Bahrain Medical Bulletin, Vol. 19, No. 2, June 1997

Achieving Earlier Thrombolysis in Acute Myocardial Infarction

Ali Akbar Murad, MS, PhD, FAMS*, Anil Kumar Chawla, MD, MRCP (UK)**
Chaveri Ashokan Nambiar, MD, DM***

Objective: Study the in-hospital delays in administering thrombolytic therapy to patients of Acute Myocardial Infarction (AMI), the reasons for such delays and if they could be avoided.

Setting: Accident and Emergency Department (A/E) and Coronary Care Unit (CCU) of the Salmaniya Medical Centre (SMC), Bahrain.

Design: Retrospective study of sixty six consecutive patients of AMI who were treated with thrombolytic drugs over a six month period from January to June 1994.

Subjects & Methods: Sixty six patients diagnosed to have AMI in the A/E were given thrombolytic therapy either in A/E or in the CCU. Besides their demographic variables, the duration of symptoms before arrival, the time lag from arrival to actual administration of thrombolytic drug and the reasons for such time lag were analysed.

Results: 80.3 % patients arrived within six hours of chest pain. 7.5 % patients were treated within an hour of arrival, 28.8 % within 1-2 hours, 25.7 % within 2-3 hours, 18.2 % within 3-4 hours and 19.7 % beyond 4 hours with an average hospital delay of 175 minutes. The major reasons for the delays were: delayed referrral from A/E, transfers to CCU and awaiting laboratory reports.

Conclusions: The hospital delay which occurs in administering a thrombolytic drug to AMI patients, reduce the benefits of such therapy and is avoidable. Steps should be taken to eliminate this delay and administer thrombolytic therapy to AMI patients at the earliest; preferably within an hour of arrival to the hospital.

Bahrain Med Bull 1997;19(2): 34-39

It is well established by large clinical trials of thrombolytic therapy, like the GISSI-1 and the ISIS-2[1,2] that time is crucial in the administration of thrombolytic drugs after the onset of chest pain in AMI. The sooner after symptoms thrombolytic drugs are administered, the greater is the reduction in morbidity and mortality from AMI. In the GISSI - 1 study, the benefit in mortality reduction at 1 hour after onset of chest pain was 47 % as compared to 18 % for the whole group who received thrombolysis treatment up to 6 hours of onset of chest pain[1].

Delay in thrombolytic drug administration could be as a result of patient-related factors at home, the problems of transportation to hospital or due to factors in the hospital itself.

Significant delay in administration of thrombolytic drugs does occur in the hospital, even when the patient has reached early[2,3]. The objective of our study was to assess the magnitude of the problem at our hospital and identify the possible reasons for the in-hospital delay.

METHODS

Salmaniya Medical Centre is the main referral hospital open to the general public. Most areas are within one hour's driving distance from the hospital by road. There is an active '999' Ambulance Service and a busy A/E Department. Almost all cases of AMI from A/E get admitted to the CCU. Some patients are treated in A/E while waiting for admission to the CCU. Case records of seventy consecutive thrombolysed patients of AMI, diagnosed at the initial presentation in A/E, on the basis of history and ECG changes, from January to June 1994, were analysed retrospectively. No cases of atypical history, non-diagnostic ECG, unstable angina or non-Q wave myocardial infarction were included. The ECG criteria used for AMI diagnosis were, an ST elevation of 1 mm or more in two consecutive chest leads, or in leads II, III, AVF. Cardiac enzymes, creatinine phosphokinase (CPK), Lactic Dehydrogenase, and CK-MB fraction of CPK were done in all cases but their elevation was not required for initiating thrombolytic therapy. The patients were first seen and

* Consultant Cardiologist & Chairman
** Medical Doctor, Cardiology
*** Consultant Cardiologist
Department of Medicine
Salmaniya Medical Centre
State of Bahrain

