Improving acute and long-term myocardial infarction care : bridging the gap between science and practice

Liem, S.S.

CHAPTER 2

MISSION!: Optimization of acute and chronic care for patients with acute myocardial infarction

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ABSTRACT

Background

Guideline implementation programs for patients with acute myocardial infarction (AMI) enhance adherence to evidence-based medicine (EBM) and improve clinical outcome. Although undertreatment of patients with AMI is well recognized in both acute and chronic phases of care, most implementation programs focus on acute and secondary prevention strategies during the index hospitalization phase only.

Hypothesis

Implementation of an all-phase integrated AMI care program maximizes EBM in daily practice and improves the care for patients with AMI.

Aim

The objective of this study is to assess the effects of the MISSION! program on adherence to EBM for patients with AMI by the use of performance indicators.

Design

The MISSION! protocol is based on the most recent American College of Cardiology/American Heart Association and European Society of Cardiology guidelines for patients with AMI. It contains a prehospital, inhospital, and outpatient clinical framework for decision making and treatment, up to 1 year after the index event. MISSION! concentrates on rapid AMI diagnosis and early reperfusion, followed by active lifestyle improvement and structured medical therapy. Because MISSION! covers both acute and chronic AMI phase, this design implies an intensive multidisciplinary collaboration among all regional health care providers.

Conclusion

Continuum of care for patients with AMI is warranted to take full advantage of EBM in day-to-day practice. This manuscript describes the rationale, design, and preliminary results of MISSION!, an all-phase integrated AMI care program.

Coronary heart disease is the leading cause of death in the western world, with an estimated 3.8 million men and 3.4 million women dying each year worldwide.(1) Furthermore, the number of chronic heart disease patients in North America and Western Europe is increasing rapidly because of better survival after acute myocardial infarction (AMI), improved treatment, and the presence of an aging population. This imposes a significant socioeconomic burden on society.(1)

To optimize care and outcome of patients with AMI, many organizations, for example, the American College of Cardiology/American Heart Association and the European Society of Cardiology, have published guidelines for treatment of patients with AMI.(2,3) These guidelines advocate early and aggressive reperfusion strategies and recommend the use of a combination of evidence-based medicine (EBM) and support programs to stimulate a healthier lifestyle. Because most of these guidelines are based on large-scale clinical trials, clinical benefit has already been established.

Nevertheless, the proven benefit and the endorsement of these guidelines by the scientific society do not seem sufficient to alter well-established daily clinical practice. Consequently, a large gap between EBM and daily practice still exists. For example, despite the fact that there is clear evidence that reperfusion therapy in the acute phase improves survival of patients with AMI, registries show that only 56% to 76% of the eligible patients actually receives this form of therapy.(4-6)

Furthermore, a recent publication of the National Registry of Myocardial Infarction reported that only 4.2% of patients with AMI transferred for primary percutaneous coronary intervention (PCI) were treated within 90 minutes, which is the benchmark recommended by the international guidelines.(7) Even worse is the situation after the acute phase: modifiable risk factors are often not controlled and optimal medication is often not prescribed.(4,8) Consequently, a significant number of patients with AMI is treated less than optimal.

Schiele et al.(9) demonstrated that the degree of guideline compliance is independently correlated with the 1-year mortality after AMI. Various guideline implementation programs, such as Guidelines Applied in Practice, Get With the Guidelines and Crusade, have been successful in improving the quality of care.(10-12) Implementation of this kind of programs resulted not only in better adherence to key indicators, but also in a lower 1-year mortality in patients with AMI.(10,13) Therefore guideline implementation programs are of paramount importance to optimize AMI care.

Still, most quality improvement programs only focus on acute care and secondary prevention strategies during the index hospitalization phase, whereas it is known that the prehospital and chronic phase is also important. Thus, to improve AMI care, we have to maximize the diffusion of EBM into daily clinical practice across practical

setting. Therefore, we developed and implemented an all-phase integrated AMI care program in the region "Hollands-Midden" The Netherlands: MISSION!.

METHODS

Study design

MISSION! is designed according to a quasi-experimental approach.(14) The MISSION! protocol is developed based on the most recent American College of Cardiol-

