

Referral pathways for reperfusion of STEMI – developing strategies for appropriate intervention

Adriaan Snyders* and Rhena Delport#

*The SA Heart Early Reperfusion Project. Wilgers Hospital, Pretoria, Gauteng, South Africa

#Department of Chemical Pathology, University of Pretoria, Pretoria, Gauteng, South Africa

Address for correspondence:

Prof Rhena Delport
Department of Chemical Pathology, Faculty of Health Sciences
University of Pretoria
Private Bag x323
Arcadia, Pretoria
0007
Gauteng
South Africa

Email:

rhena.delport@up.ac.za

INTRODUCTION

South African cardiologists frequently encounter patients with ST-segment elevation myocardial infarction (STEMI). Not infrequently, patients present for medical care long after the onset of symptoms and without having received any prior reperfusion therapy. There is no standardised management protocol for the management of STEMI in the public or private sector. The key objectives of the SA Heart STEMI Early Reperfusion Project are to improve quality of acute myocardial infarction (AMI) care and to improve the care network to ensure prompt access to reperfusion therapy and decrease mortality from AMI.

These objectives accord with the European Society of Cardiology's (ESC) Stent for Life programme to promote the implementation of their guidelines in the management of AMI and to identify the specific barriers to their implementation. A further objective is to formulate key actions to ensure that the majority of STEMI patients have access to primary percutaneous coronary intervention (p-PCI) within 120 minutes.⁽¹⁾ According to the ESC guidelines,⁽¹⁾ it is a CLASS I A recommendation that STEMI patients presenting to a hospital with PCI capability should be treated with primary PCI within 90 minutes of first medical contact (FMC), while it is a CLASS I B recommendation that STEMI patients presenting to a hospital without PCI capability, and who cannot be transferred to a PCI center and

ABSTRACT

The SA Heart Association seeks to improve the early management of ST-segment elevation myocardial infarction in South Africa. This pilot study was undertaken to establish the current time intervals present in the referral pathways to percutaneous coronary intervention (PCI) facilities in the Tshwane Metropole and to further identify the barriers to appropriate management of STEMI.

Method: Cardiologists from 5 PCI-capable hospitals recruited the patients in the catheterisation laboratory and captured the data. Interviews were conducted with three emergency medical services (EMS) to assess paramedics' scope of practice and identify hindrances to the effective management of STEMI patients.

Results: Median system delays were longer in patients requiring inter-facility transport (IFT; n=29) compared to patients with direct access to a PCI facility (DA) patients (median 3.7 vs. 30.4 hours; p<0.001). Door-to-balloon times of ≤90 minutes were achieved in only 22% DA and 33% IFT patients. Fibrinolysis within ≤30 minutes was achieved in 50% DA and 20% IFT patients. Reperfusion was attempted in <12 hours of symptom onset in significantly more DA than IFT patients (70% vs. 34%; p=0.012 respectively). Paramedics were suitably trained and ambulances reasonably equipped to manage STEMI patients. However, members of the public do not routinely summon EMS.

Conclusion: Education initiatives and improved systems of care have the potential to improve STEMI patient outcome in South-Africa. SAHeart 2015;12:74-80

undergo PCI within 90 minutes of FMC, should be treated with fibrinolytic therapy within 30 minutes of hospital presentation, unless such therapy is contraindicated.

A recent study in STEMI patients found that while p-PCI was performed in 60%, the majority of the interventions occurred later than 120 minutes, and that only 36% received fibrinolysis.⁽²⁾ This high percentage of patients receiving angiography and an invasive treatment strategy may be explained by the location of the participating centers in urban areas, almost all of which were private healthcare facilities.

Early and appropriate pre-hospital diagnosis, as well as immediate transport, are of vital importance to avoid unrec-

essary case fatalities.^(3,4) Ideally patients should have access to a referral pathway to p-PCI that is managed by informed professionals and is free of delays and bottlenecks. Patient, system and other delays contribute to the inability to meet quality targets.⁽⁴⁻⁶⁾ Factors contributing to extended referral pathways, such as cath lab activation times and door-to-balloon time, need to be identified and specifically targeted to ensure improved patient outcomes.

