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E-Transmission of ECGs for expert consultation results in improved triage and treatment of acute ischemic chest pain patients by ambulance paramedics

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ABSTRACT

Aims: In pre-hospital settings handled by paramedics, identification of myocardial infarction (MI) patients remains challenging when automated electrocardiogram ECG-interpretation is inconclusive. We aimed to identify those patients and to get them on the right track to (primary) percutaneous coronary intervention (PCI).

Methods and results: In the Rotterdam-Rijnmond region, automated ECG-devices on all ambulances were supplemented with a modem, enabling transmission of ECGs for on-line interpretation by an expert. The diagnostic protocol for acute chest pain was modified and monitored during 1 year.
Patients with an ECG that met the criteria for ST-segment elevation (STE) myocardial infarction (STEMI) were immediately transported to a PCI hospital. ECGs that did not meet the STEMI criteria, but showed total ST-deviation ≥800 μv were transmitted for on-line interpretation by the ECG-expert. On-line supervision was offered as a service in case ECGs showed conduction disorders, or had an otherwise 'suspicous' pattern according to the ambulance paramedics.

We enrolled 1076 acute ischemic chest pain patients who did not meet the automated STEMI criteria. Their mean age was 63 years; 64% were men. After on-line consultation, 735 (68%) patients were directly transported to a PCI-hospital for further treatment. PCI within 90 minutes was performed in 115 patients with a final MI diagnosis.

Conclusion: During a 1-year evaluation of the modified pre-hospital triage protocol for acute ischemic chest pain patients, over 100 MI patients with an initially inconclusive ECG received primary PCI within 90 minutes. Because of these results, we decided to continue the operation of the modified protocol.

INTRODUCTION

In patients presenting with acute chest pain suggestive of ongoing myocardial infarction (MI) early diagnosis and revascularization treatment leads to favourable clinical outcomes. Patients with ST-segment elevation (STE) myocardial infarction (STEMI) benefit most from percutaneous coronary intervention (PCI) when performed within 2 hours after symptom onset.(1-3) In The Netherlands, early mortality was reported to be as low as 1.6% in patients who receive PCI treatment in the first hour after symptom onset, compared with 4.0% in those treated after 5 hours. (4) Similarly low mortality has been reported after early PCI in non-ST-segment-elevation acute coronary syndrome (NSTE-ACS) patients with a so-called 'high-risk profile', including patients with a GRACE risk score >140.(5, 6) Thus, minimizing total ischemic time is the key to improve the prognosis of STEMI and high-risk NSTE-ACS patients, which mainly is a logistical challenge that starts in the pre-hospital setting.

For decades, the standard 12-lead electrocardiogram (ECG) has been the main diagnostic tool in the assessment of patients with acute chest pain. Worldwide, in most patients presenting with symptoms suggestive of ongoing MI in a pre-hospital setting an ECG will be obtained by the emergency medical service (EMS). Ambulances in The Netherlands, which are staffed by paramedics, are equipped with a patient-monitoring device that is capable to not only derive and register such ECGs, but to also provide an automated analysis and interpretation. Patients with an ECG that is interpreted as 'evolving MI' are then directly transported with highest emergency for coronary angiography and revascularization therapy to the nearest hospital with PCI service. Patients with an inconclusive ECG are transported to non-PCI hospitals for further diagnosis and treatment.

Satisfying results have been reported in relation to the implementation of ECG-based triage protocols,(3) also in the Rotterdam-Rijnmond region, The Netherlands, albeit in the thrombolysis era.(7) Still, in pre-hospital settings, it remains challenging to adequately identify those patients who require immediate reperfusion therapy when automated ECG analysis provides inconclusive results. In the past years, we have obtained anecdotic reports that acute ischemic chest pain patients who initially were transported to a non-PCI center in our region turned out to need immediate PCI after all. Review of their medical records showed that the automated ECG interpretation fell short to recognize the ongoing MI, and, consequently, symptom-onset-to-reperfusion times exceeded the guideline-recommended treatment criteria.

