Acute myocardial infarction treatment : from prehospital care to secondary prevention

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Standardized pre-hospital care of acute myocardial infarction patients: MISSION! guidelines applied in practice.

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ABSTRACT

Background

To improve acute myocardial infarction (AMI) care in the region "Hollands-Midden" (the Netherlands), a standardized guideline based care program was developed (MISSION!). This study aimed to evaluate outcome of the pre-hospital part of the MISSION! program and to study potential differences in pre-hospital care between four areas of residency.

Methods

Time to treatment delays, AMI risk profile, cardiac enzymes, hospital stay, in-hospital mortality, and pre-AMI medication was evaluated in consecutive AMI patients (n=863, 61±13years, 75% male) transferred to the Leiden University Medical Center for primary percutaneous coronary intervention (PCI).

Results

Median time interval between onset of symptoms and arrival at the catheterization laboratory was 150(101-280)minutes. The alert of emergency service to arrival at the hospital time was 48(40-60)minutes and the door to catheterization laboratory time was 23(13-42)minutes. Despite significant regional differences in ambulance transportation times no difference in total time from onset of symptoms to arrival at the catheterization room was found. Peak troponin T was 3.33(1.23-7.04)μg/L, hospital stay was 2(2-3)days and in-hospital mortality was 2.3%.

Twelve percent had 0 known risk factors, 30% had 1 risk factor, 45% 2-3 risk factors and 13% had ≥4 risk factors. No significant differences were observed for AMI risk profiles and medication pre-AMI.

Conclusions

This study shows that a standardized regional AMI treatment protocol achieved optimal and uniformly distributed pre-hospital performance in the region "Hollands-Midden", resulting in minimal time delays regardless of area of residence. Hospital stay was short and in-hospital mortality low. Eighty-eight percent of patients had ≥1 modifiable risk factor.

INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death in the western world. Current guidelines are therefore aimed at optimizing care and outcome of patients with acute myocardial infarction (AMI).[1;2] In the past 20 years the risk of dying from CHD in the Netherlands was successfully reduced by almost 33%.[3] This was in part the result of increased efforts to improve acute treatment and secondary prevention strategies.[3-5]

In the acute phase AMI patients require rapid diagnosis and early reperfusion to minimize infarct size and to prevent complications. Several factors determine treatment delay with its major contributors being patient-delay, physician-delay and in-hospital delay. In order to minimize treatment delay an intensive collaboration is therefore needed between primary care physicians, regional ambulance services, community hospitals (without percutaneous coronary intervention (PCI) facilities), and PCI centers.

A regional AMI guideline implementation program (MISSION!) was developed to optimize the use of evidence-based medicine in practice.[6] MISSION! contains a pre-hospital, in-hospital and out-patient clinical framework for decision making and treatment of AMI patients. The main goal of this study was to study the outcome of the pre-hospital part of MISSION! and to evaluate and identify potential regional differences in multidisciplinary performance and related patient factors in the region "Hollands-Midden".

METHODS

Patients

The geographical region studied (Hollands Midden = "Center of Holland") spans an area of 875 km^2 with a population of approximately 750.000 inhabitants. Patients included in this study were all living in the region and were admitted with the diagnosis of AMI in the years 2006-2008 at the Leiden University Medical Center for primary PCI. The study population was partitioned into four areas of residency within Hollands-Midden, classified as "Duin & Bollen" (region 1), "Leiden" (region 2), "Alphen" (region 3) and "Gouda" (region 4) (Fig. 1). AMI patients admitted for primary PCI living outside of the region Hollands-Midden were excluded.

Clinical protocol

To align AMI care, an intensive collaboration was established among primary care physicians, the regional ambulance services, three community hospitals without PCI facilities, three cardiac rehabilitation centers and the Leiden University Medical Center, serving as primary PCI facility. The MISSION! protocol was developed based on the American College of Cardiology/American Heart Association and European Society of Cardiology guidelines for AMI.[2;7]

The pre-hospital emergency care required trained ambulance personnel to obtain a 12-lead ECG at patients' home. In the case of suspect characteristics, the ECG was electronically transmitted to the PCI center. Trained coronary care unit (CCU) nurses determined patient's eligibility for primary PCI. Patients not eligible for PCI, were transferred to a community hospital for further assessment. Patients eligible for primary PCI, were transferred directly to the PCI center's Cardiac Care Unit. In the ambulance aspirin, abciximab and clopidogrel was administered to the patient. The catheterization room was operational within 20 minutes, 24 hours a day, 7 days a week. After discharge, patients were offered a cardiac rehabilitation program and benefited from intensive out-patient follow up for the period of 1 year.