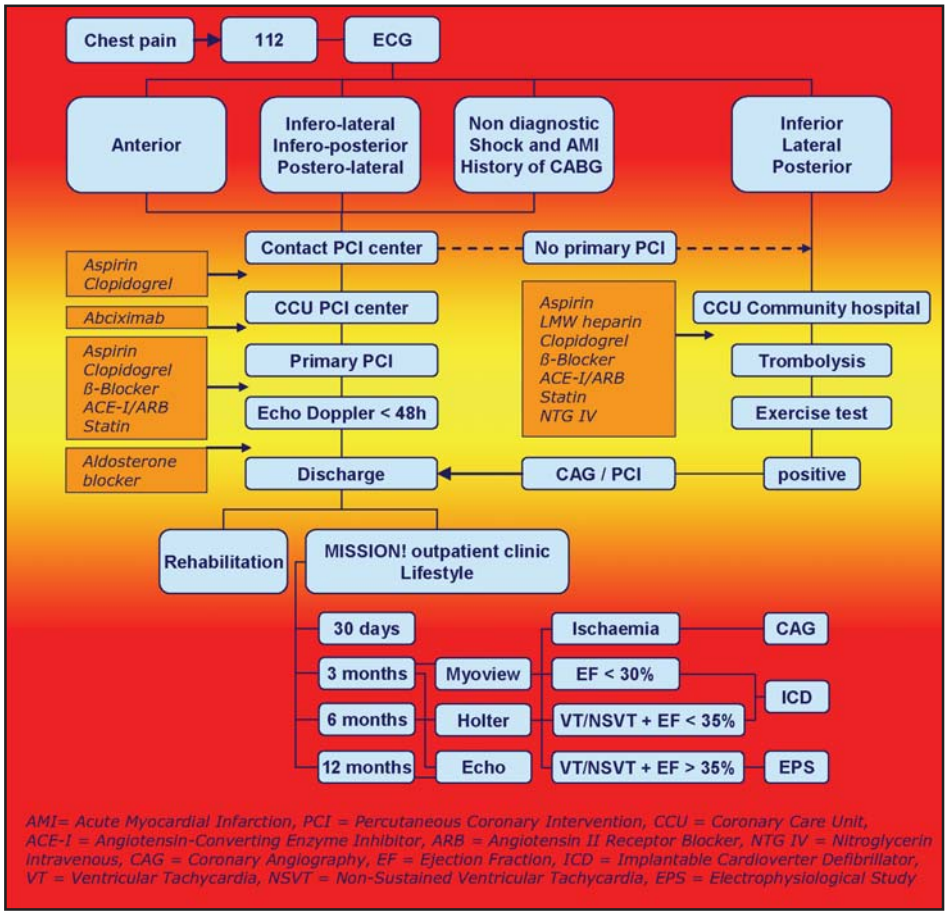

Figure 1.
The MISSION! flowchart presents the clinical framework for decision making and treatment. The flowchart covers all phases of AMI care: the prehospital and inhospital phase, followed by a structured outpatient program, up to 1 year after the index infarction.

ogy/American Heart Association and European Society of Cardiology guidelines for AMI.(2,3) It contains a prehospital, inhospital, and outpatient clinical framework for decision making and treatment, up to 1 year after the index event (Figure 1). The MISSION! goals, addressing all aspects of AMI care, are summarized in Figure 2. The Hollands-Midden region has 750.000 inhabitants and covers an area of approximately 50 x 25 miles. Based on historical data, it is estimated that approximately 1000 patients within the area will suffer from an AMI annually. An intensive collaboration has been established among primary care physicians, the regional ambulance service, 3 community hospitals (without PCI facilities), 3 cardiac rehabilitation centers, and the Leiden University Medical Center, Leiden, The Netherlands (serving as the primary PCI facility), to align AMI care. To provide insight into the rationale of the MISSION! program, we described the 3 MISSION! care phases and MISSION! care tools.

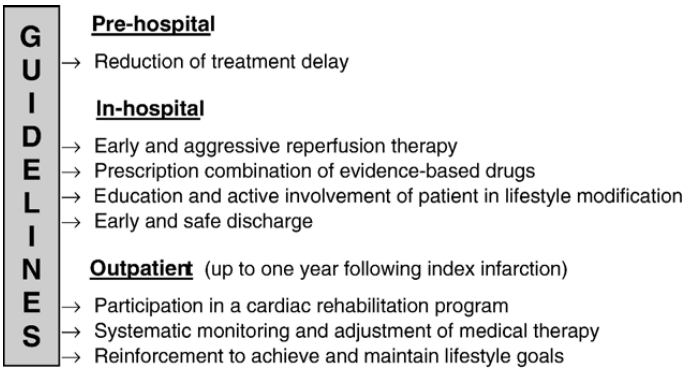

Figure 2.
The MISSION! goals, addressing all phases of AMI care, are summarized in this figure.

Prehospital phase

As advocated by the different guidelines, the cornerstones of optimal prehospital AMI care are rapid diagnosis, early risk stratification to identify patients who benefit from early intervention, minimal treatment delay, and aggressive reperfusion strategies. Prehospital triage by 12-lead electrocardiogram (ECG) in the field, thereby allowing early AMI diagnosis and rapid access to an intervention or community center, can reduce the treatment delay significantly.(15) Thereupon, primary PCI or thrombolysis prevents unnecessary infarct extension and saves lives.(16,17)

All these aspects are incorporated in the prehospital MISSION! protocol: in patients with chest pain, trained paramedics obtain a high-quality 12-lead ECG at the patient's

home (Lifepak 12 Defibrillator/Monitor Series; Medtronic, Redmond, WA). If the ECG fulfills the positive identification criteria as shown in the prehospital MISSION! standard order form (Figure 3), the ECG is transmitted directly to the computer network of the PCI hospital (Lifenet RS system; Medtronic). Trained coronary care unit (CCU) nurses analyze the ECG for determining patient's eligibility for primary PCI, based