Because of these reports, in December 2013 we decided to change the logistic system in our region. The automated ECG-devices on the ambulances were then supplemented with a modem, which enabled e-transmission of the ECGs for expert consultation. We modified the diagnostic protocol, utilizing this technical option, and we hypothesized that a substantial portion of MI patients would get on the right track to (primary) PCI faster. The implementation of the new protocol was monitored during a one year period, and this paper presents the main findings.

METHODS

Setting

At the start of this study (in 2013), the Rotterdam-Rijnmond region in the Western part of The Netherlands holds a population of 1.1 million. A total of 10 hospitals are located in the region, two of which (*Erasmus MC* and *Maasstadziekenhuis*) offer a 24/7 primary PCI service for MI patients. Most acute ischemic chest pain patients have their first medical contact with a paramedic of the ambulance crew – it should be noted that, in the Netherlands, similar to most other (European) countries, a medical doctor is not present on the ambulance. The paramedic performs a brief physical examination and provides an initial diagnosis, which is mainly based on an automated analysis of the ECG. All ambulances in the region are equipped with the Corpuls3 defibrillator-/monitoringsystem, in which Biosigna HES PRO ECG-interpretation software (algorithm Rev.2.2) was implemented. Patients with a confirmed evolving MI are then transported to a PCI-hospital, whereas the remaining patients are transported to the nearest non-PCI-hospital.

Automated ECG interpretation

In November 2013, the Corpuls devices on the ambulances in the Rotterdam-Rijnmond region were enriched with modems which enabled transmission of the ECGs for on-line interpretation by an ECG-expert: the on-call cardiologist or cardiology resident in one of the two PCI-hospitals (Erasmus MC and Maasstadziekenhuis). Since then, the ECG-protocol for pre-hospital MI diagnosis in acute ischemic chest pain patients (which is a prerequisite) is as follows (Figure 1):

The existing protocol remained unchanged for patients with an ECG that shows ST elevation ≥200 μv in ≥2 adjacent anterior leads, or ≥100 μv in ≥2 non-anterior leads (Category 2). They are directly transported to a PCI-hospital, as they meet the STEMI criteria and need immediate revascularization. An alert is sent by the

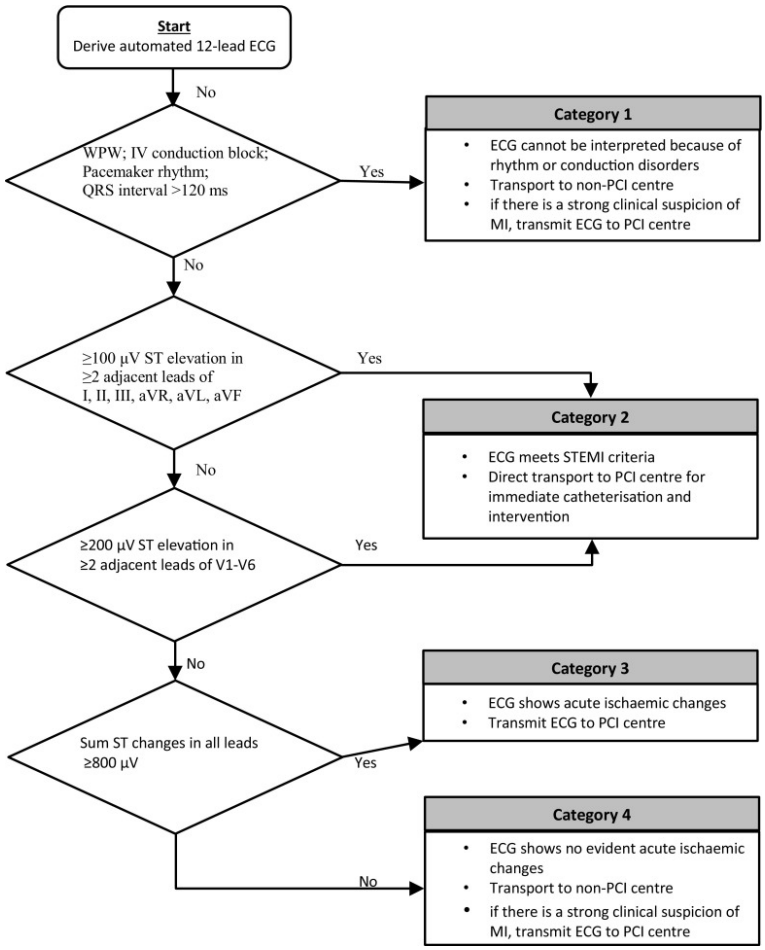

Figure 1. The ECG-protocol for pre-hospital myocardial infarction diagnosis

The following categories are distinguished by the automated ECG analysis and interpretation:

Category 1: ECG with rhythm or conduction disorders. Normally the patient is transported to a centre without facilities for PCI. If there is a strong clinical suspicion of evolving MI, the ECG will be transmitted for online interpretation by the ECG expert.

