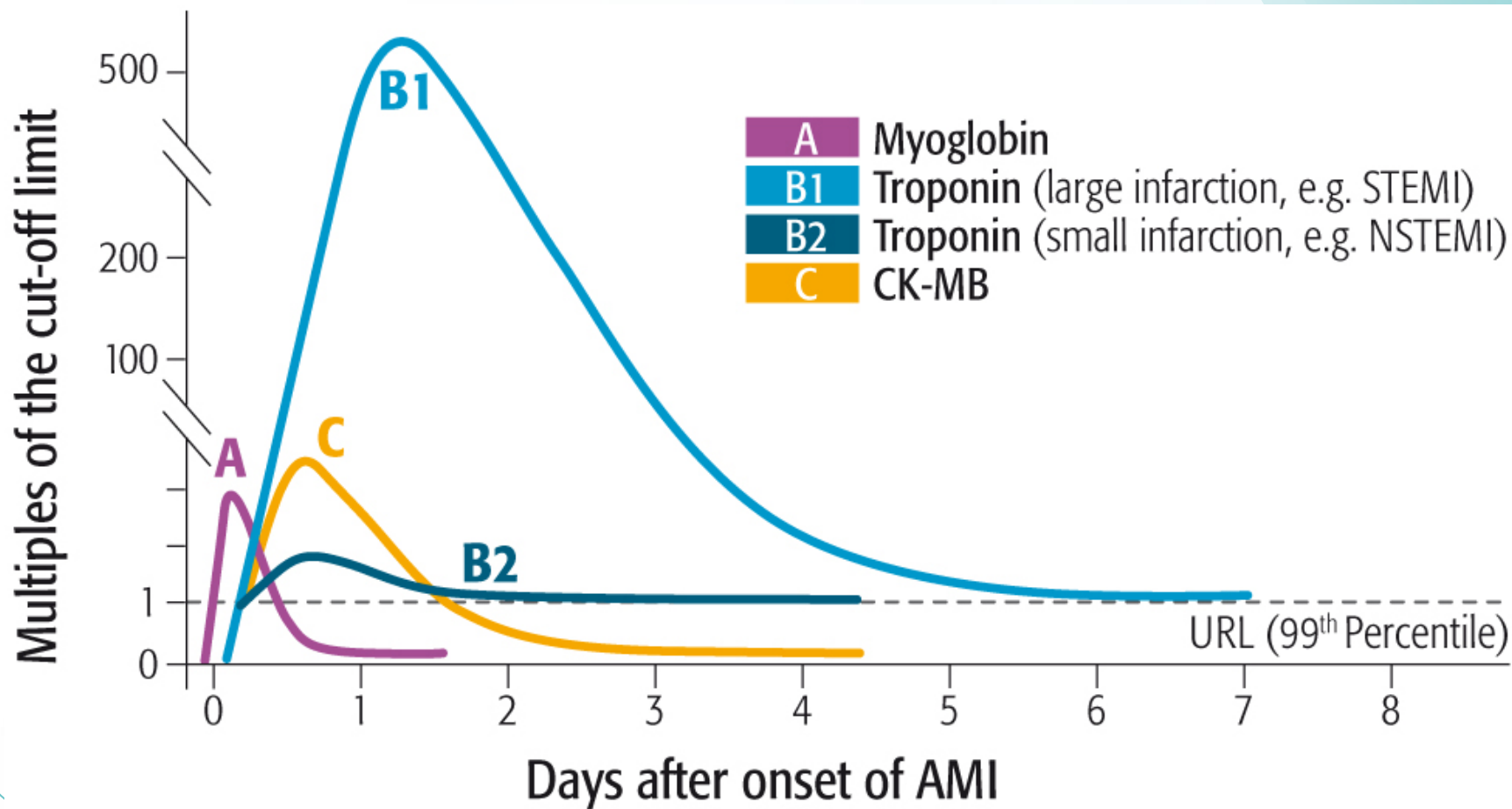


# Troponin

## What is Troponin?

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

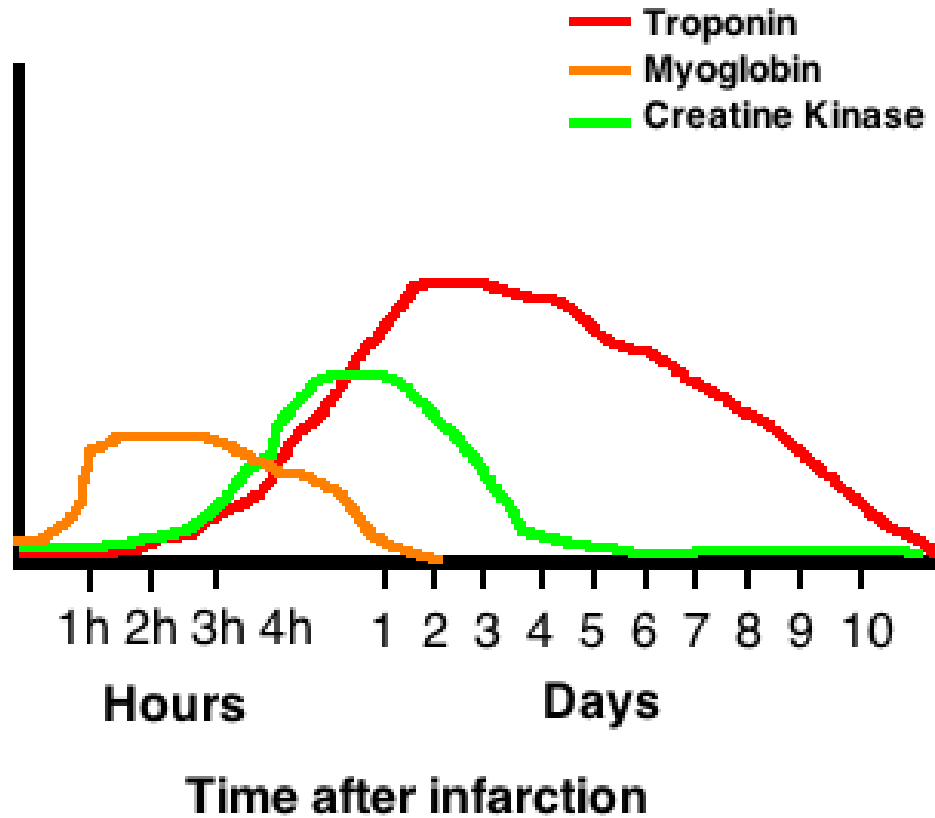
- Troponin is not normally found in the blood.
- When heart muscles become damaged, troponin is sent into the bloodstream.
- As heart damage increases, greater amounts of troponin are released in the blood
- This helps physicians dictate a patient's chance of thrombosis



# 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.

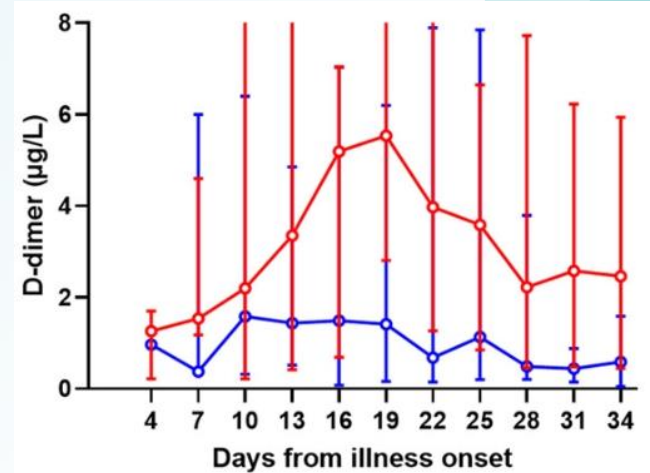
# **Relationship to COVID-19**

# 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

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# References

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