Impact of a well-organized collaborative team approach on mortality in patients with ST-segment elevation myocardial infarction

İyi planlanmış ekip yaklaşımının ST-yükselmeli miyokart enfarktüslü hastaların mortalitesine etkisi

Yalın Tolga Yaylalı, İbrahim Susam, Akın Ateş[1], Dursun Dursunoğlu

Department of Cardiology, Faculty of Medicine, Pamukkale University, Denizli
[1]Servergazi State Hospital, Denizli, Turkey

Abstract

Objective: Fibrinolytic therapy remains a legitimate option for many patients presenting with acute ST-segment elevation myocardial infarction (STEMI). Shorter time- to- treatment for patients with STEMI administered fibrinolytic therapy has repeatedly been shown to reduce mortality. A well-organized collaborative team approach was implemented in April 2007. The purpose of this study was to examine the effect of implementing a well-organized collaborative team approach on the outcome in patients with acute STEMI treated with fibrinolysis.

Methods: Sociodemographic, clinical, laboratory, and time interval data were prospectively collected on 109 consecutive patients (the study group) and 155 patients from the years 2005–2007 (the control group) retrospectively. A single-phone call was made to discuss case. Emergency department evaluation was bypassed for definitive case. An electrocardiogram was faxed to the on-call cardiologist for suspected case. Door-to-needle times were calculated as medians. Mortality was assessed by reviewing records of all patients visiting outpatient clinic. For the rest, information was obtained over the phone. Median door-to-needle times were compared using Mann-Whitney U test. The Fisher's exact test was used to compare 6-month mortalities.

Results: Improvements were seen in door-to- needle times in the study group regardless of time of presentation (reduced from 59 minutes to 29 minutes during off hours) (reduced from 35 minutes to 18 minutes during regular hours) ($p<0.0001$). Mortality was significantly reduced in the study group (2 deaths, 1.8%) compared with the control group (12 deaths, 7.7%, $p=0.048$).

Conclusion: The mortality of patients presenting with acute STEMI treated with fibrinolytic therapy was significantly reduced after optimal hospital organization. *(Anadolu Kardiyol Derg 2010 December 1; 10(6): 508-13)*

Key words: ST-segment elevation myocardial infarction, mortality, well-organized collaborative team approach

Özet

Amaç: Bu çalışmanın amacı, etkin iyi planlanmış bir ekip yaklaşımının fibrinolitik tedavi almış akut ST-segment yükselmeli miyokart enfarktüslü (STEMİ) vakaların sağkalımına etkisini araştırmaktı.

Yöntemler: Fibrinolitik tedavi akut STEMI'lı olgularda akılcı bir seçenek olmaya devam etmektedir. Fibrinolitik tedavi alan STEMI'lı olguların kısa sürede tedaviye ulaşmalarının mortalitelerini azalttığı defalarca gösterilmiştir. Nisan 2007'de iyi planlanmış bir ekip yaklaşımı başlatıldı. Sosyodemografik, klinik, laboratuvar ve zaman ölçümleri gibi bilgiler 109 çalışma hastasında prospektif olarak, 2005-2007 yıllarından 155 kontrol hastasında retrospektif olarak toplandı. Olguyu tartışmak için tek telefon konuşması yapıldı. Acil değerlendirme kesin olgularda yapılmadı. Şüpheli olgularda EKG'ler kardiyoloğa fakslandı. Kapı-iğne zamanları medyan olarak hesaplandı. Mortalite oranları kliniğe kontrole gelen hastalarda kayıtlar incelenerek, diğer tüm hastalarda telefon görüşmeleri ile belirlendi. Kapı-iğne zamanları Mann-Whitney U testi ile karşılaştırıldı. Altı aylık mortaliteler Fischer'in tam testi ile karşılaştırıldı.

Bulgular: Çalışma grubunda kapı-iğne aralığı başvurma zamanından bağımsız anlamlı olarak azaldı (mesai dışında 59 dakikadan 29 dakikaya azaldı) (mesai içinde 35 dakikadan 18 dakikaya azaldı) ($p<0.0001$). Mortalite çalışma grubunda (2 ölüm, %1.8) kontrol grubu (12 ölüm, %7.7) ile karşılaştırıldığında anlamlı olarak azaldı ($p=0.048$).