Category 2: ECG shows ST elevation ≥200 µv in ≥2 adjacent anterior leads, or ≥100 µv in ≥2 non-anterior leads. The ECG meet the criteria for STEMI. Immediate revascularisation is indicated, and patients are directly transported to a PCI hospital. The ambulance staff sends an alert to the PCI hospital, and transmits the ECG for completion of the medical dossier.

Category 3: ECGs that do not meet the STEMI criteria, but still show total ST deviation ≥800 µv must now be transmitted for online interpretation by the ECG expert.

Category 4: Abnormal ECGs without evident acute ischaemic changes.

As in Category 1, the patient is transported to a non-PCI centre. If there is a strong clinical suspicion of evolving MI, the ECG will be transmitted for online interpretation by the ECG expert (ECG electrocardiogram, IV intraventricular, MI myocardial infarction, PCI percutaneous coronary intervention, STEMI ST-elevation myocardial infarction, WPW Wolff-Parkinson-White)

ambulance staff to the PCI-hospital, and the ECG is transmitted for completion of the medical record.

With respect to the treatment of other patients, the existing protocol was extended. ECGs that do not meet the STEMI criteria, but still show total ST-deviation ≥800 µv (Category 3) must now be transmitted for on-line interpretation by the ECG-expert. According to the advice of the ECG-expert, which is provided by telephone within 5 minutes, the patient is then transported to the on-call PCI-hospital for immediate angiography, possibly followed by revascularization, or to a non-PCI-hospital for further evaluation by a cardiologist. For patients with an ECG that cannot be interpreted by the ECG-interpretation software because of conduction disorders (Category 1), as well as for patients with abnormal ECGs, but not showing evident acute ischemic changes (Category 4), on-line supervision by the ECG-expert is offered as a service that is not obliged.

Study patients and data collection

We monitored the revised protocol during the 1 year period from December 2013 to November 2014. Transmitted ECGs and primary data were collected by the ambulance personnel, including age, sex, ECG transmission date and time, and the diagnostic classification that was generated by the Corpuls device. Secondary data were collected by the first author (SA), based on a review of hospital medical records, and included medical history, risk factors, reperfusion time, final (discharge) diagnosis, and other pertinent clinical outcomes. All data were recorded in a dedicated database.

The patients who did not fullfill the STEMI criteria on the ambulance ECG were the population of main interest (Categories 1, 3, and 4). Still, we also collected information on patients who met the STEMI criteria (Category 2), and whose ECGs were transmitted.

Study endpoints

The revised protocol was developed to increase the early rule-in of MIs, and to increase the number of patients undergoing 'primary' PCI within the recommended 90 minutes window (PCI_{90min}), in particular in those patients who initially did not fullfill the STEMI criteria. PCI_{90min} was therefore defined as the main study endpoint. PCI delay was defined as the time difference between the acquirement of the ECG (time zero) and the wire crossing. The revised protocol also aimed to avoid unnecessary patient burden, invasive diagnostics (coronary catheterization) and treatments.

From this perspective, we considered patients that were immediately transported to a PCI-center, but who did not undergo PCI during the initial hospitalisation, as 'false positives'. Consequently, $PCI_{hospitalisation}$ was defined as the secondary endpoint. PCI_{90min} is an inappropriate endpoint in this respect, since it will be influenced by logistic delays.

We classified patients according to their final diagnosis as MI, Unstable Angina (UA), or 'other'. The diagnostic- and treatment criteria that were used by the treating physicians were based on prevailing European Society of Cardiology guidelines (8-10) This study was embedded in the clinical practice of the ambulance service and hospitals in the Rotterdam-Rijnmond region, and we accepted the final (hospital discharge) diagnosis that was made by the treating cardiologist. We derived this information from the hospital discharge letter, and we did not install an adjudication board to evaluate diagnoses and treatment decisions.

