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Impact of a Simple Inexpensive Quality Assurance Effort on Physician's Choice of Thrombolytic Agents and Door-to-Needle Time: Implication for Costs of Management

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Abstract. **The objective of this study were to assess the impact of a quality assurance effort on the door-to-needle time and the choice of thrombolytic agent for the management of acute myocardial infarction in the emergency department. The study design involved a prospective collection of data on a series of consecutive patients who received a thrombolytic agent for a presumed acute myocardial infarction. The study was carried out in the emergency department of a major university urban tertiary care center. A total of 349 patients were studied from September 1989 to March 1994. The quality assurance program began in 1989 and included chart review of all patients receiving thrombolytic therapy, with special attention to all patients with door-to-needle times >60 minutes to identify causes for delay. Feedback was directed to pharmacy, nursing, and physician staff. Biannual reports were distributed throughout the hospital and the emergency department. Nursing-specific feedback led to the development of protocols for all aspects of the delivery of thrombolytic agents. The choice of thrombolytic agent was not dictated by the protocol, but the physician staff was continuously updated on the results of the latest clinical trials comparing one thrombolytic agent with another. The mean age was 58 years for men and 67 years for women in this cohort consisting of 78% men and 22% women. Thirty-seven percent of the myocardial infarctions were in an anterior location and 56% were in an inferior location. The median duration of chest pain before presentation to the emergency department was 120 minutes. Hospital mortality was 3%. Median door-to-needle time fell from 46 (1989–1991) to 36 (1992–1994) minutes, $P < 0.01$. The percentage of patients with a door-to-needle time >60 minutes decreased from 35% (1989–1991) to 16% (1992–1994) minutes, $P < 0.0001$. Corresponding with the ISIS-3 report, there was a significant increase in the proportion of patients receiving streptokinase over the first 3 years of the study ($P < 0.0001$), which changed to a trend toward increased utilization of tissue plasminogen activator with the GUSTO report in the final 6 months of the study. In conclusion, a quality assurance program led to a significant reduction in the door-to-needle time, and recent megatrials were found to influence the choice of thrombolytic agent used.**

Key Words. **thrombolytic therapy, time factors, quality assurance, myocardial infarction**

Intravenous thrombolytic agents significantly lower mortality after an acute myocardial infarction when given within 12 hours of the onset of chest pain [1–3]. Recent studies have shown that early delivery of the agent, especially within the first 4 hours of symptoms, is associated with a greater mortality benefit. However, in most centers there is a substantial delay from presentation to actual drug infusion (door-to-needle time). The average door-to-needle time has been reported as 45–90 minutes [4–10]. Analysis of factors leading to delays in initiating therapy have suggested that a substantial portion of the total delay occurs after patients arrive at the hospital. For instance, in an analysis of the TIMI 2 trial, in-hospital delay accounted for 59% of the total time from the onset of symptoms of infarction to the initiation of tissue plasminogen activator (t-PA) therapy [4]. It has been said that reducing the in-hospital delay in the administration of thrombolytic therapy represents the best opportunity to further maximize the present-day treatment of myocardial infarction [4].

A recent multicenter prospective trial [11] examined the hospital attributes that correlated with a more rapid door-to-needle time. The study demonstrated that urban location, teaching hospital status, and higher case volumes were each associated with more rapid thrombolytic administration. We hypothesized that if a relatively simple and inexpensive quality assurance effort could reduce the door-to-needle time of our center, then such a program might yield even greater efficiencies in other centers.

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In addition to documenting the importance of efficient delivery of thrombolytic agents to acute myocardial infarction patients, recent megatrials have also influenced the choice of thrombolytic agents. Controversy surrounding the efficacy and cost of purported clot-specific agents has led to uncertainty as to which thrombolytic agent to use. We hypothesized that temporal trends of thrombolytic use in our emergency department would likely reflect the major reports comparing the efficacy of different thrombolytic drugs. Thus, the specific aims of our study were to determine the impact of a quality assurance program on (1) door-to-needle time and (2) the choice of thrombolytic agents in acute myocardial infarction.

Methods

Patient identification

The emergency department records of 349 consecutive patients receiving thrombolysis for an acute myocardial infarction from September 1989 through March of 1994 were reviewed. All patients included in the study met criteria for thrombolytic therapy in accord with written guidelines reported in the literature and used in our emergency department. These criteria included the presence of typical ischemic chest pain of at least 30 minutes duration (and up to 12 hours) that was unresponsive to nitrate therapy and was associated with at least 1-mm ST segment elevation in two contiguous leads or new left bundle branch block. Patients with contraindications to thrombolytic therapy were excluded from the study. Additional exclusions included patients who had received the thrombolytic agent for the index acute myocardial infarction at an outside hospital, patients who received thrombolysis for a condition other than an acute myocardial infarction, and patients in whom a thrombolytic agent was ordered but never received.