Sonuç: Akut ST yükselmeli miyokart enfarktüsü ile başvuran ve fibrinolitik tedavisi uygulanan hastaların ölüm oranları optimal hastane planlaması ile azalmıştır. *(Anadolu Kardiyol Derg 2010 Aralık 1; 10(6): 508-13)*

Anahtar kelimeler: ST segment yükselmeli miyokart enfarktüsü, mortalite, iyi planlanmış ekip yaklaşımı

Address for Correspondence/Yazışma Adresi: Dr. Yalın Tolga Yaylalı, Department of Cardiology, Faculty of Medicine, Pamukkale University, 20070, Denizli, Turkey
Phone: +90 258 444 07 28/2175 Fax: +90 258 213 49 22 E-mail: yaylalimd@gmail.com

Accepted Date/Kabul Tarihi: 12.04.2010 **Available Online Date/Çevrimiçi Yayın Tarihi:** 05.11.2010

doi:10.5152/akd.2010.167

Introduction

Mortality from ST-segment elevation myocardial infarction (STEMI) remains high. Shorter time to reperfusion in patients with STEMI treated with fibrinolytic therapy is associated with better survival (1-4).

The rapid restoration of sustained patency of the infarct-related artery with low residual stenosis is the primary goal of treatment. This can be achieved by prompt use of either fibrinolytic therapy or primary angioplasty. Even in the Western world-wide application of a primary angioplasty strategy to the majority of patients with acute myocardial infarction (MI) is not feasible. Yet almost one-third of eligible patients is not given any reperfusion therapy at all (5). For many such patients, fibrinolytic therapy remains a legitimate option. Published guidelines recommend a goal of 30 minutes for presentation at the hospital to the administration of fibrinolytic therapy (door-to-needle time) (6). No contemporary report exists about state or university hospital performance in achieving this goal for time to reperfusion in Turkey. In addition, the relation between the time to treatment and optimal hospital organization, and its impact on outcome have not been well studied.

Accordingly, the aim of this report was to examine the clinical outcome after the implementation of a well-organized collaborative team approach in patients with acute MI treated with fibrinolysis.

Methods

Study design and patient's characteristics

Patients (n=109) who presented to Servergazi State Hospital with STEMI, received fibrinolytic therapy as the reperfusion strategy and were managed according to collaborative approach (since April 2007, see below) comprised the study group (prospective follow-up group). Patients presenting with ongoing chest pain of ≤12 h in duration with ECG criteria of ST-segment elevation ≥0.1 mm in two or more electrocardiographic leads were assigned to receive either streptokinase or tissue- plasminogen activator (t-PA). Patients presenting with uncomplicated inferior MI with onset of symptoms within 3 hours before the initiation of therapy had received streptokinase. All other patients had received t-PA. Patients with previous MI, prior coronary stenting or coronary artery bypass grafting (CABG), previous history of angina pectoris, chronic renal insufficiency, chronic obstructive pulmonary disease, stroke, Killip class >1, current smoking status, heart rate ≥120 bpm were excluded. Patients who had developed stroke, re-ischemia, reinfarction, or died during index hospitalization were also excluded. Electronic records of all patients who visited our outpatient clinic were reviewed. For all other patients, information was obtained by direct telephone interview with the patient or relative.

One hundred and fifty five patients with similar demographic and clinical characteristics who had been treated with fibrinolytic therapy between August 2005 and March 2007 served as controls (restrospective analysis group).

All patients had received aspirin, β blockers, angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers, and statins while at the hospital and after discharge unless they were not tolerated or contraindicated. Clopidogrel could only be given for a month after discharge due to government's reimbursement policies.

Collaborative team approach protocol (Fig. 1)

We implemented a protocol to improve timeliness of reperfusion therapy.