Statistical analysis

Baseline characteristics between the four diagnostic categories were compared. Continuous variables are presented as mean value ± standard deviation (SD) and categorical variables are presented as numbers and percentages.

PCI_{90min} and $PCI_{hospitalisation}$ are reported in relation to the diagnostic category. We conducted logistic regression analyses to examine the relation between diagnostic category and patient characteristics as predictor variables, and $PCI_{hospitalisation}$ as outcome (Category 2 patients are excluded from this analysis). Results are presented as unadjusted and adjusted odds ratios (OR) with 95 % confidence intervals (CI). These analyses might be useful to identify patient categories in which the diagnostic system was apparently and definitely - as by judgment of the treating physician - unsuccessful.

Data were analyzed with SPSS software (SPSS 23.0 IBM corp., Armonk, NY, USA). Statistical tests were two-tailed and p-values <0.05 were considered statistically significant.

Ethics

This is an observational study. For the purpose of this study, patients were not subject to acts, or imposed to any mode of behavior, other than standard treatment. For that reason, according to the Dutch law, written informed consent for a patient to be enrolled in this study was not necessary. This study was conducted according

Table 1 - Baseline characteristics according to the automated ECG-based initial diagnosis

	Automated ECG-based initial diagnosis					
	All patients	Category 1	Category 2	Category 3	Category 4	P-value
		ECG cannot be interpreted because of rhythm disturbances	ECG meets STEMI criteria	ECG shows acute ischemic changes	ECG shows no evident acute ischemic changes	
No. of patients	1421	228	345	526	322	
Demographic characteristics						
Age, years	62 ± 17	68 ± 14	57 ± 17	62 ± 18	61 ± 15	<0.001
Men	67	72	76	61	64	<0.001
Cardiovascular risk factors†						
Hypertension	53	64	37	58	60	<0.001
Hypercholesterolemia	41	47	28	43	48	<0.001
Diabetes mellitus	20	25	11	23	22	<0.001
Current smoker	34	27	47	33	40	<0.001
Positive family history	36	28	42	33	40	0.021
Cardiovascular history†						
CAD	31	43	17	32	38	<0.001
MI	22	30	14	19	31	<0.001
PCI	20	22	13	17	29	<0.001
CABG	7	11	1	9	8	<0.001
AF	10	17	2	12	9	<0.001

Data represent mean ± standard deviation values or percentages

† Data on cardiovascular risk factors and cardiovascular history were only available for the 1022 (72%) patients who were directly transported to PCI center. Data on smoking was complete in 89% and data on family history of coronary disease in 87% of patients.

Category 1: ECG with rhythm or conduction disorders. Category 2: ECG that shows ST elevation ≥200 μv in ≥2 adjacent anterior leads, or ≥100 μv in ≥2 non-anterior leads. Category 3: ECG that show total ST-deviation ≥800 μv. Category 4: abnormal ECG, without evident acute ischemic changes.

AF, atrial fibrillation; CABG, Coronary artery bypass grafting; CAD, coronary artery disease; ECG, electrocardiogram; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

to the Privacy Policy of the Erasmus MC, and according to the Erasmus MC regulations for the appropriate use of data in patient-oriented research.

Table 2 - Final diagnosis and treatment according to the automated ECG-based initial diagnosis

