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

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Background. To improve acute myocardial infarction (AMI) care in the region 'Hollands-Midden' (the Netherlands), a standardised guideline-based care program was developed (MISSION!). This study aimed to evaluate the 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 catheterisation laboratory was 150 (interquartile range [IQR] 101-280) minutes. The alert of emergency services to arrival at the hospital time was 48 (IQR 40-60) minutes and the door-to-catheterisation laboratory time was 23 (IQR 13-42) minutes. Despite significant regional differences in ambulance transportation times no difference in total time from onset of symptoms to arrival at the catheterisation room was found. Peak troponin T was 3.33 (IQR 1.23-7.04) μg/l, hospital stay was 2 (IQR 2-3) days and in-hospital mortality was 2.3%. Twelve percent had 0 known risk factors, 30% had one risk factor, 45% two to three risk factors and 13% had four or more risk factors. No significant differences were observed for AMI risk profiles and medication pre-AMI.

Conclusions. This study shows that a standardised 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. Of the patients, 88% had ≥1 modifiable risk factor. (Neth Heart J 2010;18:408-15.)

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Coronary heart disease (CHD) is the leading cause of death in the Western world. Current guidelines are therefore aimed at optimising 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 success-
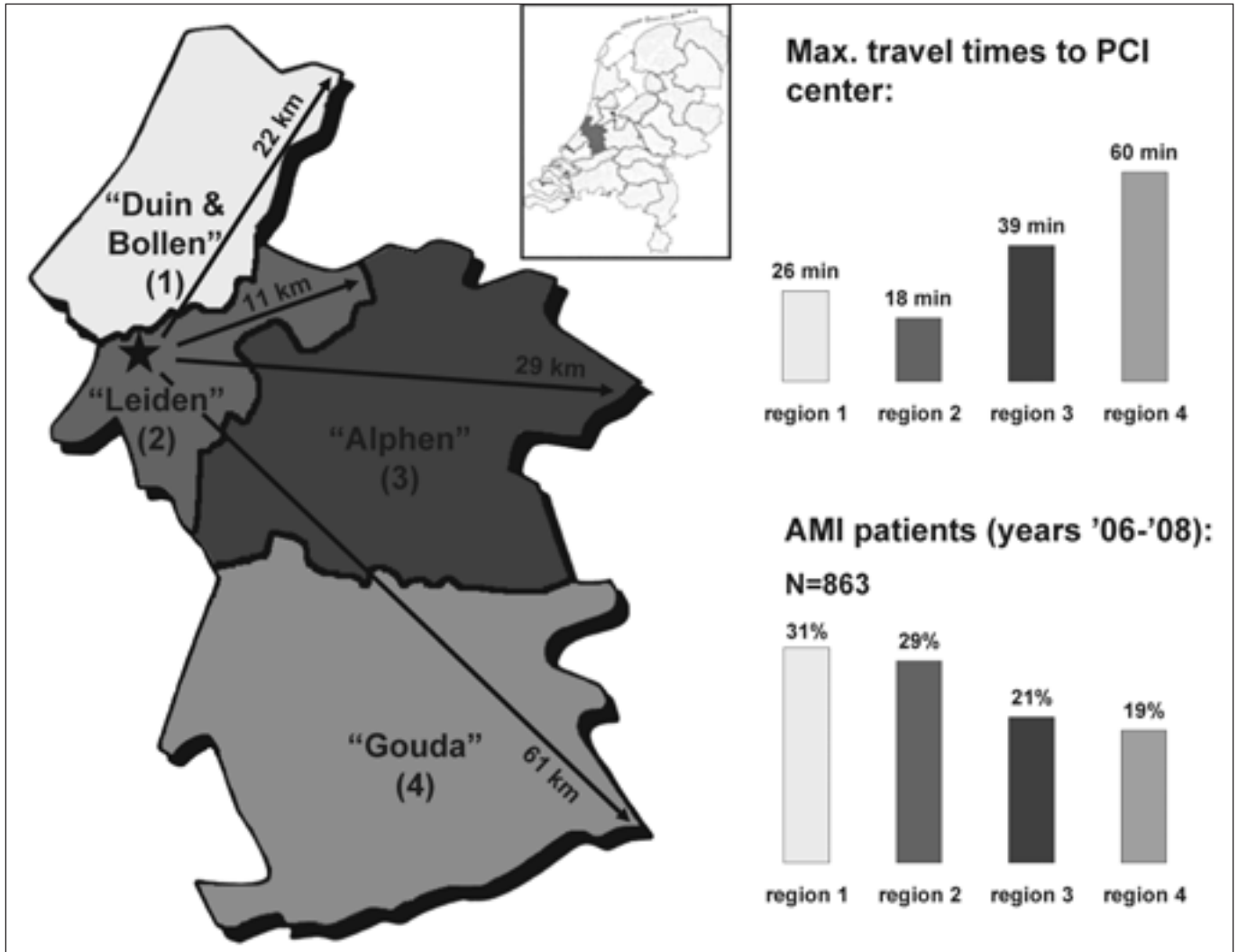
Figure 1. Schematic map of the region 'Hollands-Midden' (the Netherlands) further subdivided into the four areas of residency: 'Duin & Bollen' (region 1), 'Leiden' (region 2), 'Alphen' (region 3), 'Gouda' (region 4). The star within 'Leiden' (region 2) represents the location of the PCI centre. Maximal 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.