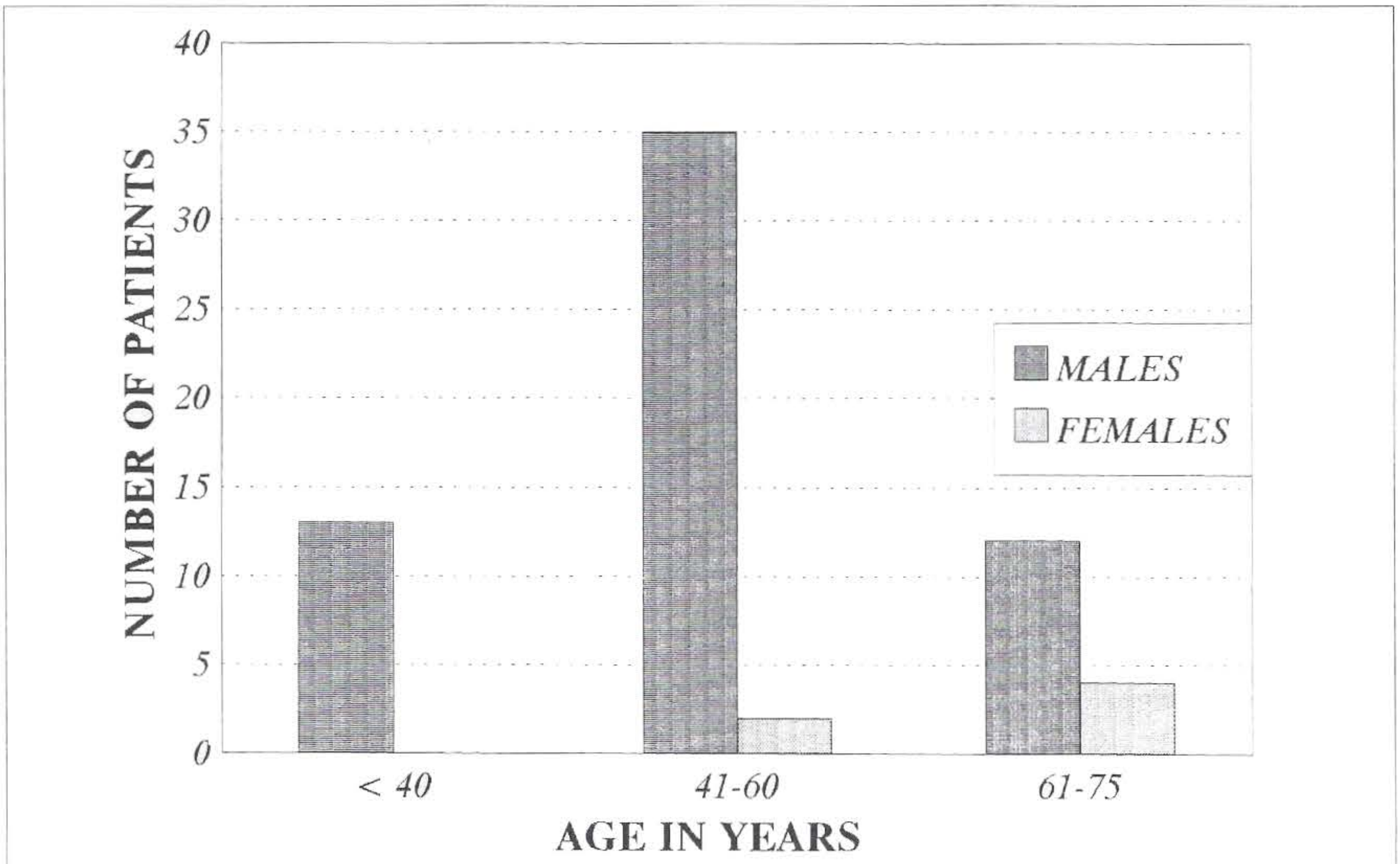

Fig 1. *Demographic variables of thrombolysed patients in acute Myocardial Infarction*

