

TROPONIN: A MIRROR OF CARDIAC HEALTH?



Professor Dr. Christoph Liebetrau (L)
Associate Professor Dr. Till Keller (R)

We discussed the significance of cardiac risk stratification with the help of troponin and possible areas of application in an interview with the cardiologists Professor Dr. Christoph Liebetrau and Associate Professor Dr. Till Keller from the Cardiac Center in Bad Nauheim.

The life expectancy of the population is increasing due to better healthcare and demographic change. As a result of this trend, there is also an increase in chronic diseases such as diabetes and heart disease. In order to enjoy a high quality of life even in old age, it is important to detect diseases at an early stage, ideally before clinical symptoms occur.

There is a range of medical parameters suitable for this prophylactic (preventative) approach. Specifically in the area of cardiac prevention, large population studies in recent years^{1,2} have shown that troponin I is particularly important in this context.

Troponin I therefore plays an important role not only for infarction diagnosis, but also as a possible sensitive marker for individual heart health.

For the first time, Abbott's High Sensitive Troponin-I diagnostic test makes it possible to assess the risk of a heart attack or other cardiac events months to years in advance.³ Studies have shown that an increased risk of heart attack and stroke is also observed in people who are considered healthy but are in the upper normal range of the troponin level.⁴

1. MODERN PATIENT CARE IN THE AREA OF CARDIOVASCULAR DISORDERS: WHAT IS THE SIGNIFICANCE OF RISK STRATIFICATION IN GENERAL?

Keller: Risk stratification plays a different role in acute and general care in the hospital compared to outpatient care, where prevention and early detection are the main focus.

Prevention plays an increasingly important role for people today. Damage to the heart and vessels can be largely avoided if the disease is detected in good time and treated properly over the long term. In the long run, health and wellness can only be maintained by means of timely medical prevention.

This examination is carried out far from the specialist centers and is based mainly on cardiac ultrasound, and partly on the determination of basic parameters in the laboratory.

A risk marker that is easy to determine as a screening test and can simultaneously indicate the risk for various cardiovascular disorders could have a high potential in this area.

Liebetrau: Managing resources is always a priority in patient risk stratification. The cardiologists' offices are becoming larger and larger and have more and more patients. Waiting times for patients are sometimes very long, and actual care becomes more difficult. A simple tool such as risk stratification by troponin could allow for better assessment of cardiac risk and better treatment of patients.

Patients with low risk based on the troponin value can be classified as in good cardiac health, and ideally will not need any further instrumental diagnostics and examination. High-risk patients can be identified based on elevated troponin values, that is sometimes overlooked due to scarce resources.

Troponin as a risk marker could be implemented very effectively in this area, because, as a cardio-specific marker, it is superior to the non-specific highly sensitive (hs) C-reactive protein (CRP).

Risk stratification with troponin is a simple tool in primary prevention to help:

- exclude cardiac risk in asymptomatic patients and
- identify and further investigate high-risk patients



HOSPITAL



RESIDENT PHYSICIAN/
CARDIOLOGIST

Diagnostics of Non-ST-Segment Elevation Acute Myocardial Infarction

- Increase/decrease of troponin

Heart failure, atrial fibrillation, heart valve and lung disease

Pre-intervention cardiology check-up

- Slightly increased troponin values indicate cardiac risk

Individual cardiac risk marker

- Cardiovascular risk assessment
- Prevention
- Identifying high-risk patients

2. EPIDEMIOLOGICAL STUDIES HAVE SHOWN THAT A DIFFERENT RISK ASSESSMENT CAN BE MADE ON THE BASIS OF GENDER-SPECIFIC THRESHOLDS. WHAT CONSEQUENCES DOES THIS HAVE ON TREATMENT FOR THE INDIVIDUAL LOW/MEDIUM/HIGH RISK GROUPS?

