Prehospital risk stratification in non-ST-elevation acute coronary syndrome; a paramedic echocardiography pilot study.

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Research

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Abstract

Background

Prehospital risk stratification and timing of revascularization in Acute Coronary Syndromes (ACS) is currently based on the electrocardiogram (ECG). ST- elevation in the ECG indicates myocardial infarction (STEMI) in need of immediate reperfusion therapy. However, a large group of ACS patients presents without ST-elevation in ECG, despite coronary occlusions. In these high risk non-ST-elevation myocardial infarctions (NSTEMI), immediate reperfusion may be just as crucial for the prognosis, but prehospital diagnostic tools to identify them are lacking.

Objective

This pilot study investigated if focused prehospital transthoracic echocardiography (TTE) images achieved by paramedics could be transferred to the in-hospital cardiologist for diagnostic evaluation, and test if this, in combination with a point-of-care (POC) high-sensitive Troponin-T (Hs-cTnT) test, facilitates prehospital identification of high risk NSTE-ACS.

Methods

Paramedics were trained to obtain focused prehospital TTE images and provide POC Hs-cTnT - testing in patients with suspected ACS. The information was transferred to the in-hospital cardiologist who determined the treatment strategy by evaluating the information provided by the paramedics.

Results

123 patients were included between November 30 th 2017 and November 30 th 2018. TTE images were interpretable in 107 cases (87%), and Hs-cTnT measures in 113 cases (93%). NSTEMI was the final diagnosis in 16 patients (13%), where 13 got admitted directly for percutaneous coronary intervention (PCI). These patients bypassed the local hospital and saved time to treatment based on the prehospital detection of NSTE-ACS.

Conclusion

Interpretable focused TTE images and POC Hs-cTnT measures can be achieved by paramedics in most patients with suspected NSTE-ACS. This information seems to aid in-hospital cardiologist admitting the right patients to the PCI hospital. The study strongly indicates that prehospital diagnostics and risk assessment of patients with suspected NSTE-ACS is feasible. A larger study is needed to clarify the diagnostic accuracy of focused prehospital TTE in suspected NSTE-ACS

Trial registration

Clinical trials NCT04223986, ID: 17/05178-2 – 522). Registered retrospectively September 23rd 2018. https://clinicaltrials.gov/show/NCT04223986.

Background

Acute Coronary Syndrome (ACS) is one of the leading causes of death and acute hospital admissions in industrialized countries (1, 2). ACS includes unstable angina pectoris, non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI). Prehospital risk stratification and timing of revascularization in ACS is challenging, and currently based on the electrocardiogram (ECG). ST-elevation on the ECG demands urgent reperfusion therapy to minimize irreversible myocardial damage caused by occlusion of a coronary artery (3). In patients without ST-elevation in ECG (NSTE-ACS), the prehospital risk stratification is challenging. Many patients with NSTE-ACS have coronary occlusions (4). Early revascularization is recommended in such cases (5), but prehospital diagnostic tools are lacking. Consequently, transport to a hospital without facilities for revascularization with percutaneous coronary intervention (PCI) might be the case (6). This introduces delays to coronary revascularization and renders a subset of patients at higher risk of major adverse cardiac events, heart failure and death (4).

Elevated cardiac biomarkers are central in defining myocardial infarction (MI) (7), but the accuracy depends on time from onset of symptoms and increases with infarction size (8). Prehospital point-of-care (POC) high-sensitive troponin T (Hs-cTnT) have high specificity in NSTEMI, but the low sensitivity and test target value limitations (cut-offs high above the 99th percentile) impair the clinical usefulness (9–11). The benefit of prehospital POC Hs-cTnT alone is therefore disputed, but still might be useful and improve patient care (9).

Transthoracic echocardiography (TTE) of patients with suspected NSTE-ACS is recommended in the European guidelines (12). Regional cardiac wall motion abnormalities (RWMA) can identify patients with myocardial infarction and total coronary occlusions (13–15). Prehospital detection of RWMA may improve patient care in NSTE-ACS, but it requires a skilled prehospital doctor (16). Outside the Franco-German EMS model (17), prehospital doctors are unlikely to be dispatched to patients with undifferentiated chest pain, so the initial evaluation is done by ambulance paramedics. This study investigates if five focused standard TTE images achieved by paramedics in the ambulance could be transferred to the cardiologist in ward for diagnostic evaluation, and test if this, in combination with a POC Hs-cTnT test and clinical assessment, facilitate prehospital identification of NSTE-ACS with a high risk of coronary occlusions.