The SA Heart Association performed this pilot survey to investigate which factors contribute to ineffective management of STEMI patients admitted by cardiologists in the Tshwane metropolitan area by determining time lapses along the referral pathway associated with direct admissions and secondary referrals to cath labs and by assessing type and timeliness of treatment. The Tshwane metropolitan area was deemed suitable for the pilot study for reasons of convenience. The total population of the City of Tshwane is approximately 2.9 million within an area of 6 368km², extending approximately 121km from west to east and 108km from north to south. The purpose of the survey was to inform the design and implementation of education initiatives to be directed at all key players aiming to improve patient access to p-PCI. Some of the findings of the pilot survey have already been described in a report on STEMI systems of care in emerging countries.⁽⁷⁾ A more detailed report on the survey findings is presented here, as well as an algorithm for treatment intervention and the project plan for the SA Heart STEMI Early Intervention Project for South Africa.

METHODS

A cross-sectional observational study was performed, employing convenience sampling, from May to October 2012 in 5 cath lab hospitals in Pretoria. Data for consecutive STEMI patients from Tshwane and surrounding areas (including 18 referring urban private hospitals in the North West, Mpumalanga and Limpopo provinces) were collected in private cath labs in Pretoria by the treating cardiologist. Common referral pathways were established, time intervals along the pathway were determined and type and timeliness of treatment was investigated. Administration of fibrinolytics was recorded pre- and post-admission to the PCI facility.

Twenty-nine inter-facility transfer (IFT) (from a non-PCI-capable hospital to a PCI-capable hospital) and 23 direct access to a PCI-capable hospital (DA) patients were included in the study following exclusion of three NSTEMI patients. Patients were classified as IFT or DA, irrespective of FMC prior to admission to a hospital. One patient could not be admitted to a PCI facility due to a lack of funds. Five patients with missing

data on more than one time point were excluded. Data regarding the onset of symptoms was not available for one DA and five IFT patients, and time of admission to cath lab was not reported for two DA patients. Patient history data was not reported for three DA and two IFT patients. First medical contact to diagnosis time was reported as zero minutes in six DA and three IFT patients. Fibrinolytic therapy was only recorded for 21 IFT and 22 DA patients.

Emergency Medical Services (EMS) in the City Of Tshwane comprise one public- and 24 private providers. Interviews were conducted with personnel from the three major EMS providers who are capable of appropriate transport and care for myocardial infarction patients (Netcare 911, ER24 and Europ Assistance) to assess their scope of practice and also to identify what they perceived as barriers to effective management of STEMI patients.

Statistical analyses were performed employing STATISIX 9, 2008 Analytical software (Tallahassee FL, USA). Between-group comparisons were performed with the Wilcoxon sign rank tests for continuous variables and the chi-square test for dichotomised variables. Logistic regression analyses were performed to identify factors contributing to treatment delay beyond defined treatment goals.

RESULTS

Ten patients were attended to by a physician prior to admission, five of whom were DA cases and five IFT cases. Two IFT patients died during PCI, one female and one male. Only one patient used EMS for transport to the hospital. This patient lived alone and first called her family, who in turn called an ambulance on her behalf. All others used their own transport (usually a family member's car) to bring them to the hospital.

Time delays associated with the process, from symptom onset to cath lab admission, and distribution of patients across referral routes are depicted in Figure 1. Five IFT and five DA patients, whose FMC was a general practitioner, came from remote areas. The other patients resided in the City of Tshwane and went directly to a non-PCI (n=24) or a PCI facility (n=18). The 24 IFT patients, whose FMC was an emergency physician at a non-PCI facility, were referred to a PCI-capable hospital for further treatment. The risk profiles of the referral pathway groups were similar although patients previously diagnosed with myocardial ischaemic events appeared more likely to follow the direct access route (Table 1).