Keller: The risk stratification of the general population based on troponin values is not widespread and the corresponding treatments have not yet been established by clinical studies. Here, a comparison could be made with the use of the highly sensitive (hs) C-reactive protein (CRP). From a certain level, patients are treated with statins. A similar approach could also be possible for slightly increased troponin. After the estimation of the clinical risk, primary prevention drugs such as statins or acetylsalicylic acid (ASA) could be used.

For example, a 65-year-old "healthy" man who comes for a cardiovascular check-up and has a troponin value above 12 ng/L should be further examined, and treated if necessary. A patient of the same age with a troponin value below 4 ng/L might not need further cardiac examinations.

Liebetrau: Troponin determination can help to better assess the risk factors of clinically healthy people. Slightly increased troponin values in a healthy person allow for an initial risk assessment, but the reason for the increase must be further investigated.

Given the high incidence of undiagnosed diabetes, the high rate of non-treated or inadequately treated hypertensive patients, and patients with unrecognized cardiac arrhythmias of any type, the troponin value is a very good screening tool to specifically check for potentially unrecognized risks.

Troponin is a simple parameter that indicates cardiac risk and allows the treatment to be adjusted and risk to be reduced in the next step.




Keller: Treatment with statins is possible, even if the primary prevention with statins is not sufficiently covered by studies.

In the West of Scotland Coronary Prevention (WOSCOP) study, the troponin level of subjects at cardiovascular risk decreased under statin therapy, with the decrease accompanied by a better prognosis.⁵ In another study, troponin was measured only at the beginning of statin therapy. In patients with a troponin I value greater than 6 ng/L, statin therapy resulted in higher absolute risk reduction compared to those with a lower troponin value.^{1,6}

Liebetrau: Consistent statin therapy reduces risk in patients with coronary heart disease (CHD), diabetes or stroke, even if LDL levels are not excessively high. However, there are no limits for lipid reduction in statin therapy; the lower the LDL, the better.

Further examinations should be performed before statin administration, such as the determination of intima-media thickness or plaque detection by imaging methods.

Highly sensitive troponin I is a parameter that indicates individual cardiovascular risk. Asymptomatic patients with slightly elevated levels should be further examined. A possibility to reduce cardiovascular risk is the treatment with statins. However, this treatment has not yet been adequately proven by clinical studies.

TROPONIN LEVEL		INTERPRETATION	POSSIBLE TREATMENT SCHEME SUGGESTED BY KELLER AND LIEBETRAU
MALE (pg/mL)	FEMALE (pg/mL)		
<6	<4	 Low risk of future cardiovascular event	No further treatment Checking of the troponin value every 2–4 years
≥6 to ≤12	≥4 to ≤10	 Moderate risk of future cardiovascular event	Possible subclinical myocardial injury <ul style="list-style-type: none"> • Healthy lifestyle • Blood pressure monitoring • Lipid monitoring • Checking of troponin value after 6–12 months
>12	>10	 Elevated risk of future cardiovascular event	Subclinical myocardial damage <ul style="list-style-type: none"> • Healthy lifestyle • Blood pressure monitoring • Lipid monitoring • Checking of the troponin value after 4–6 weeks

3. AT WHAT INTERVALS SHOULD THE TROPONIN BE MEASURED FOR THE INDIVIDUAL RISK GROUPS AFTER THE INITIAL ASSESSMENT?

Liebetrau: In acute myocardial infarction, we always want to have two troponin values within 1–3 hours. The progression of the troponin concentration in the first three hours is of central importance for the detection of patients with acute myocardial infarction.

In order to better estimate cardiovascular risk in prevention, it is certainly helpful to always have more than one value. However, it is difficult to estimate the exact time interval between the determinations. But we do know, for example, from the natriuretic peptides, that in the intensive treatment of patients with heart failure a decreasing value reflects a good prognosis, while an increase represents a greater risk.