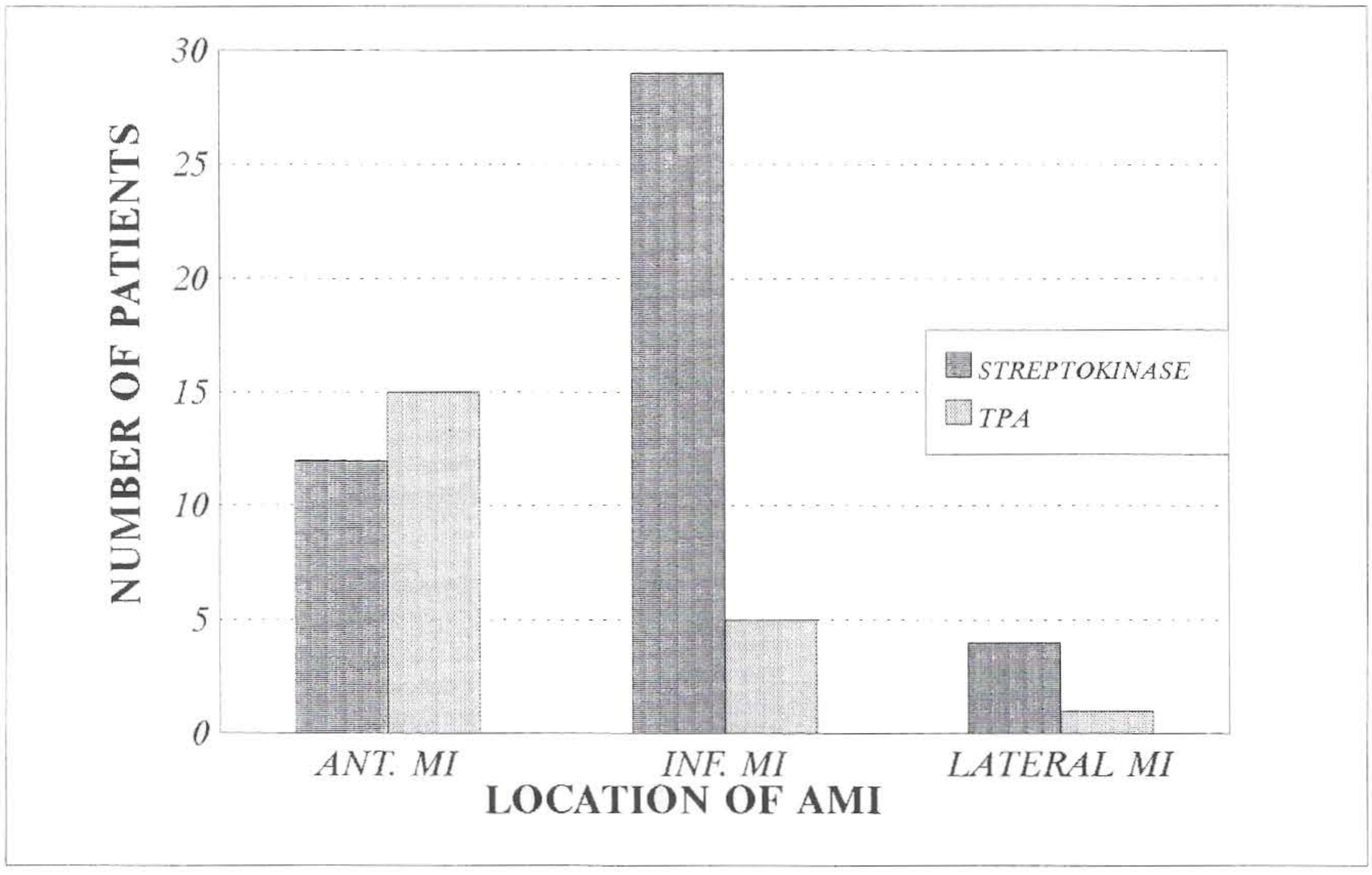

Fig 2. *Thrombolytic agent used and location of AMI*

assessed by the A/E doctor on duty and then referred to the medical registrar for opinion. The decision to give thrombolytic treatment was taken in the A/E itself by the medical doctor in consultation with the Consultant Cardiologist.

In every case, the time of patient's arrival in A/E, the time seen by the A/E doctor and the time of referral to the medical doctor were recorded. The time when a thrombolytic agent was actually administered was also recorded, so that the "door to needle time" that is the time from the patient's arrival in the emergency to the time of actual administration of the thrombolytic agent could be calculated in every case. The movement of the patient, the reasons for delay in giving thrombolytic therapy were obtained from the doctors' and nurses' notes on each patient.

Two thrombolytic agents, streptokinase and tissue plasminogen activator (tPA) were available for use and the agent was selected on the basis of whether the infarction was anterior or inferior, small or large and duration and persistence of symptoms.

RESULTS

Of the seventy patients given thrombolytic therapy, four were excluded because the initial decision in the A/E was not to give therapy because of late presentation. Therapy was later given to these patients in the wards due to recurrence of symptoms and fresh ECG changes. The demographic variables of the included sixty six patients are given in Figure 1.

The majority (53 %) of patients were in the 41 to 60 years age group and 20 % of our patients were under 40 years of age. Of the two thrombolytic agents used Streptokinase was given to 45 (68.2 %) patients and tPA was given to 21 (31.8 %) patients.

Figure 2 shows the thrombolytic agent used according to the location of AMI.

The majority of Inferior wall AMI patients (56.6 %) received Streptokinase, whereas most of the anterior wall AMI patients (71.4 %) received tPA.