Objective

Evaluate the feasibility of paramedics performing POC Hs-cTnT measurements and focused TTE for prehospital NSTE-ACS risk stratification.

Methods

Study design and setting

This pilot study was conducted at Sorlandet Hospital, Norway. The hospital is located at three different geographical locations, with only one PCI-facility serving a population of approximately 500.000 inhabitants. One emergency medical system (EMS) ambulance located 67 km southwest of the PCI hospital and serving a population of approximately 110.000 was equipped for this study. The ambulance was operational from 8 am to 8 pm, Monday through Thursday. The ambulance was equipped with Lifepac 15® (Physio Control INC, WA, USA) ECG recorder with wireless transfer via LifeNet®, mobile broadband connection (Conel LTE LR77; BB- Electronics, Ottawa USA), a laptop sized ultrasound scanner (Vivid IQ with M5Sc-RS probe, General Electric Healthcare, Horten, Norway) placed in a crash proof wall mount, and a Cobas h232 device (Roche Instr, Switzerland) for prehospital analysis of POC Hs-cTnT.

Six paramedics with no previous experience in performing ultrasound examinations were trained over two days by a cardiologist and an echo technician in focused TTE image acquisition. Hospital laboratory staff instructed paramedics in POC Hs-cTnT measurements, and performed quality control, temperature control and monthly calibration of the devices. Supervised simulation scenarios were conducted prior to the first dispatch.

Study population

All patients ≥ 18 years of age located in the study region requesting an ambulance from the local Norwegian Emergency Medical Communication Centre (EMCC) due to chest pain between November 30st 2017 and November 30st 2018 were considered for inclusion. Patients with ST- elevation were excluded and transferred for primary PCI in accordance with current guidelines. We also excluded patients with hemodynamic instability and/or severe arrythmia requiring immediate treatment, conditions affecting ability to cooperate, obvious non-cardiac origin of chest pain and pregnancy. A hospital cardiologist was contacted by paramedics to determine patient eligibility in cases of uncertainty. A flow chart illustrating the enrollment with inclusion and exclusion is presented in Fig. 1.

Study procedure

The EMCC dispatched the study ambulance in accordance with Norwegian Index for Emergency Medical Assistance criteria (table 1).

Table 1: Norwegian Emergency Medical Communication Centre (EMCC) Index v 3.0 dispatch criteria, used for study ambulance response:

A10.02 Chest pain and near fainting.
A10.03Strong pain in the middle of the chest for > 5 min
Chest pain or chest discomfort
A10.04- and difficulty breathing
A10.05- and unwell, nauseous
A10.06- and pale, moist skin
A10.07- and radiance of the pain of the jaw / shoulder / arm / back
A10.08- and suddenly powerless in the arms
A10.10- and only transient effect of nitroglycerin
A10.11Possible serious heart problem with unclear symptoms.

A 12-lead ECG was obtained at first medical contact in all patients. ECGs were digitally transmitted and interpreted by the hospital cardiologist on duty. POC Hs-cTnT was analyzed after first intravenous access. When the test results were ready after 12 minutes, they were communicated to the cardiologist by telephone. Focused prehospital TTE was performed in the ambulance, with the patient on the stretcher facing 45 degrees left towards the paramedic. Image acquisition of five standard 2D-projections (Fig. 2) were stored, transferred and immediately analyzed by the in-hospital cardiologist using EchoPac® software. The cardiologist's evaluation of RWMA was primarily based on visual analysis of myocardial segments. Further action was determined by the cardiologist in real time by evaluating subsequent information provided by the paramedics who examined the patients. Patients with presumable high-risk NSTE-ACS were admitted directly to the PCI hospital. The remaining patients were admitted to the local emergency department or referred to the emergency primary health care service in accordance with standard ambulance protocols. Point of times, medical information, and logistical decisions were registered in an electronic case report form by paramedics, cardiologists and study investigators for all included patients. TTE image interpretability was scored on a five-level Likert-type scale. Dispatch times for first medical contact, ambulance arrival, departure, hospital arrival and dispatch criteria were extracted directly from the ambulance registry. Further registered variables included age, gender, blood pressure, pulse rate, height and weight, smoking habits, diabetes mellitus, previous MI, previous PCI or previous coronary artery bypass graft. Medical journal follow-up was done at day 30 and day 90, registering 30 day mortality, test results, final diagnosis, evidence of new cardiac events or hospital re- admissions.