	All patients	Category 1 ECG cannot be interpreted because of rhythm disturbances	Category 2 ECG meets STEMI criteria	Category 3 ECG shows acute ischemic changes	Category 4 ECG shows no evident acute ischemic changes	P-value
ECG transmitted to expert	1421	228	345	526	322	
Direct transport to PCI center after expert supervison	1022 (72)	182 (80)	287 (83)	333 (63)	220 (68)	<0.001
Final diagnosis						<0.001
Acute MI	431 (42)	76 (42)	222 (77)	85 (26)	48 (22)	
NSTEMI/UAP	144 (14)	31 (17)	12 (4)	69 (21)	32 (15)	
Other	447 (44)	75 (41)	53 (19)	179 (54)	140 (64)	
PCI performed in Acute MI*						
<90min	263/385 (68)	42/68 (62)	148/202 (73)	49/70 (70)	24/45 (53)	0.007
<120min	300/385 (78)	52/68 (76)	165/202 (82)	53/70 (76)	30/45 (67)	0.013
During hospitalization	400 (93)	71 (93)	211 (95)	72 (85)	46 (96)	0.073
PCI performed in STEMI/UAP						
<90min	14/86 (16)	1/17 (6)	2/8 (25)	8/44 (18)	3/17 (18)	0.827
<120min	16/86 (19)	2/17 (12)	2/8 (25)	9/44 (20)	3/17 (18)	0.775
During hospitalization	86 (60)	17 (55)	8 (67)	44 (64)	17 (53)	0.632

Data represent numbers (percentages)

* PCI during hospitalisation was performed in 400 of 431 patients with a final diagnosis of Myocardial Infarction. The other 46 (11%) patients had no indication for PCI due to medical conditions or other circumstances such as age, multivessel disease, preferred for CABG treatment based on occlusion of multiple cardiac blood vessels or other medical history. Note that data on the timing of the PCI was available in 385 patients.

Category 1: ECG with rhythm or conduction disorders.

Category 2: ECG that shows ST elevation ≥200 μv in ≥2 adjacent anterior leads, or ≥100 μv in ≥2 non-anterior leads.

Category 3: ECG that show total ST-deviation ≥800 μv.

Category 4: abnormal ECG, without evident acute ischemic changes.

Coronary Artery Bypass Grafting, CABG; ECG, electrocardiogram; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

RESULTS

Patient characteristics

The study cohort comprised 1421 patients with a mean age of 62 ± 17 years, and 67% were men (Table 1). A total of 345 patients met the STEMI criteria (Category 2 patients). As compared with the other categories (1,3,4) patients from category 2 were younger (mean age 57 versus 61-68 years), whereas the percentage men was higher (76 versus 61-72%). Furthermore, these patients had a somewhat more favorable cardiovascular disease risk profile, as fewer patients had hypertension

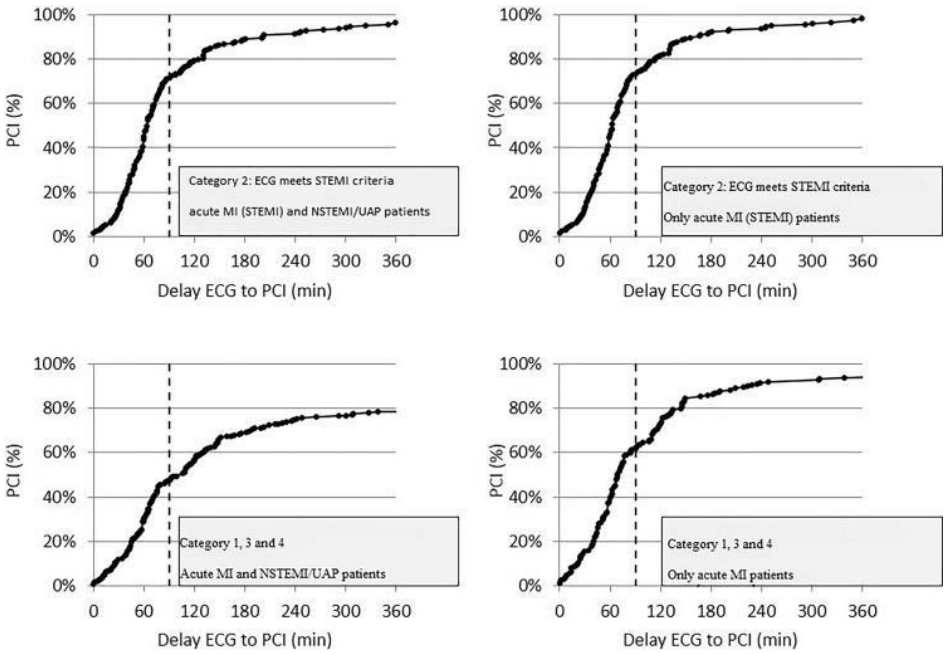

Figure 2. Time delay between ECG transmission and Percutaneous Coronary Intervention treatment

The results are presented as PCI (percentages) time delay (per minute) between the ECG transmission time and PCI treatment time for patients in Category 2 and the Categories 1, 3 and 4 combined.

