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Pre-hospital Triage of Acute Cardiac Patients: Rationale and Design HART-c, a multicenter prospective study

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Complete List of Authors:	de Koning, Enrico; Leiden Universitair Medisch Centrum, Cardiology Biersteker, Tom; Leiden Universitair Medisch Centrum, Cardiology Beeres, Saskia; Cardiology Bosch, Jan; Regionale Ambulancedienstvoorziening Hollands Midden Backus, Barbra; Leiden Universitair Medisch Centrum, Emergency Medicine Kirchhof, Charles; Alrijne Hospital, Department of Cardiology Alizadeh Dehnavi, Reza; Groene Hart Hospital Silvius, Helen; Leiden Universitair Medisch Centrum, Public Health and General Practice Schalij, Martin; LUMC, Cardiology Boogers, Mark; Leiden Universitair Medisch Centrum, Cardiology
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Adrian Aldcroft

Editor in Chief

BMJ Open

London, UK

10th of June, 2020

Dear Mr. Aldcroft,

I am writing to submit our manuscript entitled "*Pre-Hospital Triage of Acute Cardiac Patients: Rationale and Design of HART-c, a multicenter prospective study"* to consider for publication in BMJ Open.

The HART-c Study is the first study which evaluates a pre-hospital triage protocol that combines paramedic's patient assessment with a pre-hospital cardiologist consultation. To the best of our knowledge, this is the first study which allows a cardiologist direct access to live ambulance data, like ECG readings and vital parameters. Combined with a newly developed application showing real-time hospital's admission capacity and in-hospital patient data. The aim of the study is to safely reduce unnecessary cardiac presentations at the emergency departments (ED) and significantly reduce ED overcrowding.

Given that ED overcrowding is becoming a worldwide health care problem, we believe the proposed study in this paper will appeal to cardiologists, emergency physicians, general physicians, paramedics, other medical specialists and patients in the Emergency Medicine community. Also, we believe publishing our study protocol before collecting and assessing the final results helps in transparent and responsible science. Because we believe this triage protocol would be useful outside the scope of Cardiology, the broad audience of BMJ Open will allow more professionals in Emergency Medicine to benefit from the given information. Furthermore, we believe this study, wherein general practitioners, paramedics, emergency physicians, cardiologists, nurses and patients closely collaborate to improve healthcare for acutely ill cardiac patients, is a perfect example of interdisciplinary daily clinical practice.

Each of the authors confirms that this manuscript has not been previously published and is not currently under consideration by any other journal. Additionally, all of the authors have approved the contents of this paper and have agreed to the Academic Emergency Medicine's submission policies. Each named author has substantially contributed to conducting the underlying research and drafting of this manuscript. Additionally, to the best of our knowledge, the named authors have no conflict of interest, financial or otherwise.

Sincerely,

Enrico de Koning

Pre-hospital Triage of Acute Cardiac Patients: Rationale and Design HART-c, a multicenter prospective study

Keywords: Pre-hospital, Acute Care, Cardiac, Cardiology, Triage, HART-c, Emergency Medical Services, Emergency Department, overcrowding

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Author list: Enrico R de Koning MD[1], Tom E Biersteker MD[1] (shared first author), Saskia LMA Beeres MD PhD[1], Jan Bosch[2], Barbra E Backus MD PhD[3], Charles JHJ Kirchhof MD PhD[4], Reza Alizadeh Dehnavi MD PhD[5], Helen AM Silvius MD[6], Martin J Schalij Prof MD PhD[1], Mark J Boogers MD PhD[1]

1. Cardiology, Leiden University Medical Center, Leiden, the Netherlands. e.r.de_koning@lumc.nl; t.e.biersteker@lumc.nl; s.l.m.a.beeres@lumc.nl; m.j.schalij@lumc.nl; j.m.j.boogers@lumc.nl
2. Research and Development, Regional Ambulance Service Hollands-Midden (RAVHM), Leiden, the Netherlands. jbosch@ravhm.nl
3. Emergency Medicine, Leiden University Medical Center, Leiden, the Netherlands. b.e.backus@lumc.nl
4. Cardiology, Alrijne Hospital, Leiderdorp, the Netherlands. cjhjkirchhof@alrijne.nl
5. Cardiology, Groene Hart Hospital, Gouda, the Netherlands. reza.alizadeh.dehnavi@ghz.nl
6. Public Health and General Practice, Leiden University Medical Center, Leiden, the Netherlands. a.m.silvius@lumc.nl

Corresponding Author:

Mark J Boogers MD PhD
Cardiologist
Leiden University Medical Center
Albinusdreef 2, 2333 ZA, Leiden, the Netherlands
j.m.j.boogers@lumc.nl
0031 - 71 52 62 020

ABSTRACT

Introduction: Emergency department (ED) overcrowding is a major health care problem associated with worse patient outcomes and increased costs. Attempts to reduce ED overcrowding of cardiac patients have so far focused on in-hospital triage and rapid risk stratification of chest pain patients at the ED. The HART-c study aims to safely reduce unnecessary ED visits by implementing a pre-hospital triage protocol combining paramedic assessment and expert cardiologist consultation, supported by live-monitoring of vital parameters, hospital data and real-time admission capacity.

Methods and Analysis: Patients visited by the emergency medical services (EMS) for cardiac complaints are included. EMS consultation consists of medical history, physical examination and vital signs and ECG measurements. All data is transferred to a newly developed platform for the triage cardiologist. Pre-hospital data, in-hospital medical records and real-time admission capacity are evaluated. Then a shared decision is made whether admission is necessary and, if so, which hospital is most appropriate. To evaluate safety all patients referred to their general practitioner, and their GP's, are contacted for 30-day adverse events.

Ethics and dissemination: The study is approved by the LUMC's Medical Ethics Committee. Patients are asked for consent for contacting their GP's.

Conclusion: The HART-c study evaluates the efficacy, safety and feasibility of a pre-hospital triage protocol that combines pre-hospital patient assessment and direct consultation of a cardiologist who has access to live-monitored data, hospital data and real-time hospital admission capacity. We expect this triage protocol to substantially reduce unnecessary ED visits.

ARTICLE SUMMARY

- A novel pre-hospital triage protocol is presented which aims to safely decrease unnecessary ED admissions, using telemedicine for pre-hospital decision making
- All participants, including patient representatives, were involved in the design of the study
- **Strengths and limitations:**
  - This study is a real-life reflection of interdisciplinary daily clinical practice, the retrospective cohort will reflect the control group in the best way possible
  - The HART-c Study is not a randomised controlled trial. Therefore accomplished results can only be compared retrospectively

INTRODUCTION

Emergency Department (ED) overcrowding is a worldwide health care problem associated with worse patient outcomes and increased costs[1,2]. Cardiac complaints are one of the most common reasons for patients to visit the ED, with chest pain as the most frequent complaint.[3] In Europe and the United States, 15-20 million patients with chest pain are seen at the ED every year.[4] The majority will be sent home after ruling out acute cardiovascular disease: previous studies have shown that up to 80% of chest pain patients do not have an acute coronary syndrome.[5-8] However, these patients substantially contribute to overcrowding of EDs and these ED visits substantially increase healthcare costs.

Attempts to reduce ED overcrowding by cardiac patients have so far particularly focused on rapid risk stratification after presentation at the ED. For example, the HEART score stratifies patients as at low, intermediate or high risk of major adverse cardiac events (MACE) based on history, the electrocardiogram (ECG), age, risk factors and troponin levels.[9] However, as it takes 1-2 hours for the latter to be available, patients still spend a long time at the ED after which the majority can be discharged home.

Accordingly, interest has shifted from in-hospital to pre-hospital triage. Preventing patients with cardiac complaints and a very low risk of adverse cardiac events from visiting the ED will substantially help to reduce ED overcrowding. Until now, efforts to prevent ED visits are scarce and especially involve single interventions such as risk score calculation by the ambulance paramedic[10] or pre-hospital point of care testing for troponin.[11] In order to improve pre-hospital triage for cardiac patients in the entire chain of acute cardiac care, we developed a comprehensive triage protocol entitled HART-c ("Hollands-midden Acute Regional Triage - Cardiology"). This protocol combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, in-hospital data as well as real-time hospital admission capacity. By drafting

this triage protocol, we specifically aimed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. In addition, we intent to provide patient-tailored care through pre-hospital assessment of patient specific needs and circumstances. The HART-c study was designed to evaluate whether the implementation of the HART-c triage protocol results in a reduction of unnecessary ED visits.

METHODS AND ANALYSIS

Study design and patient population

The HART-c study is a multi-center prospective study with a historical control group. The intervention group comprises of adult patients visited by the regional emergency medical services (EMS) because of cardiac complaints between 1 September 2019 and 31 August 2020 in whom pre-hospital triage is performed according to the HART-c triage protocol. The historical control group consists of adult patients visited by the regional EMS because of cardiac complaints between 1 September 2018 and 31 August 2019 (1 year before the start of the HART-c triage protocol). Of note, in both groups EMS consultation could have been requested directly by the patient, through bystanders or by the patients' general practitioner (GP) who refers patients through EMS. Patients in need for urgent cardiac care, patients with complaints not suspected of cardiac origin as assessed by the ambulance paramedic, and patients unable or not willing to provide informed consent were excluded from triage according to the HART-c protocol. Table 1 displays the detailed inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria
Inclusion criteria
Patients visited by EMS for cardiac complaints
Age over 18 years
Exclusion criteria
Patients in need for urgent cardiac care because of - ST-elevation myocardial infarction - Hemodynamic instability - (Out of hospital) cardiac arrest - Suspected pulmonary embolism - Suspected acute aortic syndrome (thoracic or abdominal)
Patients with symptoms not suspected of cardiac origin
Unable or unwilling to provide informed consent

The HART-c study is coordinated by the Leiden University Medical Centre (LUMC) and conducted in the entire EMS region "Hollands-midden" which consists of over 600.000 inhabitants. The hospitals located in this region participate: the Leiden University Medical Centre, the Groene Hart hospital and the Alrijne hospital. The study is performed in close collaboration with the regional EMS (RAVHM) that employs 240 paramedics who are trained in pre-hospital cardiac care and 31 ambulance vehicles equipped with real-time monitoring. In addition, the study was performed and developed with the help of over regional 300 GPs.

Intervention group: Pre-hospital Triage using HART-c protocol

The intervention group consists of patients visited by the EMS because of symptoms suspected to be of cardiac origin such as chest pain, shortness of breath, palpitations or implanted cardiac device problems. In line with the National Protocol for Emergency Medical Care, patients at

first receive standard medical care consisting of a medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG.[12] In patients with chest pain, the pre-hospital modified HEART score (the HEART[13] score without troponin) is calculated. All acquired data are noted on a handheld device and stored on AmbuSuite, an external secure database. Afterwards, the ambulance paramedic directly contacts the on-call triage cardiologist. GPs can refer patients through EMS consultation, however in the intervention period cardiologist consultation is possible. When a GP is in doubt of referral, they can request cardiologist consultation through EMS with the HART-c protocol. The triage cardiologist evaluates the pre-hospital data, including, medical history, real-time vital parameters and 12-lead ECG and combines them with (if present) previous medical records and the actual hospital admission capacity of the regional hospitals. Based on these comprehensive data, the triage cardiologist and ambulance paramedic decide, as a shared decision with the patient, whether transfer to an ED is necessary and, if so, which hospital and which department is most suitable. The triage decision is sent immediately to the concerning ED nursing staff and the capacity of this hospital is updated automatically (Figure 2). Upon arrival at the ED, cardiac assessment is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] The right panel in Figure 1 illustrates the entire routing of patients in the intervention group.

Figure 1. Method of triage. (A) Patient routing without pre-hospital selection where patients are referred to the nearest ED or left at home. If hospital admission capacity is insufficient, patients are transferred to another hospital. (B) Patient routing with pre-hospital selection using pre- and in-hospital data where a cardiologist has insight in live vital parameters and regional hospital capacity.

Figure 2. Mobile phone triage application: Left panel showing overview of a hospital specific capacity. Right panel showing the ability to update capacity.

Intervention group: Tempus Pro Monitor, IntelliSpace Corsium, triage platform and data handling

All ambulances are equipped with a Tempus Pro Monitor[14] (Philips, The Netherlands) that allows recording of a 12-lead ECG and real-time monitoring of the following vital patient parameters: heart rate, blood pressure and pulse oximetry. The monitor can show trends in measurements and stream data for up to 10 hours. All data are encrypted and shared with the on-call triage cardiologist through secure channels. The Tempus Pro Monitor is shown in Figure 3.

Figure 3. Image of Tempus Pro Monitor.

Using a secure log-in, the on-call triage cardiologist logs in to IntelliSpace Corsium (Philips, the Netherlands) and connects digitally with a patient specific Tempus Pro Monitor. All aforementioned measurements are streamed live. Once the live streaming ends, no patient specific data are stored on the platform. This system of data-transfer is FDA approved.[15,16]

A novel triage platform was developed showing real-time admission capacity of the regional hospitals. The nursing staff in these hospitals continuously updates their admission capacity. Linking these capacity data to a local electronic patient dossier (EPD-Vision; Leiden, The Netherlands), the on-call triage cardiologist has insight into the actual bed occupancy of each hospital. After consultation, the on-call triage cardiologist notes his decision and a message is automatically sent to the nursing staff of the chosen hospital, thereby updating their admission capacity immediately.

Patient data are sent securely from Tempus Monitor to IntelliSpace Corsium. No data are stored on IntelliSpace Corsium. No patient data are transmitted to the mobile phone application. Patient data are transferred from AmbuSuite to our EPD. All patient data and decisions are stored on the EPD of the coordinating hospital and are only accessible for triage cardiologists.

Historical control group: Standard care in pre-hospital setting

The historical control group consists of patients visited by the EMS because of potential cardiac complaints in the year before the onset of the HART-c triage protocol. Upon arrival by the paramedic, standard medical care consists of medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG. All acquired data are noted on a handheld device and stored on AmbuSuite (Topicus, the Netherlands) which is an external secure database. Thereafter, the ambulance paramedic decides, based on predefined national protocols and decision rules for diagnosis, whether transfer to an ED is deemed necessary.[12] Paramedics select low risk patients for the whole pallet of medical specialties, and only transport patients with cardiac complaints when in doubt or if admission is deemed necessary. Of note, at the time of referral, the paramedic has no insight in the previous medical records and the actual hospital admission capacity. The Netherlands has a unique system, where approximately 5% of patients with cardiac complaints aren't referred to a hospital after paramedic assessment, instead these patients are directly referred to their GP. However, given the number of unnecessary ED visits, based on expert opinion, an increase in patients not referred to a hospital is possible. After paramedic assessment and hospital transport, cardiac assessment on the ED is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] If evaluation at the ED indicates that hospitalization is mandatory, the patient is admitted in the concerning hospital. However, when admission capacity is insufficient or immediate intervention is not available in the concerning hospital, ambulance transfer to another hospital is mandatory. The routing of patients in the historical control group is illustrated in the left panel of Figure 1.

