

THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION: EXPERIENCE AT A UNIVERSITY HOSPITAL IN KUWAIT

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Background: There is conclusive evidence from large clinical trials that thrombolytic therapy reduces mortality and morbidity in acute myocardial infarction (AMI). However, only a small proportion of patients receive thrombolytic treatment. Estimates have varied from 20%-50% in North America and Europe. Data from the Arab Middle East is sparse. The purpose of our study was to determine the use of thrombolytic therapy in our hospital.

Methods: We conducted a retrospective analysis of 343 patients (358 incidents of AMI), who were either discharged from or died at the coronary care unit of the Mubarak Al-Kabeer Hospital during the one-year period between June 1994 and May 1995.

Results: Our patients were relatively younger (63% were <55 years) and had a much higher prevalence (44%) of diabetes compared to European patients. We observed a high rate (62%) of thrombolysis and a lesser shortfall (8%) when compared to that reported for European patients. The main reason for withholding thrombolytic therapy was non-diagnostic electrocardiogram (ECG) on initial presentation. Women were less likely to be thrombolitized than men (38% vs. 66%, $P=0.0001$). Older patients (aged >65 years) were also less likely to be thrombolitized than younger patients (42% vs. 66%; $P=0.0006$).

Conclusion: We conclude that the use of thrombolytic therapy in this university hospital in Kuwait is appropriate. However, as observed in other reports as well, the underutilization of thrombolytic therapy in women and the elderly needs to be addressed in future studies.

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Despite definitive evidence from large randomized clinical trials in the 1980s and 1990s that thrombolytic therapy significantly reduces mortality and morbidity in acute myocardial infarction (AMI),¹ thrombolytic drugs continue to be underutilized.^{2,3} The rate of thrombolysis in North America and Europe, as reported from population-based studies, has ranged from 20% to 50%.²⁻⁵ Data from the Middle East pertaining to the use of thrombolytic therapy in Arab populations is sparse. A recent study from Bahrain reported a thrombolysis rate of 58% in patients presenting with ST-segment elevation.⁶ Previously reported factors limiting the use of thrombolytic therapy included delayed presentation to hospital, non-diagnostic ECG changes on presentation and the presence of contraindications. Old age and female gender have also limited the use of

thrombolytic therapy in some reports.^{2,7,8}

The structure and characteristics of both the population and the health care system in Kuwait vary from that of North America and Europe. Kuwait is a rapidly developing Arab country which has undergone major changes in its population structure and lifestyle during the last three decades. The use of thrombolytic therapy in this population has not been reported previously. We have, therefore, conducted a retrospective study to determine the use of thrombolytic therapy at a university hospital and compared the findings with those from other countries.

Methods

The study was conducted at the Coronary Care Unit (CCU) at Mubarak Al-Kabeer Hospital, which is a large (476 beds) university hospital. The hospital provides services to the 449,554 residents in the Hawalli Governorate. All patients with the final diagnosis of acute myocardial infarction (AMI) who were discharged from, or died at, the CCU over a one-year period between June 1994 and May 1995 were included in the study. The

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TABLE 1. Comparison of clinical characteristics of study population with a European study population.²

Characteristics	Study population (n=358)	European study (n=4035)
Sex		
Male	306 (85%)	2695 (67%)
Female	52 (15%)	1340 (33%)
Age (years)		
<55	224 (63%)	669 (17%)
55-64	77 (22%)	916 (23%)
65-74	41 (11%)	1129 (28%)
>74	16 (4%)	1321 (33%)
Diabetes		
Yes	158 (44%)	728 (18%)
No	200 (56%)	3270 (82%)
Previous myocardial infarction		
Yes	70 (20%)	955 (24%)
No	288 (80%)	3022 (76%)
ECG		
BBB	13 (4%)	238 (6%)
ST elevation	259 (72%)	2504 (63%)
ST depression	33 (9%)	831 (21%)
Other	53 (15%)	393 (10%)
Hours from onset of symptoms to admission		
0-1	59 (16%)	574 (15%)
2-3	117 (34%)	1158 (30%)
4-6	64 (18%)	798 (20%)
7-12	48 (13%)	601 (15%)
13-24	22 (6%)	434 (11%)
>24	19 (5%)	353 (9%)
Unknown	29 (8%)	-

BBB=bundle-branch-block.

diagnosis of AMI was based on any two of the following three criteria: typical chest pain, diagnostic serial ECG changes, and doubling of creatine kinase with at least 6% MB fraction.