For example, consider a patient with hypertension and a troponin value of 14 ng/L, who has an increased systolic blood pressure of 160 mmHg on the day. After three months of treatment, the average 24-hour measurement is 120 mmHg. In this patient, the troponin value should also have decreased due to the low strain on the myocardium. A relevant study from Hamburg in this area, the TEAMSTAR study, showed that the troponin value decreased under optimized drug-induced blood pressure adjustment.⁷

4. WHAT ARE THE ADVANTAGES OF TROPONIN I OVER OTHER BIOMARKERS IN RISK STRATIFICATION?

Keller: The main advantage is the cardiospecificity of troponin I, or, more precisely, the specificity for the myocardium. This is the great advantage over the natriuretic peptides that reflect the hemodynamic stress of the heart.

5. SHOULD TROPONIN DETERMINATION BECOME PART OF REGULAR HEALTH CHECK-UPS? WHICH PATIENT GROUPS WOULD BENEFIT MOST?

Liebetrau: There are various screening tests, such as the check-up 35 in Germany. I think that an investigation into cardiovascular health at the age of 35 is too early. In men, however, this can make sense from about 50 years of age, and in women later after menopause, at about 60 years of age.

At 50 years of age, if a patient has non-measurable or very low troponin in the check-up, this patient will not need further measurement for 4–5 years. If the first value is high, a second measurement should be taken at a shorter interval.

Keller: If there is a patient with slightly elevated troponin values, one should continue to look at the risk factors that exist and treat them as discussed earlier. At the moment, performing an annual examination is also recommended if there is a certain cardiovascular risk. This could be transferred to a troponin-based risk assessment. If troponin is low, the cardiovascular risk is low; if the value is moderate to high, a risk is present, which should be checked regularly/annually.

Liebetrau: However, the intervals have not yet been defined and must be defined more precisely depending on the risk in the individual case.

6. WHAT COMBINATION OF BIOMARKERS COULD FURTHER IMPROVE PATIENT CARE?

Keller: Multiple biomarkers that represent cardiovascular risks can be helpful individually or in combination. If you look at the studies that have been performed, there are only a few markers left that have successfully indicated an increased risk. These include kidney markers such as cystatin C. Inflammation markers would be desirable from a pathobiological point of view, but CRP is often non-specific; however, there is currently no better biomarker. In the end, the lipids, the troponin for the myocardium and the natriuretic peptides as hemodynamic markers are significant ones.

Liebetrau: However, before we think about even better markers, we should first make use of the currently known markers for estimating cardiovascular risk.

Lipid status is not always checked as a routine measure, and patients are treated with outdated statins. LDL is not determined and therapy is not switched to a treatment that might be better for patients. The main objective should be to implement the current guidelines as part of the routine. Unfortunately, this does not always happen everywhere.

7. WHAT ARE THE BENEFITS OF TROPONIN RISK STRATIFICATION IN EVERYDAY CLINICAL LIFE?

Keller: Risk stratification supported by troponin could be of great importance in everyday clinical life. We know from practical experience that non-cardiac surgeries require a cardiac risk assessment.

From the point of view of the clinical cardiologist, risk stratification by troponin is extremely helpful in this area. An estimation based on the troponin value in patients with high or low cardiovascular risk is performed quickly and allows the targeted examination of high-risk patients. Adjusting the risk assessment limits for this older patient population (65 years plus) could be useful.

Liebetrau: This is a very important field of application, and more and more non-cardiac operations are carried out in Germany every year. Attentiveness is high, and perioperative myocardial infarction is common, resulting in increased mortality. There are major pan-European studies that show that the release of troponin before and during surgery reflects patient outcomes. Clinical observational studies on this subject are ongoing, but no intervention study has yet been performed.⁸

Keller: In everyday clinical practice, the determination of cardiac risk can be problematic. In older patients with dyslipidemia, echocardiography is often used without any other obvious cardiac risks. This leads to a very high workload. As a consequence, the troponin value can be measured in these patients for risk assessment. Then the risk is further characterized by an echocardiography examination only in patients with elevated values. This is an example from our clinical routine, which has proved to be very helpful.

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