The safety and efficacy of implementing the PreHEART decision support tool by the Emergency Medical Service for patients with undifferentiated chest pain: a prospective randomized open blinded end-point study (PreHeart-3 study)

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Primary Objective: 1. To determine the non-inferiority of pre-hospital risk stratification and care path selection through the preHEART algorithm as compared to usual care with respect to the occurrence of unexpected serious adverse events (USAE) in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON48009

Source
ToetsingOnline

Brief title
PreHEART 3: The best care in the right place

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
"chest pain", undifferentiated chest pain

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ambulancediensten financieren zelf deels de kosten voor het onderzoek. Subsidie is aangevraagd bij ZonMW.

Intervention

Keyword: Acute coronary syndrome, Efficacy, Emergency Medical Services

Outcome measures

Primary outcome

Main study parameter/endpoint

a) Unexpected Serious Adverse Events (USAE) at 3 and 30 days from the index contact. An USAE is defined as any unexpected and undesired medical occurrence that:

• Results in death

• Is life-threatening

• Requires (prolonged) hospitalization

• Results in persistent or significant disability or incapacity

• Any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been avoided upon appropriate judgment by the investigator.

USAE do not include events that are diagnosed during the index EMS contact. For example, the suspicion of a life-threatening diagnosis (e.g. myocardial

infarction, aortic dissection, pulmonary embolism) at the initial EMS contact which resulted into conveyance to the ED where this life-threatening diagnosis was confirmed shall not be considered an USAE (as it was not unexpected). However, when a life-threatening diagnosis was not suspected at initial contact and the patient was left at home but at a later stage the diagnosis was established it will be considered an USAE. Also, a hospitalization based on the decision to transport a patient to the hospital is not USAE. Hospitalization after an initial decision to leave a patient at home is an USAE. Prolonged hospitalization due to any complications of treatment (e.g. invasive coronary angiography) is an USAE. A (re) transportation from the ED to an alternative hospital due to the need of PCI facilities is considered an USAE.

Secondary outcome

Secondary study parameters/endpoints

a) Unexpected Serious Adverse Events (USAE) at 6 months and 1 year from the index contact

b) Unexpected Major Adverse Cardiac Event (UMACE) at 3 days, 30 days, 6 months and 1 year after index contact. UMACE is defined as:

- Cardiac death
- Myocardial infarction (9)
- Invasive coronary angiography without revascularization
- Revascularization with PCI
- Revascularization with coronary artery bypass graft (CABG)

c) Cumulative healthcare-related costs/resource (according to the Health Care Insurance Board-determined costs per treatment package [DBC]) at 3 days, 30 days, 6 months and 1 year of the index contact, including:

• Ambulance personnel (EMS) evaluation and transport

• ED costs

• In-hospital workup and treatments

• GP (huisarts) evaluation and treatment

d) Quality of life at 3 days, 30 days, 6 months and 1 year of the index contact evaluated through the EuroQol 5D-5D-5L (completed through the dedicated phone or tablet app)15

Tertiary parameter/endpoint

a) Percentage of included cases with a discordant (non-)conveyance decision between the preHEART algorithm and the effective management selected in the preHEART arm of the study

Study description

Background summary

Every year, more than 100,000 patients with chest pain are evaluated by the emergency medical services (EMS) in the Netherlands. These patients undergo

triage for potentially life-threatening conditions for which early diagnosis and treatment are essential. A major component of this triage consists of an electrocardiogram (ECG) to identify individuals with and ST-elevation myocardial infarction (STEMI). Notably, when a STEMI is identified, the patient will be conveyed to the nearest hospital with percutaneous coronary intervention (PCI) facilities for treatment of the culprit lesion. This care path has been established and has demonstrated efficacy and cost-effectiveness. However, STEMI only represents a minority of the cases presenting with acute chest pain (7%), and approximately half of the patients with a myocardial infarction will not show ST-elevation on their ECG (Non-STEMI or NSTEMI).