The protocol was implemented in April 2007 and included the following strategies: (1) single-phone call for the on-call cardiologist and the emergency room (ER) physician to discuss case; (2) bypassing of emergency department evaluation for definitive case; (3) Electrocardiograms were faxed to the on-call cardiologist for suspected case; (4) multiple consultations were avoided; (5) Coronary care unit (CCU) and ER staff were educated and trained by a cardiologist; (6) One of the elevators was assigned for emergency use only; (7) Transfer of patients carried out by the CCU personnel.

The time period from hospital arrival to time of therapy can be influenced readily by changes in hospital practice patterns (7). Our well-organized collaborative team approach is shown in Figure 1. A cardiologist had seen patients when asked during regular hours (8 AM to 5 PM Monday through Friday), and after a decision for pharmacologic reperfusion was made then the patient was admitted to the CCU. When 112 was contacted for a patient during off hours (5 PM to 8 AM and at weekends), and if there was no question regarding diagnosis after initial evaluation by 112 personnel or ER personnel, the patient was admitted to the CCU. Suspected cases were also brought to the ER by 112 for further evaluation, and ER physicians contacted the cardiologist on call. Electrocardiograms (ECG) were faxed to an off-site cardiologist's notebook for confirmation. Multiple consultations were avoided. Based on the discussion with a cardiologist, a decision for pharmacologic or catheter based therapy was made. In-hospital treatment delay has been shortened to ≈20-30 min by establishing special in-hospital structures (8). The CCU and ER staff were educated and trained specifically on ECG findings and treatment of acute STEMI. One of the elevators was assigned to emergency use only. The transfer of the patients was carried out by the CCU staff.

Before April 2007, the protocol strategies were not used routinely at Servergazi State Hospital. Patients who served as controls underwent emergency department evaluation. Multiple consultations were made. Some ER personnel were unaware of treatment delays associated with increased mortality in patients with STEMI treated with fibrinolytic therapy. Previously, ECGs