Figure 3 shows the duration of chest pain before arrival to the hospital.

More than half the patients (51.5 %) presented to the hospital within two hours of onset of symptom and another third between 2 to 6 hours. Thus 80.3 % of the patients who were thrombolysed had symptoms of less than 6 hours duration. The remaining 19.7 % of patients were given thrombolysis for symptoms longer than 6 hours because of recurrent or continuing symptoms.

The "door to needle time" was calculated in every case and is shown in Figure 4 which reveals the hospital delay in administering the thrombolytic agent. Only 5 (7.5 %) patients were given the thrombolytic drug within one hour of arrival, 28.8 % within 1-2 hours, 25.7 % within 2-3 hours, 18.2 % within 3-4 hours, and the remaining 19.7 % after 4 hours. The average hospital delay was 175 minutes before the thrombolytic drug could be administered.

The reasons for delay in administering thrombolytic therapy are shown in Figure 5.

Most of the delay was found to be related to late referrals (> 30 minutes after arrival in the A/E) and logistics of patient transfers from the A/E department to the CCU. Awaiting results of Prothrombin Time (PT) and Partial Thromboplastin Time (PTT) from the laboratory before starting thrombolytic drugs also was responsible for the delay in a number of patients. In some cases, treating initial complications and equivocal initial ECG, were responsible for the delay.

DISCUSSION

Early thrombolytic therapy in patients with AMI achieves higher reperfussion and patency rates, greater myocardial salvage, better left ventricular ejection fraction and lower mortality than later administration of such therapy[1-3]. Benefits of thrombolytic therapy in terms of morbidity and mortality are almost directly proportional to the time lag from the onset of chest pain to the time that such treatment is administered.

The GISSI-1 study established that optimal benefit occurs if patients of AMI are treated within 6 hours of symptom onset, although ISIS-2 study showed some benefit to accrue to patients treated even from 6-24 hours of chest pain[1,2].

In our study, 53 (80.3 %) out of 66 patients presented to the hospital within 6 hours of symptom onset and were eligible to receive the thrombolytic therapy according to the standard inclusion criteria. The remaining (19.7 %) patients with symptom onset longer than 6 hours were included because of recurring or continuing symptoms and it was decided to give them the benefit of such late therapy as observed in ISIS-2 and other studies[2,3].

The reasons for pre-hospital delay on the part of the patient may include denial, mistaking symptoms for a more benign medical condition, a history of angina pectoris or other cardiac disease, attempts to contact personal physicians, ambulance inavailability or poor utilisation[4]. The relatively large proportion (80.3 %) of patients presenting early, within six hours, in our series is because of good ambulance services, and the advantageous geographic location of the hospital as it can be reached from anywhere within an hour by road.

