ELMER PRESS

Check for updates

Review

J Clin Med Res. 2022;14(2):80-87

False-Positive Causes in Serum Cardiac Troponin Levels

Dr. Seyed Mostafa Parizadeh
Resident of Cardiology

Introduction

Introduction

- cTns : Diagnostic & prognostic
- False-positive Dilemma

False positive:

The main causes and mechanisms & types of interference.

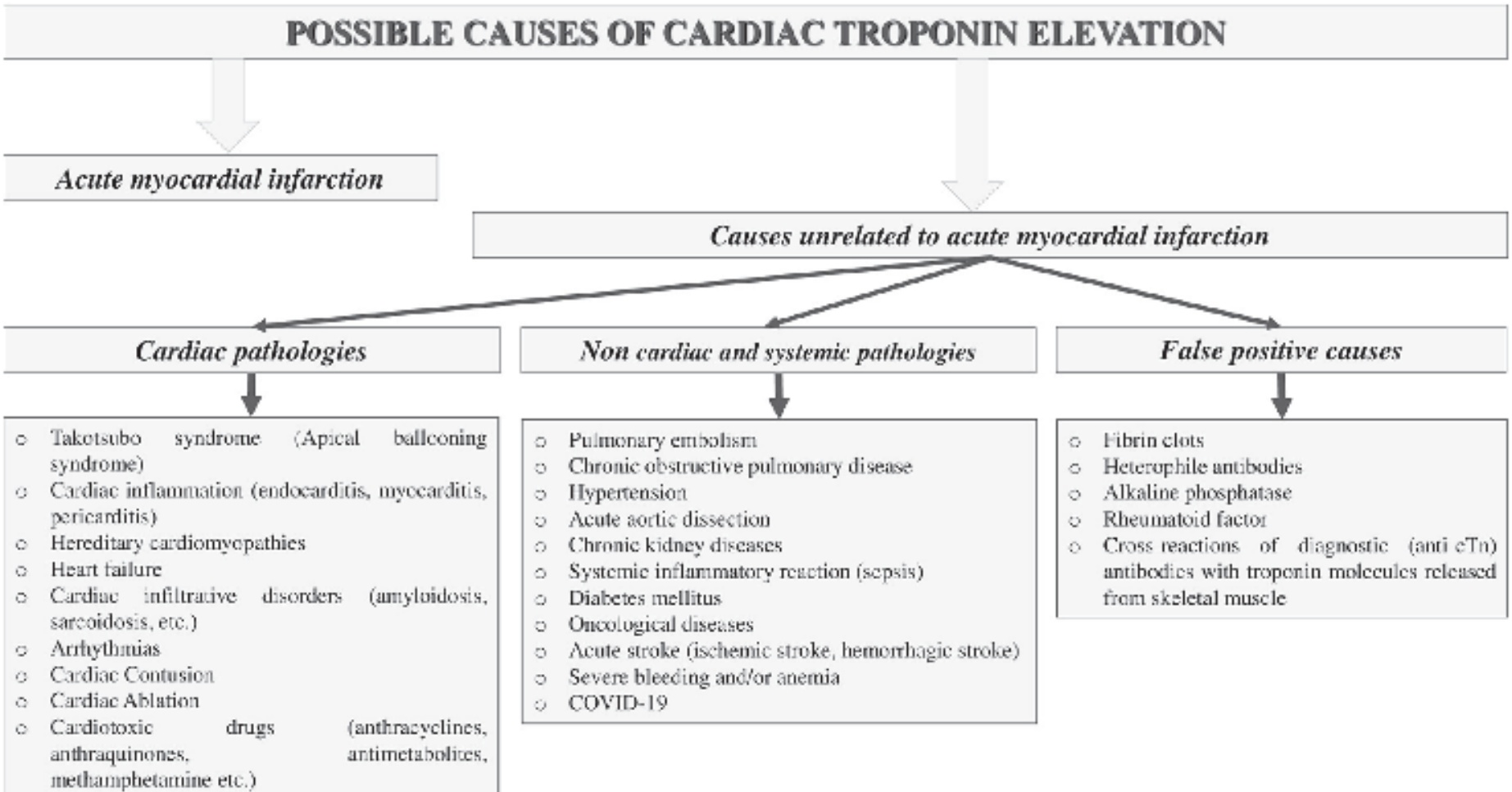

Figure 1. Possible causes of cardiac troponin elevation.