Anadolu Kardiyol Derg 2010 Aralık 1; 10(6): 508-13
doi:10.5152/akd.2010.167

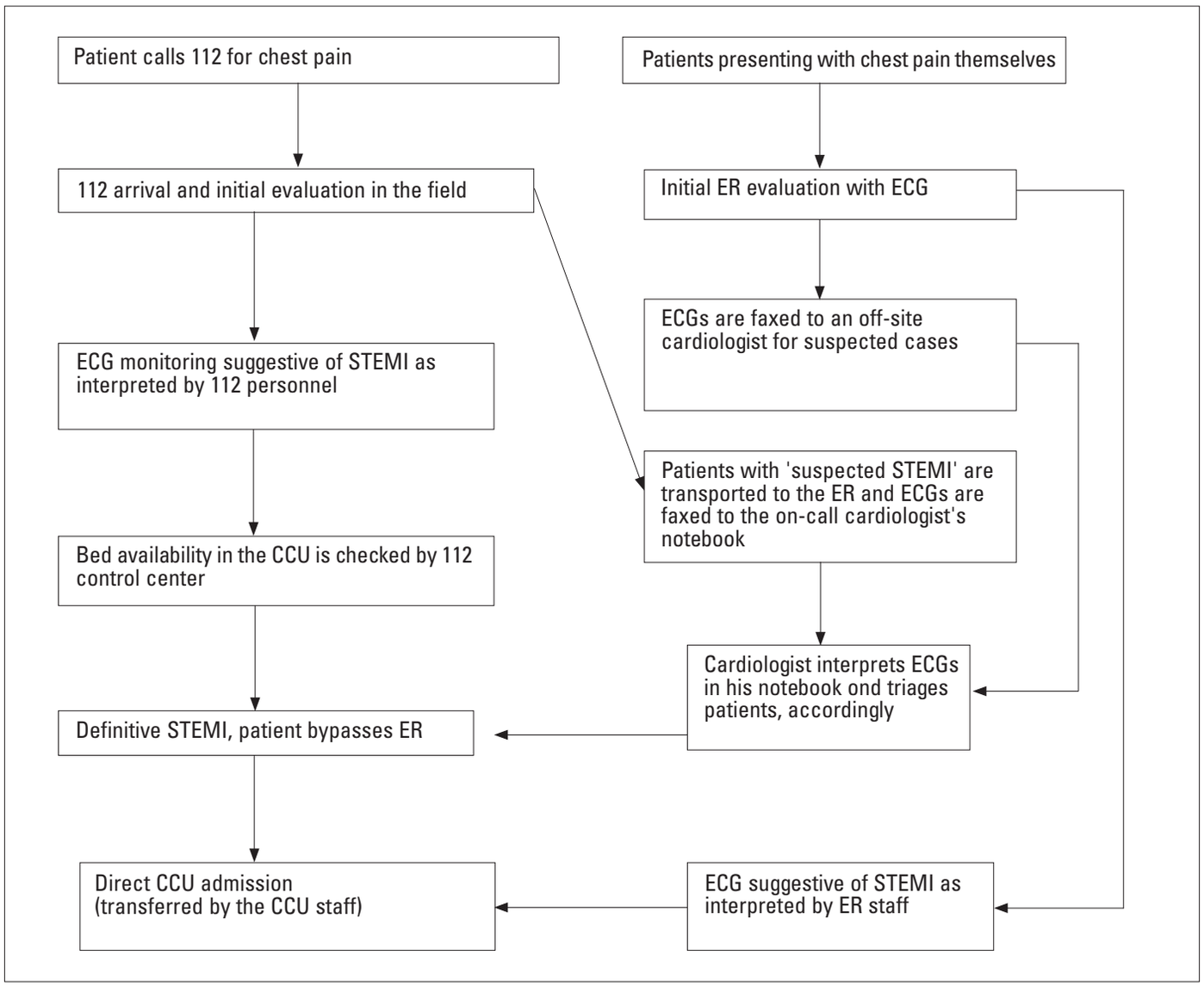

Figure 1. Schematic of optimal hospital organization

112 - emergency medical services, CCU - coronary care unit, ECG - electrocardiogram, ER - emergency room, STEMI - ST - elevation myocardial infarction

were faxed from the CCU instead of the ER. No elevator was assigned for emergency use only. Most patients were transferred to the CCU by busy ER staff. All of these had caused additional delays in time to treatment.

Data collection

Our main outcome measure was 6-month mortality. Data were obtained on all 264 patients admitted with STEMI and received fibrinolytic therapy. Time- to- treatment for fibrinolytic therapy was measured with door-to-needle (DTN) time. DTN time is the time in minutes between first hospital arrival and the delivery of reperfusion therapy. DTN times were calculated as medians. Patient demographic and clinical characteristics included sociodemographic variables (gender, age); medical history (hypertension, diabetes, dyslipidemia); the admission time of day (day, evening, or night); and admission day of week (weekday or weekend), the presence of chest pain, the location of myocardial infarction, the fibrinolytic agent used, the percentages of post-fibrinolytic TIMI-3 flow, and post-fibrinolytic CABG.

Angiographic data analysis

All angiograms were analyzed by an experienced interventional cardiologist blinded to all data apart from the coronary angiogram. TIMI (Thrombolysis In Myocardial Infarction) flow was assessed, as described previously (9).

Clinical outcomes

Records of all patients who visited our outpatient clinic were reviewed. For all other patients, information was obtained by direct telephone interview with the patient. At approximately 6 months after hospital discharge, patients were contacted to ascertain vital status.

Statistical analysis

Statistical analysis was conducted using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Median door-to-needle times in the control (pre-protocol) and the study (post-protocol) groups were compared using a Mann-Whitney U test. The Fisher's exact test was used to compare pre-protocol and post-protocol 6-month mortalities. Statistical significance was set at a level of $p<0.05$.