Objective and outcome measures

The HART-c study is designed to evaluate the efficacy, safety and feasibility of a novel comprehensive pre-hospital triage protocol which aims to safely reduce unnecessary ED visits

in patients with cardiac complaints. The primary outcome is the percentage of patients in who an ED visit can be prevented after EMS consultation. The following secondary end-points will be evaluated:

- Number of ambulance transfers to an ED because of cardiac complaints
- Number of inter-hospital transfers in cardiac patients
- Patient, triage cardiologist and GP satisfaction with the HART-c triage protocol on a 0-10 scale
- Safety of the HART-c prehospital triage protocol. This will be evaluated in intervention group patients who are not transferred to an ED and assessed by the occurrence of adverse events up to 30 days follow-up. Table 2 displays the pre-specified major and minor adverse events. To evaluate safety, a dedicated researcher will contact these patients and their GP.
- Feasibility of the HART-c prehospital triage protocol. This will be evaluated in the intervention group and defined as the absence of technical problems for the ambulance paramedic and the triage cardiologist. This means access to the live-monitored data from the ambulance, hospital data and real-time hospital admission capacity are all available. In order to swiftly manage potential technical problems, the HART-c triage protocol will start during working hours. If interim analysis reveals that the protocol is feasible, the time frame in which HART-c triage is available could be extended.

Table 2. Adverse events (30 days after EMS contact)
Major adverse events
Death
Acute coronary syndrome
Other adverse events
Renewed EMS visit for any cardiac complaint
Pulmonary embolism
ED visit or hospitalization for acute decompensated heart failure
Ventricular tachycardia or – fibrillation
Cerebrovascular accident (CVA) or transient ischemic attack (TIA)

Statistical analysis

The percentage of patients in whom an ED visit can be prevented after EMS consultation will be analyzed using a logistic regression analysis. Comparison of the total number of ambulance transfers and the number of inter hospital transfers in the intervention versus in the control group will also be evaluated using logistic regression. This study will be underpowered to detect differences in mortality and major adverse cardiac events (MACE). Accordingly, these events will only be reported and no further statistics on mortality and MACE will be done. The data will be analysed using IBM SPSS Statistics version 25. A p-value lower than 0.05 will be considered statistically significant.

Patient and public involvement

Patients were involved in the design of the study. During the design stage, representatives from the 'Harteraad', a cardiovascular patient council, were asked for input in study design, choice of outcome measures and methods of recruitment. Also, a dedicated website and e-mail address

were created to inform the public and answer questions from professionals and patients, before and during the study.

ETHICS AND DISSEMINATION

The study is approved by the LUMC's Medical Ethics Committee (P18.213). Patients are requested to provide oral informed consent for contacting their GP at 30 days follow-up. The devices used in this study are FDA and/or CE approved. No manufacturer has a role in study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any manufacturer.

DISCUSSION

Overcrowding of ED's is a major challenge in healthcare. The HART-c study is a multi-center prospective study that primarily aims to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. If this will succeed, it will contribute to more patient-tailored health care and lead to improved utilization of healthcare resources.

Although recently interest has shifted from in-hospital to pre-hospital triage, efforts to reduce the number of patients with cardiac complaints visiting at the ED are limited. As far as we know, until now only 2 study groups evaluate the added value of pre-hospital risk assessment in chest pain patients. The FAMOUS investigators aim to assess the effects of introducing a pre-hospital triage system that stratifies chest pain patients without ST segment elevation into 1) patients at high risk for NSTEMI requiring direct transfer to a PCI hospital, 2) patients at intermediate risk for major adverse cardiac events who could be evaluated at the nearest non-PCI hospital and 3) patients at low risk for major adverse cardiac events who could have further evaluation at home or in a primary care setting.[17] The study was divided in three phases. In the

first phase, a venous blood sample was drawn in the ambulance for measurement of the pre-hospital troponin T levels, in order to establish a pre-hospital HEART score (i.e. the modified HEART score) and evaluate the possibility of triage at the patient's home. All patients were transferred to the hospital and the primary end-point was the occurrence of major adverse cardiac events within 30-days after presentation. Of the 1127 chest pain patients, 36% had a low modified HEART score and none of them developed a major adverse event. Accordingly, the FAMOUS authors concluded that it seemed feasible to rule out myocardial infarction at home in patients without ST segment elevation on the ECG.[18] In the second phase, this tool will be externally validated. In the third phase, the risk stratification tool will be implemented in clinical practice. Until now, the results of the second and third phase have not been published.

Another study investigating the added value of point-of-care troponin in the pre-hospital setting is the ARTICA[11] trial. This randomized trial will include patients suspected of non-ST elevation acute coronary syndrome in whom the modified HEAR score (the HEART score without troponin) is calculated by the ambulance paramedic. If the HEAR score is less than or equal to 3, patients will be 1:1 randomized for 1) presentation at the ED or 2) point-of-care troponin T measurement and transfer of care to the GP in case of a low troponin T value. The primary objective of the ARTICA trial will be healthcare costs at 30 days. The trial is currently ongoing and aims to include 866 patients in total. The total follow-up period will be 12 months. The similarity of the currently described HART-c study and the FAMOUS and ARTICA is that all three assess whether patients with cardiac complaints who are at low risk of major adverse events can be prevented from visiting the ED. However, while the FAMOUS and ARTICA study only focus on chest pain patients, the HART-c study extents this to all patients with cardiac complaints and could therefore be of benefit for a substantially larger cohort of patients. Furthermore, the HART-c triage protocol is unique as it combines pre-hospital patient

assessment by the ambulance paramedic and direct consultation of an expert triage cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the results of current study show that the HART-c triage protocol is effective in safely reducing unnecessary ED visits of patients with all types of cardiac complaints, the next step will be to evaluate cost-effectiveness. When thereafter also cost-effectiveness can be demonstrated, we feel that the HART-c triage protocol can be expanded to other EMS regions. Furthermore, last but not least, it may potentially also be useful for other medical specialists aiming to optimize pre-hospital triage of non-cardiac patients.

CONCLUSION

The HART-c study is a multi-center prospective study evaluating the efficacy, safety and feasibility of a novel comprehensive pre-hospital triage protocol that combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the HART-c study will succeed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints, it may help to decrease ED overcrowding and ultimately reduce healthcare expenditures.

Author statement

EK, TB, JB, CK, RAD, HS, MS and MB made a substantial contribution to the concept and design of the work. EK and MB are in charge of acquisition of data, analysis and interpretation of the data. EK, TB, SB and MB contributed to the drafting of the article. EK, SB, JB, BB, CK, RAD, MS and MB all revised the manuscript critically for important intellectual content.

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Competing interest

EK, TB, SB, JB, CK, RAD, HS, MS and MB report no conflict of interest. BB is the creator of the HEART score.

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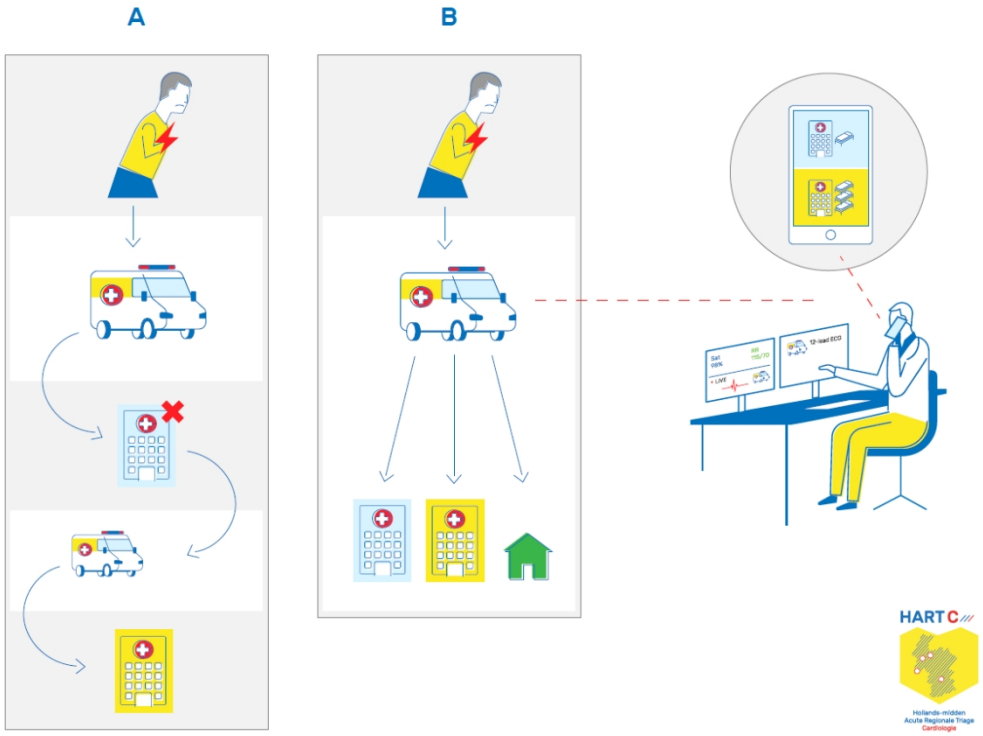

Figure 1. Method of triage

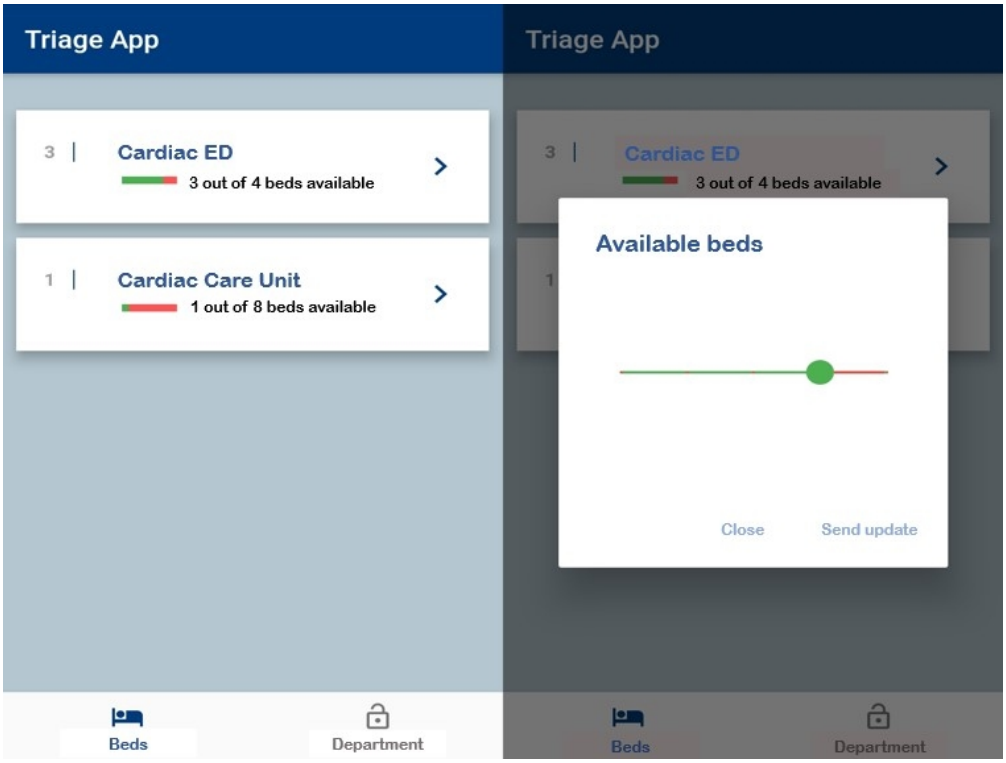

Figure 2. Mobile phone triage application

200x151mm (96 x 96 DPI)

Figure 3. Image of Tempus Pro Monitor

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Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

Keywords: Pre-hospital, Acute Care, Cardiac, Cardiology, Triage, HART-c, Emergency Medical Services, Emergency Department, overcrowding

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Author list: Enrico R de Koning MD[1], Tom E Biersteker MD[1] (shared first author), Saskia LMA Beeres MD PhD[1], Jan Bosch[2], Barbra E Backus MD PhD[3], Charles JHJ Kirchhof MD PhD[4], Reza Alizadeh Dehnavi MD PhD[5], Helen AM Silvius MD[6], Martin J Schalij Prof MD PhD[1], Mark J Boogers MD PhD[1]

1. Cardiology, Leiden University Medical Center, Leiden, the Netherlands. e.r.de_koning@lumc.nl; t.e.biersteker@lumc.nl; s.l.m.a.beeres@lumc.nl; m.j.schalij@lumc.nl; j.m.j.boogers@lumc.nl
2. Research and Development, Regional Ambulance Service Hollands-Midden (RAVHM), Leiden, the Netherlands. jbosch@ravhm.nl
3. Emergency Medicine, Leiden University Medical Center, Leiden, the Netherlands. b.e.backus@lumc.nl
4. Cardiology, Alrijne Hospital, Leiderdorp, the Netherlands. cjhjkirchhof@alrijne.nl
5. Cardiology, Groene Hart Hospital, Gouda, the Netherlands. reza.alizadeh.dehnavi@ghz.nl
6. Public Health and General Practice, Leiden University Medical Center, Leiden, the Netherlands. a.m.silvius@lumc.nl

Corresponding Author:

Mark J Boogers MD PhD
Cardiologist
Leiden University Medical Center
Albinusdreef 2, 2333 ZA, Leiden, the Netherlands
j.m.j.boogers@lumc.nl
0031 - 71 52 62 020

ABSTRACT

Introduction: Emergency department (ED) overcrowding is a major health care problem associated with worse patient outcomes and increased costs. Attempts to reduce ED overcrowding of cardiac patients have so far focused on in-hospital triage and rapid risk stratification of chest pain patients at the ED. The HART-c study aims to safely reduce unnecessary ED visits by implementing a pre-hospital triage protocol combining paramedic assessment and expert cardiologist consultation, supported by live-monitoring of vital parameters, hospital data and real-time admission capacity.

Methods and Analysis: Patients visited by the emergency medical services (EMS) for cardiac complaints are included. EMS consultation consists of medical history, physical examination and vital signs and ECG measurements. All data is transferred to a newly developed platform for the triage cardiologist. Pre-hospital data, in-hospital medical records and real-time admission capacity are evaluated. Then a shared decision is made whether admission is necessary and, if so, which hospital is most appropriate. To evaluate safety all patients referred to their general practitioner, and their GP's, are contacted for 30-day adverse events.

Ethics and dissemination: The study is approved by the LUMC's Medical Ethics Committee. Patients are asked for consent for contacting their GP's. The main results of this trial will be disseminated in one paper.

Discussion: The HART-c study evaluates the efficacy, safety and feasibility of a pre-hospital triage protocol that combines pre-hospital patient assessment and direct consultation of a cardiologist who has access to live-monitored data, hospital data and real-time hospital admission capacity. We expect this triage protocol to substantially reduce unnecessary ED visits.

ARTICLE SUMMARY

- A novel pre-hospital triage protocol is presented which aims to safely decrease unnecessary ED admissions, using telemedicine for pre-hospital decision making
- All participants, including patient representatives, were involved in the design of the study
- **Strengths and limitations:**
    - This study is a real-life reflection of interdisciplinary daily clinical practice, the retrospective cohort will reflect the control group in the best way possible
    - The HART-c Study is a non-randomised controlled trial and therefore has risk of bias as decisions from paramedics and cardiologist can be influenced by the study.

INTRODUCTION

Emergency Department (ED) overcrowding is a worldwide health care problem associated with worse patient outcomes and increased costs[1,2]. Cardiac complaints are one of the most common reasons for patients to visit the ED, with chest pain as the most frequent complaint.[3] In Europe and the United States, 15-20 million patients with chest pain are seen at the ED every year.[4] The majority will be sent home after ruling out acute cardiovascular disease: previous studies have shown that up to 80% of chest pain patients do not have an acute coronary syndrome.[5-8] However, these patients contribute to overcrowding of EDs and these ED visits substantially increase healthcare costs.