Fibrin Clots

Fibrin Clots

- Fibrin clots: one of the most important factors causing interferences in laboratory studies
- incomplete blood
- Most often this occurs in patients with coagulopathies or anticoagulant therapy.
- extra-laboratory errors
- intra-laboratory errors

Fibrin Clots *(continues…)*

- The optimal time for complete clotting of the blood sample is approximately 30 - 60 min

- Pressure from clinicians !

- Competitive interaction of fibrin clots with diagnostic antibodies (anti-cTn)

- Ways to combat fibrin clots are:
  - adherence to blood collection and sample preparation guidelines
  - careful visual inspection of the blood sample after centrifugation
  - use of whole blood or plasma as biomaterial instead of serum

Heterophile Antibodies

Heterophile Antibodies

- immunoglobulins formed by B lymphocytes

- The main reasons for the formation of heterophile antibodies in humans are:

  - Use of monoclonal antibodies
  - Frequent contact with microbial antigens, animal antigens or foreign proteins
  - Vaccination and Blood transfusion
  - Long-term persistence of viral agents in the body

Heterophile Antibodies *(continues…)*

- Prevalence of heterophile antibodies ranges from < 1% to 80%.
- Not all patients with heterophile antibodies have false-positive reactions.
- The mechanism of false-positive elevation of cTn concentrations lies in the cross-interaction of heterophile antibodies with anti-cTn
- Lum et al (2006) described an interesting clinical case of a false-positive increase in ***cTnI*** concentration in a patient without myocardial infarction.

Heterophile Antibodies *(continues…)*

- ✓A 57-year-old patient
- ✓Complaints and symptoms similar to AMI
- ✓The cTnI concentration measured on admission with the Beckman Coulter immunoassay was significantly higher than normal
- ✓other possible causes of elevated troponin I concentration were also excluded.
- ✓Troponin level is positive only with the Beckman Coulter immunoassay, whereas all other immunoassays were negative.
- ✓After adding heterophilic antibody blockers to the patient's original blood sample, the troponin I concentration decreased from normal range.

Heterophile Antibodies *(continues…)*

- ✓A 53-year old female patient
- ✓ Admitted with complaints of chest pain
- ✓Patient had been admitted with similar symptoms three times during the current year.
- ✓The Troponin concentration at the time of admission was five times the upper reference limit
- ✓ECG and coronary angiography were normal
- ✓The blood sample was sent to another laboratory, where troponin was measured and was negative.
- ✓Further analysis revealed the presence of heterophile antibodies in the patient’s blood,

Heterophile Antibodies *(continues…)*

- Lippi et al (2012) summarized 16 studies and clinical cases
- The rate of false-positive ranged from 0.1% to 3%, and in some studies, it was significantly higher, up to 50%.
- The best way to detect false-positive troponin levels caused by heterophilic antibodies is to pretreat the blood sample with heterophilic antibody blockers
- The addition of a blocking reagent led to a dramatic decrease in cTn concentrations in patients' blood.
- Prevalence of false-positive results may increase significantly in the future due to the widespread use of immunotherapy for the treatment of many diseases.

Alkaline Phosphatase

Alkaline Phosphatase (ALP)

- Alkaline is widely used to diagnose liver and biliary tract diseases
- ALP for signal amplification
- Butch et al (1989) first established that alkaline phosphatase can have a significant effect on the concentration of a cardiac-specific enzyme CKMB
- Dasgupta et al (2001) reported the effect of alkaline phosphatase on cTn concentration. A further increase in alkaline phosphatase the troponin concentration is increased

Alkaline Phosphatase *(continues…)*

- Immunoassays that do not use this enzyme should be used in patients with increased alkaline phosphatase.