Statistical analysis

Continuous variables are presented as median (min and max value /interquartile range (IQR)), and categorical variables are presented as counts and percentages of total count. To assess the demographic differences between the groups with and without NSTEMI the Fisher exact test was used for cathegorical variables, the two-sided t-test was used for normal distributed continuous variables, and the two sided Mann-Whitney U-test was used for non-normal distributed continuous variables. Shapiro-Wilk normality test was used together with qq-plot to determine normality. Further, the Levene’s test was used to test for heteroscedacity (difference in variance) in the two groups compared. The result of this test determined if the equal variance t-test or Welsh-test was used. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using R v. 3.6.1.

Results

A total of 123 patients with symptoms of ACS but without ST-elevation were included in the period from November 30th 2017 to November 30th 2018. The average inclusion rate was 0.8 patients per 12-hour shift. The incidence of NSTEMI in the study population was 13%. The median road distance from point of first medical contact (FMC) to the local hospital was 14 km (IQR 14), and 77 km (IQR 20) to the PCI-hospital. 17 (13%) patients were not admitted to any hospital, but received follow-up by outpatient medical service. None of those were admitted during the next 90 days for cardiac events. Clinical characteristics are further presented in table 2. Exept for age, no statistical significant differences were found between groups.

[Table 2: Baseline characteristics of the study population at first medical contact

Variable	Unit	NSTEMI n = 16			Without NSTEMI n = 107			p
		n	%, median (min, max)	Missing n	n	%, median (min, max)	Missing n	
Female	-	4	25%	0	44	41%	0	0.28
Age	years	-	72 (46, 86)	0	-	61 (27, 93)	0	0.03
Previous MI	-	4	25%	0	22	22%	7	0.75
Body Mass Index	kg/m^2	-	27 (20, 36)	0	-	27 (17, 48)	0	0.21
Smoking	-	11	73%	1	67	68%	8	0.77
Hypertension	-	6	40%	1	42	42%	8	1.00
Previous PCI/cABG	-	4	27%	1	20	19%	3	0.50
Statin use	-	3	20%	1	41	41%	7	0.16
Diabetes mellitus (I & II)	-	3	19%	0	19	18%	4	1.00
COPD	-	1	7%	1	12	11%	1	1.00
Systolic blood pressure	mmHg	-	149 (70, 192)	0	-	146 (76, 202)	1	0.72
Diastolic blood pressure	mmHg	-	91 (50, 110)	0	-	85 (44, 120)	1	0.46
Heart rate	bpm	-	71 (35, 103)	0	-	73 (40, 137)	0	0.18
30-day mortality	-	2	13%	0	5	5%	0	0.23

Nomination: percentage, mean, (Standard deviation), median(range). Fisher exact test was used to test for inequality between the non ST- elevation myocardial infarction (NSTEMI) and without NSTEMI groups for categorical variables and t-test for normal distributed continuous variables (Age, Systolic/Diastolic blood pressure) and Mann-Whitney was used for other continuous variables (Body Mass Index and Pulse-rate). MI: Myocardial infarction. PCI: percutaneous coronary intervention. cABG: coronary artery bypass graft. COPD: Chronic obstructive pulmonary disease]

In patients discharged with NSTEMI, two (13%) had a normal prehospital ECG. In patients discharged without evidence of NSTEMI, a normal ECG was found in 75 (65%). In five cases (5%) ECG was not fully interpretable due to digital transfer issues or low quality of the recordings.

Prehospital POC Hs-cTnT among NSTEMI patients were in nine cases ranging from 51 ng/L to 416 ng/L. In the remaining seven NSTEMI patients, the prehospital Hs-cTnT were < 50 ng/L, which is below the detection limit of the unit. Hospital admission Hs-cTnT showed clinically comparable test results (see supplemental material). All patients without NSTEMI had negative prehospital POC Hs-cTnT values (< 50 ng/L). Technical issues in measuring prehospital POC Hs-cTnT were registered in seven cases (6%). This was mostly noted as a result of too low ambient temperature. Difficulties in providing venous access were registered in three cases (2%). A total of 113 (93%) Hs-cTnT tests were successfully performed.

A total of 107 (87%) focused TTE examinations were interpretable. Interpretability scoring is presented in table 3.

Table 3: Cardiologist interpretability score of TTE images received from paramedics on scene. The Likert-type scale range from 1 (no useful information) to 5 (full interpretable information) n = 123

Score	Frequency*	
1	3	(2%)
2	8	(7%)
3	42	(34%)
4	46	(37%)
5	22	(18%)

*two cases (2%) score missing.