On the other hand, EMS contact often results in patient conveyance to the emergency department (ED), but ambulance care can alternatively result in patients not being conveyed at all. Non-conveyance is defined as *an ambulance deployment as appropriate, where the patient after examination and/or treatment on-scene does not require transport with medical personnel and equipment to the healthcare facility*. Non-conveyance includes referral to the general practitioner (GP - huisarts) and it can be due mainly to two reasons: a patient*s refusal or the professional decision of EMS personnel. Often, non-conveyance is a combination of these two categories. The current priority to conduct research on non-conveyance is reflected on the Dutch National Pre-hospital Research Agenda for EMS 2014-2018. For ambulance professionals, the (non)conveyance decision-making process is challenging and multifactorial. Competencies needed to decide on non-conveyance are marginally described, and there is a limited number of standardized support tools available for general and specific non-conveyance populations. This may compromise patient-safety.

Currently, the majority of patients with chest complaints (>75%) are conveyed to the nearest ED for further evaluation, while acute care evaluation is an increasing burden in the health care system. Overall, less than 10% of patients hospitalized for chest pain ultimately receive the diagnosis of myocardial infarction or other severe pathology. Moreover, at least 45% of the patients transported to the ED are discharged after evaluation within hours without a life-threatening condition (unnecessary ED visit)6 and approximately 6% are further (re)transported to a hospital with PCI facilities for definitive interventional care. Hence, the sequential pre-hospital and hospital approach for patients with undifferentiated chest discomfort is probably inefficient for a significant proportion of them, and there is much room for improvement.

A promising clinical tool has been the HEART risk score, which is an acronym indicating the evaluation of History of the chest discomfort, ECG findings, patient Age, the presence of cardiovascular Risk factors, and levels of Troponin I. The HEART risk score has been clinically validated in multicenter collaborations demonstrating a capacity to exclude short-term major adverse cardiovascular events (MACE) with >98% of confidence. But notably, the utility of the HEART score has been mostly evaluated in the hospital setting (i.e. the ED), while only three studies have evaluated it in the pre-hospital setting.

Recently, we have validated an adaptation of this tool for prehospital evaluation by EMS, named the preHEART risk score. This preHEART score, has demonstrated a negative predictive (NPV) value of 99.4% for the occurrence of MACE at 3 days in patients deemed as very-low risk.
It is still unknown whether prehospital implementation of the preHEART score as a decision support tool for EMS to select a dedicated care path for patients with undifferentiated chest pain is not only at least as safe but also provides more efficient care as compared to current usual care.

Study objective

Primary Objective:
1. To determine the non-inferiority of pre-hospital risk stratification and care path selection through the preHEART algorithm as compared to usual care with respect to the occurrence of unexpected serious adverse events (USAE) in patients evaluated by EMS for undifferentiated chest pain.

Secondary Objective(s):

1. To determine the non-inferiority of pre-hospital risk stratification and care path selection through the preHEART algorithm as compared to usual care with respect to the occurrence of unexpected major adverse cardiovascular events (UMACE) in patients evaluated by EMS for undifferentiated chest pain.
2. To determine the impact of pre-hospital risk stratification and care path selection through the preHEART algorithm as compared to usual care in terms of cost/resource utilization for the healthcare system in patients evaluated by EMS for undifferentiated chest pain.
3. To determine the impact of pre-hospital risk stratification and care path selection through the preHEART algorithm as compared to usual care, on patient quality of life (QoL) of patients evaluated by EMS for undifferentiated chest pain.

Study design

Due to the nature of the comparison, this study will be a pragmatic, prospectively randomized, open blinded end-point (PROBE), non-inferiority trial. This design addresses the problem of not being able to blind the EMS personnel executing the study.
Patients requesting EMS for complaints of chest pain will be screened for in- and exclusion criteria and if suitable, randomized in a 1 to 1 fashion to either receive usual care (i.e. decision of (non)conveyance to the nearest ED for further evaluation without support score) or undergo risk stratification and (non)conveyance decision (dedicated care paths) with the preHEART score algorithm (see Figure below).

All randomized patients will undergo follow-up at 3 days, 30 days, 6 months and

1 year.
The PreHEART Consortium
This project entails a continuum of health care collaborators. Therefore, it will be carried out through a consortium (the preHEART Consortium) structure involving prehospital (EMS), hospital (academic and regional hospitals with and without PCI facilities), general practice institutions (huisartspraktijken) and medical science experts (clinical, outcomes expertise, health economics, and patient participation) to ensure seamless flow of the project and patients through the areas needed to answer our research question.