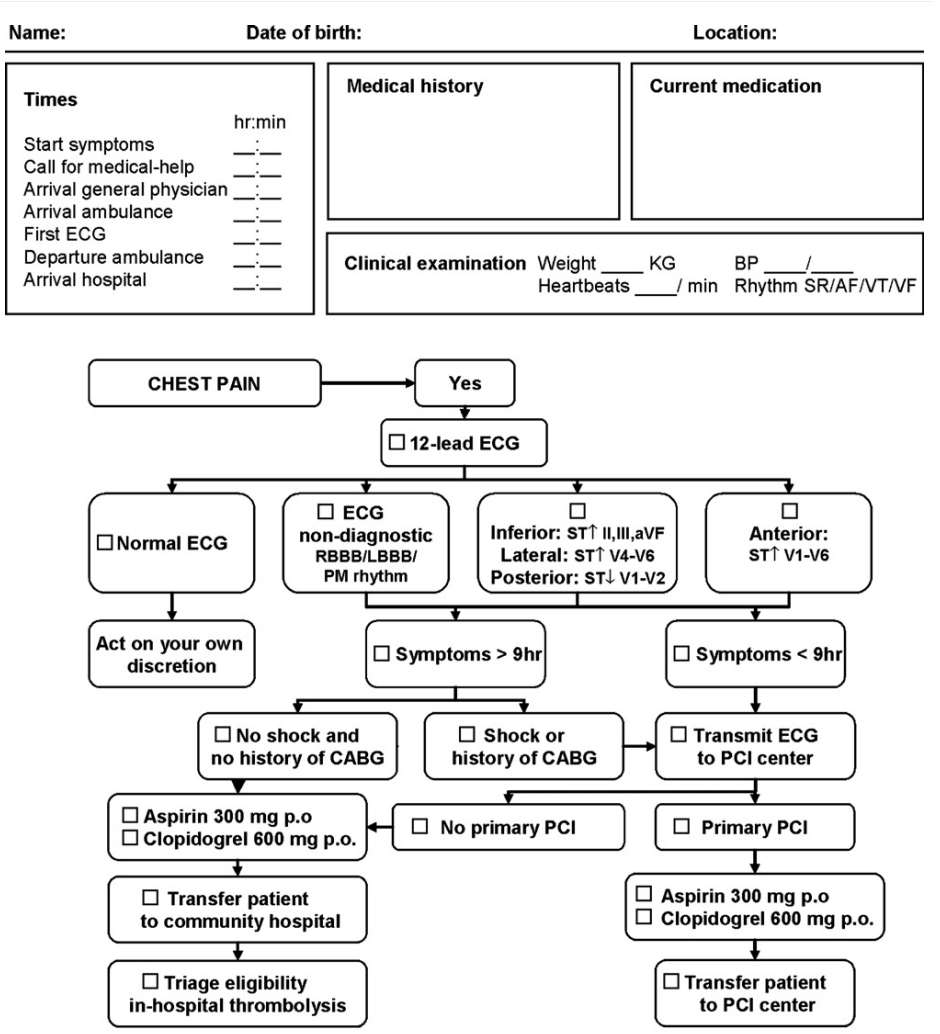

Figure 3.
Prehospital triage of patients with AMI is performed according to clinical and ECG criteria shown in this standard order: to determine the patient's eligibility for PCI or thrombolysis and to allow rapid access to the appropriate center for early and aggressive reperfusion therapy.

MISSION! **COMMUNICATION FORM AMBULANCE-CCU**

Date:	**Time call:**	**Ambulance number:**
Patient's information		
Last name, initials		
Date of birth		
Weight		
Time start symptoms		
Medical history		
Estimated duration to arrive at CCU?		

Contra-indications for abciximab ?		
Hemorrhagic disease?	Yes	No
Liver function disturbances?	Yes	No
Kidney function disturbances?	Yes	No
Blood loss in the last **3** months?	Yes	No
Operation in the last **3** months?	Yes	No
Trauma in the last **3** months?	Yes	No
TIA/CVA in the last **6** months?	Yes	No
Is the patient pregnant or does she menstruate **at this moment?**	Yes	No

If patient is accepted			
Office-hours		**Evening / Night / Weekend**	
Call Cath Lab. Ask for the person who makes the schedule for today Tel 2018		Call first the interventional cardiologist in charge	
Call the trainee *9157		Call the Cath Lab laboratory worker in charge	
Prepare abciximab		Call the trainee *9157	
		Prepare abciximab	

After patient's arrival	
Enter patient in the hospital information system/ask the secretary to do	
Call the trainee *9157	
Call the Cath Lab and tell that the patient is arrived Tel 2018	

Admission according to **MISSION!** Protocol, see nurse standard order

Figure 4.
This communication form is used by the CCU nurses, when they call the ambulance personal immediately after receiving the ECG of the primary PCI candidate.

on predefined criteria. If the patient is eligible for PCI, and after confirmation by phone, the ambulance paramedic administers clopidogrel and aspirin and the patient is transferred directly to the PCI center (Figures 3 and 4). Meanwhile, the CCU is prepared and the catheterization staff is informed. The catheterization laboratory is operational within 20 minutes, 24 hours/d, 7 days/wk.

If the ECG does not fulfill the criteria for primary PCI, but the patient may be a candidate for thrombolysis, prehospital triage for inhospital thrombolysis is performed (Figure 5). These patients also receive clopidogrel and aspirin. The patient is transferred to the nearest community hospital directly, which never exceeds 10 mi in this region, allowing rapid access.

MISSION! Standard order eligibility thrombolysis

Is the patient older than 80yrs?	Yes	**No**
Duration of symptoms >6hrs?	Yes	**No**
Does the pain consistently stay away after NTG s.l.?	Yes	**No**
History of CABG?	Yes	**No**
Decreased consciousness?	Yes	**No**
Is the patient paralyzed at this moment?	Yes	**No**
Systolic blood pressure>180 mmHg?	Yes	**No**
Does the patient suffer from a hemorrhagic disease?	Yes	**No**
Did the patient fall or bump his/her head **today**?	Yes	**No**
Is there a chance to be pregnant?	Yes	**No**
Does the patient menstruate at this moment?	Yes	**No**
Did the patient ever suffer from a TIA/CVA?	Yes	**No**
	Yes	**No**
In the last 3 months, did the patient		
- have had a severe accident?	Yes	**No**
- have had a big operation?	Yes	**No**
- have coughed blood?	Yes	**No**
- have suffered from a stomach ulcer or hemorrhage?	Yes	**No**
- have lost blood in urine or stool?	Yes	**No**
- have suffered from abnormal vaginal blood loss?	Yes	**No**

*If all questions are answered with **"NO"**, consult with the Central Post Ambulance (CPA) where to present the patient. The CPA will announce the CCU that a potential thrombolysis patient is arriving.*

Figure 5.
This form is used to determine patient's eligibility for thrombolysis.

Inhospital phase

The patient with AMI is directly admitted to the CCU, bypassing the emergency department, where all PCI patients receive abciximab (dose abciximab, 0.25 mg/kg bolus followed by an infusion of 0.125 Ag/kg per minute during 12 hours) in the absence of contraindications, and a PCI is performed (Figure 6). Likewise, thrombolysis patients receive fibrinolytic therapy immediately on arrival at the CCU of the community hospital. This approach minimizes inhospital delay as much as possible.