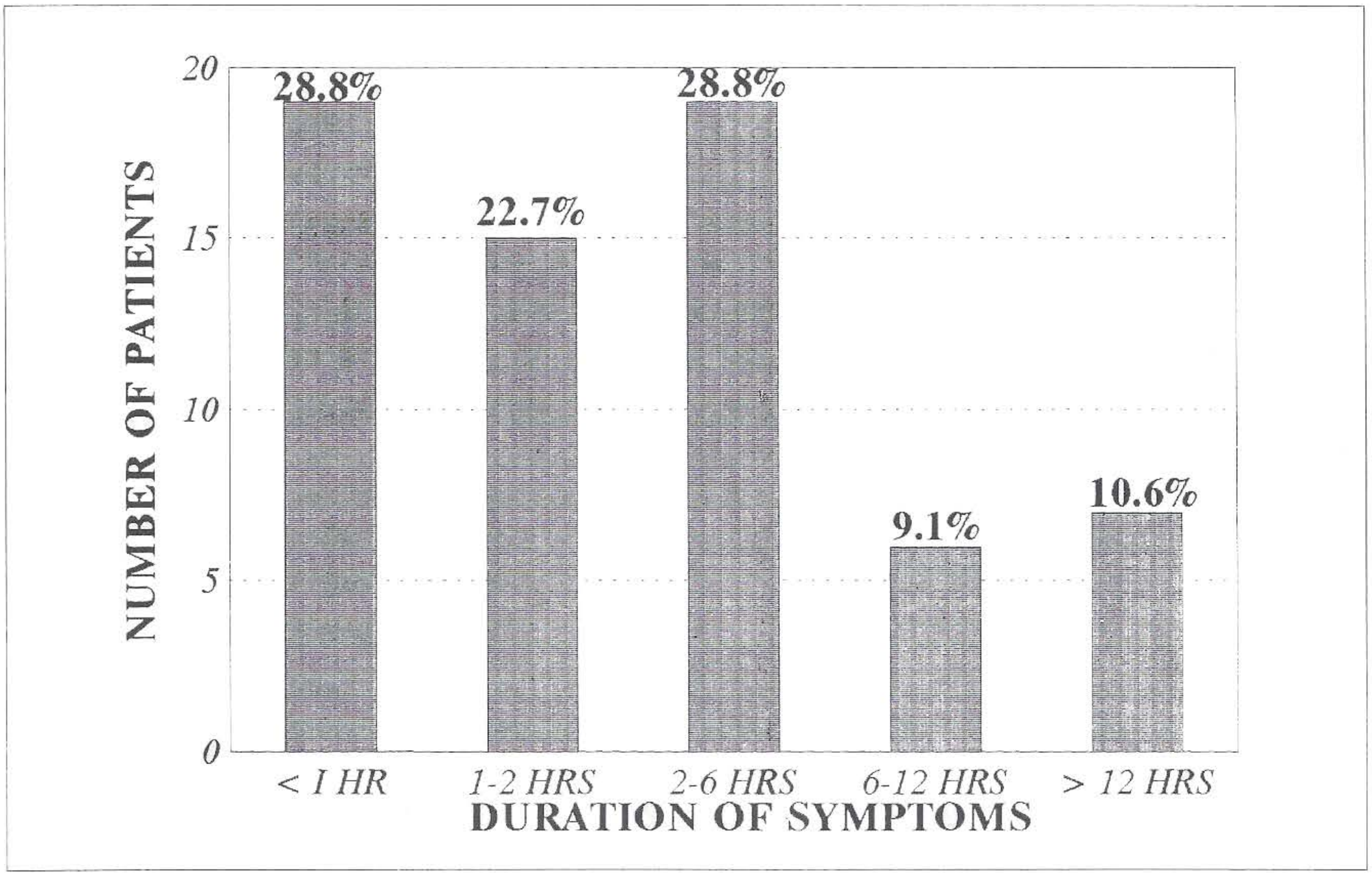

Fig 3. *Duration of symptoms in patients of AMI before arrival to the hospital*

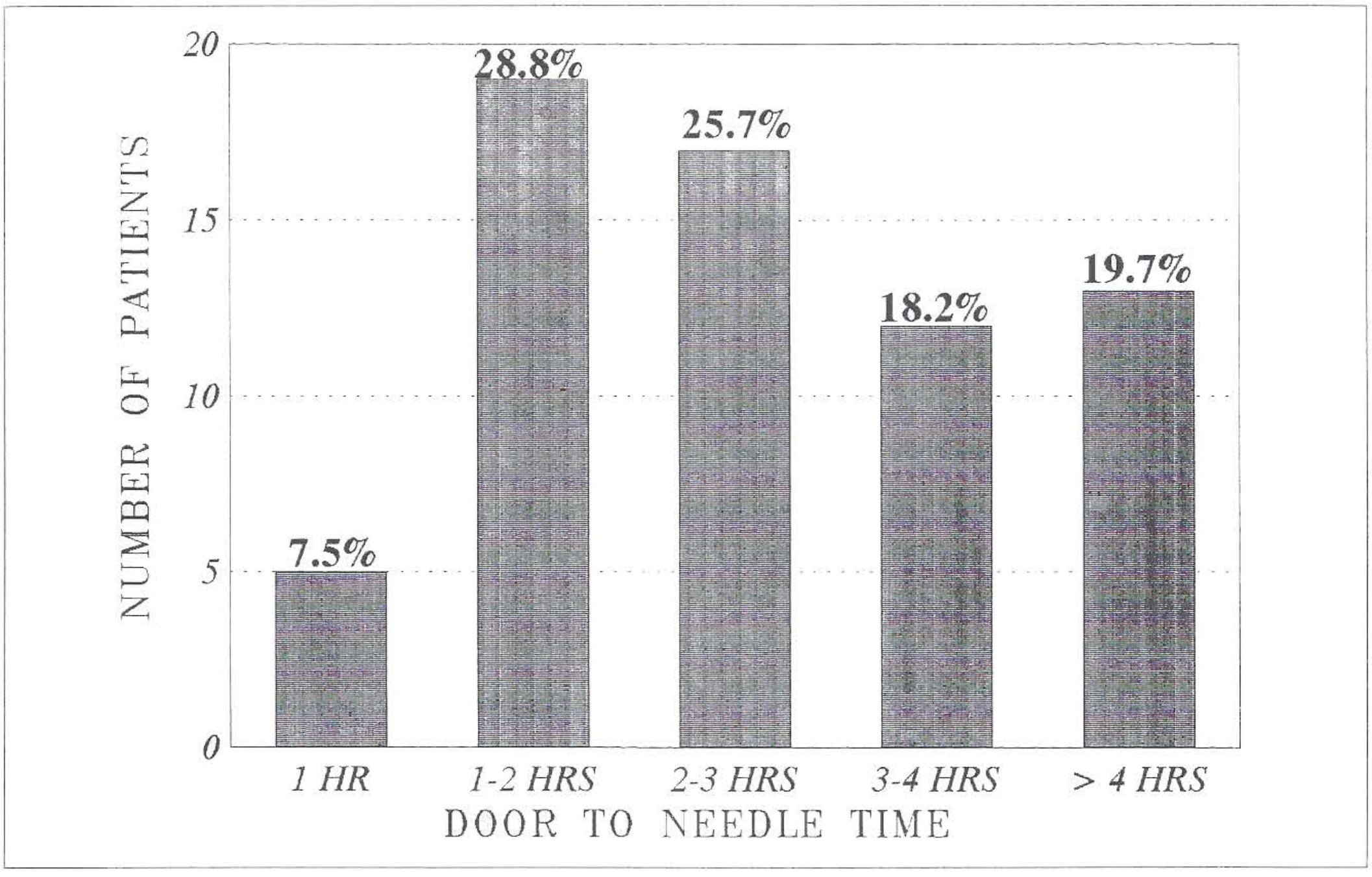

Fig 4. *Door to needle time for Thrombolysis in patients of AMI*

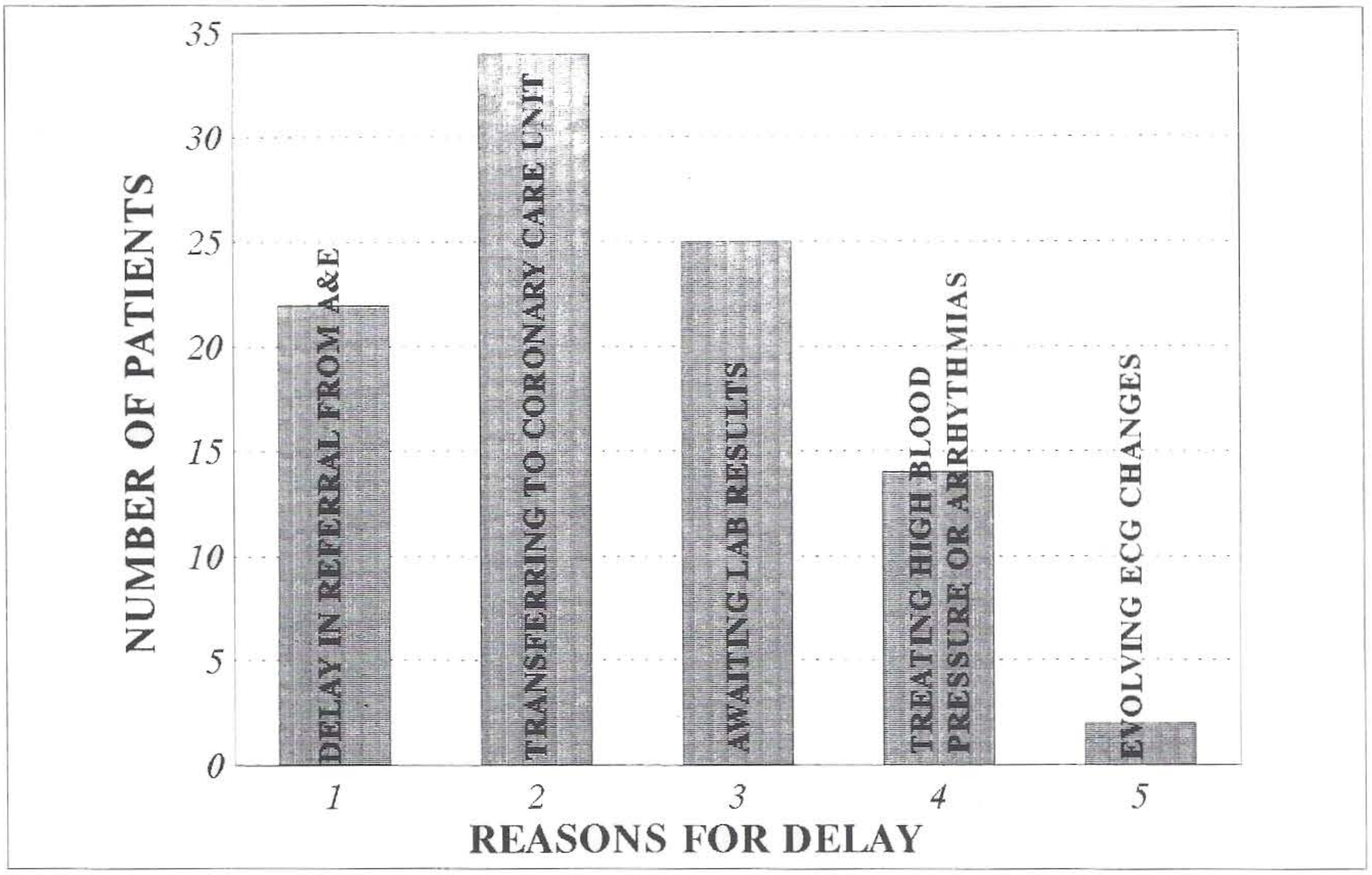

Fig 5. *Reasaons for delay in administetring thrombolytic therapy*

This is also one of the main reasons why thrombolysis utilisation in AMI here is 57.9 %, which is much better than many other centres[5]. In contrast to the pre-hospital delay which is hard to influence, significant delay occurs in the hospital and could be minimised to achieve early thrombolysis. A US study of nation wide survey of thrombolytic use showed that the elapsed time between onset of symptoms and initiation of therapy was 5.5 ± 1.4 hours[6]. Sharkey et al, in their landmark study of time delay preceding tPA treatment of AMI, found an average time lapse of 154 ± 54 minutes from symptom onset to treatment and a lapse of 90 minutes from arrival in emergency department to the initiation of thrombolytic therapy[7]. In our series, the average hospital door to needle time was 175 minutes, with 60 % of the patients receiving treatment within 180 minutes of arrival and almost 40 % taking more than 3 hours for initiation of treatment. Only 7.5 % patients received the treatment within an hour of arrival to A/E. A significant 19.7 % of the patients