Significant patient delays (delay between symptom onset and FMC) were evident in both referral groups (Table 2) but did

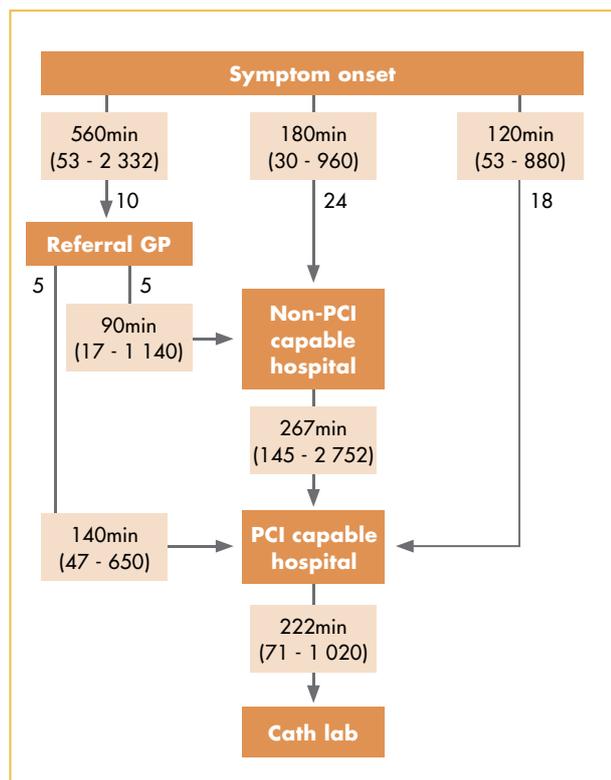


FIGURE 1: Distribution of patients across referral routes and time delays from onset of symptoms to cath lab admission associated with referral route

Median (IQR) values for time intervals are reported in minutes (min). GP: General practitioner.

not differ significantly between referral groups. Excessive system delays (delay between FMC and admission to cath lab) were also observed in both groups, with significantly longer delays for IFT patients compared to DA patients. FMC did not occur within 120 minutes in 45% and 68% of DA and IFT patients respectively. The treatment goal of performing p-PCI in ≤60 and 90 minutes from FMC was achieved only in DA patients in 13% and 22% respectively.

Ninety-six percent of DA patients and 72% of IFT patients had received fibrinolytics (Table 3) and although the 2 groups did not differ significantly with regards to the time lapse between FMC and administration of fibrinolytics, the treatment goal of administering fibrinolytics in ≤30 minutes from FMC was only achieved in 50% of DA and 20% of IFT patients (Table 2). Table 3 presents information on the different types of fibrinolytics that were administered pre-and post-admission to a PCI-capable hospital.

Reperfusion delays of more than 12 hours from symptom onset were explained by patients delays (duration to FMC dichotomised as ≤/ >120 minutes of symptom onset) (Odds ratio 16.5; 95% CI 3.0-91.8), independent of referral pathway

TABLE 1: Risk profile of patients in the different referral pathway groups

Referral groups	Direct access (n=23)	Indirect access (n=29)
Sex: % Females	4 (17%)	8 (28%)
Age (years)*	64 (30-83)	57 (32 - 76)
Hypertension	10/18 (55%)	11/27 (41%)
Diabetic	6/20 (30%)	4/25 (16%)
Hypercholesterolemia	8/18 (44%)	11/24 (46%)
Coronary Heredity	6/17 (35%)	6/26 (23%)
Smoker previous/ current	9/16 (56%)	13/24 (54%)
CABG	1/14 (7%)	1/20 (5%)
Angioplasty	1/14 (7%)	0/17 (0%)
Stent	2/14 (14%)	0/18 (0%)

*Reported as median (range).