A structured data collection form, including detailed information on medical history, physical examination, ECG, cardiac enzymes, lipid profile and blood sugar, admission and discharge diagnosis, thrombolytic therapy execution and in-hospital course, was completed from the patients' records.

During the study period, patients were considered eligible for thrombolytic therapy if they presented within 12 hours of typical cardiac pain of more than 20 minutes' duration, or acute pulmonary edema or cardiac arrest and ST elevation of ≥ 0.1 mV in two or more limb leads, or ≥ 0.2 mV in two or more contiguous precordial leads, or a new left bundle branch block (LBBB). The time limit was extended to 24 hours in selected patients with ongoing pain. There was no age barrier to treatment. Absolute contraindications for the use of thrombolytic therapy included acute internal bleeding, suspected aortic dissection, blood pressure $\geq 200/120$ not responding to treatment, non-hemorrhagic stroke within six months, hemorrhagic stroke, known intracranial neoplasms or

arteriovenous malformations, head trauma or surgery within two months, known bleeding disorder, and diabetic proliferative retinopathy. Relative contraindications included surgery or organ biopsy, gastrointestinal or genitourinary bleeding and trauma to the abdomen or chest within two weeks, prolonged or traumatic cardiopulmonary resuscitation, puncture of a non-compressible vessel, and severe renal or hepatic diseases. Two thrombolytic agents, namely, tissue plasminogen activator and streptokinase, were available for use.

In the current study, a non-diagnostic ECG means the absence of ST elevation or LBBB. The actual rate of thrombolysis is the observed thrombolysis rate. The shortfall is the percentage of patients who were eligible for, but did not receive thrombolytic treatment. The chi-squared test was used to assess the significance of association between categorical variables and the outcome.

Results

Over the one-year study period, 343 patients suffered 358 episodes of AMI. The mean age of the patients was 52 years and the age range was 25 to 93 years. Males (85%) were on average 12 years younger than females (mean age 50 vs. 62 years). Table 1 compares the baseline characteristics of the study population with a European study which included patients from 11 countries. These two patient populations had some interesting differences. This study population was much younger: 63% of the patients were younger than 55 years, compared with 17% in the European study. Only 4% were older than 74 years, compared with 33% in the European study. Diabetes was relatively more common in our study population, with 44% of the patients being diabetic, as compared to 18% among the European patients.

Table 2 summarizes the implementation of thrombolytic therapy in the study population and compares it to the European study. The observed rate of thrombolytic treatment in the whole study population was 62%, compared to 35% in the European study. The shortfall was 8%, compared to 21% in the European study. In our study, there were 252 patients eligible for thrombolytic treatment (admitted within 12 hours of symptom onset, ST elevation on admission, and no apparent contraindication). The thrombolysis rate in this group of patients was 88%, compared with 62% in the European study.

All patients were treated in the CCU, as out of hospital and emergency department thrombolysis was not practiced in Kuwait during the study period. The majority (56%) of patients received streptokinase, while 44% received tissue plasminogen activator.

The reasons for omission of thrombolytic therapy are also shown in Table 2. The main reason for not receiving

thrombolytic treatment was nondiagnostic ECG changes on admission. Time delay was the reason for omitting thrombolysis in only 7% of the patients.

Table 3 compares the observed thrombolysis rate, factors limiting the use of thrombolytic treatment and shortfall according to sex and two broad age groups. Females were less likely to receive thrombolytic therapy than males (38% vs. 66%; $P=0.0001$). When compared to males, more females presented late and more females had non-diagnostic ECG changes. The shortfall in females was also greater (14% vs. 7%). When patients aged < 65 years were compared with those aged ≥ 65 years, the older patients were less likely to receive thrombolytic treatment (42% vs. 66%, $P=0.0006$). Compared to the younger patients, more older patients presented late and had non-diagnostic ECG. The shortfall in older patients was also greater (14% vs. 7%).