received it after 4 hours. Ornato, reviewing published US thrombolytic studies suggested that the ideal in-hospital delay prior to initiating therapy should be 30 minutes or less[4]. Our door to needle time is thus much longer than the time recommended and that reported from many Western hospitals.

In the Minnesota TIMI-II study one of the most important factors resulting in in-hospital time delays was patient transfer[7]. Transferring patients from emergency department to CCU results in significant delay in starting thrombolytic therapy. Several other studies show that the treatment is received sooner if initiated in the A/E rather than if patient is transported to the critical care unit for therapy[3,4,6,7]. In our study the 7.5 % of the patients who were treated within an hour of arrival to A/E were all given thrombolytic therapy in the A/E itself. All the remaining patients were transferred to the CCU for initiating therapy although the decision to give treatment was taken in A/E itself. This involves considerable loss of valuable time in the form of nurses' transfer paper work and protocol formalities, added to the transportation time itself.

Several studies have demonstrated that thrombolytic therapy can be safely and effectively administered in the A/E departments both in tertiary care hospitals and community hospitals[8-10]. High risk patients can have thrombolytic therapy safely initiated at the site of presentation and can then be transported to the coronary care unit[11]. The A/E is a major focal point for influencing the timing of thrombolytic therapy because it is he hospital's entry point for most AMI patients who are candidates for such treatment. Such treatment is given in A/E itself to save valuable time in many hospitals[12-14].

Among several time saving measures, it is recommended that the thrombolytic drugs should be stored in the A/E itself, a qualified emergency physician could decide and

initiate thrombolytic therapy and that a cardiologist should only supervise and set up the protocols[14-16].

Pell AC et al, from Edinburgh Royal Infirmary UK, devised a fast track admission system to the CCU from the A/E and were successful in reducing by half the in-hospital delay to thrombolytic therapy administration. But they also found A/E administration of thrombolysis to be faster. We now administer thrombolysis in the A/E, whenever fast transfer of the patient to CCU is not possible. During the study period, considerable time was lost in referral from A/E to the medical registrar. However this is likely to improve with the recently introduced triage system in the A/E department where in a chest pain patient is given a red sticker, transferred to a resuscitation room where urgent ECG is done and immediate medical attention is given.