TABLE 2: Time intervals from onset of symptoms to reperfusion

	Direct access (n=22)	Inter-facility transfer (n=29)	p-value
Symptom onset to FMC	120 (54 - 1 020)	212 (34 - 2 017)	NS
FMC to cath lab admission	223 (105 - 885)	1 822 (340 - 5 106)	p=0.0001
FMC within 120 minutes of symptom onset	12 (54%)	9 (37%)	NS
FMC to Primary PCI ≤90 minutes	(≤90 minutes) 5 (22%)	(≤90 minutes) 0 (0%)	χ ² =6.52; p=0.011
Or ≤60 minutes in patients presenting within 120 minutes of symptom onset or at a PCI-capable facility	(≤60 minutes) 3/23 (13%)	(≤60 minutes) 0/12 (0%)	NS
FMC to diagnosis time	18 (0 - 60)	390 (81 - 2 051)	p=0.0007
Door-to-balloon time	222 (93 - 500)	285 (60 - 1 121)	NS
Door-to-balloon ≤90 minutes	5 (22%)	9 (33%)	NS
FMC to fibrinolysis time*	32 (19 - 71)	227 (46 - 4 628)	p=0.009
FMC to fibrinolysis ≤30 minutes	11/22 (50%)	4/21 (20%)	χ ² =4.11; p=0.043
Total time delay to reperfusion therapy by PCI	487 (205 - 1 605)	3 363 (684 - 7 847)	p=0.001
Reperfusion in all patients with 12 hours duration of symptom onset	16 (70%)	10 (34%)	χ ² =6.31; p=0.012

Time intervals are reported as minutes: Median (IQR range). FMC: First medical contact, χ²: Chi square test, *Direct access (n=22) and Inter-facility transfer (n=21).

TABLE 3: Fibrinolytic treatment administered post- and pre-arrival at PCI-capable hospitals

	Direct access (n=22)	Inter-facility transfer (n=21)
Fibrinolysis	22 (1) (1 post-PCI)	21 (8) (3 post-PCI)
Glycoprotein IIb/IIIa inhibitor	1	11 (2)
Aspirin	18 (2)	18 (7)
UFH	0	1 (1)
Enoxaparin	17 (1)	15 (6)
Fondaparinux	0	1 (1)
Clopidogrel	11 (1)	14 (6)

Pre-arrival treatment numbers reported in brackets.

and system delays dichotomised as \leq / $>$ 90 minutes of FMC. Risk for fibrinolysis being delayed more than 30 minutes after FMC increased four-fold with IFT (Odds ratio 95% CI: 1.01-15.86).

The key findings of the interviews with EMS providers were as follows:

- Ambulances are equipped with a 3-lead ECG only.
- When a patient calls in complaining of chest pain, a response vehicle is simultaneously dispatched by some emergency service providers. The response vehicle is manned by more highly qualified staff and has a 12-lead ECG.
- Some ambulances/response vehicles have the capability to transmit an ECG via cell phone to an e-mail address. This equipment costs R180 000. Others rely on the paramedic taking a photograph of the ECG and sending it to another phone.
- There have been instances in which, although the patient was delivered to a PCI-capable facility, transfer to another facility was mandated by the patient's insurer, resulting in needless delays.

DISCUSSION

In broad terms, this small observational study provides the outline on which a national survey can be planned. Significant patient and system delays were evident in both referral groups, and in particular in the IFT group (Table 2, Figure 1), with the excessive system delays compounding the risk in a significant number of patients whose FMC was beyond 120 minutes of symptom onset. Time lapses between FMC /non-PCI-capable hospitals and PCI-capable hospitals were unnecessarily long and