Attempts to reduce ED overcrowding by cardiac patients have so far particularly focused on rapid risk stratification after presentation at the ED. For example, the HEART score stratifies patients as at low, intermediate or high risk of major adverse cardiac events (MACE) based on history, the electrocardiogram (ECG), age, risk factors and troponin levels.[9] However, as it takes 1-2 hours for the latter to be available, patients still spend a long time at the ED after which the majority can be discharged home.

Accordingly, interest has shifted from in-hospital to pre-hospital triage. Preventing patients with cardiac complaints and a very low risk of adverse cardiac events from visiting the ED will substantially help to reduce ED overcrowding. Efforts to prevent ED visits especially involve interventions focused on chest pain patients such as risk score calculation by the ambulance paramedics (for example with the modified HEART[10] and HE-MACS[11]) or pre-hospital point of care testing for troponin.[12] In order to improve pre-hospital triage for cardiac patients in the entire chain of acute cardiac care, we developed a comprehensive triage protocol entitled HART-c ("Hollands-midden Acute Regional Triage - Cardiology").

Innovative in this protocol is the combination of pre-hospital patient assessment by the ambulance paramedic and expert consultation of a cardiologist who has access to live-

monitored data from the ambulance, in-hospital data and real-time hospital admission capacity in a newly developed triage application. By drafting this triage protocol, we specifically aimed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. In addition, we intent to provide patient-tailored care through pre-hospital assessment of patient specific needs and circumstances. The HART-c study was designed to evaluate whether the implementation of the HART-c triage protocol results in a reduction of unnecessary ED visits.

METHODS AND ANALYSIS

Study design and patient population

The HART-c study is a multi-center prospective study with a historical control group. The intervention group comprises of adult patients visited by the regional emergency medical services (EMS) because of cardiac complaints between 1 September 2019 and 31 August 2020 in whom pre-hospital triage is performed according to the HART-c triage protocol. The historical control group consists of adult patients visited by the regional EMS because of cardiac complaints between 1 September 2018 and 31 August 2019 (1 year before the start of the HART-c triage protocol). Of note, in both groups EMS consultation could have been requested directly by the patient, through bystanders or by the patients' general practitioner (GP) who refers patients through EMS. Patients in need for urgent cardiac care, patients with complaints not suspected of cardiac origin as assessed by the ambulance paramedic, and patients unable or not willing to provide informed consent were excluded from triage according to the HART-c protocol. Table 1 displays the detailed inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria
Inclusion criteria
Patients visited by EMS for cardiac complaints
Age over 18 years
Exclusion criteria
Patients in need for urgent cardiac care because of - **ST-elevation myocardial infarction** - **Hemodynamic instability** - **(Out of hospital) cardiac arrest** - **Suspected pulmonary embolism** - **Suspected acute aortic syndrome (thoracic or abdominal)**
Patients with symptoms not suspected of cardiac origin
Unable or unwilling to provide informed consent

The HART-c study is coordinated by the Leiden University Medical Centre (LUMC) and conducted in the entire EMS region "Hollands-midden" which consists of over 600.000 inhabitants. The hospitals located in this region participate: the Leiden University Medical Centre, the Groene Hart hospital and the Alrijne hospital. The study is performed in close collaboration with the regional EMS (RAVHM) that employs 240 paramedics who are trained in pre-hospital cardiac care and 31 ambulance vehicles equipped with real-time monitoring. In addition, the study was performed and developed with the help of over regional 300 GPs.

Intervention group: Pre-hospital Triage using HART-c protocol

The intervention group consists of patients visited by the EMS because of symptoms suspected to be of cardiac origin such as chest pain, shortness of breath, palpitations or implanted cardiac device problems. In line with the National Protocol for Emergency Medical Care, patients at

first receive standard medical care consisting of a medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG.[13] In patients with chest pain, the pre-hospital modified HEART score (the HEART[14] score without troponin) is calculated. All acquired data are noted on a handheld device and stored on AmbuSuite, an external secure database. Afterwards, the ambulance paramedic directly contacts the on-call triage cardiologist. In total, 43 cardiologist from all three reginal hospitals are scheduled so one cardiologist is on duty for the entire region. GPs can refer patients through EMS consultation, however in the intervention period cardiologist consultation is possible. When a GP is in doubt of referral, they can request cardiologist consultation through EMS with the HART-c protocol. The triage cardiologist evaluates the pre-hospital data, including, medical history, real-time vital parameters and 12-lead ECG and combines them with (if present) previous medical records and the actual hospital admission capacity of the regional hospitals. Based on these comprehensive data, the triage cardiologist and ambulance paramedic decide, as a shared decision with the patient, whether transfer to an ED is necessary and, if so, which hospital and which department is most suitable. The triage decision is sent immediately to the concerning ED nursing staff and the capacity of this hospital is updated automatically (Figure 2). Upon arrival at the ED, cardiac assessment is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] The right panel in Figure 1 illustrates the entire routing of patients in the intervention group.

Figure 1. Method of triage. (A) Patient routing without pre-hospital selection where patients are referred to the nearest ED or left at home. If hospital admission capacity is insufficient, patients are transferred to another hospital. (B) Patient routing with pre-hospital selection using pre- and in-hospital data where a cardiologist has insight in live vital parameters and regional hospital capacity.

Figure 2. Mobile phone triage application: Left panel showing overview of a hospital specific capacity. Right panel showing the ability to update capacity.

Intervention group: Tempus Pro Monitor, IntelliSpace Corsium, triage platform and data handling

All ambulances are equipped with a Tempus Pro Monitor[15] (Philips, The Netherlands) that allows recording of a 12-lead ECG and real-time monitoring of the following vital patient parameters: heart rate, blood pressure and pulse oximetry. The monitor can show trends in measurements and stream data for up to 10 hours. All data are encrypted and shared with the on-call triage cardiologist through secure channels. The Tempus Pro Monitor is shown in Figure 3.

Figure 3. Image of Tempus Pro Monitor.

Using a secure log-in, the on-call triage cardiologist logs in to IntelliSpace Corsium (Philips, the Netherlands) and connects digitally with a patient specific Tempus Pro Monitor. All aforementioned measurements are streamed live. Once the live streaming ends, no patient specific data are stored on the platform. This system of data-transfer is FDA approved.[16,17]

A novel triage platform was developed showing real-time admission capacity of the regional hospitals. The nursing staff in these hospitals continuously updates their admission capacity. Linking these capacity data to a local electronic patient dossier (EPD-Vision; Leiden, The Netherlands), the on-call triage cardiologist has insight into the actual bed occupancy of each hospital. After consultation, the on-call triage cardiologist notes his decision and a message is automatically sent to the nursing staff of the chosen hospital, thereby updating their admission capacity immediately.

Patient data are sent securely from Tempus Monitor to IntelliSpace Corsium. No data are stored on IntelliSpace Corsium. No patient data are transmitted to the mobile phone application. Patient data are transferred from AmbuSuite to our EPD. All patient data and decisions are stored on the EPD of the coordinating hospital and are only accessible for triage cardiologists.

Historical control group: Standard care in pre-hospital setting

The historical control group consists of patients visited by the EMS because of potential cardiac complaints in the year before the onset of the HART-c triage protocol. Upon arrival by the paramedic, standard medical care consists of medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG. All acquired data are noted on a handheld device and stored on AmbuSuite (Topicus, the Netherlands) which is an external secure database. Thereafter, the ambulance paramedic decides, based on predefined national protocols and decision rules for diagnosis, whether transfer to an ED is deemed necessary.[12] Paramedics are able to identify low-risk patient for all medical specialties, and decide whether admission or ED presentation is necessary on every consultation. So, even in the historical cohort group only patients with cardiac complaints deemed severe enough for presentation are presented to the ED. Of note, at the time of referral, the paramedic has no insight in the previous medical records and the actual hospital admission capacity. The Netherlands has a unique system, where, in the historical cohort in our region, approximately 5% of patients with cardiac complaints aren't referred to a hospital after paramedic assessment, instead these patients are directly referred to their GP or treated at home. However, given the number of unnecessary ED visits, there is still a large cohort of low-risk patients in whom ED presentation could be prevented. After paramedic assessment and hospital transport, cardiac assessment on the ED is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] If evaluation at the ED indicates that hospitalization is mandatory, the patient is admitted in the concerning

hospital. However, when admission capacity is insufficient or immediate intervention is not available in the concerning hospital, ambulance transfer to another hospital is mandatory. The routing of patients in the historical control group is illustrated in the left panel of Figure 1.

Objective and outcome measures

The HART-c study is designed to evaluate the efficacy, safety and feasibility of a novel comprehensive pre-hospital triage protocol which aims to safely reduce unnecessary ED visits in patients with cardiac complaints. The primary outcome is the percentage of patients in who an ED visit can be prevented after EMS consultation. The following secondary end-points will be evaluated:

- Number of ambulance transfers to an ED because of cardiac complaints.
- Number of inter-hospital transfers in cardiac patients.
- Patient, triage cardiologist and GP satisfaction with the HART-c triage protocol on a 0-10 scale.
- Time from EMS consultation to arrival at the hospital in the both study groups.
- Safety of the HART-c prehospital triage protocol. This will be evaluated in intervention group patients who are not transferred to an ED after cardiologist consultation. Safety will be assessed by the occurrence of adverse events up to 30 days follow-up. Table 2 displays the pre-specified major and non-major adverse events. To evaluate safety, a dedicated researcher will contact these patients and their GP and evaluate on a case-by-case basis. If a major adverse event is deemed directly attributable to the triage protocol, the protocol will be adjusted or the study will be terminated prematurely.
- Feasibility of the HART-c prehospital triage protocol. This will be evaluated in the intervention group and defined as the absence of technical problems for the ambulance paramedic and the triage cardiologist. This means access to the live-monitored data

from the ambulance, hospital data and real-time hospital admission capacity are all available. In order to swiftly manage potential technical problems, the HART-c triage protocol will start during working hours. If interim analysis reveals that the protocol is feasible, the time frame in which HART-c triage is available could be extended.

Table 2. Adverse events (30 days after EMS contact)

Major adverse events
Death
Acute coronary syndrome
Other adverse events
Renewed EMS or ED visit for cardiac complaint
Pulmonary embolism
ED visit or hospitalization for acute decompensated heart failure
Ventricular tachycardia or – fibrillation
Cerebrovascular accident (CVA) or transient ischemic attack (TIA)

Statistical analysis

The prevention of an ED visit after EMS consultation will be analysed using a logistic regression analysis. Ambulance transfers and inter hospital transfers in the intervention versus the control group will also be evaluated using logistic regression. Baseline characteristics will be reported as mean and standard deviation or median and interquartile range and compared between historical cohort and intervention. This study will be underpowered to detect differences in mortality and major adverse cardiac events (MACE). Accordingly, these events will only be reported and no further statistics on mortality and MACE will be done. The data

will be analysed using IBM SPSS Statistics version 25. A p-value lower than 0.05 will be considered statistically significant.

Patient and public involvement

Patients were involved in the design of the study. During the design stage, representatives from the 'Harteraad', a cardiovascular patient council, were asked for input in study design, choice of outcome measures and methods of recruitment. Also, a dedicated website and e-mail address were created to inform the public and answer questions from professionals and patients, before and during the study.

ETHICS AND DISSEMINATION

The study is approved by the LUMC's Medical Ethics Committee (P18.213). Patients are requested to provide oral informed consent for contacting their GP at 30 days follow-up. Oral informed consent is requested for cardiologist consultation and study participation by paramedics which is then noted in AmbuSuite. Written informed consent was not deemed feasible or necessary in this urgent setting. The devices used in this study are FDA and/or CE approved. No manufacturer has a role in study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any manufacturer. The main results of this trial will be disseminated in one paper.

DISCUSSION

Overcrowding of ED's is a major challenge in healthcare. The HART-c study is a multi-centre prospective study that primarily aims to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. By selecting the hospital best suited for every patient, this

protocol will contribute to more patient-tailored health care and lead to improved utilization of all available healthcare resources in the region.

Recently, interest has shifted from in-hospital - to pre-hospital triage. Pre-hospital cardiologist consultation has been standard procedure for some time in many hospitals in the Netherlands for quick catheterization lab activation when paramedics suspect chest pain patients of STEMI.[18] For all other cardiac complaints no pre-hospital triage procedure is in place for emergency evaluations. However, there have been some studies assessing the possibility of pre-hospital triage and pre-hospital selection of low-risk cardiac patients.

The History and ECG-only Manchester ACS (HE-MACS) decision aid was developed for pre-hospital triage using history, physical examination and ECG. It was derived in 796 patients and validated in cohorts of 474 and 659 patients. 9.4% of all validated patients were identified as 'very low risk' in which ACS could be 'ruled out' with a sensitivity of 99.5%. It's impact, however, was not prospectively evaluated in this study.

The FAMOUS investigators aim to assess the effects of introducing a pre-hospital triage system that stratifies chest pain patients without ST segment elevation into 1) patients at high risk for NSTEMI requiring direct transfer to a PCI hospital, 2) patients at intermediate risk for major adverse cardiac events who could be evaluated at the nearest non-PCI hospital and 3) patients at low risk for major adverse cardiac events who could have further evaluation at home or in a primary care setting.[19] The study was divided in three phases. In the first phase, a venous blood sample was drawn in the ambulance for measurement of the pre-hospital troponin T levels, in order to establish a pre-hospital HEART score and evaluate the possibility of triage at the patient's home. Of the 1127 chest pain patients, 36% had a low modified HEART score and none of them developed a major adverse event. Accordingly, the FAMOUS authors concluded that it seemed feasible to rule out myocardial infarction at home in patients without ST segment elevation on the ECG.[20] After this first phase proving feasibility, further studies have been done

in the pre-hospital setting by the FAMOUS TRIAGE study group. In a prospective observational study, including 700 patients with suspected NSTE-ACS, 24.6 % (172 patients) were stratified as low risk with a MACE occurrence of 2.9% as opposed to 21.0% MACE occurrence in the intermediate to high risk group. This study showed nicely that pre-hospital risk stratification by ambulance paramedics using the HEART score was accurate in differentiating in low and intermediate to high risk.[21]

Another study investigating the added value of point-of-care troponin in the pre-hospital setting is the ARTICA[12] trial. This randomized trial will include patients suspected of non-ST elevation acute coronary syndrome in whom the modified HEAR score (the HEART score without troponin) is calculated by the ambulance paramedic. If the HEAR score is less than or equal to 3, patients will be 1:1 randomized for 1) presentation at the ED or 2) point-of-care troponin T measurement and transfer of care to the GP in case of a low troponin T value. The primary objective of the ARTICA trial will be healthcare costs at 30 days. The trial is currently ongoing and aims to include 866 patients in 12 months.

The similarity of the currently described HART-c study and the HE-MACS, FAMOUS and ARTICA studies is that all three assess whether patients with chest pain who are at low risk of major adverse events can be identified before presenting to the ED. However, the HART-c study has some added benefit as opposed to earlier known studies. First, the HART-c study does not only identify patients at low-risk for events, but also aims to effectively prevent low-risk patients from actually visiting the ED by combining pre-hospital risk stratification by the paramedic and real-time cardiologist consultation with insight in live vital parameters and ECG. Secondly, while these studies study only focus on chest pain patients, the HART-c study extends this to all patients with cardiac complaints and could therefore be of benefit for a substantially larger cohort of patients. Furthermore, the HART-c triage protocol is unique as it combines pre-hospital patient assessment by the ambulance paramedic and direct consultation

of an expert triage cardiologist who has access to live-monitored data from the ambulance for all cardiac patients, as opposed to only STEMI patients. Besides these novelties, the HART-c study incorporates hospital data as well as real-time hospital admission capacity to decide which regional hospital is best suited for every patient.