Data acquisition

This was a retrospective analysis of a prospective cohort study with data on demographic information, vital signs, myocardial infarction location, choice of thrombolytic agent, and hospital mortality analyzed by review of medical records. The door-to-needle time was calculated from the time of initial triage in the emergency department to the time when the infusion of streptokinase or t-PA was started. In patients who received both streptokinase and t-PA, only the time to infusion of the first thrombolytic agent was included in the analysis.

Quality assurance program (Table 1)

The quality assurance program begun in September of 1989 included a monthly review of the emergency department records of all patients who received thrombolytic agents by a clinical nurse specialist and/or attending physician. Issues targeted for review included whether the documentation was completed by nursing (e.g., the infusion rate and dose) and physicians (e.g., the time the order was written) and an assessment of the door-to-needle time. The time for drug preparation was analyzed separately where possible. The records of patients who had a door-to-needle time exceeding >1 hour were reviewed in detail by the physician director of the quality assurance program to identify the reasons for delay. When appropriate, individuals involved in the care of that patient were contacted to clarify the possible causes for a delay. Per protocol, the emergency department staff physician made the decision to administer thrombolytic therapy without obtaining a cardiology consult (unless the patient had chest pain for more than 12 hours and/or the indications for thrombolysis were unclear).

A protocol-driven physician–nurse team approach at the bedside was instituted. Intravenous access was obtained immediately, and a decision was rendered regarding which drug would be used in a patient meeting the criteria for thrombolysis. Updated protocols that were mounted on the wall of every acute care cubicle were followed in a timely fashion. While the thrombolytic agent was infusing, additional drugs were administered, a chest x-ray was obtained, and blood samples were sent. Thrombolytic agents were

Table 1. *Components of the quality assurance program*

1. Immediate ECG
2. Updated protocols posted in every acute care cubicle in the emergency department
3. Team approach (a protocol-driven physician-nurse team)
4. Thrombolytic agent stocked in emergency department
5. Thrombolytic therapy begun in the emergency department (no delays in transfer to the CCU)
6. Thrombolytic therapy begun by emergency department physician, except in ambiguous cases (minimal consulation delays)
7. Review of all thrombolytic-treated MI patients by M.D. or nurse clinical specialists
8. Measure of door-to-needle time
9. Focused review/feedback of patients with door-to-needle times >1 hr
10. Biannual status report
11. Nursing feedback sessions on documentation, thrombolytic drug protocol, drug preparation, etc.
12. House staff teaching conference reviewing current literature/monthly orientation lectures in the emergency department

mandated to be available in the emergency department pharmacy at all times.

A biannual status report of the Thrombolysis Quality Assurance Program was distributed throughout the hospital (including the hospital administration, pharmacy, nursing, and the Department of Internal Medicine). The Department of Nursing held formal feedback sessions targeting the areas of adequate documentation, review of the thrombolysis protocol, and timely preparation and administration of drugs. Teaching conferences were held for the house staff reviewing conclusions from our own database and that of the thrombolytic literature. Also, a monthly orientation was given in the emergency department for new house officers and a medical grand rounds was held annually, reviewing the goals of thrombolytic therapy.

Data analysis

Statistical analysis was done using the BMDP statistical program [12]. Fisher's exact tests were used to compare categorical variables. Student's t-test was used to compare independent means of continuous variables. *P* values reflect two-sided tests. Findings were considered significant when the two-sided *P* value was <0.05. Data are summarized as means with standard deviations as measures of dispersion. Median values are reported for variables that were not normally distributed. For the analysis, patients who received thrombolytic therapy during the first 2 years of implementing the quality assurance effort in 1989–1991 (group A) were compared with patients who received thrombolytic therapy during the latter 2 years of the study in 1992–1994 (group B), after the quality assurance program had become an established component of the emergency department routine.

Results

Of 349 study patients, 78% were men and 22% were women, with a mean age of 58 ± 1 and 67 ± 1 years, respectively ($P < .001$). The mean age increased from 58 $\pm$ 11 years for group A to 62 ± 12 years for group B ($P < .005$; Table 2). The location of myocardial infarctions was similar between group A and B, and consisted of 39% anterior (including anteroseptal and anterolateral myocardial infarctions), 58% inferior, and 3% lateral myocardial infarctions. There was no statistically significant difference in gender or duration of symptoms between groups A and B. The overall in-hospital mortality for patients who received thrombolytic agents was 3%.