After reperfusion therapy, the patient stays for 24 hours at the CCU. Electrocardiogram and hemodynamic monitoring are performed continuously. According to protocol, all patients receive supplemental oxygen (3 L/min or more, according to the oxygen need) for the first 6 hours. If no contraindications exist, β-blockers, angiotensin-converting enzyme (ACE) inhibitors, and statins are administrated within 24 hours of admission. Reasons for not prescribing these drugs are documented. Respective drugs are titrated to control heart rate (target heart rate, 60-70 beats/min) and blood pressure (target level, <140/90 mm Hg or <130/80 mm Hg for patients with diabetes or chronic renal disease).

LUMC cardiology **MISSION!** NURSE STANDARD ORDER

1. Admission CCU

- □ Connect patient to the ECG monitor □ Obtain a 12-lead ECG □ Insert 2 intravenous catheters □ Nasal O_2 at 3L/min
- □ Check if clopidogrel and aspirin are administered in the ambulance
- □ Start Abciximab Time start Abciximab: ____/____
- □ Print patient's labels to the Cath Lab □ Transfer the patient immediately to the Cath Lab with ECG monitoring
- □ Bring blood-tubes to the Cath Lab to obtain blood for laboratory studies

2. After primary PCI

- □ Connect patient to the ECG monitor □ Obtain a 12-lead ECG □ Chest X-ray
- □ Nasal O_2 at 3L/min for minimal 6h and according to patients needs.
- □ Control vital parameters, insertion side and medication.
- □ Stop abciximab after 12 hrs.

Time stop Abciximab: ____/____

- □ **Medication:** clopidogrel, aspirin, metoprolol, statin, perindopril, pantoprazol
- □ Start enoxaparin after finishing abciximab
- □ Complete MISSION! standard order set *(application forms for laboratory tests, echo, physiotherapist, id.)*

- □ Remove the sheath 4 hrs after prim PCI and apply Safeguard™. Time removal sheath: ____/____
- □ 2 hours after applying Safeguard™ deflate and inflate Safeguard™, according to protocol. Time: ____/____
- □ 4 hours after applying Safeguard™ deflate Safeguard™. Inspection of the insertion side by MD. Time: ____/____
- □ When Angio-Seal is used: 2 hours bedrest in a lying position of 30°.
- □ After these 2 hrs: remove bandage and inspection of the insertion side by MD Time: ____/____
- □ If no clinical contra-indications: start telemetry and mobilization scheme.
- □ After 12-24 hours: stable patient to Cardiac Stepdown Unit

ECG and laboratory test scheme

- □ 6 hrs after admission: ECG Time: ____/____
  Studies: CK, Troponin-T
- □ 12 hrs after admission: ECG Time: ____/____
  Studies: CK, ASAT, ALAT, LDH, K, Ureum, Creat, Troponin-T, Hb, Htc, Trombo
- □ 18 hrs after admission: ECG Time: ____/____
  Studies: CK, Troponin-T
- □ 24 hrs after admission: Studies: CK, according to this protocol until CK have reached the highest value Time: ____/____
  CK max.....U/L **Troponin-T max.....µg/L**

- □ After CK have reached the highest value: CK once daily, till the 3rd day after prim. PCI
- □ ECG once daily
- □ Echo heart within 48 hrs after admission
- □ MISSION! talk by MISSION! MD
- □ Educate patient to fill in his/her MISSION! brochure and stimulate patient to keep it up-to-date.
- □ Weight patient:_____ Kg. (Instruct patient to fill his/her weight into his/her patient brochure)
- □ Educate the patient the benefit of drug compliance, the possibility to reduce his/her risk by changing unhealthy lifestyles and draw patient's attention to existing resources to succeed in these lifestyle changes

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3. Discharge

When Angio-seal is used: □ Give discharge instructions □ Give Angio-Seal patient card

- □ MISSION! outpatient visits arranged by secretary
- □ Check if MISSION! brochure is completely filled in by patient: medication list, cholesterol, blood pressure id.
- □ Give discharge letter □ Give Medication prescriptions

Figure 6.
This order function as a check for nurse to maximize EBM in practice. Adequate feedback can be given by the use of check boxes.

Patients free of recurrent ischemic symptoms, symptoms of heart failure, or hemodynamically compromising arrhythmias start a mobilization program within 12 hours

postreperfusion (supervised by a physiotherapist) and are transferred to a stepdown unit within 24 hours. In the presence of complications, the patient remains at the CCU until clinical stable.

Resting 2-dimensional echocardiography is performed within 48 hours after admission, and left ventricular ejection fraction (LVEF) is calculated to evaluate the need for aldosterone inhibition (ie, LVEF <40% and existence of either symptomatic heart failure or diabetes) (Figure 1).

An important part of the inhospital MISSION! protocol is to educate and involve the patient actively in changing the lifestyle (smoking cessation, healthy diet, exercise, and weight management) and to emphasize the need for drug compliance. This secondary prevention program is provided by a multidisciplinary team (physicians, nurses, and a nurse practitioner) and is continued in the outpatient cardiac rehabilitation program and during follow-up.

Furthermore, in an era of growing economic pressure in health care, attention is paid to early and safe discharge of the uncomplicated patient. Patients without complications are discharged at day 3. Complications include stroke, reinfarction, ischemia, cardiogenic shock, heart failure (Killip class >1), bypass surgery, balloon pumping, emergency cardiac catheterization, or need for cardioversion or defibrillation. Although the risk of uncomplicated patients to develop adverse events after discharge is low, the strategy of early discharge inquires the possibility of rapid access to medical help.(18) Therefore, we provide a network: first, before discharge, patient and family members are informed how to recognize acute cardiac symptoms and how to take appropriate actions in response (ie, calling the emergency number 1-1-2); second, the general practitioner is informed concerning the diagnosis and treatment at discharge; third, all patients are contacted by phone within 1 week after discharge; and fourth, all patients are offered an outpatient rehabilitation program starting within 2 weeks after discharge.