partially explain why 30% of DA and 65% of IFT patients failed to receive timely reperfusion. Patient reaction times suggest that they were uninformed regarding possible symptoms, the importance of timely treatment and the importance of being treated in a PCI-capable hospital. Upon analysis of the South Africa Heart Association registry data, Shamroth, et al.⁽²⁾ reported median (IQ range) time intervals of 3.6 (1.6; 9.5) hours between the onset of symptoms and arrival at a hospital in a population in which 64% of patients lived within a 30-minute drive from the admitting hospital. The longer time intervals reported in our study may reflect the longer distances patients need to travel from referral hospitals to PCI-capable facilities. Although the pharmaco-invasive strategy is advocated for STEMI patients living in remote areas with no ready access to PCI facilities, only 65% of IFT patients received a fibrinolytic agent and treatment was delayed until admission to a PCI facility in four of the 23 patients. In addition, fibrinolysis was performed at a median time of four hours and 34 minutes (range 00:02-09:09 hrs:min), well beyond the recommended limit of \leq 30 minutes.⁽¹⁾ Difficulty in diagnosing STEMI in IFT patients has been reported previously and has been ascribed to symptoms and early ECG changes being less clear in this cohort of patients.⁽⁶⁾ The authors suggest that "initial triage to a non-primary PCI center may be justifiable due to diagnostic uncertainty, and that guideline time metrics should be amended appropriately".⁽⁶⁾ However, IFT due to misdiagnosis is associated with significantly higher 1-year mortality.⁽⁸⁾

A recent retrospective study in Cape Town (2008 - 2010) reported a median "door-to-needle" time of 54 minutes (range 13 - 553 minutes).⁽⁹⁾ A fibrinolytic agent was administered in only 44.7% of cases despite 88.8% typical symptoms of myocardial infarction. A "door-to-needle" time of 30 minutes or less was achieved in 33 (20.5%) patients; 51.3% of these patients arrived by ambulance; 34% had a pre-hospital 12-lead ECG. These deviations from recommended practice were ascribed to a lack of senior doctors, difficulty interpreting ECGs, atypical presentations and delays in emergency centers. Of note, 51.3% of the patients enrolled for this study were transported by ambulance and a 12-lead ECG was performed pre-hospital in 34% of patients.⁽⁹⁾

"Time to treatment" and "door-to-balloon" time are both significant determinants of mortality in STEMI.⁽⁴⁾ Total time delays to reperfusion therapy by PCI of approximately eight hours for DA patients and 56 hours for IFT patients were observed in this study, and "door-to-balloon" time of \leq 90 minutes was only achieved in 22% of DA and 33% of IFT patients. Of concern is that only 22% of DA and none of

the IFT patients received p-PCI within 90 minutes of FMC. System delays with DA need to be scrutinised in particular in national follow-up studies for targeted intervention to optimise outcome in this referral group.

Findings relating to Emergency Medical Service (EMS) provision

The scope of practice of emergency care providers for the different levels of training is as follows:⁽¹⁰⁾

- A Basic Ambulance Assistant (BAA) provides basic life support and is able to administer oxygen and interpret vital signs. They do not have access to any medication, nor may they administer drugs. They are unable to attach or interpret an ECG.
- Ambulance Emergency Assistants (AEA) and Emergency Care Technicians are qualified to provide intermediate life support. They may set up an intravenous infusion, administer aspirin and attach and interpret a 3-lead ECG (to recognise ST elevation or depression and interpret critical cardiac arrhythmias).
- The Critical Care Assistant (CCA) provides advanced life support. They are licensed to administer nitrates and morphine. Some may be able to attach, perform and interpret a 12-lead ECG.
- Emergency Care Practitioners (Bachelors Degree in Technology or Bachelors Degree in Emergency Medical Care) are qualified to administer thrombolytic therapy.

Four of the 5 qualifications for emergency care providers include interpretation of an ECG within their scope of practice, which implies that EMS personnel are well equipped to recognise and manage STEMI patients appropriately while those with a Bachelors Degree in Technology or in Emergency Medical Care are qualified to administer fibrinolytic treatment. Ambulances are equipped with a 3-lead ECG only, while response vehicles have 12-lead ECG machines on board. Solutions need to be found for the immediate transmission of the ECG to a control center for early diagnosis and appropriate referral of the patient. All paramedics should be adequately trained to make the “time-sensitive” diagnosis of STEMI and triage the patients successfully as this has the potential to have major impact on patient outcome.⁽¹¹⁾ Ideally EMS should be mandated to promptly activate the cath lab team.⁽¹²⁾ The finding that EMS is not routinely solicited by the public prompts urgent implementation of public awareness initiatives.