Results

The characteristics of the patients in the study group (n=109) and the control group (n=155) are displayed in Table 1. Both groups had similar ages and similar percentages of men, hypertension, diabetes, dyslipidemia, chest pain, and anterior wall infarctions on presentation, the use of streptokinase as the fibrinolytic agent, and similar percentages of TIMI-3 flow restoration, and the need for coronary artery bypass grafting. Time interval measurements according to time of day are presented in Table 2. For groups the study and the control, median (25th and 75th percentiles) door-to-needle times were 29 (19, 37) and 59 (31, 93) minutes during off hours ($p<0.0001$); 18 (12, 26) and 35 (22, 74) minutes during regular hours ($p<0.0001$), respectively.

Mortality was significantly reduced in the study group (2 deaths, 1.8%) compared with the control group (12 deaths, 7.7%, $p=0.048$) (Table 1).

Table 1. Clinical characteristics of the patient groups

Variables	Control Subjects (n=155)	Study Subjects (n=109)	p*
Demographics			
Age, years	60.71±11.33 (33-74)	63.54±7.55 (36-77)	NS
Men, n (%)	131 (85)	88 (81)	NS
Medical history			
Hypertension, n (%)	55 (35)	40 (37)	NS
Diabetes, n (%)	46 (30)	30 (28)	NS
Dyslipidemia, n (%)	26 (17)	22 (20)	NS
Presentation			
Chest pain, n (%)	147 (95)	101 (93)	NS
Anterior location, n (%)	77 (50)	52 (48)	NS
Fibrinolytic agent			
Streptokinase, n (%)	7 (4.5)	6 (5.5)	NS
Post-fibrinolytic			
TIMI-3 flow, n (%)	62 (40)	43 (39)	NS
Post-fibrinolytic			
CABG, n (%)	54 (35)	39 (36)	NS
Death at 6 months, n (%)	12 (7.7)	2 (1.8)	0.048

Values are given as numbers/percentages or means±SD (range)
*Mann-Whitney-U test and Fisher's exact test
CABG - coronary artery bypass grafting, NS - nonsignificant, TIMI - thrombolysis in myocardial infarction

Table 2. Time-to- treatment according to the time of the day

Variables	Study subjects (n=109)	Control subjects (n=155)	p*
Off hours, min (25th, 75th percentiles), n	29 (19.37) (n=79)	59 (31.93) (n=106)	<0.0001
Regular hours, min (25th, 75th percentiles), n	18 (12.26) (n=30)	35 (22.74) (n=49)	<0.0001

Values are given as medians (25th, 75th percentiles).
Off hours: 5 PM to 8 AM and at weekends; regular hours: 8 am to 5 pm Monday-Friday.
*Mann-Whitney-U test

Discussion

The principal novel finding of this study was that by reducing time to treatment with the implementation of a well-organized in-hospital pharmacological reperfusion strategy, we have positively influenced our patients' outcomes.

Treatment with fibrinolytic therapy remains the most common mode of reperfusion for patients presenting with STEMI (10, 11). Yet fibrinolytic therapy is a missed opportunity for many patients, especially those in rural areas, requiring long transportation times to the referral hospitals. Fibrinolytic agents are most effective when administered within 2 to 3 hours from symptom onset (12-15) with longer treatment delays leading to worse clinical outcomes (16). Because it requires at least an additional 30-45 minutes from the beginning of treatment until successful vessel reperfusion (17). Time-to-treatment for STEMI are still prolonged. Throughout the last decade, time-to-treatment remained unchanged for patients treated with fibrinolysis (18). Infarct size is significantly affected by the duration of coronary occlusion (19-21). Therefore, late reperfusion is expected to result in less myocardial salvage and a higher mortality rate. De Luca et al. (22) found that patients with successful reperfusion had a significantly shorter ischemic time. Early reperfusion with fibrinolytic therapy in patients with evolving acute myocardial infarction (MI) has been clearly demonstrated to reduce mortality and salvage myocardium (23). Early and sustained patency of the infarct-related artery has been related to improved in-hospital and late survival (24, 25), recovery of left ventricular function (24, 26-28), prevention of ventricular aneurysm formation (29), and cardiac rupture (30), and enhanced electrical stability (31). In addition, previous studies have demonstrated that only the acute restoration of TIMI grade 3 flow, present in ≈50% to 60% of vessels after fibrinolysis, is independently predictive of in-hospital survival and reduction in infarct size (26, 32, 33). It has been demonstrated that treatment delays with fibrinolytic therapy were associated with higher 6-month mortality in patients with STEMI receiving reperfusion therapy.