The current study focused on the pre-PCI phase of the MISSION! protocol.

Data collection

Data was recorded by ambulance personnel and medical staff at the hospital. All the data was registered in a departmental electronic patient system (EPD-Vision, LUMC, Leiden, The Netherlands).

Endpoints

Pre-clinical performance in the four residence areas was measured by the following time intervals (minutes): Onset of Symptoms to Alert of Emergency Services (patient delay), Onset of Symptoms to Arrival at Catheterization Room (Cath-Lab), Door to Cath-Lab (hospital delay) and Interval between the Alert of Emergency Services to Arrival at the Hospital. Additional endpoints of interest were peak Troponin T and peak Creatine Phosphokinase (CPK) levels.

Furthermore, risk profile for CHD was compared between the 4 areas of residency within Hollands-Midden, including risk factors like smoking, hypertension, hyperlipidemia, positive family history, diabetes mellitus and prior myocardial infarction. Lastly, drug treatment before occurrence of AMI was studied. Pre-admission medication use of interest was beta-blockers, statins, aspirin, ACE-inhibitors, angiotensine II (AT2)-antagonists, diuretics and calcium-antagonists.

Statistical Analysis

Sample comparisons were made with a Pearson χ^2 test for categorical variables using Yate's correction where appropriate. A Kruskal-Wallis one-way analysis of variance was employed for the comparison of not normally distributed continuous variables such as time intervals. All tests were two-sided, a p-value of < 0.05 was considered significant (using Bonferroni correction where appropriate). All data were analyzed with SPSS 16.0.02.

RESULTS

Study population

A total of 1002 consecutive AMI patients were admitted at the PCI center between 2006 and 2008. Of these patients, 863 (86%) were Hollands-Midden residents and included in the final study population. Baseline characteristics are shown in Table 1. The majority of patients was male (75%) and the mean age was 61 ± 13 years. The distribution of patients from the areas of residence 1, 2, 3 and 4 was 31%, 29%, 21% and 19%, respectively (Fig. 1).

Table 1. Patient characteristics.

Patient Characteristics (n=863)	
Male (%)	646 (74.9)
Age (years)	61 ± 13
BMI (kg/m^2)	28.4 (24.9-41.1)
BMI ≥30 kg/m^2 (%)	374 (43.3)
Region of residency (%)	
1	265 (30.7)
2	253 (29.3)
3	185 (21.4)
4	160 (18.5)
Risk factors for coronary diseases (%)	
Smoking	462 (53.5)
Hypertension	307 (35.6)
Hyperlipidemia	167 (19.4)
Family History	358 (41.5)
Diabetes Mellitus	108 (12.5)
Prior Myocardial Infarction	90 (10.4)
Median time intervals in minutes (IQR)	
Onset Symptoms - Arrival at Cath-Lab	150 (101-280)
Door - Arrival at Cath-Lab	23 (13-42)
Onset Symptoms – Alert of Emergency Services	61 (25-158)
Alert of Emergency Services – Arrival at Hospital	48 (40-60)
Hospitalization	
Days hospitalized (median [IQR])	2 (2-3)
In-hospital mortality (%)	20 (2.3)

