Door to Balloon and Door to Needle: Temporal Trends in Delays to Reperfusion

Arik Wolak MD, Harel Gilutz MD, Guy Amit MD, Carlos Cafri MD, Reuben Ilia MD and Doron Zahger MD

Department of Cardiology, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

Key words: ST elevation, myocardial infarction, thrombolysis, primary percutaneous coronary intervention, time delay

Abstract

Background: Reperfusion practices have changed markedly over the last few years with the introduction of primary percutaneous coronary intervention. This technique has gained growing popularity in Israel, but little published data are available regarding the delays to primary PCI in real life in this country.

Objectives: To examine temporal trends in time to reperfusion achieved in a large tertiary center over 6 years.

Results: Between 1997 and 2002, 1,031 patients were admitted to our hospital with ST elevation myocardial infarction. Of these, 62% underwent thrombolysis and 38% primary PCI. The proportion of patients referred for primary PCI increased steadily, from 14% in 1997 to 68% in 2002. Door to treatment time among patients referred for thrombolysis or primary PCI was 54 $\pm$ 42 and 117 $\pm$ 77 minutes, respectively ($P < 0.00001$). The door to needle time in patients given thrombolysis remained virtually unchanged during the study period at around 54 minutes. In contrast, the door to balloon time progressively and substantially decreased, from 175 $\pm$ 164 minutes in 1997 to 96 $\pm$ 52 minutes in 2002.

Conclusions: There is a steady increase in the proportion of patients referred for primary PCI than for thrombolysis. The door to needle delay in patients given thrombolysis substantially exceeds the recommended time. The door to balloon time has declined considerably but still slightly exceeds the recommended time. Given the inherent delay between initiation of lysis and arterial recanalization, it appears from our experience that PCI does not substantially delay arterial reperfusion as compared to thrombolysis. Efforts should continue to minimize delays to reperfusion therapy.

IMAJ 2003;5:852–855

Reperfusion practices for ST segment elevation myocardial infarction have changed over the last few years with the introduction of primary percutaneous coronary intervention. Available evidence points toward a greater benefit from catheter-based intervention as compared to pharmacologic reperfusion [1–5]. Current guidelines identify primary PCI as a reperfusion modality that is either equivalent [6] or even superior to thrombolysis [7], provided it can be performed in a timely manner by an experienced team. According to current guidelines, in-hospital delays to thrombolysis and primary PCI should not exceed 30 minutes and 60–90 minutes, respectively. The superiority of primary PCI over thrombolysis depends heavily on time to balloon delays [8,9]. Adoption of a primary PCI strategy for ST elevation MI may not be beneficial, and may even be harmful, if door to balloon delays exceed 60–90 minutes. It is therefore extremely important to assess whether in any given setting the door to balloon delays achieved in real life are acceptable.

Primary PCI has gained growing popularity in Israel over the last few years, but little published data are available regarding the delays to primary PCI in real life in this country. We therefore examined the trends in time to reperfusion achieved in a large tertiary center over 6 years.

Patients and Methods

We retrospectively reviewed the charts of all consecutive patients with ST segment elevation MI admitted to our Coronary Care Unit between 1997 and 2002. Patients were included if they had ischemic type chest discomfort accompanied by ST segment elevation or new, or presumably new, left bundle branch block as well as elevated cardiac markers. Patients who did not receive reperfusion therapy were excluded. Primary angioplasty was available at all times; outside normal working hours it was performed by an on-call team that was summoned from home as needed. Patients were referred for thrombolysis or primary angioplasty at the discretion of the attending physician. Thrombolytic therapy was given in the CCU. The clock time of pain onset, hospital arrival, CCU admission and initiation of reperfusion therapy were routinely recorded for each patient. We compared patients given thrombolysis with those treated by primary PCI in terms of age, gender, Killip class on admission, time of day of admission, and time interval from Emergency Department admission to either thrombolytic therapy or primary PCI (door to needle and door to balloon time, respectively). Daytime hours were defined as 08:00 hours to 16:00 hours and the rest of the day was defined as nighttime.

Statistical analysis

Results are expressed as mean $\pm$ SD. Proportions were compared using chi-square statistics. Simple linear regression was used to test the association between continuous variables. The differences were calculated using Student's *t*-test. To assess the associations between multiple variables ANOVA was used. The level of significance was 0.05. Analysis was performed with WinSTAT 2001.1 software.

PCI = percutaneous coronary intervention
MI = myocardial infarction

CCU = Coronary Care Unit

Results

Altogether, 1,031 patients were admitted to our hospital with ST segment elevation MI and were given reperfusion therapy during the study period. Of these, 637 (62%) received thrombolysis and 394 (38%) underwent primary angioplasty. Table 1 describes the patients' characteristics. Patients' age was 60 ± 13 years and did not change significantly during the study period. The Killip score on admission was 1.3 ± 0.7, and it increased gradually and significantly from 1.2 ± 0.6 in 1997 to 1.5 ± 0.9 in 2002

Table 1. Baseline characteristics

	Thrombolysis (n=637)	Primary PCI (n=394)	*P* value
Age (mean ± SD)	59±12	62±14	<0.01
Males (%)	79	78	NS
Dyslipidemia (%)	54	50	NS
Hypertension (%)	44	51	<0.05
Current smoking (%)	45	38	<0.05
Diabetes mellitus (%)	24	25	NS
Killip score (mean ± SD)	1.2±0.5	1.6±0.9	<0.05