Equipment-related technical TTE issues were reported in four (3%) patients, resulting in uncompleted or failed examinations. RWMA were detected in 11 (69%) patients with NSTEMI and in six (6%) patients without NSTEMI. Median time consumption in performing focused prehospital TTE was 11 minutes (IQR 8), counting from “probe- to- skin” until all five images were stored. The cardiologists registered a median time consumption of five minutes (IQR 3) for image interpretation, risk stratification and determining course of action. The individual and combined diagnostic results of utilizing ECG, Hs-cTnT and focused TTE are summarized in table 4 and Fig. 3. RWMA was the most common positive prehospital finding among the NSTEMI patients, while 13% still had no initial findings.

Table 4: Prehospital diagnostic characteristics of individual patients, showing the frequency of positive tests among patients diagnosed NSTEMI.

Test combinations	n = 16
RWMA+	69%
TnT+	56%
ECG+	31%
RWMA + and TnT + combined	38%
RWMA + and ECG + combined	25%
TnT + and ECG + combined	19%
TnT + RWMA + and ECG + combined	13%
All three prehospital tests negative	13%

The combined result illustrates the frequency of individual patients with more than one test suspicious of NSTE-ACS present at the same time. RWMA+: Regional wall motion abnormalities on prehospital transthoracic echocardiogram findings, as interpreted by the cardiologist visual evaluation. TnT+: High sensitive troponin -T point of care test > 50 ng/L. ECG+: ST -depression and/ or T- wave inversion on the prehospital electrocardiogram (ST- elevations were already excluded from the study)]

13 of the 16 NSTEMI patients were transported directly to the PCI hospital based on prehospital risk stratification. The median time from FMC to the PCI procedure startup was 93 minutes (IQR 82). Of the remaining three NSTEMI, two patients were admitted to the local (non-PCI) hospital after negative prehospital risk stratification, but later transferred for revascularization because of clinical deterioration and positive cardiac biomarkers. The third patient had prehospital assessment suggestive of high-risk NSTE-ACS, but was due to co-morbidity, age and previously confirmed non-treatable coronary heart disease admitted to the local hospital for palliative care.

Four (4%) patients without a NSTEMI were directly transferred to the PCI-hospital due to suspected high-risk NSTE-ACS, but no acute angiography was performed. Of these four, two had uninterpretable prehospital TTE and negative Hs-cTnT, but the combination of clinical suspicion and ongoing pain led to the admission. The third had suspicious TTE findings, and the last had prehospital TTE findings later confirmed as moderate to severe aortic valvular stenosis.

Coronary angiography was performed in 15 patients diagnosed with NSTEMI, and they all underwent acute coronary revascularization by PCI. Six (38%) of these patients had total coronary occlusion, subdivided into right coronary artery (three patients), circumflex artery (two patients) and left anterior descending artery (one patient). In the remaining nine, established coronary artery disease was noted, and conditions like a major stenosis, plaque rupture or subtotal stenosis were treated.

Discussion

To our knowledge, this is the first study to evaluate the feasibility of focused prehospital TTE obtained by paramedics in suspected NSTE- ACS (18). This study confirmed that paramedics could acquire and transfer interpretable TTE images in most patients with NSTE-ACS. Based on clinical features, prehospital ECGs, POC Hs-cTnT and TTE images, it might be possible to identify many high-risk NSTE-ACS in the ambulance, and consequently admit the patients directly to a PCI hospital.

The implementation and use of prehospital ECG since the 1990´s for patients with suspected ACS has been a success in improving patient care (19, 20). However, our observations of two normal ECGs among NSTEMI patients and several pathological ECGs outside the NSTEMI group, seem to correlate to the inferiority of ECG alone in ACS risk stratification previously shown (21, 22). The absence of ST-segment elevation in the prehospital ECG could conventionally exclude these patients from an emergent invasive approach.

Single test Hs-cTnT is not sufficient for the MI diagnosis (7), but elevated values rise clinical suspicion of ACS. Prehospital POC Hs-cTnT measurements are technically feasible (9, 23) and positive test results are comparable to first in-hospital measurements in our patient group. Still, seven patients with confirmed NSTEMI presented with negative prehospital POC Hs-cTnT values (< 50 ng/L). This emphasizes the time-dependency and cut-off-value limitations of prehospital POC Hs-cTnT (24). Similar to the case of ECG, a single negative or positive POC Hs-cTnT test is usually not sufficient to exclude or identify ACS (25).