Values expressed as n (%), normally distributed data as mean ± standard deviation, otherwise as median (interquartile range [IQR]: 25th-75th percentile).
BMI = Body Mass Index, Cath-Lab = Catheterization Room.
Hyperlipidemia= Total cholesterol ≥190 mg/dl or previous pharmacological treatment.
Hypertension = Blood pressure ≥140/90 mm Hg or previous pharmacological treatment.
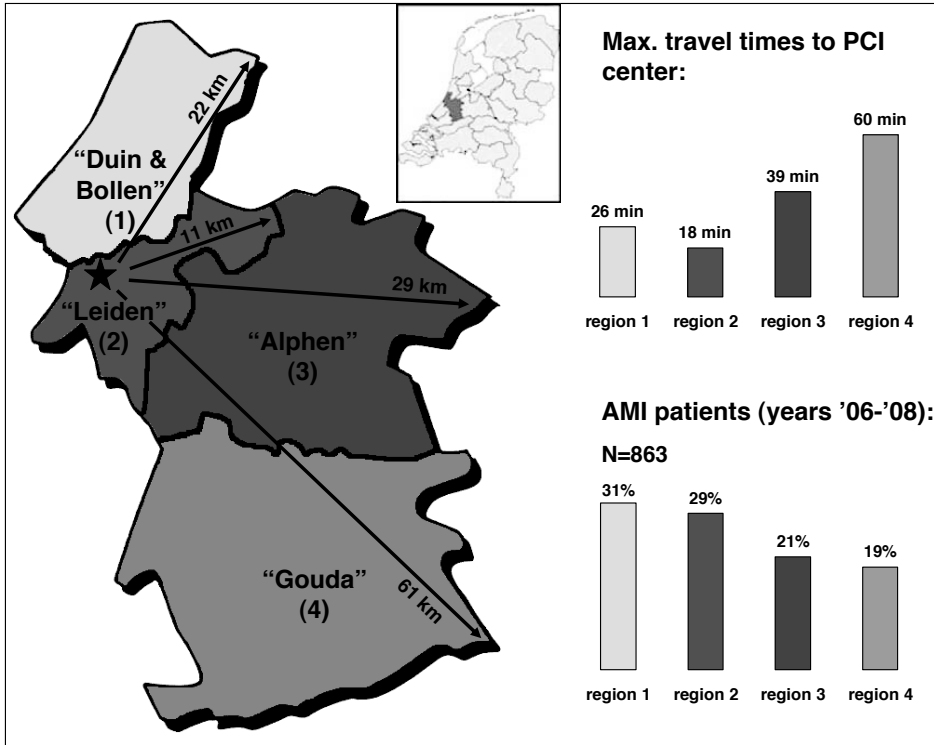
Figure 1. The region of "Hollands-Midden" as divided into four areas of residency.
Schematic map of the region "Hollands-Midden" (The Netherlands) further subdivided into the four areas of residency: "Duin & Bollen" (region 1), "Leiden" (region 2), "Alphen" (region 3), "Gouda" (region 4). The star within "Leiden" (region 2) represents the location of the PCI center. Maximal travel time to each area of residency (minutes) and percentage of patients per area are shown in the bar graphs on the right.
AMI = acute myocardial infarction, KM = kilometers, Max. = maximal, PCI = percutaneous coronary intervention.

The four most common risk factors were smoking (54%), a family history of coronary artery disease (CAD) which was present in 42% of patients, a Body Mass Index (BMI) $\geq$30 kg/m^2 (43%) and hypertension in 36% of patients.

Median duration from onset of symptoms to arrival at the Cath-Lab was 150 minutes (101-280 min). Median patient delay, measured as time between the onset of symptoms and the moment of alerting the emergency service, was 61 minutes (25-158 min), whereas the median time between the alert of emergency services and the arrival at the hospital was 48 minutes (40-60 min). Median Door to Cath-Lab time was 23 minutes (13-42 min). Hospital stay was only 2 (2-3) days and in-hospital mortality was 2.3% (20/863). Total 30 day mortality was 3.5% (30/863, including in-hospital mortality).

Clinical characteristics per area of residency

Clinical characteristics according to the area of residency are shown in Table 2. In summary, comparisons revealed a similar age and gender distribution between the 4 areas and similar

Table 2. Patients' medical history per region of residency.