Another area which needed improvement was the time taken to get coagulation profile laboratory reports. This problem has been overcome by starting thrombolytic therapy if on clinical grounds bleeding disorders are unlikely.

Realising the benefits of auditing the time to thrombolysis and of fostering a healthy competition among A/E physicians for faster times, Peter Cummings recommends such audits to be the routine part of the quality assurance audit of A/E departments[18].

The delay because of treating initial serious complications like arrhythmia or shock or elevated BP seems unavoidable. Since "time is muscle" following an AMI, for an earlier reperfusion, myocardial salvage, and lower mortality, all these urgent steps have to be taken to reduce the door to needle time. The goal should be to treat all patients of AMI in less than one hour[18].

CONCLUSION

In conclusion we emphasise that with close cooperation of the Cardiology Division of Medicine and A/E department, it should be possible to cut down considerably the in-hospital delay in thrombolysis. The excellent thrombolysis utilisation in AMI of 57.9 % at our centre[5] would be more beneficial to the patient if a corresponding improvement is made in the "door to needle" time and measures have been adopted to advance towards this goal.

REFERENCES

1. Gruppo Italiano per Studio della Streptochinasi nell' Infarto Micocardico (GISSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986;1:397-401.
2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both or neither in 17187 cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988;2:249-60.
3. Maynard C, Althouse R, Olsurufka M, et al. Early versus late hospital arrival for acute myocardial infarction in the Western Washington thrombolytic therapy trials. Am J Cardiol 1989;63:1296-300.
4. Ornato JP. Role of the emergency department in decreasing the time to thrombolytic therapy in acute myocardial infarction. Clin Cardiol 1990;13:48-52.
5. Chawla AK, Nambiar CA, Murad AA. Thrombolysis Utilisation in acute myocardial infarction in Bahrain. Indian Heart J 1996;March-April:155-8.
6. Grasela TH, Green JA. A nationwide survey of prescribing patterns for thrombolytic drugs in acute myocardial infarction. Pharmacotherapy 1990;10:35-41.
7. Sharkey SW, Brunette DD, Ruiz E, et al. An analysis of time delays preceding thrombolysis for acute myocardial infarction. JAMA 1989;262:3171-4.
8. Hartmann JR, Mckeever LM, et al. Intravenous streptokinase in acute myocardial infarction: Experience of community hospitals served by paramedics. Am Heart J 1986;111:1030-4.
9. Verheugt FWA, Funke-Kupper AJ. Emergency room infusion of intravenous streptokinase in acute myocardial infarction: feasibility, safety and consequences. Am Heart J 1989;117:1018-22.
10. Topol EJ, Bates ER, Walton JA, et al. Community hospital administration of intravenous tissue plasminogen activator in acute myocardial infarction: improved timing, thrombolytic efficacy and ventricular function. J Am Coll Cardiol 1987;10:1173-7.
11. Topol EJ, Fung AV, Kline E, et al. Safety of helicopter transport and out-of-hospital intravenous fibrinolytic therapy in patients with evolving myocardial infarction. Cathet Cardiovasc Diagn 1985;12:151-5.
12. Smith M, Eisenberg MS. Thrombolytic therapy for myocardial infarction: Pivotal role for emergency medicine. Ann Emerg Med 1987;16:592-3.
13. Eisenberg MS, Smith M. The farmer and the cowman should be friends. Emergency physicians and cardiologists must work together to ensure rapid initiation of thrombolytic therapy. Ann Emerg Med 1988;17:653-4.
14. Gpza ER, et al. Hospital delays and problems with thrombolytic administration in patients receiving thrombolytic therapy. Ann Emerg Med 1992;21:10.
15. Malacrida R, Weaver WD. The avoidable delay [Editorial]. Ann Emerg Med 1992;21:10, 1243-4.
16. Hilleman DE, Gannon JM. Reducing time delays in the administration of thrombolytic therapy to patients with acute myocardial infarction. DICP Ann Pharmacother 1991;25:1096-100.
17. Pell ACH, et al. Effect of "fast track" admission for acute myocardial infarction on delay to thrombolysis. BMJ 1992;304:83-7.
18. Cummings P. improving the time to thrombolytic therapy for myocardial infarction by using a quality assurance audit. Ann Emerg Med 1992;21:1107-10.