Outpatient phase

The patient visits the MISSION! outpatient clinic 4 times during the first year after AMI. According to the protocol, a number of functional tests are obtained during these visits. If necessary, further tests/interventions are performed (Figure 1). The achieved medical and lifestyle goals are monitored, and if required, the physician and nurse practitioner emphasize the principles of secondary prevention. Each patient receives the appointment schedule for the first year at discharge to stress the importance of active participation of the patient.

After 1 year of follow-up, patients are referred either to the general practitioner (asymptomatic patients and an LVEF > 45%), to a regional cardiologist (patients with symptoms or an LVEF between 35% and 45%), or to the outpatient clinic of the university hospital (LVEF < 35%, after implantation of a device or in case of serious symptoms).

MISSION! care tools

We created guideline-oriented care tools for each phase of the MISSION! protocol. These care tools were developed to facilitate adherence to the MISSION! protocol and function as a check for physician, nurses and patients to maximize EBM in practice.(10) The following MISSION! care tools are customized and implemented: standard orders with check boxes for each clinical decision-making step and medical

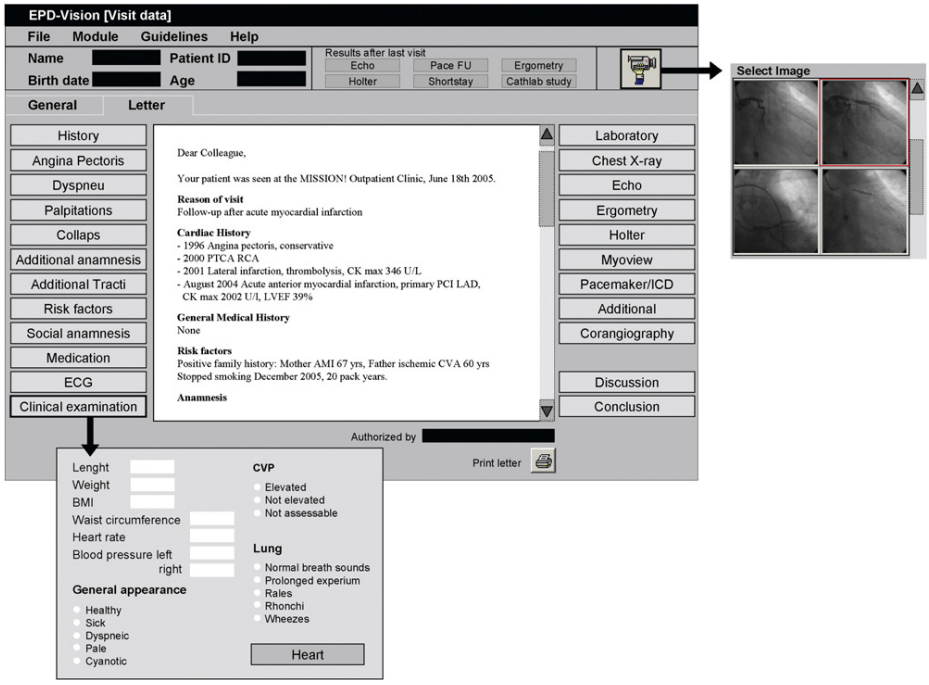

Figure 7.

EPD-VISION 6.01 is the electronic patient file and data management system that is used to store all the information of each patient, using a unique identification number. After applying the medical information in the inhospital and outpatient setting, this system produces automatically a letter concerning the diagnosis and treatment, which is electronically sent to the patient's primary care physician.

intervention (Figures 3-6), a guideline-based electronic patient file and data management system (EPD-VISION 6.01, Leiden University Medical Center) (Figure 7), a personal digital assistant (PDA) MISSION! protocol, chart stickers, patients' brochures, posters with lifestyle advices, and a MISSION! website for patients and professionals. Physicians and nurses are trained to use these care tools. The use of these care tools is guaranteed by handing out as standard order sets for each patient and the use of EPD-VISION inhospital and in the outpatient setting.

Patients

Patients who comply with the predefined criteria mentioned in the prehospital flowchart are included in the prehospital MISSION! protocol (Figure 3). Inhospital, the AMI diagnosis is confirmed by the presence of an unstable coronary lesion on acute angiography and/or the presence of enzymatic myocardial damage, defined as an increase in cardiac biomarker(s) above normal level(s). Also, patients who are presenting without typical ST-elevation inhospital, but with elevated cardiac biomarker(s), are diagnosed as patients with AMI. Based on this "a posteriori" diagnosis, patients with AMI follow the subacute inhospital and outpatient MISSION! program. Patients who need mechanical ventilation at the time of index event are excluded for the prehospital and inhospital MISSION! protocol. However, these patients are treated according to the outpatient MISSION! protocol after discharge.

No specific age threshold for exclusion is defined. Nevertheless, carefulness is needed in elderly patients, given the relative low number of studies and lack of consensus of optimal treatment strategies in this group. Elderly people with severe preexisting comorbidities are excluded. No informed consent is required, whereas MISSION! is the standard AMI care regimen in the region Hollands-Midden, The Netherlands.

Control group

MISSION! data are compared with data of AMI, patients treated with primary PCI at the Leiden University Medical Center from January 2003 until December 2003. This historical group was treated just before implementation of MISSION!, thereby limiting the effect of changes in, for example, drug regimen and/or technical aspects of PCI procedures. Although a randomized design to compare the effects of MISSION! with routine care would have been better, this was considered unethical. The patients of the historical group were selected by using the code for "primary PCI" in EPD-VISION. We retrospectively included only those with an "a posteriori" AMI diagnoses by using the same criteria as in the MISSION! patients' group. After

approval by the institutional ethical committee, all patients of the control group gave written informed consent.