Anadolu Kardiyol Derg 2010 Aralık 1; 10(6): 508-13
doi:10.5152/akd.2010.167

Our study showed that mortality was significantly reduced in the study group compared with the control group after the initiation of an optimal hospital organization. There was a significant reduction in DTN times after the introduction of the protocol. These included earlier transfer of fibrinolytic eligible patients from the field to the coronary care unit equipped for such therapy with an experienced staff, single-call activation of the CCU, and a well-organized team-based approach with direct routing of patients to the CCU. These measures are consistent with the strategies articulated by the door-to-treatment time workgroup (34). In addition, by earlier notification of a cardiologist, unnecessary multiple consultations were avoided. Emergency room and CCU personnel were specifically trained. All these measures helped reduce time to treatment consistent with a previous report, which showed that in-hospital delay has been shortened by establishing special in-hospital structures (8). Thus, one explanation for our finding is a greater extent of early myocardial salvage as the result of a shorter time to treatment. In an animal study, it has been shown that the final infarct size is very sensitive to the duration of ischemia before reperfusion (20). The ischemia time to recanalization also affects the severity of microvascular damage (35). It has also been shown that there was a progressive decline in the extent of myocardium salvaged as the interval between symptoms and therapy increased (36). Earlier treatment that improves myocardial (microvascular) reperfusion might have enhanced our patients' survival.

Thus, all efforts should be made to shorten total ischemic time. Coordinated efforts among community services, hospitals, and physicians will be necessary to achieve the goal of shortening time to treatment. Organizational culture, physician leadership, interrelationship between cardiology and emergency physicians and staff, emergency medical systems, and administrative support need to be identified and used by hospitals for performance improvement programs to decrease door-to-needle and decrease mortality from STEMI. Resources should be directed to early recognition of the acute myocardial infarction, improved utilization of emergency services for transportation, and prehospital diagnosis and triaging. The literature would suggest that prehospital 12-lead electrocardiogram and advanced emergency department notification reduces in hospital time to fibrinolysis (37). McNamara et al. (11) found that improving time to fibrinolytic therapy could have an important effect on improving survival rates for patients presenting with STEMI. Our results also further highlight the importance of reducing the time delay between symptom onset and the initiation of thrombolytic therapy in patients with AMI. Meaningful reductions in fibrinolytic treatment times can be achieved with a better organization at an institutional level. Moreover, this could translate into better patient outcomes.

Study limitations

Several limitations of this study should be mentioned. Its limited sample size is one of the weaknesses of the study. Information was obtained by direct telephone interview with patients who had not visited our outpatient clinic. Thus, we largely relied on their recollection for the events. Time to treatment was calculated from when the patient was first registered with the front desk in the ER to the initiation of fibrinolytic therapy in the CCU. Sometimes registration took place after patients' transfer from the ER. Some patients might have discontinued their medications (beta- blockers, ACE-Is, statins) for some reason against our advice.

Conclusion

We implemented a protocol and achieved door-to-needle times that were close to what is recommended in the guidelines. We showed that mortality of patients presenting with STEMI was significantly reduced after a well-organized collaborative team approach has been implemented. We demonstrated that novel and simple strategies and coordination of systems of care make these times achievable and improve patients' outcomes. Since fibrinolytic therapy remains the most accessible therapy for such patients, a well-organized collaborative team approach can be broadly applied to decrease their mortality.

Acknowledgements

The authors thank the physicians (Dr. Mustafa Ölçek, Dr. M. Ali Abdüloğlu, Dr. Zeki Gürlesin) and nurses (Ms. Hatice Arman, Ms. Banu Yıldırım, Ms. Gülfidan Düzgün, Ms. Sibel Kadıoğlu, Ms. Selda Kiraz) for participating in the project and assistance with data collection.