FUTURE STRATEGIES

Strategy to establish functional regions

The goals to be attained within the next 24 months are defined as follows:

- Recruiting a key cardiologist in each region to drive the project.
- Establishment of contact with all relevant stakeholders to inform them of what the project entails and to solicit their collaboration.
- Commencement of the Early Reperfusion Project training, once buy-in has been obtained, in the following sequence:
 - Hospitals with a cath lab (involving personnel in intensive care units, emergency department, hospital manager, nursing manager);
 - Hospitals without cath labs (involving personnel in emergency rooms from all city hospitals and other referring suburban centers, and also referring GP practices); and
 - EMS personnel.
- Launching of a patient awareness programme through the Heart and Stroke Foundation (HSF) within the broader context of acute coronary syndrome management.
- Establishment of a network amongst STEMI care providers, central and local government, medical insurance companies, private sector funders.
- Establishment of a registry with meticulous data collection and follow up to ensure the collection of reliable outcome data. A study protocol has been developed to establish the effectiveness of the education and networking initiatives and to identify remaining constraints, unmet training needs and organisational shortfalls across other regions. The objective of the proposed study is to inform the compilation of South African STEMI treatment guidelines and to define standards against which the systems of care are monitored.

The patient awareness programme needs to be prioritised, based on the finding of this pilot study that risk for missing the treatment goal for reperfusion <12 hours duration of symptom onset increases seventeen-fold if duration to FMC exceeds 120 minutes of symptom onset, independent of referral pathway.

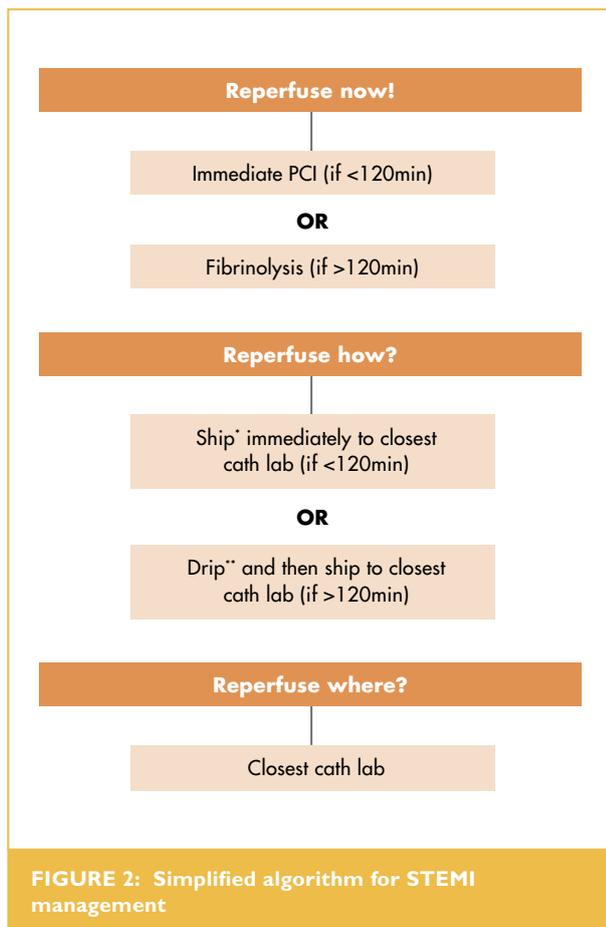
Following this strategy it is hoped that concerted action amongst the role players will ensure early reperfusion by appropriate intervention and that the DA strategy will be followed whenever possible.

STEMI management algorithm

This simple algorithm has been developed to facilitate effective STEMI management (Figure 2).

