TIGER STUDY

High-Sensitivity Troponin I in Addition to Guideline-Based Care in Emergency Medical Service - an Open Randomized Controlled Trial

2025-05-15

NCT number:

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Study Protocol

Introduction

In Sweden, a myocardial infarction (MI) occurs approximately every twenty minutes, affecting individuals across all ages and genders. Early detection of these cases is critical to enable the prompt initiation of life-saving interventions. Within the emergency medical service (EMS) of Region Stockholm—handling over 200,000 patient cases annually—chest pain accounts for between 10% and 12% of all assignments. However, currently only a limited proportion of patients with MI can be diagnosed prehospitally using ECG, requiring the majority of patients to undergo further evaluation through high-sensitivity troponin blood testing at emergency departments. Streamlining this diagnostic process within the prehospital emergency care setting has the potential to optimize patient flow, reduce unnecessary healthcare costs, and—most importantly—significantly shorten patient suffering.

The objective of the study is to evaluate the clinical utility of a point-of-care high-sensitivity Troponin I analysis in prehospital emergency care, in patients presenting with chest pain or in whom ambulance personnel suspect a MI. By facilitating earlier diagnosis of myocardial infarction, the project seeks to improve patient outcomes through more rapid identification and treatment of this time-critical condition.

Sponsor: Region Stockholm, through Ambulance Services in Greater Stockholm (AISAB)
Principal Investigator: Jakob Lederman, jakob.lederman@ki.se
Responsible for Current Study Information: Sebastian Bjöhle, sebastian.bjohle@ki.se
Original Protocol Version Date: 2024-03-21
Most Recent Protocol Amendment Date: 2025-05-15
Condition Studied: Myocardial Infarction

Research question

What is the added value of using high-sensitivity Troponin I in prehospital emergency care—beyond current guideline-based care —for the early identification of patients with myocardial infarction?

Materials and Methods

Study Design

This is an open, randomized controlled trial with a 2:1 allocation ratio. After obtaining informed consent from the patient, the ambulance personnel will perform digital randomization to either the intervention or control group.

Sample Size Calculation

To ensure sufficient statistical power, a power calculation was conducted. It is based on the assumption that the use of high-sensitivity Troponin I in prehospital emergency care will result in a 50% improvement in the identification of patients with MI, with a 2:1 ratio between the intervention and control groups. With a significance level (alpha) of 0.05 and a power of 80%, the total number of required participants was calculated. To account for potential dropouts—such as unsuccessful sampling or incomplete data—an additional 10% was added. This resulted in a total required sample size of 1,419 participants, distributed as 946 in the intervention group and 473 in the control group.

Interim Analysis

An interim analysis will be conducted by external researchers after the inclusion of the first 150 participants. The purpose is to ensure the validity and reliability of the study, confirm adherence to the protocol, and identify any unforeseen risks. The principal investigator will make the final decision regarding any potential discontinuation of the study.

Overall Study Design

This is an open, randomized controlled trial with parallel group allocation (intervention or control) using an intention-to-treat (ITT) approach. In the intervention group, blood sampling will be performed during the prehospital care period by ambulance personnel. The result is communicated via the EMS medical record system (FRAPP), along with the transmitted ECG and during verbal handover to the receiving hospital. Final clinical decisions are made by the receiving physician based on the overall clinical assessment. Follow-up will only be conducted by the research team via electronic health record review and data extraction from the Swedeheart register, no direct follow-up with participants will take place.

Procedures and Flowchart

All EMS personnel participating in the study will undergo training on the use of the point-of-care testing device and receive study-specific information prior to study initiation. In addition, they will be informed by the Principal Investigator about legal requirements and procedures for obtaining informed consent. Only EMS personnel who have completed this training will be authorized to recruit and collect samples from participants.

When a patient is assessed as eligible for inclusion, informed consent will be obtained. The responsible prehospital emergency nurse (or other nurse with specialist training) at each study site must ensure that the participant receives comprehensive oral and written information about the study, its purpose, potential risks and benefits, and inclusion/exclusion criteria. Participants must be informed of their right to withdraw at any time without providing a reason. Adequate time must be given for questions and consideration. If a patient is deemed unable to understand the provided information, they will be excluded from participation.