fully 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 minimise 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 minimise 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 optimise the use of evidence-based medicine in practice.[6] MIS-SION! contains a pre-hospital, in-hospital and outpatient clinical framework for decision-making and treatment of AMI patients. The main goal of this study was to investigate 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, meaning the centre 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 to the Leiden University Medical Center for primary PCI in the years 2006 to 2008. 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) (figure 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 centres 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 the patient's home. In the case of suspect characteristics, the ECG was electronically transmitted to the PCI centre. 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 centre's Cardiac Care Unit. In the ambulance aspirin, abciximab and clopidogrel were administered to the patient. The catheterisation 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 outpatient follow-up for the period of one year. The current study focused on the pre-PCI phase of the MISSION! protocol.

Data collection
Data were recorded by ambulance personnel and medical staff at the hospital. All the data were 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 catheterisation room (cath lab), door-to-cath lab (hospital delay) and interval between the alert of emergency services and 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 four areas of residency within Hol-

lands-Midden, including risk factors such as smoking, hypertension, hyperlipidaemia, 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 β-blockers, statins, aspirin, ACE inhibitors, angiotensin 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 analysed with SPSS 16.0.02.

Results

Study population
A total of 1002 consecutive AMI patients were admitted at the PCI centre 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 (figure 1). 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) ≥30 kg/m² (43%) and hypertension in 36% of patients. Median duration from onset of symptoms to arrival at the cath lab was 150 minutes (IQR 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 (IQR 25-158 min), whereas the median time between the alert of emergency services and the arrival at the hospital was 48 minutes (IQR 40-60 min). Median door-to-cath lab time was 23 minutes (IQR 13-42 min). Hospital stay was only 2 (IQR 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 four areas and similar risk profiles for CHD.
Medication prior to AMI was similar between the four patient groups except for a significantly larger percentage of patients using AT2-antagonist

Table 1. Patient characteristics (n=863).

Male (%)	646 (74.9)
Age (years)	61±13
BMI (kg/m²)	28.4 (24.9-41.1)
- BMI ≥30 kg/m² (%)	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)
- Hyperlipidaemia	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)
Hospitalisation	
- Days hospitalised (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=catheterisation room.

living in region 3 when compared with patients living in the region 1 (13.7 vs. 5.7%, respectively).

Pre-hospital care
Pre-hospital time delays per area of residency are illustrated in figure 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 catheterisation laboratory was also similar for patients from 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 furthermore 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).

Figure 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 of the 911 call) in addition to the amount of time needed to transport the patient to the PCI centre (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 centre (≥50 min). Transportation time of patients

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
- BMI (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
- Hyperlipidaemia	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 MI	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 AP	33 (12.6)	43 (17.5)	28 (15.6)	25 (15.8)	0.498
No. 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 (%)					
- β-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
- Ang 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
- Calcium 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, ANG=angiotensin, AP=angina pectoris, BMI=body mass index, CABG=coronary artery bypass surgery, CPK=creatine phosphokinase, LVEF=left ventricular ejection fraction, MI=myocardial infarction, PCI=percutaneous coronary intervention.