The median door-to-needle time fell significantly from 46 minutes during 1989–1991 to 36 minutes in 1992–1994 ($P < .01$). The percentage of patients with door-to-needle times >60 minutes fell from 35% in 1989–1991 to 16% in 1992–1994, ($P < .0001$; See Table 3). Over the entire study period, 65% of patients received only streptokinase, 32% received t-PA, and 3% received both. As shown in Figure 1, the proportion of streptokinase versus t-PA increased from 60% for group A to 75% for group B ($P < .01$). Streptokinase use in anterior myocardial infarctions also increased from 55% during the 1989–1991 period to 73% during the 1992–1994 period ($P < .05$). In addition, the tendency for streptokinase use in inferior myocardial infarctions increased from 68% during the 1989–1991 period to 80% during the 1992–1994 period ($P < .09$). For

Table 2. *Demographic information (n = 349)*

	Group A 1989–1991	Group B 1992–1994	*P* value
Age			
<40 years	10 (5%)	6 (4%)	NS
41–64 years	115 (61%)	79 (50%)	<0.05
>65 years	62 (33%)	71 (45%)	<0.02
Mean ± SD	58 ± 11	62 ± 12	<0.005
Gender			
Female	47 (25%)	36 (23%)	NS
Male	143 (75%)	122 (77%)	NS
Duration of symptoms			
² 6 hours	58 (31%)	45 (28%)	NS
>6 hours	120 (63%)	104 (65%)	NS
Type of thrombolytic agent			
Streptokinase	112(59%)	113 (72%)	<0.02
t-PA	72(38%)	38 (24%)	<0.007
Streptokinase 1 t-PA	6(3%)	5 (3%)	NS
Death during hospitalization	4(2%)	7 (4%)	NS

Table 3. *Impact of quality assurance on thrombolytic therapy*

	Group A 1989–1991	Group B 1992–1994	*P* Value
Approximate hours of symptoms prior to ED arrival (median in hours)	2 hours	2 hours	
Door-to-needle time (median in minutes)	46	36	>0.01
Patients with door-to-needle time >60 minutes	35%	16%	>0.0001

ED = emergency department.

lateral infarcts, streptokinase and t-PA were used in similar proportions. The proportion of patients receiving streptokinase increased significantly over the first 3 years of the study ($P < .0001$). Analysis of the final 6 months of the study, however, revealed a significant increase in the proportion of patients receiving t-PA, a clear reversal of prior trends. This trend for increased utilization of t-PA was seen following the reporting of the GUSTO trial. Figure 1 illustrates the proportion of streptokinase versus t-PA use in 6-month intervals (the period in which the results of ISIS-3 and GUSTO became available are indicated).

Discussion

We reduced the median time from initial triage to treatment by 10 minutes (21%) after implementing a quality assurance program (see Table 1). Our program was simple and focused on physician/nurse education and feedback, as well as a bedside team approach. In addition, the hospital administration and pharmacy director were involved. While an absolute reduction of 10 minutes may seem marginal from a clinical viewpoint, it is significant in the context of a hospital that already has a door-to-needle time significantly below the national average of approximately 90 minutes [10]. The most recent report from the National Registry of Myocardial Infarction notes a 9-minute reduction in the median time to treatment (52.5 vs. 43.5 minutes) when comparing their first enrollment interval in January 1991 to December 1993, but this registry is admittedly predominantly composed of tertiary academic centers.

When data across all 904 hospitals that volunteered to participate in the National Registry of Myocardial Infarction were considered, the median time from hospital presentation to treatment was >55 minutes, with ~63% of patients receiving thrombolytic therapy within 1 hour [13]. This national trend toward decreasing the time to treatment is encouraging, given that our experience with a quality assurance program in a single center resulted in a greater than 50% reduction in the number of patients who received thrombolysis >1 hour after presentation. The American Medical Association and the NIH (National Heart, Lung, and Blood Institute) and National Heart Attack Alert Coordinating Committee recommend treating all acute myocardial infarction patients who are eligible for thromboytic therapy within 30–60 minutes after arrival in the emergency department [14,15]. We believe that opportunities for even greater impact and clinical benefit exist in hospitals in which the door-to-needle time remains 60–90 minutes.