If the results of current study show that the HART-c triage protocol is effective in safely reducing unnecessary ED visits of patients with all types of cardiac complaints, the next step will be to evaluate cost-effectiveness. When cost-effectiveness can be demonstrated, we feel that the HART-c triage protocol can be expanded to other EMS regions. Furthermore, last but not least, it may potentially also be useful for other medical specialists aiming to optimize pre-hospital triage of non-cardiac patients. Eventual improvements in pre-hospital triage, such as pre-hospital high sensitive Troponin sampling with a point-of-care test or newly developed and proven risk scores, could always be implemented in this triage protocol.

To conclude, the HART-c study is a multi-center prospective study evaluating the efficacy, safety and feasibility of a novel comprehensive pre-hospital triage protocol that combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the HART-c study will succeed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints, it may help to decrease ED overcrowding and ultimately reduce healthcare expenditures.

Author statement

EK, TB, JB, CK, RAD, HS, MS and MB made a substantial contribution to the concept and design of the work. EK and MB are in charge of acquisition of data, analysis and interpretation of the data. EK, TB, SB and MB contributed to the drafting of the article. EK, SB, JB, BB, CK, RAD, MS and MB all revised the manuscript critically for important intellectual content.

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Competing interest

EK, TB, SB, JB, CK, RAD, HS, MS and MB report no conflict of interest. BB is the creator of the HEART score.

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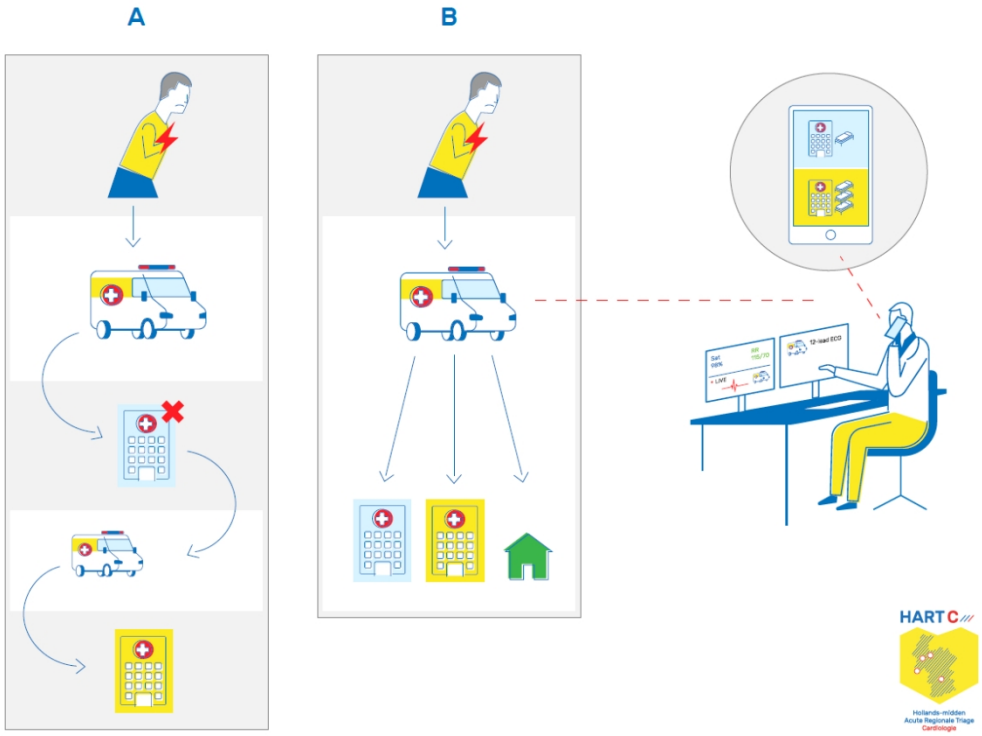

Figure 1. Method of triage

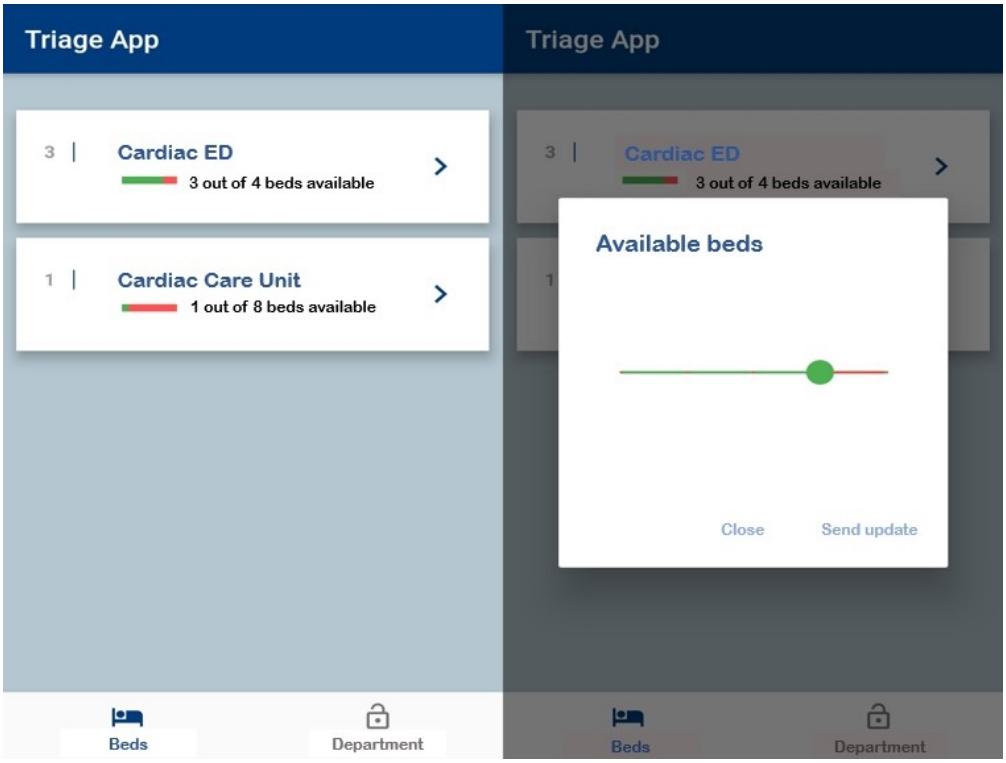

Figure 2. Mobile phone triage application

200x151mm (96 x 96 DPI)

Figure 3. Image of Tempus Pro Monitor

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Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

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Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

Keywords: Pre-hospital, Acute Care, Cardiac, Cardiology, Triage, HART-c, Emergency Medical Services, Emergency Department, overcrowding
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Author list: Enrico de Koning MD[1], Tom E Biersteker MD[1] (shared first author), Saskia Beeres MD PhD[1], Jan Bosch[2], Barbra E Backus MD PhD[3], Charles JHJ Kirchhof MD PhD[4], Reza Alizadeh Dehnavi MD PhD[5], Helen AM Silvius MD[6], Martin Schalij Prof MD PhD[1], Mark J Boogers MD PhD[1]

1. Cardiology, Leiden University Medical Center, Leiden, the Netherlands. e.r.de_koning@lumc.nl; t.e.biersteker@lumc.nl; s.l.m.a.beeres@lumc.nl; m.j.schalij@lumc.nl; j.m.j.boogers@lumc.nl
2. Research and Development, Regional Ambulance Service Hollands-Midden (RAVHM), Leiden, the Netherlands. jbosch@ravhm.nl
3. Emergency Medicine, Leiden University Medical Center, Leiden, the Netherlands. b.e.backus@lumc.nl
4. Cardiology, Alrijne Hospital, Leiderdorp, the Netherlands. cjhjkirchhof@alrijne.nl
5. Cardiology, Groene Hart Hospital, Gouda, the Netherlands. reza.alizadeh.dehnavi@ghz.nl
6. Public Health and General Practice, Leiden University Medical Center, Leiden, the Netherlands. a.m.silvius@lumc.nl

Corresponding Author:

Mark J Boogers MD PhD
Cardiologist
Leiden University Medical Center
Albinusdreef 2, 2333 ZA, Leiden, the Netherlands
j.m.j.boogers@lumc.nl
0031 - 71 52 62 020

ABSTRACT

Introduction: Emergency department (ED) overcrowding is a major health care problem associated with worse patient outcomes and increased costs. Attempts to reduce ED overcrowding of cardiac patients have so far focused on in-hospital triage and rapid risk stratification of chest pain patients at the ED. The HART-c study aims to assess the amount of patients left at home in usual ambulance care as compared to the new pre-hospital triage protocol. This protocol combines paramedic assessment and expert cardiologist consultation using live-monitoring, hospital data and real-time admission capacity.

Methods and Analysis: Patients visited by the emergency medical services (EMS) for cardiac complaints are included. EMS consultation consists of medical history, physical examination and vital signs and ECG measurements. All data is transferred to a newly developed platform for the triage cardiologist. Pre-hospital data, in-hospital medical records and real-time admission capacity are evaluated. Then a shared decision is made whether admission is necessary and, if so, which hospital is most appropriate. To evaluate safety, all patients left at home and their GP's, are contacted for 30-day adverse events.

Ethics and dissemination: The study is approved by the LUMC's Medical Ethics Committee. Patients are asked for consent for contacting their GP's. The main results of this trial will be disseminated in one paper.

Discussion: The HART-c study evaluates the efficacy and feasibility of a pre-hospital triage protocol that combines pre-hospital patient assessment and direct consultation of a cardiologist who has access to live-monitored data, hospital data and real-time hospital admission capacity. We expect this triage protocol to substantially reduce unnecessary ED visits.

ARTICLE SUMMARY

- A novel pre-hospital triage protocol is presented which aims to safely decrease unnecessary ED admissions, using telemedicine for pre-hospital decision making
- All participants, including patient representatives, were involved in the design of the study
- **Strengths and limitations:**
    - This study is a real-life reflection of interdisciplinary daily clinical practice, the retrospective cohort will reflect the control group in the best way possible
    - The HART-c Study is a non-randomised controlled trial and therefore has risk of bias as decisions from paramedics and cardiologist can be influenced by the study.

INTRODUCTION

Emergency Department (ED) overcrowding is a worldwide health care problem associated with worse patient outcomes and increased costs[1,2]. Cardiac complaints are one of the most common reasons for patients to visit the ED, with chest pain as the most frequent complaint.[3] In Europe and the United States, 15-20 million patients with chest pain are seen at the ED every year.[4] The majority will be sent home after ruling out acute cardiovascular disease: previous studies have shown that up to 80% of chest pain patients do not have an acute coronary syndrome.[5-8] However, these patients contribute to overcrowding of EDs and these ED visits substantially increase healthcare costs.

Attempts to reduce ED overcrowding by cardiac patients have so far particularly focused on rapid risk stratification after presentation at the ED. For example, the HEART score stratifies patients as at low, intermediate or high risk of major adverse cardiac events (MACE) based on history, the electrocardiogram (ECG), age, risk factors and troponin levels.[9] However, as it takes 1-2 hours for the latter to be available, patients still spend a long time at the ED after which the majority can be discharged home.

Accordingly, interest has shifted from in-hospital to pre-hospital triage. Preventing patients with cardiac complaints and a very low risk of adverse cardiac events from visiting the ED will substantially help to reduce ED overcrowding. Efforts to prevent ED visits especially involve interventions focused on chest pain patients such as risk score calculation by the ambulance paramedics (for example with the HEART score[10] and HE-MACS[11]) or pre-hospital point of care testing for troponin.[12] In order to improve pre-hospital triage for cardiac patients in the entire chain of acute cardiac care, we developed a comprehensive triage protocol entitled HART-c ("Hollands-midden Acute Regional Triage - Cardiology").

Innovative in this protocol is the combination of pre-hospital patient assessment by the ambulance paramedic and expert consultation of a cardiologist who has access to live-

monitored data from the ambulance, in-hospital data and real-time hospital admission capacity in a newly developed triage application. By drafting this triage protocol, we specifically aimed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. In addition, we intent to provide patient-tailored care through pre-hospital assessment of patient specific needs and circumstances. The HART-c study was designed to evaluate whether the implementation of the HART-c triage protocol results in a reduction of unnecessary ED visits.

METHODS AND ANALYSIS

Study design and patient population

The HART-c study is a multi-center prospective study with a historical control group. The intervention group comprises of adult patients visited by the regional emergency medical services (EMS) because of cardiac complaints between 1 September 2019 and 31 August 2020 in whom pre-hospital triage is performed according to the HART-c triage protocol. The historical control group consists of adult patients visited by the regional EMS because of cardiac complaints between 1 September 2018 and 31 August 2019 (1 year before the start of the HART-c triage protocol). Of note, in both groups EMS consultation could have been requested directly by the patient, through bystanders or by the patients' general practitioner (GP) who refers patients through EMS. Patients in need for urgent cardiac care, patients with complaints not suspected of cardiac origin as assessed by the ambulance paramedic, and patients unable or not willing to provide informed consent were excluded from triage according to the HART-c protocol. Table 1 displays the detailed inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria
Inclusion criteria
Patients visited by EMS for cardiac complaints
Age over 18 years
Exclusion criteria
Patients in need for urgent cardiac care because of - **ST-elevation myocardial infarction** - **Hemodynamic instability** - **(Out of hospital) cardiac arrest** - **Suspected pulmonary embolism** - **Suspected acute aortic syndrome (thoracic or abdominal)**
Patients with symptoms not suspected of cardiac origin
Unable or unwilling to provide informed consent

The HART-c study is coordinated by the Leiden University Medical Centre (LUMC) and conducted in the entire EMS region "Hollands-midden" which consists of over 600.000 inhabitants. The hospitals located in this region participate: the Leiden University Medical Centre, the Groene Hart hospital and the Alrijne hospital. The study is performed in close collaboration with the regional EMS (RAVHM) that employs 240 paramedics who are trained in pre-hospital cardiac care and 31 ambulance vehicles equipped with real-time monitoring. In addition, the study was performed and developed with the help of over regional 300 GPs.