Discussion

This is the first report of the use of thrombolytic therapy in AMI in Kuwait. It is worth noting that the majority of patients in our study were younger than 55 years and that almost half were known to be diabetic. These findings are consistent with a young population structure (about 93% of the population in Kuwait is younger than 50 years) and a high prevalence of diabetes.⁹

With regard to the use of thrombolytic treatment, we observed a high rate of thrombolysis in our study and a lesser shortfall when compared to other studies. This study demonstrated that about two-thirds of the patients admitted to our CCU with AMI received thrombolytic therapy. This is one of the highest reported rates of thrombolysis, especially when considering that we used the final discharge diagnosis to identify patients with AMI. If we were to include only those with suspected AMI at the initial presentation (by excluding patients without ST elevation on admission) our rate of thrombolysis would be even higher (76%). This observed high thrombolysis rate could have several explanations. One explanation is that our patients were younger than those in other studies, and were therefore less likely to have contraindications to thrombolysis. Other studies^{2,8} have also demonstrated that the rate of thrombolysis is higher in younger patients and in males. Another explanation for the high thrombolysis rate may lie in our daily systematic monitoring of treatment. All treatment decisions are discussed daily in a morning round, and our staff are encouraged to adhere to the unit's guidelines for the use of thrombolytic therapy.

The main reason for exclusion from thrombolysis in our study was non-diagnostic ECG changes at the time of presentation. Data from the fibrinolytic trials have shown that there is no benefit from administering thrombolytic treatment to patients with AMI who present with ST

TABLE 2. Comparison of observed thrombolysis rate, factors limiting thrombolysis and shortfall between study population and a European study.²

	Study population (n=358)	European study (n=4035)
Thrombolysed	223 (62%)	1397 (35%)
Not thrombolysed	135 (38%)	2638 (65%)
Time delay or uncertain time	26 (7%)	847 (21%)
Initial diagnosis not AMI	0	261 (7%)
Non-diagnostic ECG changes	63 (18%)	610 (15%)
Contraindications	17 (5%)	85 (2%)
Shortfall	29 (8%)	835 (20%)

* >12 hours.

TABLE 3. Observed thrombolysis rate, factors limiting thrombolysis and shortfall according to gender and age.

	Male (306)	Female (n=52)	Age <65 (n=301)	Age ≥ 65 (n=57)
Thrombolysed	203 (66%)	20 (38%)*	199 (66%)	24 (42%) [†]
Not thrombolysed				
Time delay or uncertain time	16 (5%)	10 (19%)	18 (6%)	8 (14%)
Non-diagnostic ECG changes	51 (17%)	12 (23%)	50 (17%)	13 (23%)
Contraindications	14 (5%)	3 (6%)	13 (4%)	4 (7%)
Shortfall	22 (7%)	7 (14%)	21 (7%)	8 (14%)

* >12 hours; ** $P=0.0001$ male patients vs. female patients; [†] $P=0.0006$ patients <65 years vs. older patients.

depression.¹ The presence of contraindications to thrombolysis was rarely a limiting factor in our study. Most of the study patients presented within the first six hours and only 7% of the patients were excluded due to time delay.

In our study, we found that females were less likely to receive thrombolytic treatment in comparison to males. This gender difference has been reported in other studies,^{2,10} and extends to other modalities of management, such as coronary artery bypass graft surgery and percutaneous transluminal coronary angioplasty.^{11,12} We also found that the older patients received thrombolytic treatment less often than the younger patients. This has been the finding in many previous studies.^{2,7,8} The age effect seems to reflect the reluctance of physicians to administer thrombolytic treatment to older patients, perhaps out of fear of hemorrhagic complications. The study population was too small to allow performance of regression analysis to see whether these gender and age differences were independent of other factors, such as delayed presentation or non-diagnostic ECG changes.

We realize that this study has potential limitations, including the retrospective design and the relatively small number of female patients. It is possible that the practice in our hospital may not be representative of the practice in other hospitals in Kuwait. A population-based study, including patients from all the hospitals in Kuwait, would more accurately reflect the practice in our country. The

development of a national registry for acute myocardial infarction is another way to document thrombolysis implementation in Kuwait.

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