Echocardiography is usually reserved for cardiologists, and RWMA evaluations are an advanced TTE skill (26). This concept of telemedical prehospital TTE does not fit into the focused cardiac ultrasound (FoCUS) definition, as the images are acquired POC, but the assessment is carried out elsewhere. The degree of TTE interpretability appears to be high in the study, but this finding should be interpreted with caution, since there was no retrospective quality assessment of the images. Even expert-assessed echocardiograms have limitations, and assessing all myocardial segments based on only five projections is challenging. Common factors such as obesity and chronic lung disease often result in technically difficult echocardiograms, and are known limitations of TTE in general. This might have caused shortcomings also in our system. Theoretically, significant coronary occlusions should show RWMA every time when assessing the affected coronary wall by TTE. We observed 69% positive RWMA among the NSTEMI cases (table 3), probably providing diagnostic aid, but it still remains unclear how much the presence or absence of RWMA contributed to the diagnosis. The finding of 6% RWMA incidence in the group without ACS, underlines the importance of seeing the whole clinical picture, and not trusting only one single test in a heterogenous patient group like ACS.

When considering the reported mean of 24 hours delay before PCI revascularization in occlusive NSTEMI (4), being able to transfer NSTE-ACS patients to the PCI lab within two hours (despite substantial road distance), indicates that this concept has great potential. But care should be taken to prevent time delay, since patients suffering from serious non-cardiac conditions might experience postponed admittance to the local hospital due to the prehospital diagnostic procedures.

Outside the Franco-German EMS model (17), emergency physicians are not routinely dispatched to the large group of patients with undifferentiated chest pain, as patients are more efficiently evaluated by regular ambulance paramedics (27). Improved competency and expanded procedure repertory among paramedics seem promising in improving patient care (28), and telemedicine is helpful to provide expert knowledge to the scene (29). We believe the interdisciplinary cooperation between the in-hospital cardiologist and paramedics could be a considerable patient benefit through individual assessment in the early phase of the disease. This probably plays a great role in the risk stratification success. Despite the noticeable shortcomings of both Hs-cTnT and focused TTE, introducing such tools could improve patient care in the paramedic-based EMS.

Some major limitations are present in our study. The pilot sample size is low because of low inclusion rate. The national myocardial infarction registry indicates that the one specially equipped ambulance was only dispatched to about half the NSTEMI cases expected in the area of interest in the time period (30, 31). This could be caused by multiple factors, i.e. limited operational time, concurrency conflicts and failure to identify the right patient-population at the EMCC and thereby lack of dispatching and inclusion. The TTE images were only assessed during the initial consultation and were not retrospectively reviewed. Thereby misinterpretations may have occurred, calling for a separate blinded image review in the future. The recruitment of highly motivated paramedics to this study might be a limitation to the generalizability, since several technical skills and multitasking capabilities are required. Equipping an ambulance with a high-end ultrasound scanner instead of a pocket ultrasound device could limit implementation due to financial issues, but choosing high-end was considered a prerequisite for adequate image quality. Future development of improved ultrasound devices might overcome this barrier.

Conclusion

Interpretable focused TTE images and POC Hs-cTnT measures can be achieved by paramedics in most patients with suspected NSTE-ACS. This information seems to aid the in-hospital cardiologist in admitting the right patients to the PCI hospital, and indicates improved prehospital diagnostics and risk stratification of patients with suspected NSTE-ACS. A larger study is needed to clarify the diagnostic accuracy of focused prehospital TTE in suspected NSTE-ACS.

Declarations

Ethical Approval and Consent to participate:

This study was approved by the Norwegian regional ethics committee (REK# 2017/ 701). All patients included in this study have signed a written consent after an initial verbal consent. Data has been processed according to The EU General Data Protection Regulation (EU 2016/679 GDPR).

Consent for publication:

All authors have approved the submitted version, and agree to be personally accountable for the quality of the contents. All listed authors confirms concent for publication of this work.

Availability of supporting data:

The anonymized part of the pilot study dataset is available on request as a .CSV file from the corresponding author by e- mail until November 2023.

Competing interests:

All the authors declare that they have no competing interests.

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Authors' contributions:

LJ, JJ, TD, RBO, BG, KGB, all contributed to the study design, implementation and draft. JJ, EEM, LJ and TD contributed to data acquisition and patient assessments, LJ, JJ, KT and KGB contributed to data interpretation, EEM, BG, RBO, KGB, KT and JJ substantively revised the manuscript.