	Region 1 n = 265	Region 2 n = 253	Region 3 n = 185	Region 4 n = 160	p-value
Patient Characteristics					
Male (%)	203 (76.6)	190 (75.1)	130 (70.3)	123 (76.9)	0.415
Age (years)	61 ± 13	61 ± 13	61 ± 13	62 ± 12	0.931
Body Mass Index (kg/m^2)	28.7 (25.5-42.6)	28.4 (25.0-40.4)	27.5 (24.5-39.6)	27.8 (24.7-42.3)	0.466
Risk factors (%)					
Smoking	151 (57.0)	128 (50.8)	105 (57.1)	78 (49.1)	0.239
Hypertension	102 (38.5)	86 (34.3)	68 (37.0)	51 (32.1)	0.540
Hyperlipidemia	50 (18.9)	49 (19.4)	35 (19.0)	33 (20.8)	0.969
Family History	115 (43.4)	99 (39.3)	81 (44.0)	63 (39.6)	0.658
Diabetes Mellitus	29 (11.0)	36 (14.3)	26 (14.1)	17 (10.7)	0.533
Prior Myocardial Infarction	24 (9.1)	34 (13.5)	16 (8.7)	16 (10.1)	0.304
Prior PCI	21 (8.0)	22 (8.7)	10 (5.4)	9 (5.7)	0.471
CABG in past	6 (2.3)	8 (3.2)	3 (1.6)	3 (1.9)	0.724
History of Angina Pectoris	33 (12.6)	43 (17.5)	28 (15.6)	25 (15.8)	0.498
Nr. of risk factors					
0	39 (14.7)	31 (12.3)	12 (6.5)	20 (12.5)	0.063
1-2	139 (52.5)	145 (57.3)	119 (64.3)	97 (60.6)	0.076
3-4	73 (27.5)	63 (24.9)	45 (24.3)	37 (23.1)	0.747
≥ 4	36 (13.6)	39 (15.4)	23 (12.4)	15 (9.4)	0.352
Medication before MI (%)					
Beta-blocker	67 (25.4)	45 (18.0)	41 (22.4)	27 (17.0)	0.104
Aspirin	51 (19.2)	52 (20.8)	33 (18.0)	20 (12.6)	0.195
Statin	52 (19.7)	48 (19.2)	34 (18.6)	21 (13.2)	0.354
ACE-inhibitor	35 (13.2)	33 (13.2)	20 (10.9)	17 (10.7)	0.779
Angiotensine II-antagonist	15 (5.7)*	16 (6.4)	25 (13.7)*	10 (6.3)	0.008*
Diuretic	31 (11.7)	25 (10.0)	22 (12.0)	23 (14.5)	0.598
Ca-antagonist	30 (11.3)	25 (10.0)	21 (11.5)	15 (9.4)	0.893
Peak troponin T (µg/L)	3.45 (1.28-7.14)	2.81 (0.92-6.39)	3.34 (1.24-6.68)	3.95 (1.98-7.87)	0.083
Peak CPK (U/L)	1388 (587-2618)	997 (448-2165)	1323 (522-2727)	1586 (755-3146)	0.008*
LVEF 3 months post-MI (%)	56 (47-64)	56 (47-64)	55 (49-63)	55 (47-63)	0.887

Values expressed as n (%), normally distributed data as mean ± standard deviation, otherwise as median (interquartile range [IQR]: 25th-75th percentile). * p<0.05
ACE = Angiotensin-Converting Enzyme, Ca = Calcium, CABG = coronary artery bypass surgery, CPK = Creatine Phosphokinase, LVEF = Left ventricular ejection fraction, MI = myocardial infarction, PCI = percutaneous coronary intervention.

risk profiles for CHD. Medication prior to AMI was similar between the 4 patient groups except for a significantly larger percentage of patients using AT2-antagonist living in region 3 when compared to patients living in the region 1 (13.7% versus 5.7%, respectively).

Pre-hospital care

Pre-hospital time delays per area of residency are illustrated in Fig. 2. Patient delays were similar between the four areas of residency as revealed by the median time between onset of symptoms to alert of emergency services (Panel A: range of a median 51 min for region 2 to a median 74 min for region 1; p=0.796).

In addition, total time elapsing between the onset of symptoms and the arrival at the catheterization laboratory was also similar for patients of all four areas of residency (Panel B: median 148 min for region 3 to median 165 min for region 4; p=0.809). Panel C further-more shows that median in-hospital delay was relatively short (median 17 min for region 4 to median 28 min for region 2) and comparable between the patient groups (p=0.056).