Category 1: ECG with rhythm or conduction disorders. Category 2: ECG that shows ST elevation ≥200 µv in ≥2 adjacent anterior leads, or ≥100 µv in ≥2 non-anterior leads. Category 3: ECG that shows total ST deviation ≥800 µv. Category 4: abnormal ECG, without evident acute ischaemic changes

(ECG electrocardiogram, MI myocardial infarction, PCI percutaneous coronary intervention, NSTEMI non-ST-elevation myocardial infarction, STEMI ST-elevation myocardial infarction, UAP unstable angina pectoris)

(37 versus 58-64%), hypercholesterolemia (29 versus 43-47%), diabetes mellitus (11 versus 22-25%) and a history of coronary artery disease (17 versus 32-43%).

Initial diagnostic category and treatment decisions

As Table 2 demonstrates, a total of 287 (83%) of Category 2 patients were directly transported to a PCI-hospital. The reasons why the remaining 17% stayed home or were transported to a non-PCI hospital were not recorded. The final diagnosis was MI in 222 (77%) and UA in 12 (4%). Other diagnoses included pericarditis, costomyalgia and cardiomyopathy. $PCI_{hospitalisation}$ was performed in 211 (95%) cases with a

final MI diagnosis, whereas 73% had PCI_{90min}. A total of 8 (67%) patients with a final UA diagnosis had $PCI_{hospitalisation}$, and 25% had PCI_{90min}.

After on-line consultation with the ECG-expert, 735 (68%) Category 1, 3 and 4 patients were directly transported to a PCI-hospital for catheterization and further treatment. Final diagnosis was MI in 209 (28%) and UA in 132 (18%) patients. An indication for PCI was present in 189 of the MI patients. The remaining patients had (relative) contraindication for PCI because of advanced age, or had an indication for Coronary Artery Bypass Grafting (CABG) treatment.. The percentage of patients with a final diagnosis MI ranged from 22% in Category 4 to 42% in Category 1, whereas, in these MI patients, PCI_{90min} ranged from 53% (Category 4) to 70% (Category 3). Figure 2 shows details of time delays between ECG transmission and PCI treatment. Apparently, delays were longer for patients with an initial ECG that did not meet the STEMI criteria.

Determinants of $PCI_{hospitalisation}$ treatment

Table 3 shows determinants of $PCI_{hospitalisation}$. Patients presenting with an initial ECG that shows rhythm or conduction disturbances, which for that reason could not be analysed by the ECG-interpretation software, had considerably higher odds to receive $PCI_{hospitalisation}$ than those with abnormal, but interpretable ECGs (49 versus 30%, $OR_{adjusted}$ 2.7). Interestingly, patients with a history of atrial fibrillation had apparently lower odds for $PCI_{hospitalisation}$ than patients with normal rhythm (20 versus 41%, $OR_{adjusted}$ 0.25). Women had lower odds than men (31 versus 42%, $OR_{adjusted}$ 0.56), whereas elderly patients had higher odds ($OR_{adjusted}$ 1.04 per year). Also smoking status and a positive family history of coronary artery disease (CAD) appeared to be related to $PCI_{hospitalisation}$ treatment.

DISCUSSION

During a 1-year evaluation of the modified pre-hospital triage protocol for acute ischemic chest pain patients in the Rotterdam-Rijnmond region, 115 MI patients with an initially inconclusive ECG received primary PCI within 90 minutes, whereas another 20 received PCI within 90-120 minutes. Because of these results, we have decided to continue the operation of the modified protocol.