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List Of Abbreviations

ACS	acute coronary syndrome
ECG	electrocardiogram

EMCC	emergency medical communication center
EMS	emergency medical services
ESC	European Society of Cardiology
FMC	first medical contact
FoCUS	focused cardiac ultrasound
Hs-cTnT	high-sensitive cardiac Troponin (T) -protein
MI	myocardial infarction
NSTE- ACS	non-ST-elevation acute coronary syndromes
NSTEMI	non-ST-elevation myocardial infarction
PCI	percutaneous coronary intervention
POC	point of care
RWMA	regional wall motion abnormality
STEMI	ST-elevation myocardial infarction
TTE	transthoracic echocardiography

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Figures

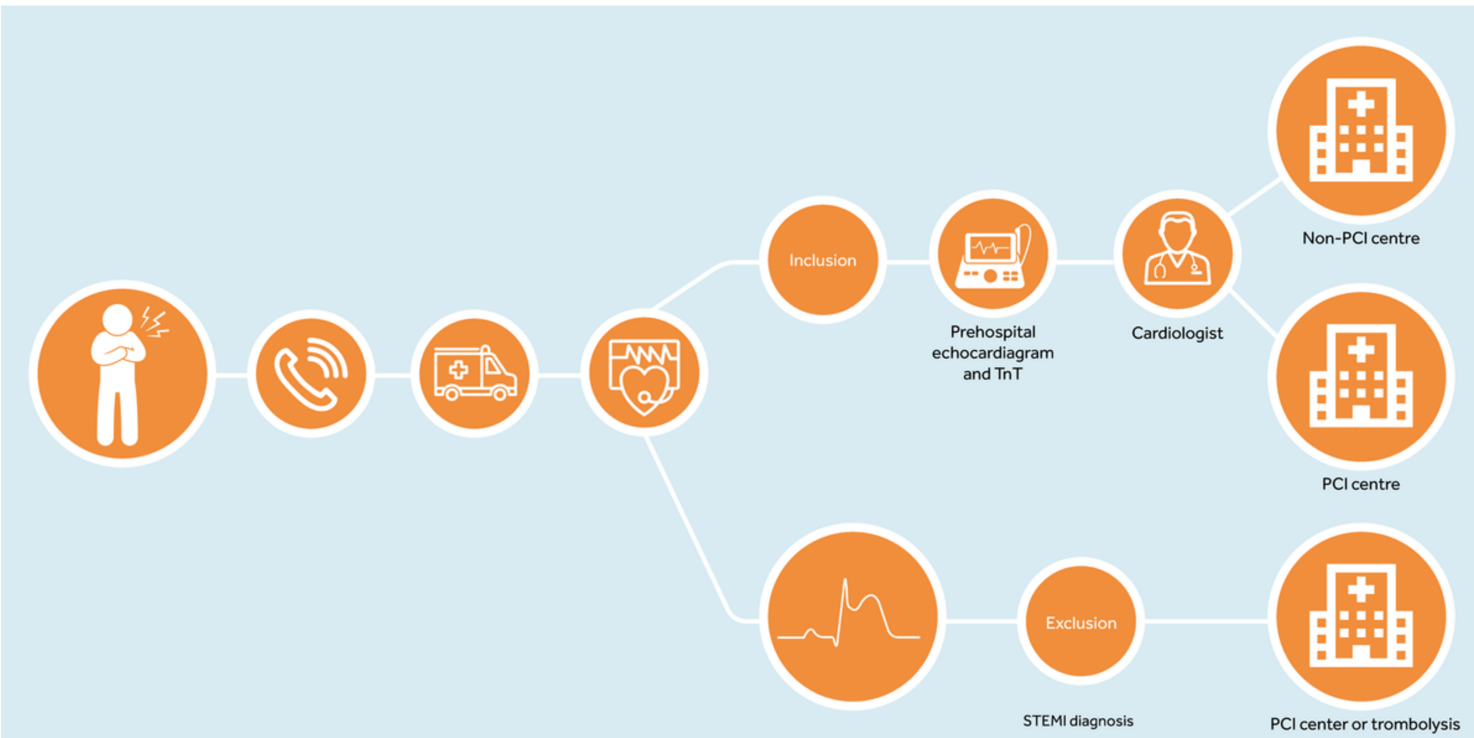
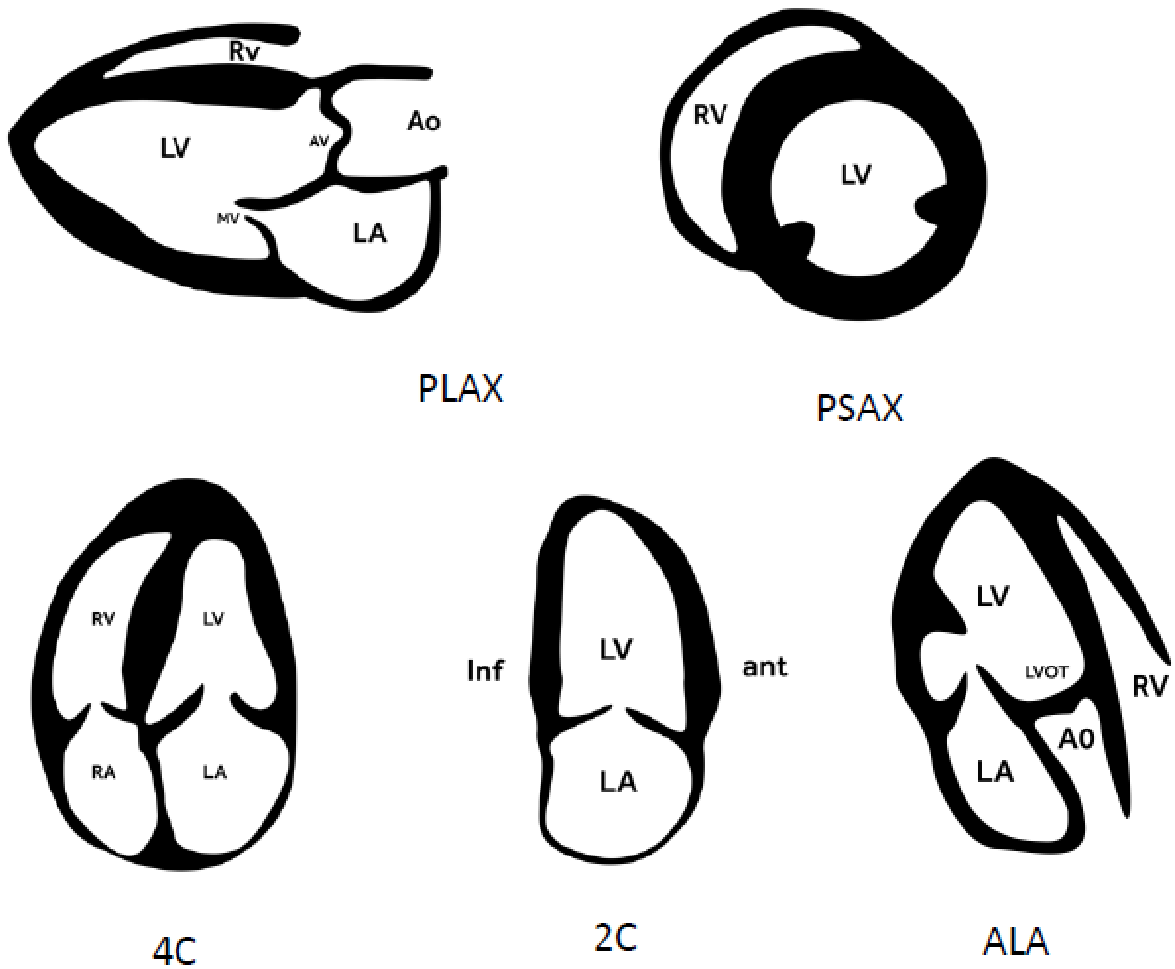