Several studies have examined the causes of delays in initiating thrombolytic drugs in emergency departments [4,11]. The two largest studies of in-hospital time delay [4,11] found several factors that appear to be important. A policy of transporting the patient to the coronary care unit prior to initiating thrombolytic therapy caused delays ranging from 10 to 35 minutes [4,11]. Significant delays were also related to waiting for the patient's private physician to initiate treatment rather than having the emergency physician alone or with an on-site cardiology consultant initiate therapy. Finally, both studies suggested that transporting the drug from the pharmacy to the emergency department consumed valuable time and led to unnecessary delays in preparing and administering the drug. Maynard et al., in evaluating factors influencing the time from hospital presentation to the initiation of thrombolytic treatment based on data from the National Registry of Myocardial Infarction, also found that the most important factor associated with a shorter time to treatment was a policy whereby thrombolytic treatment is given in the emergency department rather than the coronary care unit (47 vs. 73 minutes, $P < 0.0001$) [13].

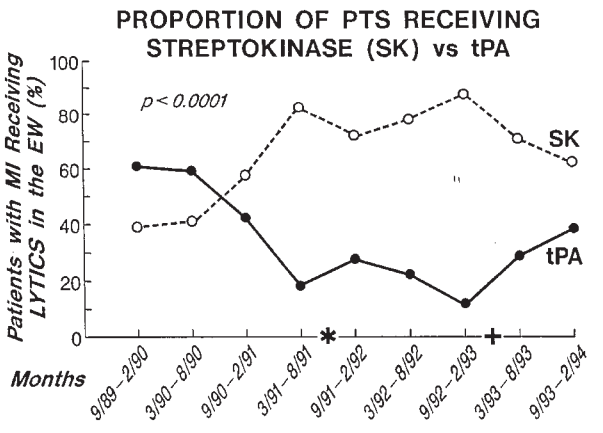

Figure 1. *Potential Influence of megatrials on thrombolytic choice. The proportion of patients meeting acute myocardial infarction criteria receiving SK (streptokinase) versus t-PA (tissue plasminogen activator) in 6-month intervals. * ISIS-3 results reported/disseminated to physician staff. + GUSTO I results reported/disseminated to physician staff.*

While it is agreed that the most important determinant of maximal thrombolytic benefit is the appropriate early administration of the drug, there have been relatively few studies that address how to reduce the door-to-needle time through an intervention. The Western Washington trials are the largest to date to examine the effect of a quality assurance program on the utilization of thrombolytic agents [8]. The authors compared the time to treatment during 1983–1986 to the time to treatment during 1987–1988 and demonstrated a reduction from an average of 97 minutes to 52 minutes with a program that streamlined the drug-delivery protocol and educated the staff in time-saving measures.

In a study of 24 patients in the emergency department at Hennepin County Medical Center, an average time from triage to treatment of 67 minutes was documented. By streamlining procedures for thrombolytic administration, the time to treatment fell to a mean of 30 minutes (range 17–44) in the nine subsequent patients studied [4]. Several community hospitals have also demonstrated a reduction in the time to treatment after a quality assurance program [16]. One recent report examined the impact of a quality assurance program in a community hospital in California that included physician and nurse education, feedback sessions, a mandate that treatment decisions be made by the emergency department physicians, and a team approach to bedside care [16]. The mean time from arrival in the emergency department to thrombolytic therapy was 63 minutes in 1988 and fell to 38 minutes by 1990 ($P < 0.0002$). Through a similar quality assurance program (see Table 1), we were able to reduce the time from initial triage to treatment by 10 minutes (~21%).

One might argue that prehospital thrombolytic treatment is the most efficient method of improving the timeliness of treatment for myocardial infarction, particularly in light of reports of in-hospital delays averaging 45–90 minutes, as noted earlier [4]. In support of this concept, the MITI trial demonstrated a time savings of 30 minutes with administration of prehospital thrombolysis [17]. However, in the MITI trial, only 5% of patients with chest pain were candidates for prehospital thrombolysis and hospital arrival was delayed by at least 15 minutes. Also, it is known that for hospitals with active emergency departments, less than 50% of patients with acute myocardial infarctions arrive by ambulance [4]. Recently, the American College of Emergency Physicians elected not to endorse the routine prehospital use of thrombolytic agents until further research proves its benefit. In particular, the college suggested the prehospital treatment was no substitute for unnecessary delays incurred within the emergency department [9].