Fig. 3 shows that significant differences were present between the four areas of residence in the total time needed for emergency services to arrive at the patient (from the moment
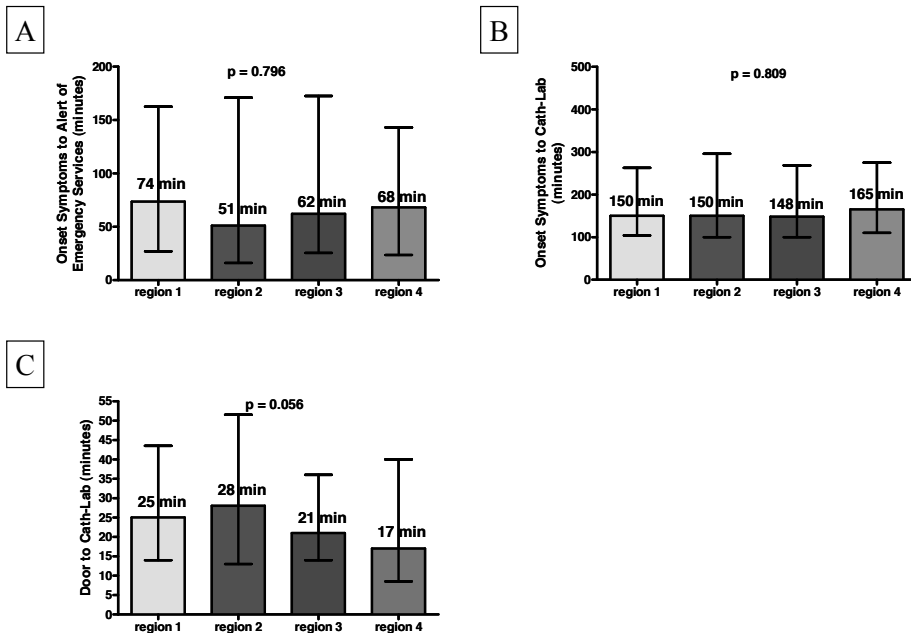
Figure 2. Time to treatment delay.
Bar graphs showing: (Panel A) patient delay defined as time from onset of symptoms to alert of emergency services, (Panel B) time interval from symptom onset to arrival at the catheterization room ("cath-lab"), and (Panel C) hospital delay expressed as time from arrival at the hospital to arrival at the cath-lab. Top of bar represents median time (minutes). Error bars indicate 25th and 75th percentile (minutes). Abbreviations as in figure 1.
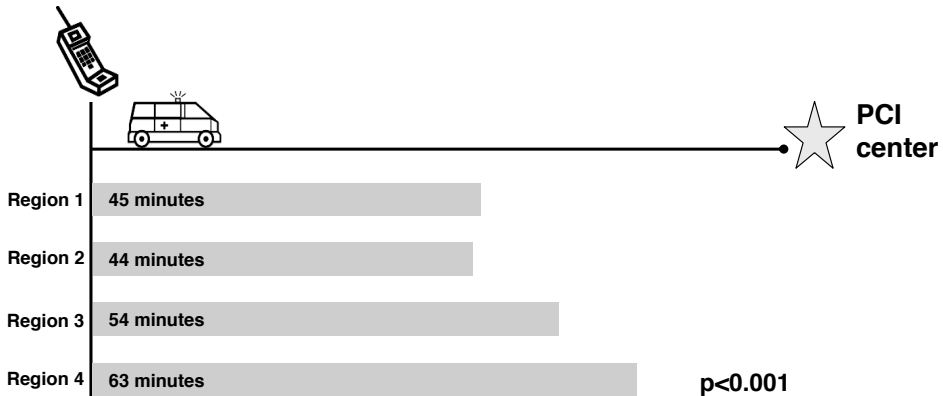
Figure 3. Time from alert of emergency services to arrival at PCI center.
Bars represent time interval (median minutes) from 911 call to the arrival at PCI center (represented by star) per region of residency. Abbreviations as in figure 1.

of the 911 call) in addition to the amount of time needed to transport the patient to the PCI center (p<0.001). Only two areas of residency did not differ significantly: Region 1 and region 2 (median of 45 min and 44 min respectively). Patients living outside of this area all needed significantly more time to reach the PCI center (≥50 min). Transportation time of patients from region 4 was the longest (median of 63 min). Of interest, these patients had the shortest door to Cath-Lab time (17 min) when compared to patients from other areas.

DISCUSSION

The main findings of this study were: (1) the pre-hospital MISSION protocol succeeded in achieving equally high quality pre-hospital performance in all areas of the region Hollands-Midden regardless of the distance from the PCI center, (2) time delay due to geographical distance ("Gouda"[region 4] patients) was counterbalanced by a short in-hospital delay, and (3) there was no significant difference in pre-AMI medication use and risk profile of patients between the four areas of residency.