In essence, time to treatment is critical during the first two to three hours after symptom onset. Therefore, anti-platelet therapy and immediate p-PCI is favoured within the first two hours following onset of pain. After 3 hours p-PCI is preferred if it can be performed within 2 hours of FMC. If this is not possible, an immediate pharmacoinvasive strategy with fibrinolysis followed by transfer for PCI within the next 3 to 24 hours is recommended because late reperfusion may improve myocardial salvage and survival. Immediate or "rescue" PCI should be performed for failed reperfusion after fibrinolysis.

Lack of first-line treatment of STEMI with Aspirin is of specific concern, especially with inter-facility transfer of patients, as is evident from this pilot study (Table 3), and needs to be addressed. Furthermore, the choice of fibrinolytic agent is important to ensure effective reperfusion and there is a need to replace streptokinase in the public sector with a fibrin-specific agent.



*Ship: Transfer, **Drip: Administer fibrinolytics.

Additional considerations

No single practitioner working in isolation can alter outcomes, as evidenced by results from abroad.⁽⁷⁾ We hope to establish an effective network between the various stakeholders and create a fully functional central hub that oversees all initiatives and monitors progress through the maintenance of a registry. The mismatch between need and availability of PCI-capable facilities remains a concern⁽⁷⁾ but success stories relating to government involvement in other countries are encouraging.^(7,13,14)

Perceived South African healthcare challenges (personal observations) that need to be considered relate to:

- **Public/private sector mismatch:** 70% of South African patients in the public (government) sector being cared for by 30% of doctors, and 30% percent of South African patients being treated by private cardiologists;
- **Shortage of cardiologists:** 4 out of 11 provinces not having one registered cardiologist;
- **Treatment constraints:** 20% of private patients having varying levels of medical insurance;
- **Collaboration amongst cardiologists:** Cardiologists tend to work as individuals and not as a team in hospitals that belong to 1 of the 4 major private groups; and
- **National fiscal constraints:** South Africa implementing National Health Insurance (NHI) while currently struggling to deliver healthcare.

Limited human resources and financial constraints may affect the establishment of an effective STEMI system of care. Although private cardiologists assist with the training of cardiologists and with patient care in the public sector, it is questionable whether closer cooperation between these sectors is possible because of regulatory and logistic constraints. Involvement of private funders may alleviate some of the financial burdens of the project and will contribute to successful STEMI management in South Africa, but key to the success of the project probably lies an individual commitment towards education of all parties involved and encouraging collaboration within regions. Although the primary focus of the project is the management of STEMI patients, all acute coronary syndrome (ACS) patients are expected to benefit from the intervention.

Strategies to establish functional regions have been identified and the follow-up national study investigating the causes of delay in early reperfusion in STEMI patients in South Africa has commenced. Although the challenges appear daunting, the

lessons learnt from other countries are encouraging⁽⁷⁾ and much may be learnt from their experiences in treating patients coming from remote areas.^(15,16)

LIMITATIONS

The limitations of this pilot study relate to the small sample size and the incompleteness of the data. A true reflection of the distribution of cases, in accordance with treatment guidelines across the different referral pathways, is lacking. Ideally a distinction should be made between p-PCI, coronary angiography with follow-on PCI in patients presenting >12 hours of the onset of symptoms, coronary angiography with follow-on rescue PCI within 60 - 90 minutes after administration of fibrinolytics in patients with failed reperfusion, and coronary angiography with follow-on rescue PCI in patients with recurrent myocardial ischemia after fibrinolysis. The timeliness of all types of PCI interventions, as defined above, is worthy of consideration in the national survey to follow.

CONCLUSION

This pilot study demonstrates that there are a number of barriers to the effective treatment of STEMI patients in South Africa. Fostering collaboration between all role players and encouraging concerted action in the various regions in managing these patients should ensure that better outcomes are achieved, not only for them, but for all patients with an acute coronary syndrome.

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Conflict of interest: none declared.

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