Conflict of interest: None declared.

References

1. Berger AK, Radford MJ, Krumholz HM. Factors associated with delay in reperfusion therapy in elderly patients with acute myocardial infarction: analysis of the cooperative cardiovascular project. Am Heart J 2000; 139: 985-92.
2. Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV, et al. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). Am J Cardiol 1998; 82: 259-64.
3. Zijlstra F, Patel A, Jones M, Grines CL, Ellis S, Garcia E, et al. Clinical characteristics and outcome of patients with early (<2 h), intermediate (2-4 h) and late (>4 h) presentation treated by primary coronary angioplasty or thrombolytic therapy for acute myocardial infarction. Eur Heart J 2002; 23: 550-7.
4. Gibson CM, Murphy SA, Kirtane AJ, Giugliano RP, Cannon CP, Antman EM, et al. Association of duration of symptoms at presentation with angiographic and clinical outcomes after fibrinolytic therapy in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol 2004; 44: 980-7.
5. Barron HV, Bowlby LJ, Breen T, Rogers WJ, Canto JG, Zhang Y, et al. Use of reperfusion therapy for acute myocardial infarction in the United States: data from the National Registry of Myocardial Infarction 2. Circulation 1998; 97: 1150-6.
6. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with

ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). Circulation 2004; 110: 588-636.
7. Shry EA, Eckart RE, Winslow JB, Rollefson WA, Simpson DE. Effect of monitoring of physician performance on door-to-balloon time for primary angioplasty in acute myocardial infarction. Am J Cardiol 2003; 91: 867-9.
8. MacCallum AG, Stafford PJ, Jones C, Vincent R, Perez-Avila C, Chamberlain DA. Reduction in hospital time to thrombolytic therapy by audit of policy guidelines. Eur Heart J 1990; 11: 48-52.
9. Chesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: A comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987; 76: 142-54.
10. Rogers WJ, Bowlby LJ, Chandra NC, French WJ, Gore JM, Lambrew CT, et al. Treatment of myocardial infarction in the United States (1990 to 1993). Observations from the National Registry of Myocardial Infarction. Circulation 1994; 90: 2103-14.
11. McNamara RL, Herrin J, Bradley EH, Portnay EL, Curtis JP, Wang Y, et al. Hospital improvement in time to reperfusion in patients with acute myocardial infarction, 1999 to 2002. J Am Coll Cardiol 2006; 47: 45-51.
12. Kalla K, Christ G, Karnik R, Malzer R, Norman G, Prachar H, et al. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). Circulation 2006; 113: 2398-405.
13. Fernandez-Avilés F, Alonso JJ, Castro-Beiras A, Vázquez N, Blanco J, Alonso-Briales J, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. Lancet 2004; 364: 1045-53.
14. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation 2003; 108: 2851-6.
15. Widimsky P, Budesínsky T, Vorác D, Groch L, Zelízko M, Aschermann M, et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial-PRAGUE-2. Eur Heart J 2003; 24: 94-104.
16. Newby LK, Rutsch WR, Califf RM, Simoons ML, Aylward PE, Armstrong PW, et al. Time from symptom onset to treatment and outcomes after thrombolytic therapy. GUSTO-1 Investigators. J Am Coll Cardiol 1996; 27: 1646-55.
17. Collen D. Thrombolytic therapy. Thromb Haemost 1997; 78: 742-6.
18. Barbagelata A, Perna ER, Clemmensen P, Uretsky BF, Canella JP, Califf RM, et al. Time to reperfusion in acute myocardial infarction. It is time to reduce it! J Electrocardiol 2007; 40: 257-64.
19. Flameng W, Lesaffre E, Vanhaecke J. Determinants of infarct size in non-human primates. Basic Res Cardiol 1990; 85: 392-403.
20. Reimer KA, Vander Heide RS, Richard VJ. Reperfusion in acute myocardial infarction: effect of timing and modulating factors in experimental models. Am J Cardiol 1993; 72: 13G-21G.