Figure 1

Inclusion timeline. The patient calls the Emergency Medical Communication Centre (EMCC) with chest pain complaint, suspicious of cardiac origin. First prehospital electrocardiogram (ECG) decide inclusion or not; Non-ST elevation ECG´s permits inclusion (upon informed consent). Cardiologist decide after evaluation and testing for immediate admitting suspected ACS to the PCI hospital by the ambulance.



Parasternal long axis (PLAX), parasternal short axis (PSAX), apical 4 chamber (4C), apical two chamber(2C) and apical long axis (ALA). RV= right ventricle. RA=right atrium. LV= left ventricle. LA= left atrium. MV=mitral valve. AV= atrial valve. LVOT= left ventricular outlet tract. AO= aorta.

Figure 2

The five standard TTE projections, stored as ECG synchronized cineloops on the EchoPac server:

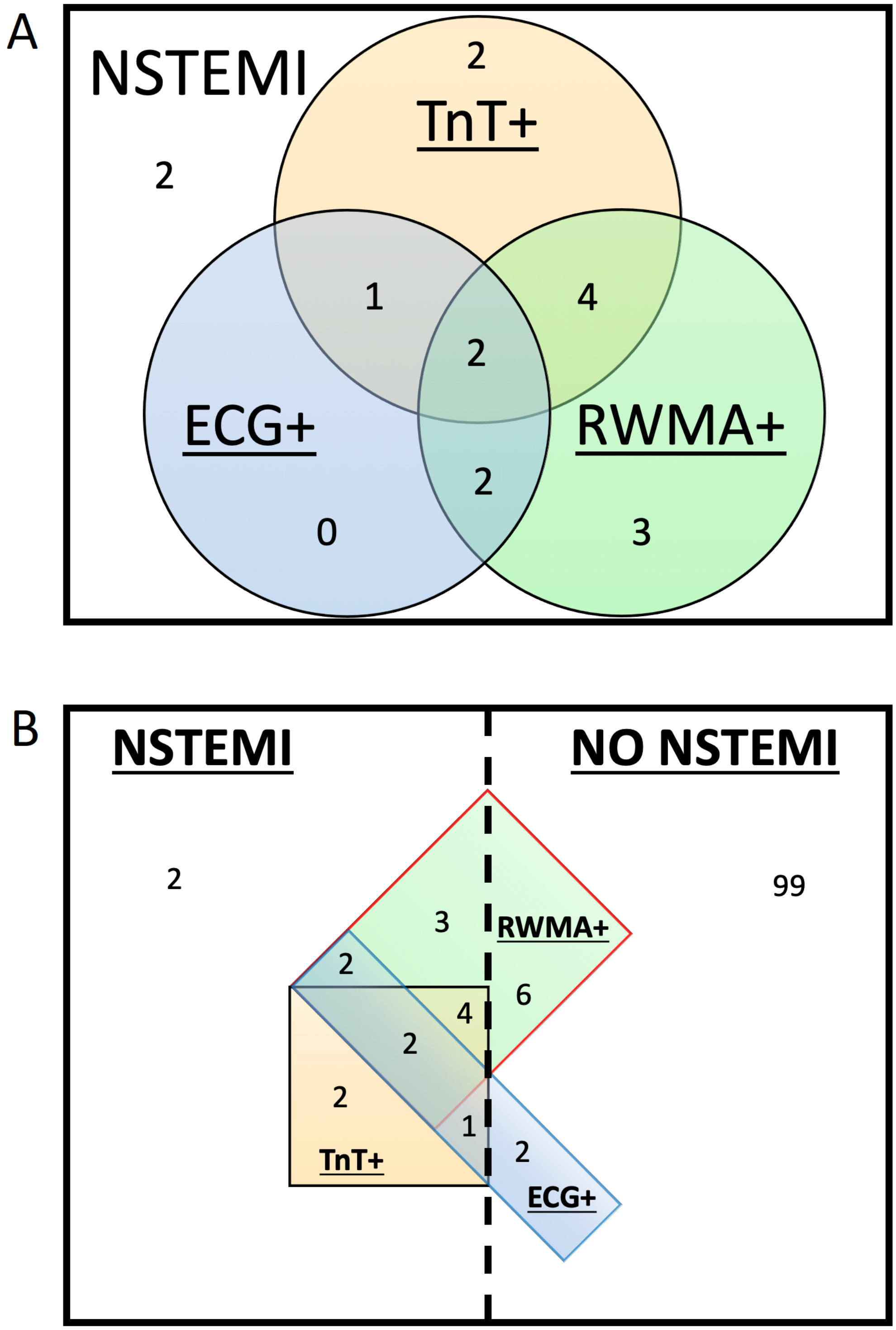


Figure 3

Prehospital diagnostic characteristics of individual patients, showing the frequency of positive and negative tests. The Venn diagram a) shows the absolute numbers from table 4 where overlapping segments illustrate test combinations. The overlapping circles illustrates the frequency of individual patients with more than one test suspicious of NSTE-ACS present at the same time. The number outside the circles illustrate patients without no prehospital findings. The Euler diagram b) shows the occurrence of positive test results in both NSTEMI and no NSTEMI groups. RWMA+: Regional wall motion abnormalities on prehospital transthoracic echocardiogram findings, as interpreted by the cardiologist visual evaluation. TnT+: High sensitive troponin -T point of care test >50 ng/L ECG+: ST -depression and/or T- wave inversion on the prehospital electrocardiogram (ST- elevations were already excluded from the study)

Supplementary Files

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- SupplementalmaterialPreACS.pdf