If the patient agrees to participate, the consent form is signed electronically, and a copy is provided to the participant. The signed and dated consent must be obtained and documented in the Case Report Form (CRF) before any study-specific procedures are carried out. Each participant will be assigned a unique study ID, and consent will include permission for the research team to access their medical records and source data. If new relevant information arises during the study, participants will have the opportunity to reassess their continued participation.

Following consent, a CRF will be initiated, and randomization to the intervention or control group will take place electronically within the CRF system.
Control Group: Will receive guideline-based care (i.e. standard of care) according to current medical guidelines.

Intervention Group: Will receive guideline-based care (i.e. standard of care) according to current medical guidelines plus a point-of-care high-sensitivity Troponin I test.

The Troponin I test will be performed on 0.03–0.1 mL of capillary or venous blood, preferably collected in parallel with EKG registration or IV access to avoid delays in care. The test is open-label, and results will be visible to EMS personnel and the patient within approximately 8 minutes.

The Troponin I level is communicated via the EMS medical record system (FRAPP), along with the transmitted ECG and during verbal handover to the receiving hospital. Final clinical decisions are made by the receiving physician based on the overall clinical assessment. Follow-up will only be conducted through the participant's electronic health records and data extraction by the research team. No additional contact will be made with the participant.

Point-of-care testing device:
Siemens Atellica VTLi

Data Collection

Following informed consent, data will be collected using an electronic Case Report Form (eCRF) via REDCap, completed by EMS personnel. Additional data sources include the patient's electronic medical record, the EMS medical record system (FRAPP), Region Stockholm healthcare administrative data warehouse (VAL), and the national quality registry Swedeheart via UCR (Uppsala Clinical Research Center).

Screening

Before randomization, it must be confirmed that the participant meets all **inclusion criteria** and does not meet any **exclusion criteria**. The inclusion decision should be made in parallel with ongoing patient care to avoid delaying transport to the hospital.

Inclusion Criteria

- Adult patients (≥18 years)
- Presenting with chest pain or with a clinical suspicion of myocardial infarction as assessed by EMS personnel

Exclusion Criteria

- No valid Swedish personal identity number
- Lacks the capacity to provide informed consent
- Not a primary EMS assignment
- Trauma Level 1 case

Randomization

Electronic randomization with a 2:1 allocation ratio will be performed during the prehospital care phase by EMS personnel using REDCap, after informed consent has been obtained. Participants will be randomized into one of the following study arms:

- **Study Arm 1: Intervention Group**
  Participants will receive guideline-based care (i.e. standard of care) according to current medical guidelines plus a point-of-care high-sensitivity Troponin I test.
- **Study Arm 2: Control Group**
  Will receive guideline-based care (i.e. standard of care) according to current medical guidelines.

Blinding

The study will be conducted using an open-label design**.**

Statistical Analyses

See separate statistical analysis plan for the TIGER study.

Potential Confounders

Potential confounding factors include conditions that may elevate troponin levels in the absence of MI, such as pulmonary embolism, sepsis, renal failure, atrial fibrillation, and heart failure. Additional potential confounders include sex, frailty, age, and time from symptom onset.

Outcome Measures

Primary Outcome Measure

1. Time from First Medical Contact (FMC) to PCI (minutes)
   Defined as the time from ambulance arrival to percutaneous coronary intervention (PCI).

Secondary Outcome Measures

1. Length of Stay (hours)
   Total duration of care (prehospital and in-hospital) per study arm. Subgroup analyses will be conducted based on potential confounders.

2. MACE (Major Adverse Cardiac Events) within 72 hours and 30 days
   Occurrence of MACE in each study arm. Subgroup analyses will be performed based on potential confounders.
   MACE is defined as:
   a) *MI*
   b) *Angina Pectoris*
   c) *New-onset heart failure (HFrEF)*
   d) *Stroke*
   e) *All-cause death*

3. *Intervention*
   Description: Number and type of interventions
   Time Frame: FMC-to-hospital discharge

4. Level of care

Distribution of admission location in each study arm, with subgroup analyses by potential confounders:

a) *Emergency Department (ED)*
b) *Coronary Care Unit (CCU)*
c) *Direct PCI*
d) *Other intermediate care unit*
e) *Other cardiac unit*
f) *Other general ward*
g) *Other healthcare facility*

5. **Clinical Utility of Point-of-Care Troponin I Testing in EMS**

Assessment of the diagnostic performance of Troponin I for early identification of MI in the prehospital setting (Sensitivity, Specificity, Negative Predictive Value (NPV) and Positive Predictive Value (PPV))

Subgroup analyses will be conducted based on potential confounders:
Overall
By time from symptom onset (≤120 min, 121–179 min, ≥180 min)

6. **Incidence of Time-Critical Diagnoses Other Than MI (within 30 days)**

Number of patients in the intervention group (Study Arm 1) with negative vs positive troponin results who receive a discharge diagnosis of another time-critical condition (excluding MI). Subgroup analyses will be performed based on potential confounders.