It is unclear whether recommendations for reducing the door-to-needle time to less than 30 minutes are realistic [18]. As determined by a Medline review, there has not been a study in the United States that has achieved a mean time to treatment under 30 minutes for in-hospital evaluation and therapy. Cannon et al. mention a study in which the door-to-needle time was reduced from 76 minutes to 48 minutes after implementation of an acute myocardial infarction protocol; in the last 3 months of the study, a 29-minute average door-to-needle time trend was statistically significant [20]. Two studies outside the United States, one in New Zealand and the other in Scotland, were able to achieve a time to thrombolysis of less than or equal to 40 minutes. Porter et al. in New Zealand, through a staff education program to fast track the management of patients eligible for thrombolysis, demonstrated a decrease in the median door-to-needle time from 59 to 40 minutes [19]. Currie et al. in Scotland, through a similar audit that included staff education regarding thrombolysis guidelines, decreased the time to thrombolysis from a median of 55 minutes to 38 minutes [21]. In the United States, the series from Hennepin County [8] is the only study that was able to achieve a mean 30-minute door-to-needle time and that was only in nine patients. Our study is one of the few to achieve a door-to-needle time <40 minutes. As mentioned earlier, Cummings, using a similar quality assurance effort in a nonacademic community hospital was able to reduce the mean time from emergency department arrival to thrombolytic therapy from 63 to 38 minutes ($P < .002$) [16]. In a community hospital setting with a university affiliation, Anderson et al. implemented a quality improvement effort and decreased the mean time from arrival to thrombolytics from 93 ± 66 to 53.5 ± 43 minutes ($P < .001$) [22]. In a retrospective study using historical controls in a nonacademic setting, Krall and Reese noted after the implementation of a continuous quality improvement intervention, which included chart review, intensive systems analysis, and staff feedback, there was a reduction in the triage to thrombolytic time from 72 ± 25 to 40 ± 22 minutes [23].

Trends in usage of thrombolytic agents

This study suggests that conformity to megatrials may be a function of both physician education and immediate feedback regarding current institutional practice. Given the recent abstract in *Circulation* [24] reporting that physician practice often does not conform to published guidelines, or even the compelling evidence of the esteemed megatrial, this result is particulary interesting. Early trials of thrombolytic therapy, such as the European Cooperative study, suggested that t-PA resulted in greater patency of the infarct-related artery (IRA) at 90 minutes [25]. However, several subsequent megatrials, such as GISSI-2 (n = 20,891) [26] followed by ISIS-3 (n = 39,713) [27], demonstrated that no additional survival benefit was conferred by t-PA when compared with the less expensive agent, streptokinase.

In the spring of 1993, the results of the GUSTO trial [28] became available, demonstrating a mortality re-

duction of 14% when accelerated t-PA was used rather than streptokinase. Although the ISIS-3 trial (demonstrating comparable efficacy among streptokinase, anistreplase (APSAC), and t-PA) was published in the *Lancet* in March 1992, preliminary results were known and discussed in conferences with our house staff by December 1991 and were part of our ongoing quality assurance efforts. Using the method of comparing the patients treated during the first 2 years of implementing the quality assurance effort to the latter 2 years of the established program, our data happened to coincide with the advent of information regarding ISIS-3, allowing for a pre- and post-megatrial comparison. Similarly, preliminary results of the GUSTO trial, published in September of 1993, were available in the spring of 1993 and were shared with our myocardial infarction management teams.

In our study, the use of streptokinase increased from 1989–1991 to 1992–1994 (60–75%), after ISIS-3 was published ($P < .01$). When the 4-year period is divided into 6-month intervals, there was an increase in the use of streptokinase, trending toward statistical significance after the preliminary results of ISIS-3 became available in December 1991. This trend continued until the time interval in the spring of 1993, when the results of GUSTO become available and the use of t-PA increased (and that of streptokinase decreased). These data support the broadly held belief that large multicenter controlled trials have an almost immediate impact on practice behavior, perhaps particularly in large, urban, teaching institutions such as ours. At a time when cost effectiveness is an increasingly important consideration, understanding how megatrials impact physician practices has important implications for overall healthcare costs.

Conclusions

Thrombolytic therapy has dramatically altered the prognosis of patients with acute myocardial infarction. However, this survival benefit is dependent on the time interval from the inception of ischemia to the delivery of the thrombolytic agent. Clearly, a substantial component of the delay to treatment is attributable to the patient's delay in seeking medical attention. Thus intensive patient education has an important role in optimizing the benefits of thrombolytic agents. However, it has been demonstrated that the in-hospital delay is often greater than the interval from the onset of symptoms to arrival in the emergency department [4]. We believe that quality assurance programs in the emergency department can significantly decrease the critical time to thrombolytic therapy. This study of the effect of a relatively simple quality assurance program on the door-to-needle time in the emergency department of a major teaching hospital could serve as a model for others trying to achieve reductions in the time to treatment of appropriate patients.

Finally, our data add further evidence that reports of megatrials can rapidly and significantly influence clinical practice. This has profound implications for the costs of care for hospitals and underscores industry's preoccupation with megatrials.

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