Intervention group: Pre-hospital Triage using HART-c protocol

The intervention group consists of patients visited by the EMS because of symptoms suspected to be of cardiac origin such as chest pain, shortness of breath, palpitations or implanted cardiac device problems. In line with the National Protocol for Emergency Medical Care, patients at

first receive standard medical care consisting of a medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG.[13] In patients with chest pain, the pre-hospital modified HEART score (the HEART[14] score without troponin) is calculated. All acquired data are noted on a handheld device and stored on AmbuSuite, an external secure database. Afterwards, the ambulance paramedic directly contacts the on-call triage cardiologist. The right panel in Figure 1 illustrates the entire routing of patients in the intervention group. In total, 43 cardiologist from all three reginal hospitals are scheduled so one cardiologist is on duty for the entire region. GPs can refer patients through EMS consultation, however in the intervention period cardiologist consultation is possible. When a GP is in doubt of referral, they can request cardiologist consultation through EMS with the HART-c protocol. The triage cardiologist evaluates the pre-hospital data, including, medical history, real-time vital parameters and 12-lead ECG and combines them with (if present) previous medical records and the actual hospital admission capacity of the regional hospitals. Also, we developed decision aids for chest pain, dyspnoea and arrhythmia as guidance for triage cardiologists. These decisions aids can help the triage cardiologist in decision making and are added, as addendum 1 for chest pain, addendum 2 for dyspnoea and addendum 3 for arrhythmia, to this manuscript. Based on these comprehensive data, the triage cardiologist and ambulance paramedic decide, as a shared decision with the patient, whether transfer to an ED is necessary and, if so, which hospital and which department is most suitable. The triage decision is sent immediately to the concerning ED nursing staff and the capacity of this hospital is updated automatically (Figure 2). Upon arrival at the ED, cardiac assessment is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9]

Figure 1. Method of triage. (A) Patient routing without pre-hospital selection where patients are referred to the nearest ED or left at home. If hospital admission capacity is insufficient, patients are transferred to another hospital. (B) Patient routing with pre-hospital selection using pre- and in-hospital data where a cardiologist has insight in live vital parameters and regional hospital capacity.

Figure 2. Mobile phone triage application: Left panel showing overview of a hospital specific capacity. Right panel showing the ability to update capacity.

Intervention group: Tempus Pro Monitor, IntelliSpace Corsium, triage platform and data handling

All ambulances are equipped with a Tempus Pro Monitor[15] (Philips, The Netherlands) that allows recording of a 12-lead ECG and real-time monitoring of the following vital patient parameters: heart rate, blood pressure and pulse oximetry. The monitor can show trends in measurements and stream data for up to 10 hours. All data are encrypted and shared with the on-call triage cardiologist through secure channels. The Tempus Pro Monitor is shown in Figure 3.

Figure 3. Image of Tempus Pro Monitor.

Using a secure log-in, the on-call triage cardiologist logs in to IntelliSpace Corsium (Philips, the Netherlands) and connects digitally with a patient specific Tempus Pro Monitor. All aforementioned measurements are streamed live. Once the live streaming ends, no patient specific data are stored on the platform. This system of data-transfer is FDA approved.[16,17]

A novel triage platform was developed showing real-time admission capacity of the regional hospitals. The nursing staff in these hospitals continuously updates their admission capacity. Linking these capacity data to a local electronic patient dossier (EPD-Vision; Leiden, The

Netherlands), the on-call triage cardiologist has insight into the actual bed occupancy of each hospital. After consultation, the on-call triage cardiologist notes his decision and a message is automatically sent to the nursing staff of the chosen hospital, thereby updating their admission capacity immediately.

Patient data are sent securely from Tempus Monitor to IntelliSpace Corsium. No data are stored on IntelliSpace Corsium. No patient data are transmitted to the mobile phone application. Patient data are transferred from AmbuSuite to our EPD. All patient data and decisions are stored on the EPD of the coordinating hospital and are only accessible for triage cardiologists.

Historical control group: Standard care in pre-hospital setting

The historical control group consists of patients visited by the EMS because of potential cardiac complaints in the year before the onset of the HART-c triage protocol. Upon arrival by the paramedic, standard medical care consists of medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG. All acquired data are noted on a handheld device and stored on AmbuSuite (Topicus, the Netherlands) which is an external secure database. Thereafter, the ambulance paramedic decides, based on predefined national protocols and decision rules for diagnosis, whether transfer to an ED is deemed necessary.[12] Paramedics are able to identify low-risk patient for all medical specialties, and decide whether admission or ED presentation is necessary on every consultation. So, even in the historical cohort group only patients with cardiac complaints deemed severe enough for presentation are presented to the ED. Of note, at the time of referral, the paramedic has no insight in the previous medical records and the actual hospital admission capacity. The Netherlands has a unique system, where, in the historical cohort in our region, approximately 5% of patients with cardiac complaints aren't referred to a hospital after paramedic assessment, instead these patients are directly referred to their GP or treated at home. However, given the number of unnecessary ED visits, there is still a large

cohort of low-risk patients in whom ED presentation could be prevented. After paramedic assessment and hospital transport, cardiac assessment on the ED is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] If evaluation at the ED indicates that hospitalization is mandatory, the patient is admitted in the concerning hospital. However, when admission capacity is insufficient or immediate intervention is not available in the concerning hospital, ambulance transfer to another hospital is mandatory. The routing of patients in the historical control group is illustrated in the left panel of Figure 1.

Objective and outcome measures

The HART-c study is designed to evaluate the efficacy and feasibility of a novel comprehensive pre-hospital triage protocol which aims to safely reduce unnecessary ED visits in patients with cardiac complaints. The primary outcome is the percentage of patients in who an ED visit can be prevented after EMS consultation. The following secondary end-points will be evaluated:

- Number of ambulance transfers to an ED because of cardiac complaints.
- Number of inter-hospital transfers in cardiac patients.
- Patient, triage cardiologist and GP satisfaction with the HART-c triage protocol on a 0-10 scale.
- Time from EMS consultation to arrival at the hospital in the both study groups.
- Safety of the HART-c prehospital triage protocol. This will be evaluated in intervention group patients who are not transferred to an ED after cardiologist consultation. Safety will be assessed by the occurrence of adverse events up to 30 days follow-up. Table 2 displays the pre-specified major and non-major adverse events. To evaluate safety, a dedicated researcher will contact these patients and their GP and evaluate on a case-by-case basis. If a major adverse event is deemed directly attributable to the triage protocol,

the protocol will be adjusted or the study will be terminated prematurely. The study will be deemed safe if the percentage of major adverse events is 1% or lower.

- Feasibility of the HART-c prehospital triage protocol. This will be evaluated in the intervention group and defined as the absence of technical problems for the ambulance paramedic and the triage cardiologist. This means access to the live-monitored data from the ambulance, hospital data and real-time hospital admission capacity are all available. In order to swiftly manage potential technical problems, the HART-c triage protocol will start during working hours. If interim analysis reveals that the protocol is feasible, the time frame in which HART-c triage is available could be extended.

Table 2. Adverse events (30 days after EMS contact)

Major adverse events
Death
Acute coronary syndrome
Other adverse events
Renewed EMS or ED visit for cardiac complaint
Pulmonary embolism
ED visit or hospitalization for acute decompensated heart failure
Ventricular tachycardia or – fibrillation
Cerebrovascular accident (CVA) or transient ischemic attack (TIA)

Statistical analysis

The prevention of an ED visit after EMS consultation will be analysed using a logistic regression analysis. Ambulance transfers and inter hospital transfers in the intervention versus the control group will also be evaluated using logistic regression. Baseline characteristics will

be reported as mean and standard deviation or median and interquartile range and compared between historical cohort and intervention. This study will be underpowered to detect differences in mortality and major adverse cardiac events (MACE). Accordingly, these events will only be reported and no further statistics on mortality and MACE will be done. The data will be analysed using IBM SPSS Statistics version 25. A p-value lower than 0.05 will be considered statistically significant.

Patient and public involvement

Patients were involved in the design of the study. During the design stage, representatives from the 'Harteraad', a cardiovascular patient council, were asked for input in study design, choice of outcome measures and methods of recruitment. Also, a dedicated website, www.hartc.nl, was created to inform the public and answer questions from professionals and patients, before and during the study.

ETHICS AND DISSEMINATION

The study is approved by the LUMC's Medical Ethics Committee (P18.213). Patients are requested to provide oral informed consent for contacting their GP at 30 days follow-up. Oral informed consent is requested for cardiologist consultation and study participation by paramedics which is then noted in AmbuSuite. The need for written informed consent was waived by the Medical Ethics Committee. The devices used in this study are FDA and/or CE approved. No manufacturer has a role in study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any manufacturer. The main results of this trial will be disseminated in one paper.

DISCUSSION

Overcrowding of ED's is a major challenge in healthcare. The HART-c study is a multi-centre prospective study that primarily aims to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. By selecting the hospital best suited for every patient, this protocol will contribute to more patient-tailored health care and lead to improved utilization of all available healthcare resources in the region.

Recently, interest has shifted from in-hospital - to pre-hospital triage. Pre-hospital cardiologist consultation has been standard procedure for some time in many hospitals in the Netherlands for quick catheterization lab activation when paramedics suspect chest pain patients of STEMI.[18] For all other cardiac complaints no pre-hospital triage procedure is in place for emergency evaluations. However, there have been some studies assessing the possibility of pre-hospital triage and pre-hospital selection of low-risk cardiac patients.

The History and ECG-only Manchester ACS (HE-MACS) decision aid was developed for pre-hospital triage using history, physical examination and ECG. It was derived in 796 patients and validated in cohorts of 474 and 659 patients. 9.4% of all validated patients were identified as 'very low risk' in which ACS could be 'ruled out' with a sensitivity of 99.5%. It's impact, however, was not prospectively evaluated in this study.

The FAMOUS investigators aim to assess the effects of introducing a pre-hospital triage system that stratifies chest pain patients without ST segment elevation into 1) patients at high risk for NSTEMI requiring direct transfer to a PCI hospital, 2) patients at intermediate risk for major adverse cardiac events who could be evaluated at the nearest non-PCI hospital and 3) patients at low risk for major adverse cardiac events who could have further evaluation at home or in a primary care setting.[19] The study was divided in three phases. In the first phase, a venous blood sample was drawn in the ambulance for measurement of the pre-hospital troponin T levels, in order to establish a pre-hospital HEART score and evaluate the possibility of triage at the

patient's home. Of the 1127 chest pain patients, 36% had a low modified HEART score and none of them developed a major adverse event.[20] After this first phase proving feasibility, further studies have been done in the pre-hospital setting by the FAMOUS TRIAGE study group. Phase 2, a prospective observational study including 700 patients with suspected NSTE-ACS, showed nicely that pre-hospital risk stratification by ambulance paramedics using the HEART score was accurate in differentiating in low and intermediate to high risk.[21] Recently the design of phase 3 has been published, where the FAMOUS study investigators aim to determine if use of the HEART score, including point-of-care Troponin measurement, is non-inferior to routine management. In this phase referral decisions are based on pre-hospital acquired risk stratification. [22]

Another study investigating the added value of point-of-care troponin in the pre-hospital setting is the ARTICA[12] trial. This randomized trial will include patients suspected of non-ST elevation acute coronary syndrome in whom the modified HEAR score (the HEART score without troponin) is calculated by the ambulance paramedic. If the HEAR score is less than or equal to 3, patients will be 1:1 randomized for 1) presentation at the ED or 2) point-of-care troponin T measurement and transfer of care to the GP in case of a low troponin T value. The primary objective of the ARTICA trial will be healthcare costs at 30 days. The trial is currently ongoing and aims to include 866 patients in 12 months.

The similarity of the currently described HART-c study and the HE-MACS, FAMOUS and ARTICA studies is that all three assess whether patients with chest pain who are at low risk of major adverse events can be identified before presenting to the ED. However, the HART-c study has some added benefit as opposed to earlier known studies. First, the HART-c study does not only identify patients at low-risk for events, but also aims to effectively prevent low-risk patients from actually visiting the ED, as well as further phases from FAMOUS and ARTICA did, by combining pre-hospital risk stratification by the paramedic and real-time

cardiologist consultation with insight in live vital parameters and ECG. Secondly, while these studies study only focus on chest pain patients, the HART-c study extends this to all patients with cardiac complaints and could therefore be of benefit for a substantially larger cohort of patients. Furthermore, the HART-c triage protocol is unique as it combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of an expert triage cardiologist who has access to live-monitored data from the ambulance for all cardiac patients, as opposed to only STEMI patients. Besides these novelties, the HART-c study incorporates hospital data as well as real-time hospital admission capacity to decide which regional hospital is best suited for every patient.

If the results of current study show that the HART-c triage protocol is effective in safely reducing unnecessary ED visits of patients with all types of cardiac complaints, the next step will be to evaluate cost-effectiveness. When cost-effectiveness can be demonstrated, we feel that the HART-c triage protocol can be expanded to other EMS regions. Furthermore, last but not least, it may potentially also be useful for other medical specialists aiming to optimize pre-hospital triage of non-cardiac patients. Eventual improvements in pre-hospital triage, such as pre-hospital high sensitive Troponin sampling with a point-of-care test or newly developed and proven risk scores, could always be implemented in this triage protocol.

To conclude, the HART-c study is a multi-center prospective study evaluating the efficacy, and feasibility of a novel comprehensive pre-hospital triage protocol that combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the HART-c study will succeed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints, it may help to decrease ED overcrowding and ultimately reduce healthcare expenditures.

Author statement

EdK, TEB, JB, CJHJK, RAD, HAMS, MS and MJB made a substantial contribution to the concept and design of the work. EdK and MJB are in charge of acquisition of data, analysis and interpretation of the data. EdK, TEB, SB and MJB contributed to the drafting of the article. EdK, SB, JB, BEB, CJHJK, RAD, MS and MJB all revised the manuscript critically for important intellectual content.

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Competing interest

EdK, TEB, SB, JB, CJHJK, RAD, HAMS, MS and MJB report no conflict of interest. BEB is the creator of the HEART score.

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Addendum 1. Decision aid for chest pain. The T stands for Triage cardiologist consultation.

Addendum 2. Decision aid for dyspnoea. The T stands for Triage cardiologist consultation.

Addendum 3. Decision aid for arrhythmia. The T stands for Triage cardiologist consultation.