Data collection

Data are systematically collected for each MISSION! patient in EPD-VISION, using a unique identification number. This database includes patient's medical history, symptoms on arrival, electrocardiographic examination, medication at the time of index, index times (ie, time onset symptoms, time call for medical help, time of first medical contact, time arrival hospital, needle time, time of first balloon inflation), inhospital treatment and events, clinical examination at admission and discharge, discharge treatment, clinical examination at follow-up, follow-up treatment and events, laboratory measurements, functional tests, achieved lifestyle changes and the use of prescribed drugs. Similar data were extracted retrospectively from the hospitals' patient files in the historical patients with AMI group treated in 2003.

Data analysis

To assess the impact of MISSION!, we developed performance indicators (Table 1). The MISSION! performance indicators are based on key indicators used in previous studies, but in an extended version in accordance with the most recent guidelines. (19) This extended version creates the opportunity to assess the quality of care of all phases of the MISSION! protocol. For each performance indicator, a target level of improvement is given. We extracted these target levels from the Euro Heart Survey and EuroAspire registry.(6,20,21) For performance indicators without prior predefined target levels, we determined target levels that we considered reasonable and achievable based on clinical experiences, prior performance data, and prevalence rates of risk factors.(6,20-23) The indicators will be calculated for both levels of eligibility, in "eligible" patients and "ideal" patients, as reported in previous studies. (19) Although not the main object, we also measure clinical end points, that is, all-cause mortality and reinfarction, at 30 days, at 6 months, and at 1 year. Analyses are only performed in those patients with an "a posteriori" diagnosis of AMI. The efficacy of the MISSION! guideline implementation program is assessed in the first 300 patients with AMI. This sample size was calculated based on Dutch performance and cardiovascular risk factors' prevalence data and the predefined targets levels of improvement for each performance indicator.(6,20-23) Sample comparisons are made using a $\chi 2$ test for categorical variables and a paired t test for continuous variables. All P values will be 2 tailed with an α of .05. All data will be analyzed in SPSS 12.0.1 (SPSS Inc, Chicago, IL).

Performance indicators \ Time points of measurement	<24 hours	Discharge	30 days	6 months	12 months	TARGET
Primary PCI Door-to-Balloon <90 min	X					> 75%
Abciximab before PCI	X					> 90%
Thrombolysis Door-to-Needle <30 min	X					> 75%
Aspirin	X	X	X	X	X	> 90%
Clopidogrel	X	X	X	X	X	> 90%
Beta-blocker	X	X	X	X	X	> 75%
Angiotensin-Converting enzyme inhibitor / Angiotensin-II receptor blocker	X	X	X	X	X	> 75%
Statin	X	X	X	X	X	> 90%
Bloodpressure < 140/90 mm Hg		X	X	X	X	> 90%
Total cholesterol < 4.5 mmol/L (180 mg/dl)			X	X	X	> 90%
LDL cholesterol < 2.5 mmol/L (100 mg/dl)			X	X	X	> 90%
Complete smoking cessation			X	X	X	> 50%
Moderate physical activity minimal 3 X 30 min/week			X	X	X	> 75%
BMI < 27 Kg/m^2			X	X	X	> 60%
Waist circumference women < 88 cm, men < 102 cm			X	X	X	> 60%
Participation cardiac rehabilitation program			X	X	X	> 75%

Table 1. MISSION! Performance indicators, time points of measurement and targets. PCI = Percutaneous Coronary Intervention, LDL Cholesterol = Low Density Lipoprotein Cholesterol, BMI = Body Mass Index

PRELIMINARY RESULTS

MISSION! is a multifaceted intervention. Figure 8 shows the timeline of implementation of the MISSION! protocol. The development of the MISSION! protocol started in October 2003. The first patients were enrolled in February 2004. Until now, 300

patients are included in the inhospital and outpatient MISSION! protocol. The communication between a limited number of ambulances and the PCI center started as a pilot in September 2004. Since January 2005, all ambulances are participating.

Baseline characteristics are shown in Table 2. The MISSION! patients were more often diabetics, were less known with hyperlipidemia, and exhibited higher blood pressures at the time of presentation compared with the historical group. In the MISSION! group, 56% presented with an anterior infarction compared with 70% in the historical group (P = .02). No significant difference in treatment strategy could be observed (96% vs 95% primary PCI, P = 1) (Table 3). After implementation of the prehospital MISSION! protocol, more patients were treated within the recommended 90-minute door-to-balloon time (80% vs 63%, P = .01), and a significant reduction of door-to-balloon time of 16 minutes was observed (67 ± 38 minutes [n = 106] vs 83

Baseline characteristics	Historical group 2003 n=100	MISSION! n=300	P-value
Demographics			
Male	77 (77%)	233 (78%)	1
Age (years)	58.8 ± 11.5 (33-81)	60.1 ± 11.8 (28-84)	0.3
Non-white	8 (8%)	25 (8%)	0.9
Medical history			
Diabetes	5 (5%)	37 (12%)	0.06
Hyperlipidemia	30 (30%)	56 (19%)	0.02
Hypertension	32 (32%)	86 (29%)	0.6
Current smokers	53 (53%)	148 (49%)	0.6
Ischaemic heart disease	13 (13%)	22 (7%)	0.1
Family history	43 (43%)	129 (43%)	0.9
Clinical			
Blood pressure (mm Hg)			
Systolic	125 ± 3 (60-190)	136 ± 26 (60-233)	<0.001
Diastolic	74 ± 2 (20-125)	79 ± 17 (30-120)	0.01
Killip class at admission			
I	93 (93%)	270 (90%)	0.5
II	4 (4%)	17 (5.7%)	0.7
III or IV	3 (3%)	13 (4.3%)	0.8
Body Mass Index (kg/m2)	27.2 ± 3 (18-38)	26.5 ± 4 (18-46)	0.3
Anterior myocardial infarction	70 (70%)	167 (56%)	0.02