- In the absence of such a possibility, the results of patients who have elevated serum/plasma alkaline phosphatase activity should be interpreted with care.

Rheumatoid Factor

Rheumatoid Factor (RF)

- Elevated levels of RF are not only of diagnostic value, but can also have a significant impact on the results of laboratory tests.

- In patients with autoimmune diseases (such as RA or SLE) the main cause of falsely elevated troponins is rheumatoid factor.

- Al-Awadhi et al (2007): 10% of patients with sero-positive RA had troponin I concentrations above diagnostic threshold for AMI, while none of patients with sero-negative RA had troponin I concentrations above the reference limit.

Rheumatoid Factor *(continues…)*

- A large multi-center study included patients with autoimmune diseases associated with elevated RF about 8.7% of troponin were false-positive.
- Use polyclonal antisera against rheumatoid factor t eliminate the interference
- Oonly a small fraction of the false-positives results (21%) were corrected with a blocking reagent
- Clinicians should be very careful when interpreting laboratory immunochemical studies in patients with autoimmune diseases and elevated serum rheumatoid factor levels.

Cross-Reactions of Diagnostic Antibodies (Anti-cTn) With Troponin Molecules Released From Skeletal Muscle

Cross-Reactions of Diagnostic Antibodies (Anti-cTn) With Troponin Molecules Released From Skeletal Muscle

- Damage to skeletal muscle in congenital and acquired diseases can lead to a false-positive increase in cTn levels

- Skeletal muscle biopsy specimen revealed absence of cTns expression in skeletal muscle.

- There are two possible mechanisms for increase in the levels of cTns in diseases and injuries of skeletal muscles:
  - re-expression of cTn molecules in skeletal muscles after injury
  - cross-reactions of diagnostic antibodies with skeletal troponin

Cross-Reactions of Diagnostic Antibodies (Anti-cTn) With Troponin Molecules Released From Skeletal Muscle *(continues…)*

- A number of studies have reported elevated serum cTn levels in many patients with skeletal myopathies even in the absence of ischemia and myocardial injury.

- Punukollu et al (2004): elevated serum cardiac Troponin T concentrations in 20% of patients with rhabdomyolysis with no signs of coronary artery damage.

- Egholm et al (2015): significant increase in high-sensitivity Troponin T (hs-TnT) in a 48-year-old patient with drug-induced rhabdomyolysis.

Cross-Reactions of Diagnostic Antibodies (Anti-cTn) With Troponin Molecules Released From Skeletal Muscle *(continues…)*

- A significant increase in only one cardiac troponin isoform (cTnT or cTnI), would be more indicative of cross-reactivity of the diagnostic antibodies

- In another study, cTns levels were measured in 78 patients with skeletal myopathies. The cTnT was increased in 72.8% of patients and cTnI in only 2.6% of patients.

- Schmid et al (2018): hs-TnT levels were elevated in a much larger number of patients compared with hs-cTnI levels. Serial measurements of hs-TnT concentrations revealed a chronic elevation of hs-cTnT in most patients.

Conclusions

Conclusions

- Fast detection of false-positive elevation of cTn levels is important in the emergency diagnosis of AMI. Physicians should also keep in mind that there are a significant number of factors that cause false-positive elevations in cTns.
- Understanding these causes and mechanisms of a false-positive increase in cTns in blood serum will help practitioners and researchers improve the diagnosis of cardiovascular diseases, in particular myocardial infarction, and reduce the risk of misdiagnoses.

- It is possible only with the coordinated interaction of clinicians and laboratory diagnostics specialists. This is due to the fact that laboratory diagnosticians only have access to laboratory results.

- An important role in identifying a possible false-positive result of troponin is played by clinicians. If the laboratory results are inconsistent with the clinical and instrumental data, clinicians should notify the diagnostic laboratory and initiate further investigation


با تشکر از توجه شما