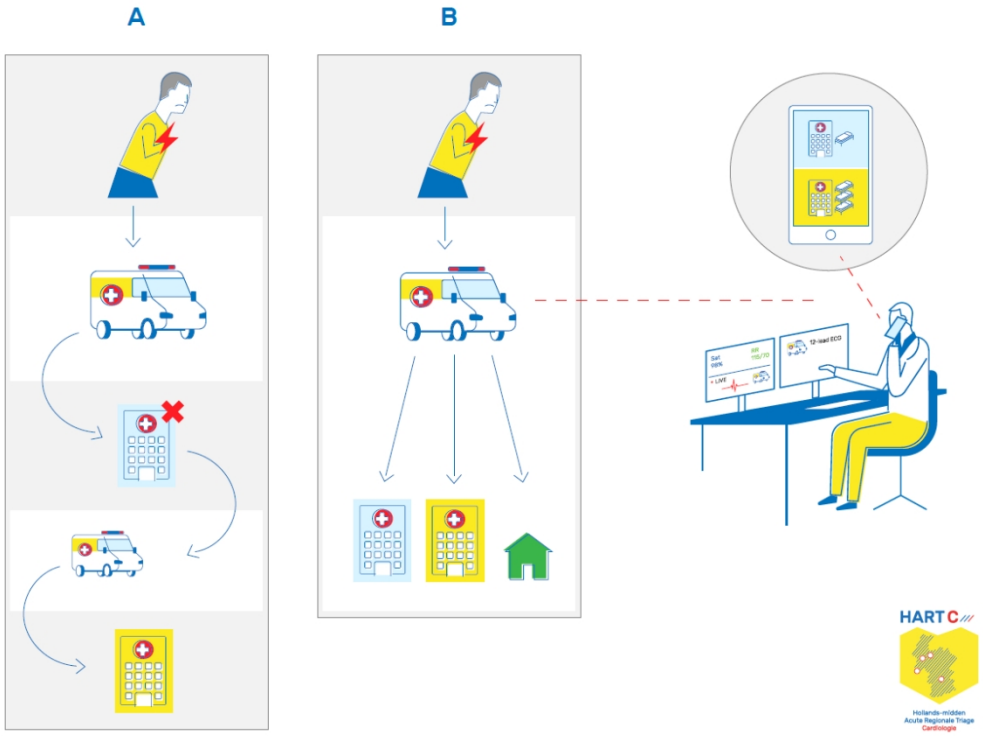


Figure 1. Method of triage

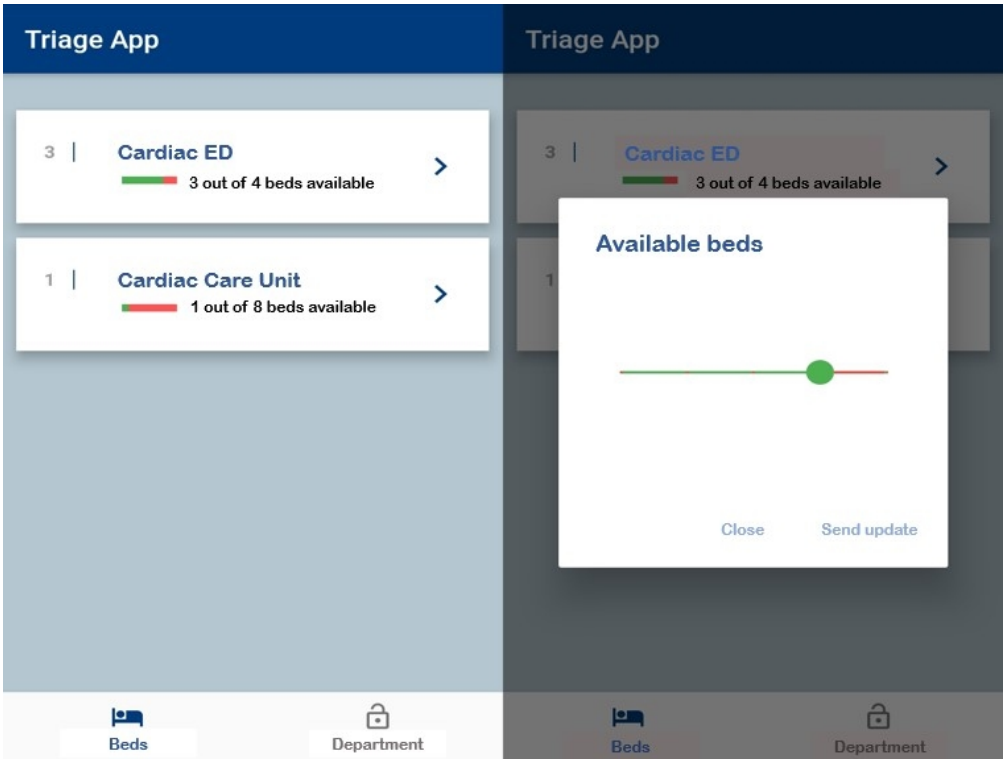
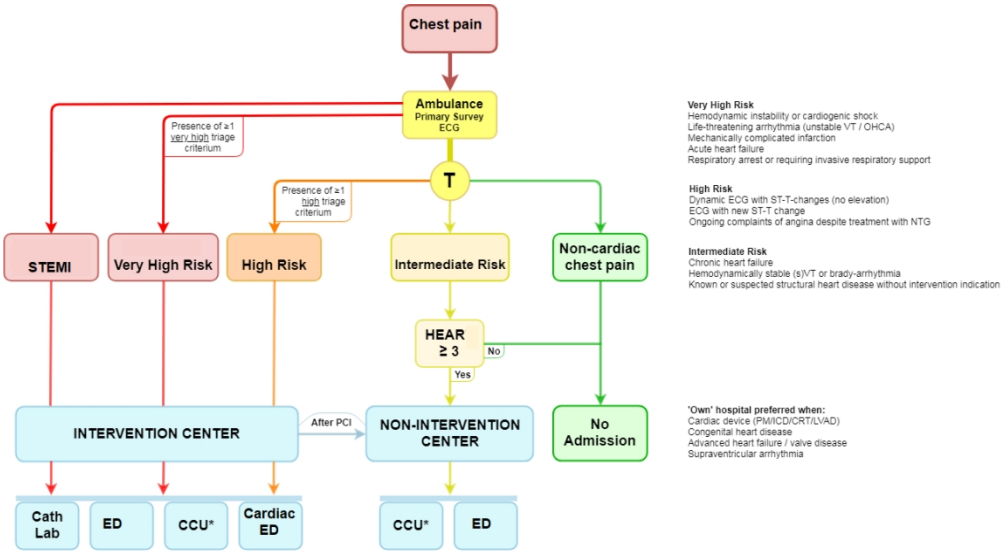
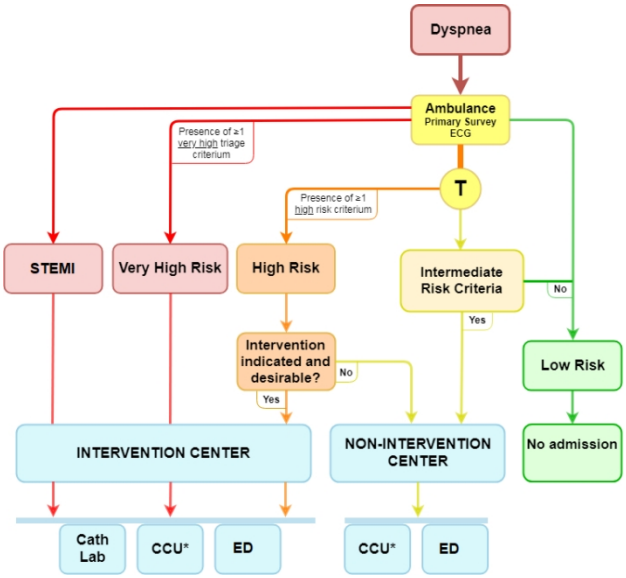


Figure 2. Mobile phone triage application

200x151mm (96 x 96 DPI)

Figure 3. Image of Tempus Pro Monitor


Chest pain
Ambulance
Primary Survey
ECG
Presence of ≥1 very high triage criterium
Presence of ≥1 high triage criterium
T
STEMI
Very High Risk
High Risk
Intermediate Risk
Non-cardiac chest pain
HEAR ≥ 3
No
Yes
INTERVENTION CENTER
After PCI
NON-INTERVENTION CENTER
No Admission
Cath Lab
ED
CCU*
Cardiac ED
CCU*
ED
Very High Risk
Hemodynamic instability or cardiogenic shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated infarction
Acute heart failure
Respiratory arrest or requiring invasive respiratory support
High Risk
Dynamic ECG with ST-T-changes (no elevation)
ECG with new ST-T change
Ongoing complaints of angina despite treatment with NTG
Intermediate Risk
Chronic heart failure
Hemodynamically stable (s)VT or brady-arrhythmia
Known or suspected structural heart disease without intervention indication
'Own' hospital preferred when:
Cardiac device (PM/ICD/CRT/LVAD)
Congenital heart disease
Advanced heart failure / valve disease
Supraventricular arrhythmia

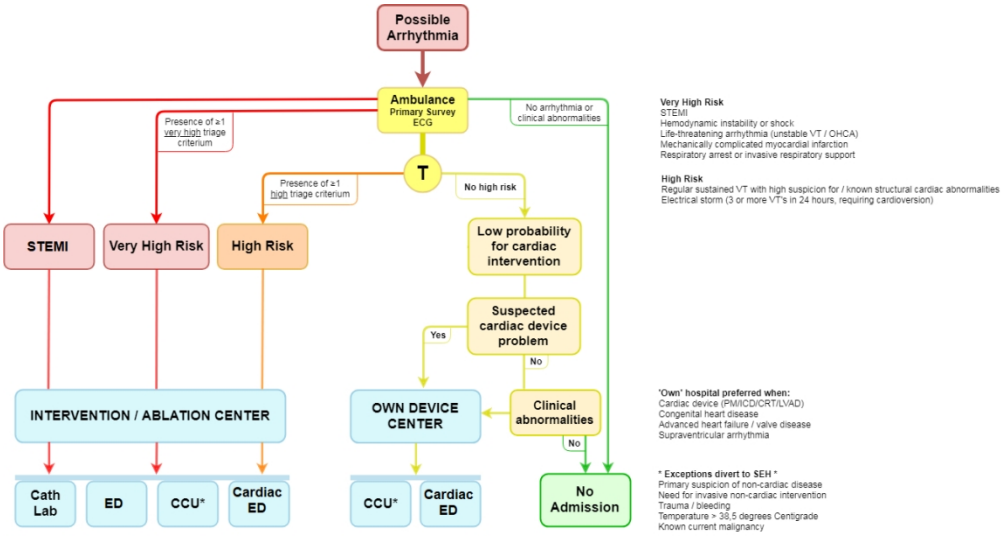


Very High Risk
STEMI
Hemodynamic instability or shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated MI
Respiratory arrest or invasive respiratory support

High Risk
Acute heart failure with the need for invasive support
Suspicion of acute or ongoing ischemia
VAD in situ OR
Scheduled VAD intervention
Respiratory distress < 2 weeks after thoracic intervention

Intermediate Risk
Hypertensive/normotensive acute heart failure
Chronic decompensation
Hemodynamically stable (s)VT or brady-arrhythmia
Known or suspected structural heart disease without intervention indication

General rules of triage: preference for own treating hospital when
Device implantation or guiding center
Congenital heart disease / aortic connective tissue disease
Heart failure
Arrhythmia / ablation


Possible Arrhythmia
Ambulance
Primary Survey
ECG
No arrhythmia or clinical abnormalities
Presence of ≥1 very high triage criterium
Presence of ≥1 high triage criterium
T
No high risk
STEMI
Very High Risk
High Risk
Low probability for cardiac intervention
Suspected cardiac device problem
Yes
No
INTERVENTION / ABLATION CENTER
OWN DEVICE CENTER
Clinical abnormalities
No
Cath Lab
ED
CCU*
Cardiac ED
CCU*
Cardiac ED
No Admission
Very High Risk
STEMI
Hemodynamic instability or shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated myocardial infarction
Respiratory arrest or invasive respiratory support
High Risk
Regular sustained VT with high suspicion for / known structural cardiac abnormalities
Electrical storm (3 or more VT's in 24 hours, requiring cardioversion)
'Own' hospital preferred when:
Cardiac device (PM/ICD/CRT/LVAD)
Congenital heart disease
Advanced heart failure / valve disease
Supraventricular arrhythmia
* Exceptions divert to SEH *
Primary suspicion of non-cardiac disease
Need for invasive non-cardiac intervention
Trauma / bleeding
Temperature > 38,5 degrees Centigrade
Known current malignancy

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Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

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Pre-hospital Triage of Acute Cardiac Patients: Study Protocol of HART-c, a multicenter prospective study

Keywords: Pre-hospital, Acute Care, Cardiac, Cardiology, Triage, HART-c, Emergency Medical Services, Emergency Department, overcrowding
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Author list: Enrico de Koning MD[1], Tom E Biersteker MD[1] (shared first author), Saskia Beeres MD PhD[1], Jan Bosch[2], Barbra E Backus MD PhD[3], Charles JHJ Kirchhof MD PhD[4], Reza Alizadeh Dehnavi MD PhD[5], Helen AM Silvius MD[6], Martin Schalij Prof MD PhD[1], Mark J Boogers MD PhD[1]

1. Cardiology, Leiden University Medical Center, Leiden, the Netherlands. e.r.de_koning@lumc.nl; t.e.biersteker@lumc.nl; s.l.m.a.beeres@lumc.nl; m.j.schalij@lumc.nl; j.m.j.boogers@lumc.nl
2. Research and Development, Regional Ambulance Service Hollands-Midden (RAVHM), Leiden, the Netherlands. jbosch@ravhm.nl
3. Emergency Medicine, Leiden University Medical Center, Leiden, the Netherlands. b.e.backus@lumc.nl
4. Cardiology, Alrijne Hospital, Leiderdorp, the Netherlands. cjhjkirchhof@alrijne.nl
5. Cardiology, Groene Hart Hospital, Gouda, the Netherlands. reza.alizadeh.dehnavi@ghz.nl
6. Public Health and General Practice, Leiden University Medical Center, Leiden, the Netherlands. a.m.silvius@lumc.nl

Corresponding Author:

Mark J Boogers MD PhD
Cardiologist
Leiden University Medical Center
Albinusdreef 2, 2333 ZA, Leiden, the Netherlands
j.m.j.boogers@lumc.nl
0031 - 71 52 62 020

ABSTRACT

Introduction: Emergency department (ED) overcrowding is a major health care problem associated with worse patient outcomes and increased costs. Attempts to reduce ED overcrowding of cardiac patients have so far focused on in-hospital triage and rapid risk stratification of chest pain patients at the ED. The HART-c study aims to assess the amount of patients left at home in usual ambulance care as compared to the new pre-hospital triage method. This method combines paramedic assessment and expert cardiologist consultation using live-monitoring, hospital data and real-time admission capacity.

Methods and Analysis: Patients visited by the emergency medical services (EMS) for cardiac complaints are included. EMS consultation consists of medical history, physical examination and vital signs and ECG measurements. All data is transferred to a newly developed platform for the triage cardiologist. Pre-hospital data, in-hospital medical records and real-time admission capacity are evaluated. Then a shared decision is made whether admission is necessary and, if so, which hospital is most appropriate. To evaluate safety, all patients left at home and their GP's, are contacted for 30-day adverse events.

Ethics and dissemination: The study is approved by the LUMC's Medical Ethics Committee. Patients are asked for consent for contacting their GP's. The main results of this trial will be disseminated in one paper.

Discussion: The HART-c study evaluates the efficacy and feasibility of a pre-hospital triage method that combines pre-hospital patient assessment and direct consultation of a cardiologist who has access to live-monitored data, hospital data and real-time hospital admission capacity. We expect this triage method to substantially reduce unnecessary ED visits.

STRENGHTS AND LIMITATIONS

- A novel pre-hospital triage method is presented which aims to safely decrease unnecessary ED admissions, using telemedicine for pre-hospital decision making
- All participants, including patient representatives, were involved in the design of the study
- This study is a real-life reflection of interdisciplinary daily clinical practice, the retrospective cohort will reflect the control group in the best way possible
- The HART-c Study is a non-randomised controlled trial and therefore has risk of bias as decisions from paramedics and cardiologist can be influenced by the study.

INTRODUCTION

Emergency Department (ED) overcrowding is a worldwide health care problem associated with worse patient outcomes and increased costs[1,2]. Cardiac complaints are one of the most common reasons for patients to visit the ED, with chest pain as the most frequent complaint.[3] In Europe and the United States, 15-20 million patients with chest pain are seen at the ED every year.[4] The majority will be sent home after ruling out acute cardiovascular disease: previous studies have shown that up to 80% of chest pain patients do not have an acute coronary syndrome.[5-8] However, these patients contribute to overcrowding of EDs and these ED visits substantially increase healthcare costs.

Attempts to reduce ED overcrowding by cardiac patients have so far particularly focused on rapid risk stratification after presentation at the ED. For example, the HEART score stratifies patients as at low, intermediate or high risk of major adverse cardiac events (MACE) based on history, the electrocardiogram (ECG), age, risk factors and troponin levels.[9] However, as it takes 1-2 hours for the latter to be available, patients still spend a long time at the ED after which the majority can be discharged home.