Structured care for AMI patients
Previous reports demonstrated that a standardized guideline-based treatment system can improve the quality of AMI care and can even result in a lower in-hospital and 1-year mortality.[8-11] Collaboration between general practitioner, ambulance services and hospital is essential in prevention, acute care and rehabilitation of (potential) AMI patients. Results of this study demonstrate the efficacy of the pre-hospital MISSION! protocol in achieving predefined targets.[6] Furthermore despite significant differences in transportation time (due to differences in distance from the PCI center) similar time intervals between the onset

of symptoms to arrival at the Cath-Lab in all 4 areas of residence demonstrate that the multidisciplinary pre-hospital care is uniformly distributed and well organized in the region Hollands-Midden. Furthermore, even though physical distance was of influence on the time needed to get the patient to the hospital (from the start of symptoms), the short door to Cath-Lab time (median 23 min) leveled out these differences.

Benefits of the standardized pre-hospital care program are also reflected in short admission duration (median 2 days) and low in-hospital mortality (2.3%). Peak cardiac enzyme levels per area of residency, such as troponin T levels demonstrated that final infarct size was similar, regardless of the geographical distance. Moreover, it corresponded well with left ventricular ejection fraction of patients as measured 3 months post myocardial infarction by stress/rest myocardial perfusion scanning (Table 2).

Hardly any significant differences were observed in medications prescribed by general practitioners prior to AMI and in risk factors for CHD between the four areas of residence within Hollands Midden. Investigators of the EUROASPIRE Study investigated risk factor control in several countries in Europe.[12] Compared with their most recent data, risk factors for CHD were less prevalent in our study population, except for smoking (this study: 54.0% vs. EUROASPIRE: 18.3%) and BMI $\geq$30 kg/m^2 (43% vs. 38.0%).[13] Lower prevalence of hypertension (35.6% vs. 60.9%), hyperlipidemia (19.4% vs. 46.2%) and diabetes (12.5% vs. 28.0%) point to a relatively successful risk factor control in the region 'Hollands Midden'. Possibly, greater attention for modifiable lifestyle factors, particularly smoking and obesity, may facilitate in further improving prevention of AMI in the region Hollands-Midden in the future.

Inconsistency of guideline implementation

Many organizations have recommended early reperfusion strategies and use of evidence-based medicine, together with long-term support programs to stimulate healthier lifestyle for the treatment of patients with AMI.[1;2] Although benefit of these guidelines has already been established, their implementation in the treatment of AMI patients is still inconsistent. Broer et al. showed that there were regional differences in pre-hospital time delays for AMI patients in the Netherlands.[14] The EURASPIRE survey showed that there were significant differences in risk factor control and cardioprotective drug prescription between European countries.[13]

While guidelines recommend having at least 75% of patients treated within 90 minutes of presentation at the hospital, a study using the United States National Registry of Myocardial Infarction led investigators to conclude that this benchmark is rarely achieved for patients undergoing primary PCI in the United States. Only 4.2% of 4278 patients transferred for primary PCI at 419 hospitals were treated within 90 minutes and median door-to-ballon time was 180 minutes.[15] More recently, the reported percentage of patients with door-to-balloon times of <90 minutes in a community-wide surveillance study of patients hospitalized with

AMI (in a large central New England community in the United States) was less than 10%.[16] In another Dutch study conducted by Broer et al, investigators reported hospital delays of 60-72 min.[14] In contrast, the present study achieved a median door-to-Cath-Lab time of 23 minutes, with 90% of patients reaching the Cath-Lab in <90 minutes.

Clinical implications

Standardized protocols like MISSION! contribute to improved adherence to evidence-based medicine in routine clinical practice and to the uniform implementation of structured care for patients with AMI, stressing the importance of close collaboration with all partners.

Limitations

No comparisons could be made between the current study population and a population not treated according to the MISSION! protocol in the region Hollands-Midden. Nevertheless, compared to previous studies, the MISSION! protocol performed well in the care of AMI patients.[14-16]

As this was a single center, single region study conclusions may not pertain to larger regions. Furthermore, as data on prevalence of risk factors and medication use was derived in part from patient self-report, it should be considered with the necessary caution.

CONCLUSION

This study shows that a standardized regional AMI treatment protocol achieved optimal and uniformly distributed pre-hospital performance in the region Hollands-Midden, resulting in minimal time delays to treatment regardless of the area of residence. Furthermore hospital stay was short and in-hospital mortality low. Eighty-eight percent of patients had 1 or more modifiable risk-factors.

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