21. Garcia-Dorado D, Théroux P, Elizaga J, Galiñanes M, Solares J, Riesgo M, et al. Myocardial reperfusion in the pig heart model: infarct size and duration of coronary occlusion. Cardiovasc Res 1987; 21: 537-44.
22. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation 2004; 109: 1223-5.
23. Wilcox RG, von der Lippe G, Olsson CG, Jensen G, Skene AM, Hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction. Anglo-Scandinavian Study of Early Thrombolysis (ASSET). Lancet 1988; 2: 525-30.
24. O'Keefe JH Jr, Rutherford BD, McConahay DR, Ligon RW, Johnson WL Jr, Giorgi LV, et al. Early and late results of coronary angioplasty without antecedent thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1989; 64: 1221-30.
25. Kennedy JW, Ritchie JL, Davis KB, Stadius ML, Maynard C, Fritz JK. The western Washington randomized trial of intracoronary streptokinase in acute myocardial infarction. A 12-month follow-up report. N Engl J Med 1985; 312: 1073-8.
26. Topol EJ, Califf RM, George BS, Kereiakes DJ, Lee KL. Insights derived from the thrombolysis and angioplasty in myocardial infarction (TAMI) trials. J Am Coll Cardiol 1988; 12: 24A-31A.
27. Rothbaum DA, Linnemeier TJ, Landin RJ, Steinmetz EF, Hillis JS, Hallam CC, et al. Emergency percutaneous transluminal coronary angioplasty in acute myocardial infarction: a 3-year experience. J Am Coll Cardiol 1987; 10: 264-72.
28. Stack RS, Califf RM, Hinohara T, Phillips HR, Pryor DB, Simonton CA, et al. Survival and cardiac event rates in the first year after emergency coronary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1988; 11: 1141-9.
29. Hochman JS, Choo H. Limitation of myocardial infarct expansion by reperfusion independent of myocardial salvage. Circulation 1987; 75: 299-306.
30. Gertz SD, Kalan JM, Kragel AH, Roberts WC, Braunwald E. Cardiac morphologic findings in patients with acute myocardial infarction treated with recombinant tissue plasminogen activator. Am J Cardiol 1990; 65: 953-61.
31. Brugada P, Waldecker B, Kersschot Y, Zehender M, Wellens HJ. Ventricular arrhythmias initiated by programmed stimulation in four groups of patients with healed myocardial infarction. J Am Coll Cardiol 1986; 8: 1035-40.
32. Vogt A, von Essen R, Tebbe U, Feuerer W, Appel KF, Neuhaus KL. Impact of early perfusion status of the infarct-related artery on short-term mortality after thrombolysis for acute myocardial infarction: retrospective analysis of four German multicenter studies. J Am Coll Cardiol 1993; 21: 1391-5.
33. Karagounis L, Sorensen SG, Menlove RL, Moreno F, Anderson JL. Does thrombolysis in myocardial infarction (TIMI) perfusion grade 2 represent a mostly patent artery or a mostly occluded artery? Enzymatic and electrocardiographic evidence from the TEAM-2 study. Second Multicenter Thrombolysis Trial of Eminase in Acute Myocardial Infarction. J Am Coll Cardiol 1992; 19: 1-10.
34. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. N Engl J Med 2006; 355: 2308-20.
35. Kondo M, Nakano A, Saito D, Shimono Y. Assessment of "microvascular no-reflow phenomenon" using technetium-99m macroaggregated albumin scintigraphy in patients with acute myocardial infarction. J Am Coll Cardiol 1998; 32: 898-903.
36. Raitt MH, Maynard C, Wagner GS, Cerqueira MD, Selvester RH, Weaver WD. Relation between symptom duration before thrombolytic therapy and final myocardial infarct size. Circulation 1996; 93: 48-53.
37. Morrison LJ, Brooks S, Sawadsky B, McDonald A, Verbeek PR. Prehospital 12-lead electrocardiography impact on acute myocardial infarction treatment times and mortality: a systematic review. Acad Emerg Med 2006; 13: 84-9.