Table 2.
Baseline characteristics of the historical group and the MISSION! patients

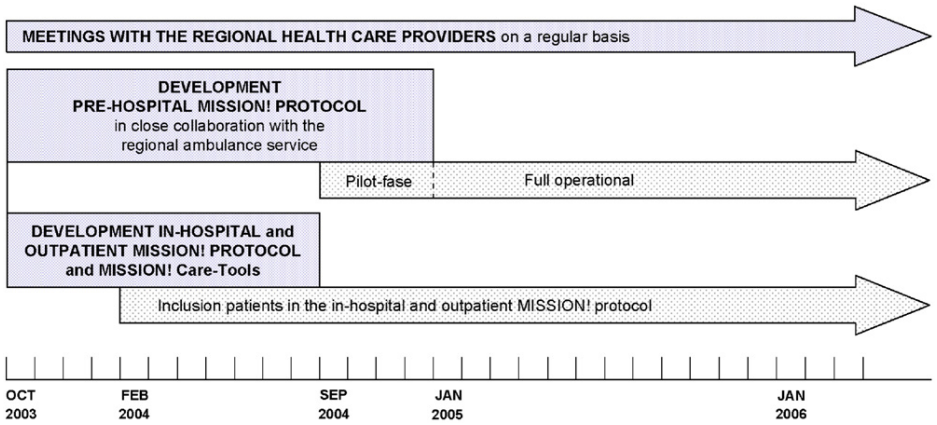

Figure 8.
MISSION! is a multifaceted intervention. The timeline of implementation of the MISSION! protocol is given.

± 33 minutes, P < .01). The MISSION! patients received more frequently β-blocker (83% vs 64%, P < .001) and ACE-inhibitor therapy (85% vs 34%, P < .001) within 24 hours after admission, and more patients were discharged with an ACE inhibitor (96% vs 73%, P < .01). MISSION! patients were discharged earlier compared with the historical group (3.9 ± 2.8 vs 7.3 ± 8.2 days, P < .001).

DISCUSSION

The treatment of patients with AMI has expanded and improved tremendously over the last 2 decades. However, widespread dissemination of EBM in daily practice is still lacking, and a significant number of patients with AMI is undertreated.(4-8) Prior AMI guideline implementation programs succeeded to increase the uptake of guidelines in daily care.(10,11,13) However, these programs mainly focus on inhospital AMI care, whereas it is known that the prehospital and chronic care for patients with AMI is equally important. Therefore, we developed and implemented an all-phase integrated AMI care program, MISSION!. The aim of MISSION! is to maximize the use of EBM across practical settings and thereby to further improve the care for patients with AMI in real life.

MISSION! is a multifaceted intervention. Lessons learned from prior studies are incorporated in the MISSION! program.(24) Changing routine care into a systematic process of care is essential to improve AMI care in real life.(24) Furthermore, imple-

	Historical group 2003 n=100	MISSION! n=300	P-value
Primary PCI	96 (96%)	286 (95%)	1
Door-to-Balloon time < 90 min (%)	63	80*	0.01
Abxicimab before PCI (%)	90	91*	0.9
Medical therapy <24 h (%)			
Aspirin	97	95	0.6
Clopidogrel	98	97	0.9
Statin	98	96	0.5
Beta-blocker	64	83	<0.001
ACE-inhibitor	34	85	<0.001
Medical therapy at discharge (%)			
Aspirin	96	98	0.5
Clopidogrel	100	98	0.3
Statin	98	100	0.3
Beta-blocker	94	90	0.3
ACE-inhibitor	73	96	<0.001
Blood pressure < 140/90 mm Hg at discharge (%)	89	94	0.1
Length of stay (days)	7.3 ± 8.2 (1-44)	3.9 ± 2.8 (1-18)	<0.001
In-hospital mortality	5 (5%)	7 (2.3%)	0.3

Table 3. In-hospital preformance and outcome
* % out of n=106 patients, since the pre-hospital MISSION! protocol started January 2005

mentation of guideline-orientated care tools makes this consistent and structural approach of patients with AMI possible and thereby enhances adherence of EBM. (24)

During the development and implementation of MISSION!, we encountered the following problems. First, financial resources are mandatory to build and implement such a comprehensive project as MISSION!. Therefore, we developed a clear statement of the intended improvements. We obtained financial support from the Dutch Heart Foundation and The Netherlands Society of Cardiology. Second, because MISSION! covers all phases of AMI care, an intensive collaboration among all regional healthcare providers had to be established. Before MISSION!, these settings operated as distinct independent institutions with their own policies, (financial) interests, and individual guidelines resulting in a dispersion of AMI care. The university center served as a key initiator. We organized meetings for all healthcare providers concern-

ing AMI care in our region. In addition, we enraptured leaders in each practical setting to create a MISSION! working group. These working groups are responsible for the implementation of MISSION! and monitoring of the care processes. Furthermore, these groups provide educational activities at a regular basis. Short- and long-term feedback is given and received to optimize the care process. When necessary, the protocol is adjusted and updated according to new evidence, taking into account that quality improvement is a continuous process.(25) It takes a lot of effort to establish such a project. However, taking responsibility and persuasively underscoring the need for alignment of regional AMI care are the way to accomplish patient-centered care and improve AMI care in real life.