The PreHEART consortium covers the full path of health care for chest pain and follows the clinical development proposed by Hartnet Noord Nederland. The three Northern Durch provinces will be involved. Two ambulance services (UMCG Ambulancezorg and Kijlstra Fryslan) with a total of 70 ambulances, providing emergency care in this region are key partners in this project and will be recruiting the intended sample size (5150 patients). Furthermore, ten hospitals are involved: the academic medical center (UMCG) and 9 regional hospitals. All hospitals have an ED and coronary care, while three also have onsite PCI facilities. The involvement of specialists from the two EMS, ten hospitals and three general practices ensure that we will be able to recruit patients and obtain accurate follow-up on their health care consumption. In particular, the three general practices in the consortium spread through the area to provide robust data and insights on patients referred to the GP under the conditions of this proposal.
The recently concluded preHEART3 study (Sagel et al. 2019, submitted) provides a relevant background for the feasibility and efficacy of the proposed intervention. The results of that study highlighted the benefit expected from the establishment of a working consortium as described in this subsection. All parties have agreed to participate in the consortium and to perform the study to achieve the stated goal.

Intervention

Subjects with undifferentiated chest pain will be randomized between two different care arms. In the intervention arm, subjects will be evaluated with additional information provided by a support tool to reach a (non-) conveyance decision and in the control arm, the decision is based without this support tool. No treatment elements are added to these programs for research purposes. In the intervention arm (preHEART algorithm arm), (non-)conveyance decisions will be made based on the decision support tool (the preHEART risk score) applied by the ambulance personnel.

The preHEART score has been developed and validated by our group based on the original HEART score. The preHEART score is based on the scoring of 5 domains with a possible range from 0 to 10 points (see Methods - Study Procedures). Based on the obtained preHEART score, patients will be stratified into 3 groups and a dedicated care path will be followed for their management:

• Very-low risk group (* 38%*) (preHEART score 0-3 points): patients will be informed about their very low risk assessment and it will be suggested not to be conveyed to the ED. If the patient agrees, he/she will not be transported to the ED and will be advised to make an appointment to see their primary care physician (huisarts) for evaluation of their symptomatology in an elective setting within 24 hours. Such evaluation will also contemplate non-cardiac etiologies of the undifferentiated chest discomfort presented.
• Intermediate risk group (* 55%*) (preHEART score 4-7 points): patients will be transported to the nearest ED for further evaluation.
• Very-high risk group: (* 7%*) (preHEART score 8-10 points): patients will be directly conveyed to the ED of a hospital with PCI capabilities (not necessarily the nearest) for further evaluation.
* Of note: the approximate percentages are based on our prior observational data available in the 75% of patients transported to the hospital.

Study burden and risks

Participation in the proposed study conveys a very low risk of adverse clinical events due to misdiagnosis of a serious condition in patients stratified as low preHEART risk. At the same time, these patients may benefit from the being reassured and allowed to remain at their residence, as well as from having to undergo unnecessary diagnostic testing that potentially carries discomfort and risk of false positive findings.
Patients with a high preHEART risk may carry the burden of anticipation of unfavorable outcomes based on their initial trial tag. However, the benefit is also expected from a prompter recognition and treatment of ACS. This is paired with less unnecessary diagnostics (due to an already high probability of the condition) and avoidance of unnecessary transports between hospitals (as they will be delivered in a facility with PCI capabilities). An additional overall burden for all participants will be the need to fill in an informed consent form and the follow-up questionnaires at 3-time points after the event.

There will be no direct compensation for participation in the PreHEART3 study. However, when a patient is not transported to a hospital they do not have to pay from their "own risk" contribution, as regulated by Dutch law. This could vary between 385 till 850 euro.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients above 17years old,
Patients with undifferentiated chest discomfort
Ability to communicate in Dutch or English

Exclusion criteria

Communication barrier (e.g. language, understanding),
ST-segment elevation myocardial infarction (electrocardiogram on scene is standard workup),
Any obvious etiology for the symptoms requiring direct treatment (e.g. trauma),
Being previously evaluated by EMS for the same complaint (already considered for participation)
High clinical suspicion of a life-threating condition (e.g. sudden death survivor, hypothermia, shock, aortic dissection, hypoxia or intoxication),
Cognitive impairment,
End-stage renal disease,
Pregnancy,
Inability or unwillingness to provide informed consent,

Not registered with a GP (huisarts).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2020
Enrollment:	5150
Type:	Actual

Ethics review

Approved WMO Date:	06-09-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-02-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-07-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-10-2020

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL69886.042.19
Other	NL7867