Risk-Benefit Assessment

In today's healthcare system, emergency departments face increasing pressure from overcrowding, while the number of EMS dispatches for chest pain continues to rise. Despite this, only a small proportion of these cases result in a confirmed diagnosis of MI, a time-critical condition. According to the latest treatment guidelines from the European Society of Cardiology (ESC), a growing share of patients requires urgent coronary intervention. There is potential benefit in enabling EMS personnel to identify MI at an earlier stage, which may facilitate faster monitoring and treatment and thereby reduce the risk of complications and mortality.

This study aims to explore the clinical value of introducing early point-of-care testing for Troponin I to improve prehospital detection of MI. Patients are included based on EMS personnel's clinical judgment and the provision of informed consent. Only EMS personnel who have received specialized training will be authorized to enroll participants. This training, provided in collaboration with the principal investigator, covers procedures for obtaining informed consent, cardiac care principles, Troponin testing, and the use of relevant equipment.

The study does not alter standard clinical management, aside from an additional blood sample analyzed using a point-of-care device. Troponin testing is already standard procedure at hospitals and results are interpreted in accordance with medical directives. If an elevated

troponin level is detected prehospitally, the cardiologist on call is informed either by phone or via the digital communication platform used by EMS. Blood sampling may cause minor discomfort, which is minimized by coordinating sampling with the establishment of peripheral IV access or other routine procedures.

Participants receive both oral and written information about the study and are informed of their right to withdraw at any time. The study's impact on length of hospital stay will be monitored through interim analyses conducted by an independent researcher. Should a significant increase in treatment time be observed, the principal investigator will consider discontinuing the study or modifying its procedures.

The risks to participating patients are considered low. Potential benefits include earlier detection of MI and thus more rapid access to treatment. This interventional study aims to enhance early decision-making by introducing high-sensitivity troponin testing into prehospital care. The implementation of point-of-care diagnostics is viewed as a strategic reinforcement of EMS capabilities.

The informed consent process is critical and includes thorough patient education, assurance of the right to withdraw without consequence, and confirmation that standard care will not be negatively affected. Privacy risks are minimized through pseudonymization and restricted data access.

In conclusion, a comprehensive evaluation indicates that the risks to participants are low, while the potential for improved early detection and timely treatment of MI—ultimately reducing morbidity and mortality—represents a substantial benefit. From an ethical perspective, the consent process is robust and safeguards patient autonomy, resulting in an overall favorable risk-benefit profile.

Biological Sampling Procedures

Handling, Storage, and Destruction of Biological Samples

No biological material will be stored after the analysis has been completed during the relevant episode of care in prehospital emergency services. The blood sample will be destroyed by the responsible EMS personnel after the care encounter, in accordance with standard operating procedures in EMS.

Total Blood Volume per Participant

The total blood volume collected from each participant during the trial will not exceed 0.1 mL.

Biobank

No samples collected during the trial will be stored. No biobank will be established. All samples will be destroyed after the care episode, following EMS standard procedures.

Trial Termination

The trial will conclude once follow-up of the final participant has been completed. The study may be terminated early if necessary for safety reasons that impact the risk-benefit assessment or if participant recruitment cannot be achieved within a reasonable timeframe. Decisions regarding early termination or modification of the study process will be made by the Principal Investigator.

Withdrawal Criteria and Incident Management

Participants may withdraw from the trial at any time without any consequences for their ongoing medical care or treatment. If a participant withdraws consent during the course of the study, data collected up to that point will be retained and used for analysis and reporting. However, any further data collection will cease upon receipt of the withdrawal, and no additional information will be gathered from the participant. This approach ensures respect for individual autonomy while allowing for the ethical and responsible use of previously collected research data.

Incidents will be reported and followed up according to the standard deviation reporting procedures in EMS. The outcomes of interim analyses will be reviewed by the research team. The Principal Investigator holds responsibility for deciding whether the study should be discontinued.

Authorship

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