The preliminary data of the first 300 MISSION! patients are promising. Baseline characteristics among the historical and MISSION! group differ (Table 2). However, prior studies have shown that patients with AMI who actually receive reperfusion therapy in routine care are less likely diabetic, are more known with hyperlypidemia and are more often present with an anterior AMI.(5) A shift in these variables is observed between the 2 groups. Hence, it can be concluded that MISSION! succeeded in changing the care system into a system in which more eligible patients benefit from EBM in real life than in the past. Implementation of the prehospital MISSION! protocol resulted in a significant reduction of door-to-balloon time compared with the historical group and an increase of patients treated within the recommended 90 minutes. Although the historical performance in the prescription of evidence-based drugs was good, MISSION! improved the performance in early use of β-blockers and ACE inhibitors, and discharge ACE inhibitors. It is known that prescription of medication before discharge increases the compliance during follow-up.(13) Moreover, Mukherjee et al(26) demonstrated marked survival advantage in patients with acute coronary syndromes, if a combination of evidence-based drugs were prescribed. Finally, MISSION! decreased the length of inhospital stay in low-risk patients with AMI. In an era of increasing economic pressures in health care, the efficient use of medical resources is mandatory.

CONCLUSIONS

MISSION! adds a new dimension in the field of AMI quality improvement initiatives, by integrating all AMI care phases in 1 structured patient-centered care program. The aim of MISSION! is to improve AMI care by implementing the most recent AMI guidelines across practical settings in real life. The preliminary results of MISSION!

are promising. If this integrated approach of AMI care proves to work, MISSION! may function as a guideline implementation program beyond our region.

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LETTER TO THE EDITOR

Dear Sir, I read with interest the article on the MISSION! program on adherence to guidelines and evidence-based medicine in patients with an ST-elevation acute myocardial infarction by Liem et al.(1) The authors must be congratulated with this initiative aiming at improving daily clinical practice. The authors have developed a nice clinical framework for decision making in the acute phase. They provide criteria for selecting primary percutaneous coronary intervention versus thrombolytic therapy. However, they do not mention prehospital thrombolysis as a reperfusion option. If the decision to give thrombolytic therapy is taken, it is to the benefit of the patient that this treatment is started already in the ambulance even if the distance to the hospital is relatively short. Traffic jams and overwork at the emergency department of the hospital may significantly delay the start of thrombolytic treatment. Randomized trials have shown a 17% reduction in inhospital mortality if fibrinolytic therapy is started in the ambulance compared with inhospital administration.(2) Also, the recent ASSENT-3 PLUS trial showed an almost 50-minute earlier onset of treatment with ambulance administration of fibrinolytic therapy.(3) Figure 5 of the article indirectly suggests that age of >80 years is an exclusion criterion for fibrinolytic therapy. There are no data in the literature indicating that thrombolytic therapy is ineffective or particularly harmful for age of >80 years. On the contrary, the SENIOR PAMI trial results suggest that thrombolytic therapy may even be slightly better than primary percutaneous coronary intervention in the very elderly (>80 years).(4) I would suggest that the authors incorporate these remarks in their otherwise excellent protocol.

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RESPONSE TO THE LETTER TO THE EDITOR BY VAN DE WERF

Dear Sir, It is with interest that we read the "Letter to the Editor" and the stimulating comments by van de Werf referring to our recently published article, which presented the study design of MISSION!, an all-phases integrated guideline implementation program for patients with an acute myocardial infarction in the region of Holland-Midden, The Netherlands.(1) Van de Werf critically remarked that we use inhospital fibrinolysis instead of prehospital fibrinolysis despite the benefit of earlier administration and the evidence of reduction of inhospital mortality when choosing the latter.(2,3) Indeed, we fully agree that prehospital fibrinolysis is preferred to inhospital fibrinolysis, looking at the available outcome data. However, we have chosen inhospital fibrinolysis for several reasons: 1) implementation of such a comprehensive protocol requires a lot of coordination and efforts; all regional health care providers across practical settings (ie, primary physicians, ambulance personnel, cardiologists, and coronary care unit nurses) are involved and collaborate closely to establish this program. Therefore, we tried to keep our MISSION! prehospital protocol as simple, manageable, and workable as possible. 2) In line with this, timely and efficient administration of prehospital fibrinolysis demands experience and practice. Although, most of our patients (>90%) are treated with primary percutaneous coronary intervention (PCI) according to our predefined criteria.(1) Hence, we primarily focused on training the ambulance personnel to perform high-quality 12-lead electrocardiogram in the field and what to do afterward to get rapid access to the appropriate center. 3) Finally, as van de Werf mentioned, benefit of prehospital administration of fibrinolysis would probably remain even if distances are relatively short as is in our region, for example, because of overwork at the emergency department. We tried to avoid the last by paging the coronary care unit of the nearest community hospital already en route to the hospital and directly transferring the fibrinolysis candidate to the coronary care unit, thereby bypassing the emergency department.

With regard to the exclusion of patients >80 years for fibrinolysis, consensus of optimal reperfusion therapy in this subpopulation, a population which exhibits high risk for mortality and severe bleeding complications, is still lacking.(3-6) This is caused by the systematic exclusion of these patients from large clinical trials, and if they are included they are often underrepresented.(4) In the beginning of MISSION!, we used >80 years as an exclusion criterion for primary PCI. However, we are confronted with elderly patients who are vital and do not have any contraindications for PCI. Therefore, >80 years per se is not an exclusion criterion anymore. With regard to fibrinolysis use, the threshold of >80 years is defined to be rather too

cautious than too aggressive. However, if an eligible patient >80 years is presented at the nearest emergency department by the ambulance, fibrinolysis indeed remains an option. MISSION! is not written and designed "as if", but demands individual assessment and tailoring, specially in a subpopulation in whom best practice is still a subject of debate. Moreover, as quality improvement is an ongoing process, clearly targeted large-scale clinical trials are needed to evaluate the relative merits of available reperfusion strategies in the elderly with ST-segment elevation myocardial infarction.(4,5,7)

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