We initiated our project because we obtained anecdotical reports of acute ischemic chest pain patients in our region with an initially inconclusive ECG, who were transported to a non-PCI center, and who ultimately underwent immediate PCI for

MI. We intentionally designed an implementation study, and not a randomized trial, neither an observational before-after study. Accordingly, we cannot conclude with entire certainty that the observed early treatment was the direct consequence of a change in patient flow that was induced by the new triage protocol. Still, however, it must be appreciated that the original protocol recommended that these patients be transferred to a regional non-PCI hospital for further evaluation, whereas Miedema et al. observed that inter-hospital transfer was the most frequent cause of treatment delay in STEMI patients.(11) Wang et al. demonstrated in the Acute Coronary Treatment and Intervention Outcomes Network (ACTION) registry that door-in-door-out times from non-PCI- to PCI-hospitals might be as long as 68 minutes in 50% of patients.(12) Prior studies showed that <10% of STEMI patients with inter-hospital transfer were treated within 90 minutes and only 15% to 36% within 120 minutes.(13) These data support the benefits of the modified prehospital triage protocol in our region.

Several studies support the use of pre-hospital ECGs to reduce ischemic times in patients presenting with STEMI or NSTE-ACS.(14-16) Health care systems that involve trained paramedics for ECG interpretation,(17, 18) as well as systems that implemented automated ECG interpretation (19, 20) had satisfactory diagnostic performance and ditto beneficial results. Nevertheless, it has been demonstrated that a cardiologist or medical doctor overview and confirmation improves diagnostic accuracy,(21) while treatment delays are not increased.(22) In particular, ECG artifacts will then be avoided.(23) Our observation of an improved sensitivity to diagnose acute MI by the combination of automated ECG-interpretation and expert-consultation is in agreement with these studies.

It is equally important to filter out normal ECGs to avoid unnecessary treatments, and overcrowding at the PCI hospital.(24, 25) In our study, 64% of the Category 1, 3 and 4 patients that were immediately transported to a PCI center after on-line supervision by the ECG-expert did not undergo revascularisation during hospitalisation. Apparently, CAD requiring immediate treatment, and thus evolving MI, was excluded by the treating physician. In view of the observed benefits, we consider the 36/64 ratio acceptable, although there is room for improvement. Adding diagnostic- and risk-stratification tools could be helpful in this respect. We found that $PCI_{hospitalisation}$ was less likely in women, in younger patients, in non-smokers and in those without a family history of CAD. Still, differences were not large enough to justify a stratified approach according to these characteristics. The application of established risk stratifications scores in the pre-hospital setting, such as the Throm-

bolysis in Myocardial infarction (TIMI) risk score, Global Registry of Acute Coronary Events risk score (GRACE), or the history, ECG, age, risk factor and troponin (HEART) score might be beneficial to improve the diagnostic system.(26-28) Finally, research is warranted to evaluate the diagnostic performance of the combination of automated ECG-interpretation and out-of-hospital point-of-care troponin tests, which recently have become available.(29, 30)

Limitations

As by design, our study has several limitations that need to be mentioned. First, the telephone conversation between the ambulance-paramedic and the on-call ECG-expert was neither protocolized nor reported. As a result, we could not evaluate the factors that actually affected the reason for acceptance or refusal for immediate transportation to the PCI center. This is particular relevant for patients living in the zip code area of the PCI capable hospital. Most likely, the threshold to undergo early CAG in these patients is lower than for their counterparts living at further distance. Second, it is possible that the phone call, in which the clinical condition was discussed, had led to the admission, and not the transmitted and reviewed ECG per se. Unfortunately, however, we are not able to disentangle the influence of both phenomenon. Third, we did not follow-up the patients who stayed at home, or who were transported to a non-PCI center. We appreciate that patients who ultimately had MI might still have been missed in the prehospital phase, but, consequently, we cannot quantify their number. This is particularly the case for patients that were labelled by the ECG-interpretation software as Category 1 or 4. Fourth, we did not measure clinical outcomes. Thus - apart from the fact that our study is not a randomised trial - we are not able to demonstrate the benefit of the revised diagnostic system in terms of patient outcomes.

Conclusion

In conclusion, by applying the modified pre-hospital triage protocol for acute ischemic chest pain patients in the Rotterdam-Rijnmond region, during a 1-year period, over 100 MI patients with an initially inconclusive ECG received primary PCI within 90 minutes. The ‘false positive’ rate of 64% is considered acceptable. Still, further research is warranted to improve the specificity of the triage protocol, so that unnecessary burden to the patient and the system will be avoided.

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