Accordingly, interest has shifted from in-hospital to pre-hospital triage. Preventing patients with cardiac complaints and a very low risk of adverse cardiac events from visiting the ED will substantially help to reduce ED overcrowding. Efforts to prevent ED visits especially involve interventions focused on chest pain patients such as risk score calculation by the ambulance paramedics (for example with the HEART score[10] and HE-MACS[11]) or pre-hospital point of care testing for troponin.[12] In order to improve pre-hospital triage for cardiac patients in the entire chain of acute cardiac care, we developed a comprehensive triage method entitled HART-c ("Hollands-midden Acute Regional Triage - Cardiology").

Innovative in this approach is the combination of pre-hospital patient assessment by the ambulance paramedic and expert consultation of a cardiologist who has access to live-

monitored data from the ambulance, in-hospital data and real-time hospital admission capacity in a newly developed triage application. By drafting this triage method, we specifically aimed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints. In addition, we intent to provide patient-tailored care through pre-hospital assessment of patient specific needs and circumstances. The HART-c study was designed to evaluate whether the implementation of the HART-c triage method results in a reduction of unnecessary ED visits.

METHODS AND ANALYSIS

Study design and patient population

The HART-c study is a multi-center prospective study with a historical control group. The intervention group comprises of adult patients visited by the regional emergency medical services (EMS) because of cardiac complaints between 1 September 2019 and 31 August 2020 in whom pre-hospital triage is performed according to the HART-c triage method. The historical control group consists of adult patients visited by the regional EMS because of cardiac complaints between 1 September 2018 and 31 August 2019 (1 year before the start of the HART-c triage method). Of note, in both groups EMS consultation could have been requested directly by the patient, through bystanders or by the patients' general practitioner (GP) who refers patients through EMS. Patients in need for urgent cardiac care, patients with complaints not suspected of cardiac origin as assessed by the ambulance paramedic, and patients unable or not willing to provide informed consent were excluded from triage according to the HART-c method. Table 1 displays the detailed inclusion and exclusion criteria.

Table 1. Inclusion and exclusion criteria
Inclusion criteria
Patients visited by EMS for cardiac complaints
Age over 18 years
Exclusion criteria
Patients in need for urgent cardiac care because of - **ST-elevation myocardial infarction** - **Hemodynamic instability** - **(Out of hospital) cardiac arrest** - **Suspected pulmonary embolism** - **Suspected acute aortic syndrome (thoracic or abdominal)**
Patients with symptoms not suspected of cardiac origin
Unable or unwilling to provide informed consent

The HART-c study is coordinated by the Leiden University Medical Centre (LUMC) and conducted in the entire EMS region "Hollands-midden" which consists of over 600.000 inhabitants. The hospitals located in this region participate: the Leiden University Medical Centre, the Groene Hart hospital and the Alrijne hospital. The study is performed in close collaboration with the regional EMS (RAVHM) that employs 240 paramedics who are trained in pre-hospital cardiac care and 31 ambulance vehicles equipped with real-time monitoring. In addition, the study was performed and developed with the help of over regional 300 GPs.

Intervention group: Pre-hospital Triage using HART-c method

The intervention group consists of patients visited by the EMS because of symptoms suspected to be of cardiac origin such as chest pain, shortness of breath, palpitations or implanted cardiac device problems. In line with the National Protocol for Emergency Medical Care, patients at

first receive standard medical care consisting of a medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG.[13] In patients with chest pain, the pre-hospital modified HEART score (the HEART[14] score without troponin) is calculated. All acquired data are noted on a handheld device and stored on AmbuSuite, an external secure database. Afterwards, the ambulance paramedic directly contacts the on-call triage cardiologist. The right panel in Figure 1 illustrates the entire routing of patients in the intervention group. In total, 43 cardiologist from all three reginal hospitals are scheduled so one cardiologist is on duty for the entire region. GPs can refer patients through EMS consultation, however in the intervention period cardiologist consultation is possible. When a GP is in doubt of referral, they can request cardiologist consultation through EMS with the HART-c method. The triage cardiologist evaluates the pre-hospital data, including, medical history, real-time vital parameters and 12-lead ECG and combines them with (if present) previous medical records and the actual hospital admission capacity of the regional hospitals. Also, we developed decision aids for chest pain, dyspnoea and arrhythmia as guidance for triage cardiologists. These decisions aids can help the triage cardiologist in decision making and are added, as addendum 1 for chest pain, addendum 2 for dyspnoea and addendum 3 for arrhythmia, to this manuscript. Based on these comprehensive data, the triage cardiologist and ambulance paramedic decide, as a shared decision with the patient, whether transfer to an ED is necessary and, if so, which hospital and which department is most suitable. The triage decision is sent immediately to the concerning ED nursing staff and the capacity of this hospital is updated automatically (Figure 2). Upon arrival at the ED, cardiac assessment is based on in-house clinical decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9]

Figure 1. Method of triage. (A) Patient routing without pre-hospital selection where patients are referred to the nearest ED or left at home. If hospital admission capacity is insufficient, patients are transferred to another hospital. (B) Patient routing with pre-hospital selection

using pre- and in-hospital data where a cardiologist has insight in live vital parameters and regional hospital capacity.

Figure 2. Mobile phone triage application: Left panel showing overview of a hospital specific capacity. Right panel showing the ability to update capacity.

Intervention group: Tempus Pro Monitor, IntelliSpace Corsium, triage platform and data handling

All ambulances are equipped with a Tempus Pro Monitor[15] (Philips, The Netherlands) that allows recording of a 12-lead ECG and real-time monitoring of the following vital patient parameters: heart rate, blood pressure and pulse oximetry. The monitor can show trends in measurements and stream data for up to 10 hours. All data are encrypted and shared with the on-call triage cardiologist through secure channels. The Tempus Pro Monitor is shown in Figure 3.

Figure 3. Image of Tempus Pro Monitor.

Using a secure log-in, the on-call triage cardiologist logs in to IntelliSpace Corsium (Philips, the Netherlands) and connects digitally with a patient specific Tempus Pro Monitor. All aforementioned measurements are streamed live. Once the live streaming ends, no patient specific data are stored on the platform. This system of data-transfer is FDA approved.[16,17]

A novel triage platform was developed showing real-time admission capacity of the regional hospitals. The nursing staff in these hospitals continuously updates their admission capacity. Linking these capacity data to a local electronic patient dossier (EPD-Vision; Leiden, The Netherlands), the on-call triage cardiologist has insight into the actual bed occupancy of each hospital. After consultation, the on-call triage cardiologist notes his decision and a message is

automatically sent to the nursing staff of the chosen hospital, thereby updating their admission capacity immediately.

Patient data are sent securely from Tempus Monitor to IntelliSpace Corsium. No data are stored on IntelliSpace Corsium. No patient data are transmitted to the mobile phone application. Patient data are transferred from AmbuSuite to our EPD. All patient data and decisions are stored on the EPD of the coordinating hospital and are only accessible for triage cardiologists.

Historical control group: Standard care in pre-hospital setting

The historical control group consists of patients visited by the EMS because of potential cardiac complaints in the year before the onset of the HART-c triage method. Upon arrival by the paramedic, standard medical care consists of medical history, physical examination with vital sign monitoring (blood pressure, heart rate, pulse oximetry) and a 12-lead ECG. All acquired data are noted on a handheld device and stored on AmbuSuite (Topicus, the Netherlands) which is an external secure database. Thereafter, the ambulance paramedic decides, based on predefined national protocols and decision rules for diagnosis, whether transfer to an ED is deemed necessary.[12] Paramedics are able to identify low-risk patient for all medical specialties, and decide whether admission or ED presentation is necessary on every consultation. So, even in the historical cohort group only patients with cardiac complaints deemed severe enough for presentation are presented to the ED. Of note, at the time of referral, the paramedic has no insight in the previous medical records and the actual hospital admission capacity. The Netherlands has a unique system, where, in the historical cohort in our region, approximately 5% of patients with cardiac complaints aren't referred to a hospital after paramedic assessment, instead these patients are directly referred to their GP or treated at home. However, given the number of unnecessary ED visits, there is still a large cohort of low-risk patients in whom ED presentation could be prevented. After paramedic assessment and hospital transport, cardiac assessment on the ED is based on in-house clinical

decision rules as guidelines prescribe, 12-lead ECG and laboratory findings.[9] If evaluation at the ED indicates that hospitalization is mandatory, the patient is admitted in the concerning hospital. However, when admission capacity is insufficient or immediate intervention is not available in the concerning hospital, ambulance transfer to another hospital is mandatory. The routing of patients in the historical control group is illustrated in the left panel of Figure 1.

Objective and outcome measures

The HART-c study is designed to evaluate the efficacy and feasibility of a novel comprehensive pre-hospital triage method which aims to safely reduce unnecessary ED visits in patients with cardiac complaints. The primary outcome is the percentage of patients in who an ED visit can be prevented after EMS consultation. The following secondary end-points will be evaluated:

- Number of ambulance transfers to an ED because of cardiac complaints.
- Number of inter-hospital transfers in cardiac patients.
- Patient, triage cardiologist and GP satisfaction with the HART-c triage method on a 0-10 scale.
- Time from EMS consultation to arrival at the hospital in the both study groups.
- Safety of the HART-c prehospital triage method. This will be evaluated in intervention group patients who are not transferred to an ED after cardiologist consultation. Safety will be assessed by the occurrence of adverse events up to 30 days follow-up. Table 2 displays the pre-specified major and non-major adverse events. To evaluate safety, a dedicated researcher will contact these patients and their GP and evaluate on a case-by-case basis. If a major adverse event is deemed directly attributable to the triage method, the protocol will be adjusted or the study will be terminated prematurely. The study will be deemed safe if the percentage of major adverse events is 1% or lower.

- Feasibility of the HART-c prehospital triage method. This will be evaluated in the intervention group and defined as the absence of technical problems for the ambulance paramedic and the triage cardiologist. This means access to the live-monitored data from the ambulance, hospital data and real-time hospital admission capacity are all available. In order to swiftly manage potential technical problems, the HART-c triage method will start during working hours. If interim analysis reveals that the method is feasible, the time frame in which HART-c triage is available could be extended.

Table 2. Adverse events (30 days after EMS contact)

Major adverse events
Death
Acute coronary syndrome
Other adverse events
Renewed EMS or ED visit for cardiac complaint
Pulmonary embolism
ED visit or hospitalization for acute decompensated heart failure
Ventricular tachycardia or – fibrillation
Cerebrovascular accident (CVA) or transient ischemic attack (TIA)

Statistical analysis

The prevention of an ED visit after EMS consultation will be analysed using a logistic regression analysis. Ambulance transfers and inter hospital transfers in the intervention versus the control group will also be evaluated using logistic regression. Baseline characteristics will be reported as mean and standard deviation or median and interquartile range and compared between historical cohort and intervention. This study will be underpowered to detect

differences in mortality and major adverse cardiac events (MACE). Accordingly, these events will only be reported and no further statistics on mortality and MACE will be done. The data will be analysed using IBM SPSS Statistics version 25. A p-value lower than 0.05 will be considered statistically significant.

Patient and public involvement

Patients were involved in the design of the study. During the design stage, representatives from the 'Harteraad', a cardiovascular patient council, were asked for input in study design, choice of outcome measures and methods of recruitment. Also, a dedicated website, www.hartc.nl, was created to inform the public and answer questions from professionals and patients, before and during the study.

ETHICS AND DISSEMINATION

The study is approved by the LUMC's Medical Ethics Committee (P18.213). Patients are requested to provide oral informed consent for contacting their GP at 30 days follow-up. Oral informed consent is requested for cardiologist consultation and study participation by paramedics which is then noted in AmbuSuite. The need for written informed consent was waived by the Medical Ethics Committee. The devices used in this study are FDA and/or CE approved. No manufacturer has a role in study design, data collection, statistical analysis or writing of the manuscript. No financial support is received for this study from any manufacturer. The main results of this trial will be disseminated in one paper.

DISCUSSION

Overcrowding of ED's is a major challenge in healthcare. The HART-c study is a multi-centre prospective study that primarily aims to safely reduce unnecessary ED visits of patients with

all types of cardiac complaints. By selecting the hospital best suited for every patient, this method will contribute to more patient-tailored health care and lead to improved utilization of all available healthcare resources in the region.

Recently, interest has shifted from in-hospital - to pre-hospital triage. Pre-hospital cardiologist consultation has been standard procedure for some time in many hospitals in the Netherlands for quick catheterization lab activation when paramedics suspect chest pain patients of STEMI.[18] For all other cardiac complaints no pre-hospital triage procedure is in place for emergency evaluations. However, there have been some studies assessing the possibility of pre-hospital triage and pre-hospital selection of low-risk cardiac patients.

The History and ECG-only Manchester ACS (HE-MACS) decision aid was developed for pre-hospital triage using history, physical examination and ECG. It was derived in 796 patients and validated in cohorts of 474 and 659 patients. 9.4% of all validated patients were identified as 'very low risk' in which ACS could be 'ruled out' with a sensitivity of 99.5%. It's impact, however, was not prospectively evaluated in this study.

The FAMOUS investigators aim to assess the effects of introducing a pre-hospital triage system that stratifies chest pain patients without ST segment elevation into 1) patients at high risk for NSTEMI requiring direct transfer to a PCI hospital, 2) patients at intermediate risk for major adverse cardiac events who could be evaluated at the nearest non-PCI hospital and 3) patients at low risk for major adverse cardiac events who could have further evaluation at home or in a primary care setting.[19] The study was divided in three phases. In the first phase, a venous blood sample was drawn in the ambulance for measurement of the pre-hospital troponin T levels, in order to establish a pre-hospital HEART score and evaluate the possibility of triage at the patient's home. Of the 1127 chest pain patients, 36% had a low modified HEART score and none of them developed a major adverse event.[20] After this first phase proving feasibility, further studies have been done in the pre-hospital setting by the FAMOUS TRIAGE study

group. Phase 2, a prospective observational study including 700 patients with suspected NSTE-ACS, showed nicely that pre-hospital risk stratification by ambulance paramedics using the HEART score was accurate in differentiating in low and intermediate to high risk.[21] Recently the design of phase 3 has been published, where the FAMOUS study investigators aim to determine if use of the HEART score, including point-of-care Troponin measurement, is non-inferior to routine management. In this phase referral decisions are based on pre-hospital acquired risk stratification. [22]

Another study investigating the added value of point-of-care troponin in the pre-hospital setting is the ARTICA[12] trial. This randomized trial will include patients suspected of non-ST elevation acute coronary syndrome in whom the modified HEAR score (the HEART score without troponin) is calculated by the ambulance paramedic. If the HEAR score is less than or equal to 3, patients will be 1:1 randomized for 1) presentation at the ED or 2) point-of-care troponin T measurement and transfer of care to the GP in case of a low troponin T value. The primary objective of the ARTICA trial will be healthcare costs at 30 days. The trial is currently ongoing and aims to include 866 patients in 12 months.