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 with 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 centre, (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 standardised guideline-based treatment system can improve the quality of AMI care and can even result in a lower in-hospital and one-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
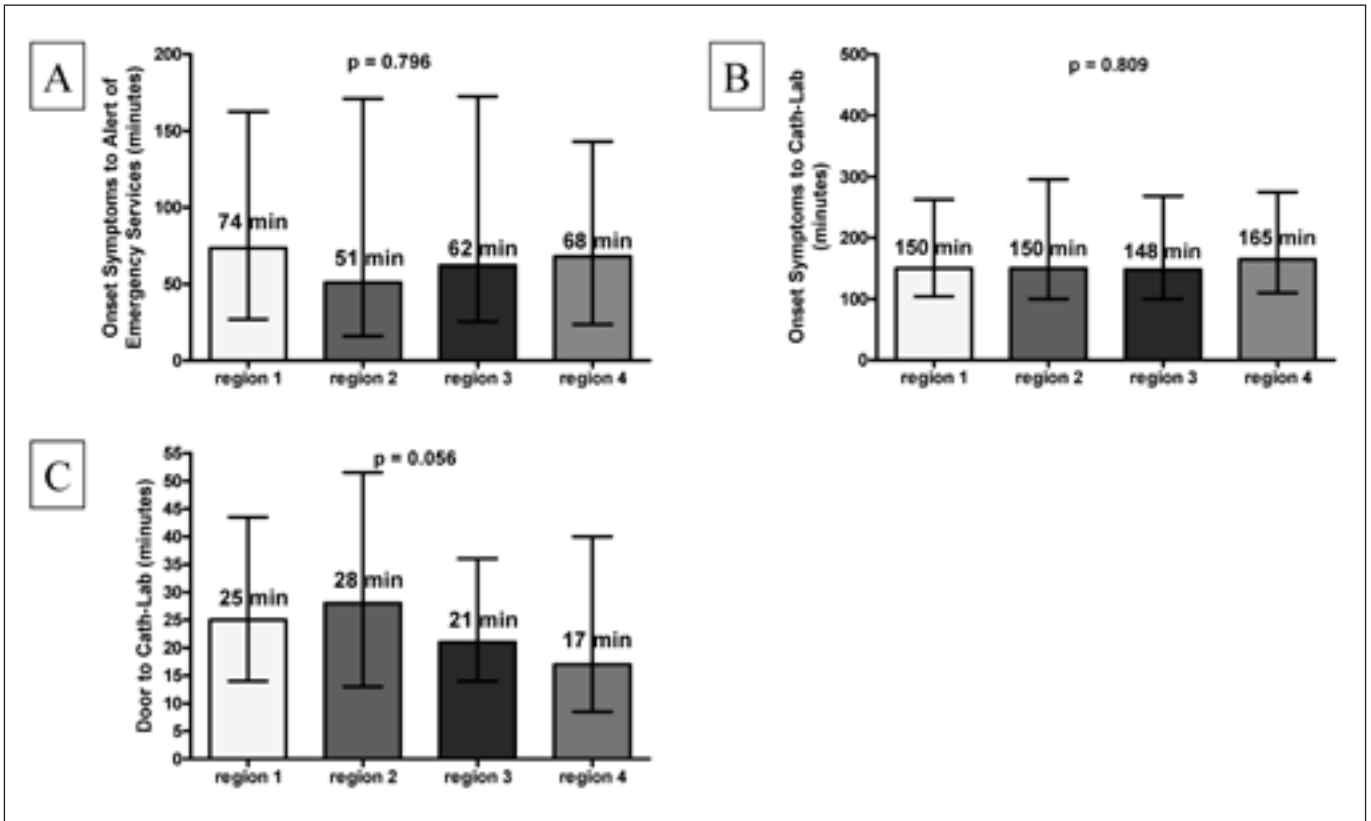
Figure 2. Time to treatment delay. Bar graphs showing patient delay defined as time from onset of symptoms to alert of emergency services (panel A); time interval from symptom onset to arrival at the catheterisation room (cath lab) (panel B) and hospital delay expressed as time from arrival at the hospital to arrival at the cath lab (panel C). Top of bar represents median time (minutes). Error bars indicate 25th and 75th percentile (minutes). Abbreviations as in figure 1.
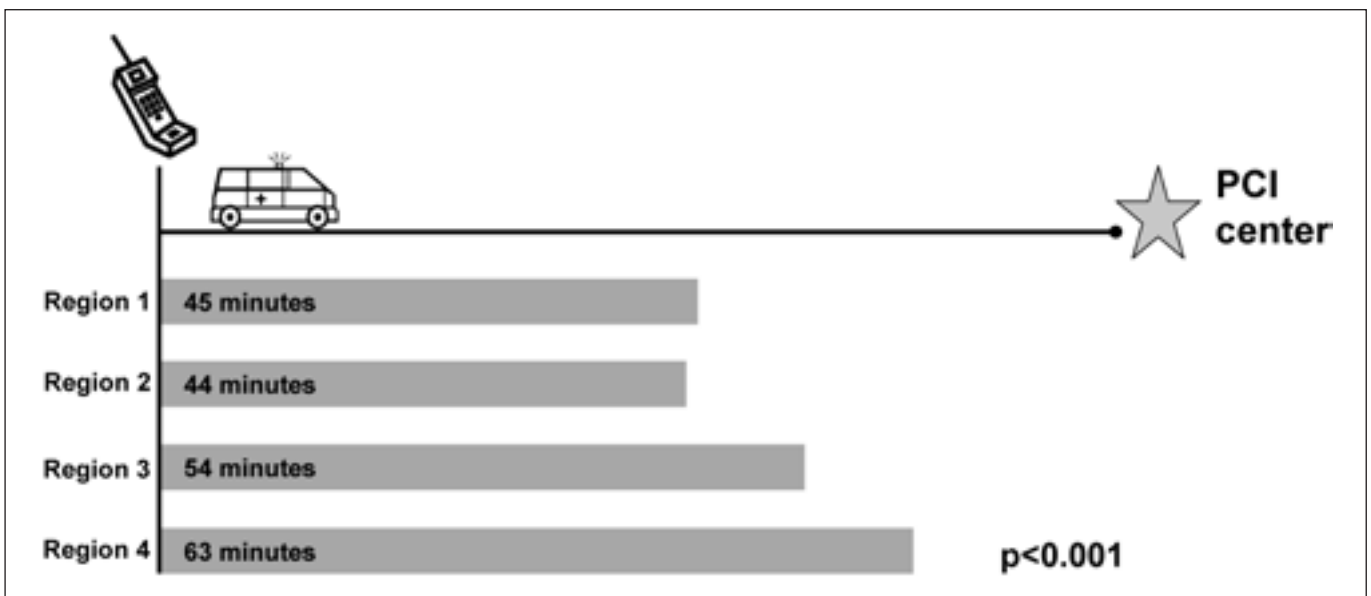

Figure 3. Time from alert of emergency services to arrival at PCI centre. Bars represent time interval (median minutes) from 911 call to the arrival at PCI centre (represented by star) per region of residency. Abbreviations as in figure 1.

predefined targets.[6] Furthermore, despite significant differences in transportation time (due to differences in distance from the PCI centre) similar time intervals between the onset of symptoms to arrival at the cath lab in all four areas of residence demonstrate that the multidisciplinary pre-hospital care is uniformly distributed and well organised 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) levelled out these differences.

Benefits of the standardised 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 the final infarct size was similar, regardless of the geographical distance. Moreover, it corresponded well with left ventricular ejection fraction of patients as measured three 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 EURO-ASPIRE 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 ≥30 kg/m² (43% vs. 38.0%).[13] Lower prevalence of hypertension (35.6% vs. 60.9%), hyperlipidaemia (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 organisations have recommended early reperfusion strategies and use of evidence-based medicine, together with long-term support programmes 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 car-

dioprotective 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-balloon 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 hospitalised 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 to 72 minutes.[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

Standardised protocols such as 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 with previous studies, the MISSION! protocol performed well in the care of AMI patients.[14-16]

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

Conclusion

This study shows that a standardised 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 one or more modifiable risk factors. ■

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