The similarity of the currently described HART-c study and the HE-MACS, FAMOUS and ARTICA studies is that all three assess whether patients with chest pain who are at low risk of major adverse events can be identified before presenting to the ED. However, the HART-c study has some added benefit as opposed to earlier known studies. First, the HART-c study does not only identify patients at low-risk for events, but also aims to effectively prevent low-risk patients from actually visiting the ED, as well as further phases from FAMOUS and ARTICA did, by combining pre-hospital risk stratification by the paramedic and real-time cardiologist consultation with insight in live vital parameters and ECG. Secondly, while these studies study only focus on chest pain patients, the HART-c study extends this to all patients with cardiac complaints and could therefore be of benefit for a substantially larger cohort of

patients. Furthermore, the HART-c triage method is unique as it combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of an expert triage cardiologist who has access to live-monitored data from the ambulance for all cardiac patients, as opposed to only STEMI patients. Besides these novelties, the HART-c study incorporates hospital data as well as real-time hospital admission capacity to decide which regional hospital is best suited for every patient. In the future, it would be helpful to have pre-hospital information integrated in all hospitals electronic patient dossier. At this moment, however, that is not the case.

If the results of current study show that the HART-c triage method is effective in safely reducing unnecessary ED visits of patients with all types of cardiac complaints, the next step will be to evaluate cost-effectiveness. When cost-effectiveness can be demonstrated, we feel that the HART-c triage method can be expanded to other EMS regions. Furthermore, last but not least, it may potentially also be useful for other medical specialists aiming to optimize pre-hospital triage of non-cardiac patients. Eventual improvements in pre-hospital triage, such as pre-hospital high sensitive Troponin sampling with a point-of-care test or newly developed and proven risk scores, could always be implemented in this triage protocol.

To conclude, the HART-c study is a multi-center prospective study evaluating the efficacy, and feasibility of a novel comprehensive pre-hospital triage method that combines pre-hospital patient assessment by the ambulance paramedic and direct consultation of a cardiologist who has access to live-monitored data from the ambulance, hospital data as well as real-time hospital admission capacity. If the HART-c study will succeed to safely reduce unnecessary ED visits of patients with all types of cardiac complaints, it may help to decrease ED overcrowding and ultimately reduce healthcare expenditures.

Author statement

EdK, TEB, JB, CJHJK, RAD, HAMS, MS and MJB made a substantial contribution to the concept and design of the work. EdK and MJB are in charge of acquisition of data, analysis and interpretation of the data. EdK, TEB, SB and MJB contributed to the drafting of the article. EdK, SB, JB, BEB, CJHJK, RAD, MS and MJB all revised the manuscript critically for important intellectual content.

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Competing interest

EdK, TEB, SB, JB, CJHJK, RAD, HAMS, MS and MJB report no conflict of interest. BEB is the creator of the HEART score.

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Addendum 1. Decision aid for chest pain. The T stands for Triage cardiologist consultation.

Addendum 2. Decision aid for dyspnoea. The T stands for Triage cardiologist consultation.

Addendum 3. Decision aid for arrhythmia. The T stands for Triage cardiologist consultation.

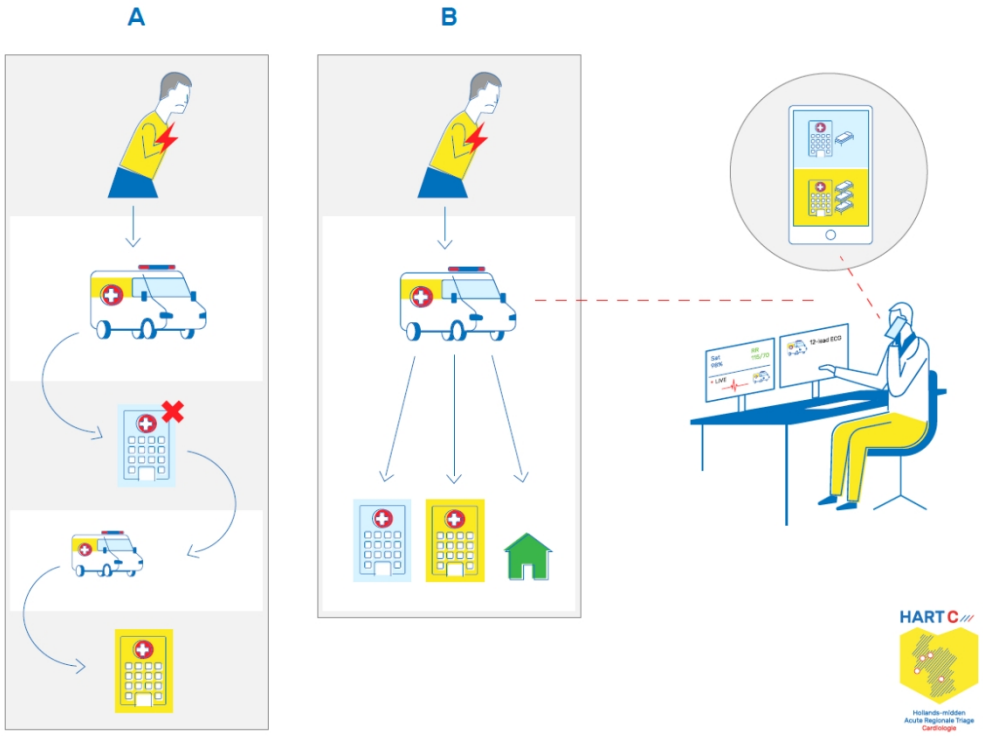


Figure 1. Method of triage

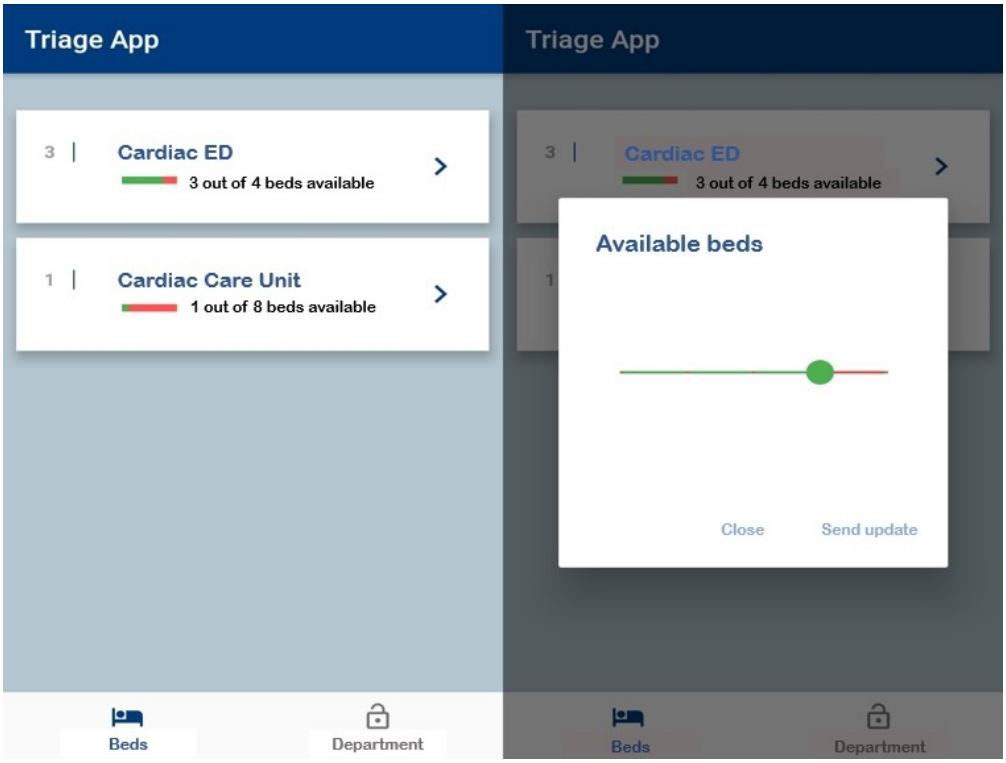
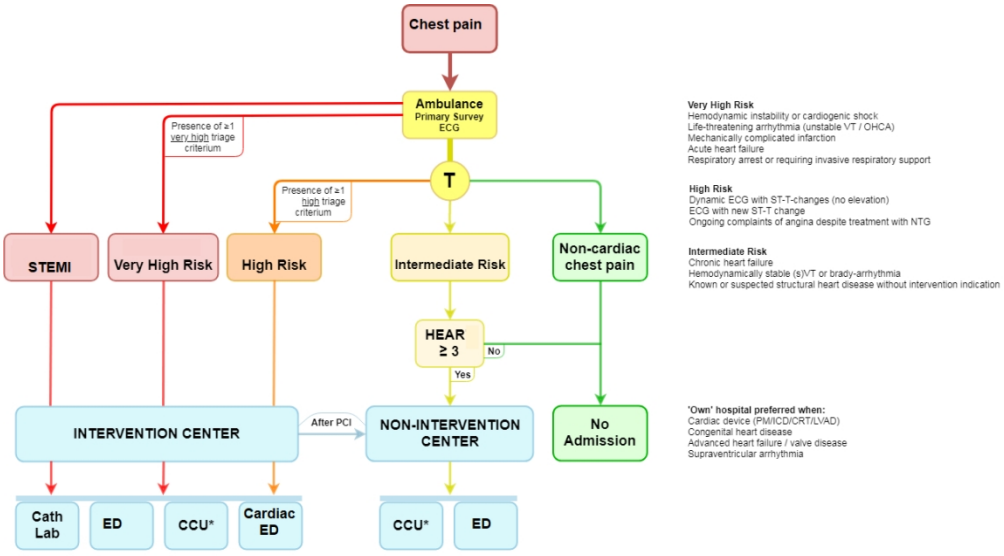
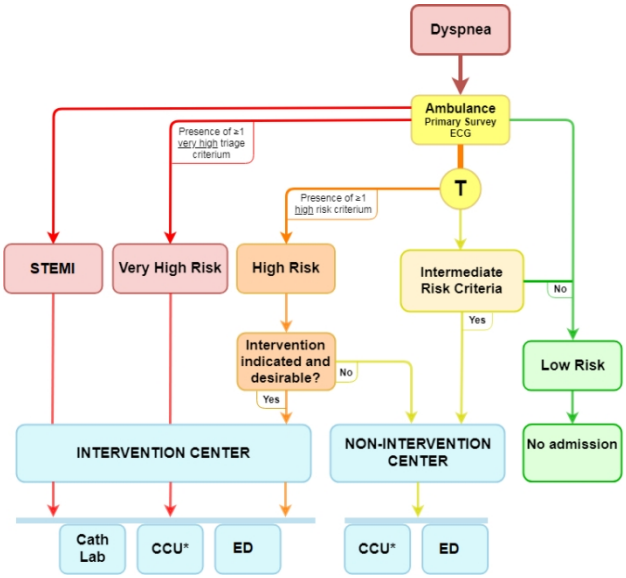


Figure 2. Mobile phone triage application

200x151mm (96 x 96 DPI)

Figure 3. Image of Tempus Pro Monitor


Chest pain
Ambulance
Primary Survey
ECG
Presence of ≥1 very high triage criterium
Presence of ≥1 high triage criterium
T
STEMI
Very High Risk
High Risk
Intermediate Risk
Non-cardiac chest pain
HEAR ≥ 3
No
Yes
INTERVENTION CENTER
After PCI
NON-INTERVENTION CENTER
No Admission
Cath Lab
ED
CCU*
Cardiac ED
CCU*
ED
Very High Risk
Hemodynamic instability or cardiogenic shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated infarction
Acute heart failure
Respiratory arrest or requiring invasive respiratory support
High Risk
Dynamic ECG with ST-T-changes (no elevation)
ECG with new ST-T change
Ongoing complaints of angina despite treatment with NTG
Intermediate Risk
Chronic heart failure
Hemodynamically stable (s)VT or brady-arrhythmia
Known or suspected structural heart disease without intervention indication
'Own' hospital preferred when:
Cardiac device (PM/ICD/CRT/LVAD)
Congenital heart disease
Advanced heart failure / valve disease
Supraventricular arrhythmia

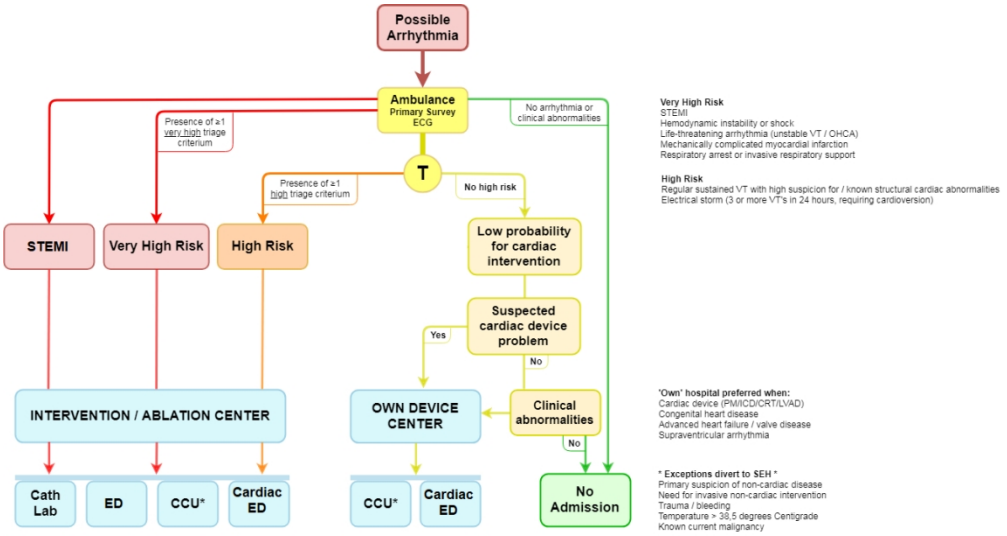


Very High Risk
STEMI
Hemodynamic instability or shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated MI
Respiratory arrest or invasive respiratory support

High Risk
Acute heart failure with the need for invasive support
Suspicion of acute or ongoing ischemia
VAD in situ OR
Scheduled VAD intervention
Respiratory distress < 2 weeks after thoracic intervention

Intermediate Risk
Hypertensive/normotensive acute heart failure
Chronic decompensation
Hemodynamically stable (s)VT or brady-arrhythmia
Known or suspected structural heart disease without intervention indication

General rules of triage: preference for own treating hospital when
Device implantation or guiding center
Congenital heart disease / aortic connective tissue disease
Heart failure
Arrhythmia / ablation


Possible Arrhythmia
Ambulance
Primary Survey
ECG
No arrhythmia or clinical abnormalities
Presence of ≥1 very high triage criterium
Presence of ≥1 high triage criterium
T
No high risk
STEMI
Very High Risk
High Risk
Low probability for cardiac intervention
Suspected cardiac device problem
Yes
No
INTERVENTION / ABLATION CENTER
OWN DEVICE CENTER
Clinical abnormalities
No
Cath Lab
ED
CCU*
Cardiac ED
CCU*
Cardiac ED
No Admission
Very High Risk
STEMI
Hemodynamic instability or shock
Life-threatening arrhythmia (unstable VT / OHCA)
Mechanically complicated myocardial infarction
Respiratory arrest or invasive respiratory support
High Risk
Regular sustained VT with high suspicion for / known structural cardiac abnormalities
Electrical storm (3 or more VT's in 24 hours, requiring cardioversion)
'Own' hospital preferred when:
Cardiac device (PM/ICD/CRT/LVAD)
Congenital heart disease
Advanced heart failure / valve disease
Supraventricular arrhythmia
* Exceptions divert to SEH *
Primary suspicion of non-cardiac disease
Need for invasive non-cardiac intervention
Trauma / bleeding
Temperature > 38,5 degrees Centigrade
Known current malignancy