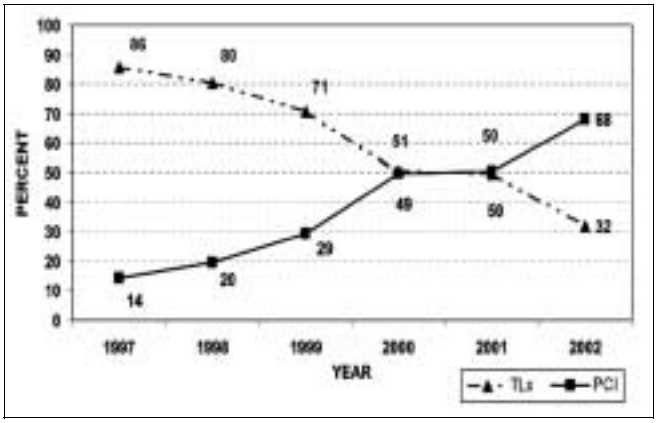

Figure 1. Trends in selection of reperfusion strategy (thrombolytic therapy and primary PC) during the 6 years of the study. TLx = thrombolysis.

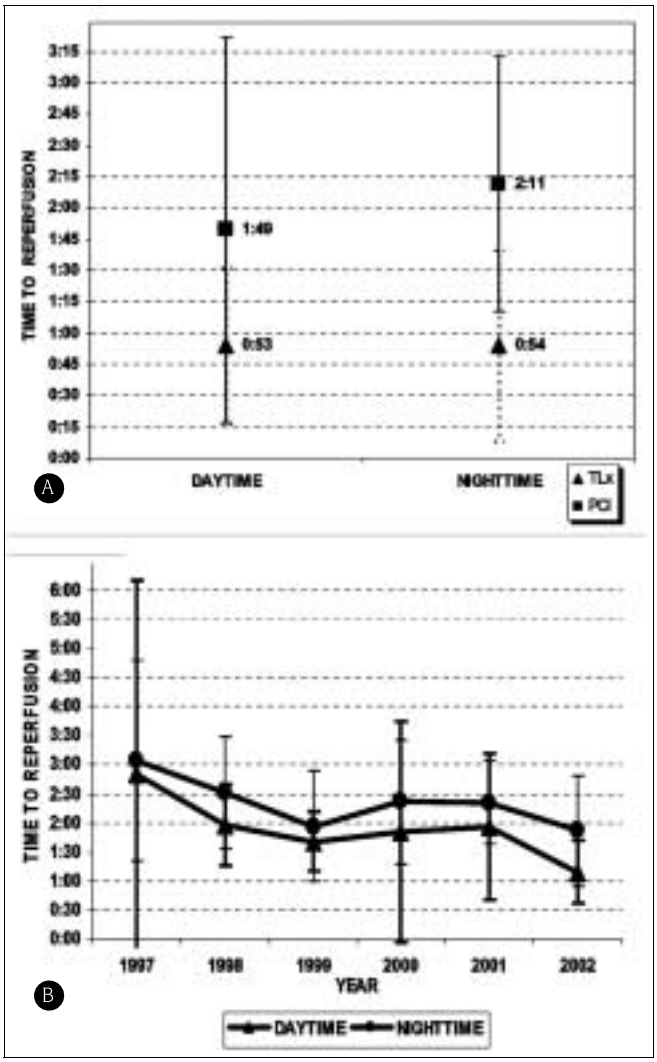

Figure 3. [A] Overall time to reperfusion (h:mm) for thrombolytic therapy and primary PCI during daytime vs. nighttime. **[B]** Time to balloon (h:mm) for daytime and nighttime during the 6 years of the study.

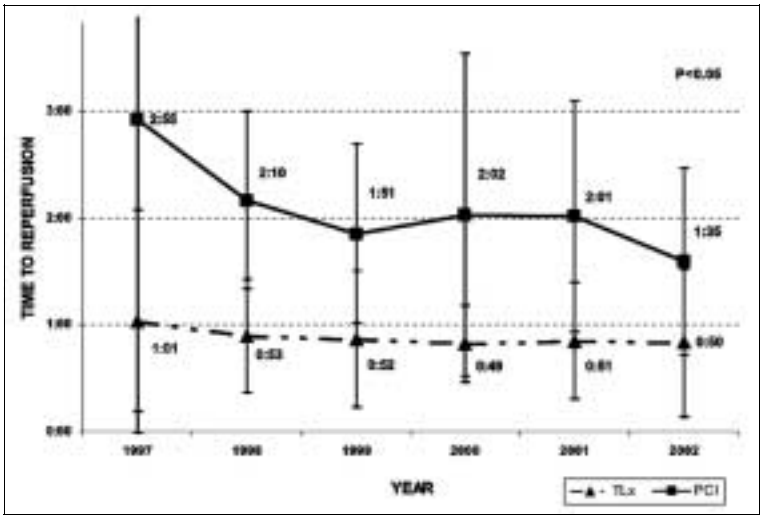

Figure 2. Trends in time to reperfusion (h:mm) for thrombolytic therapy and primary PCI during the 6 years of the study.

(*P* < 0.05). Patients referred for primary PCI had a higher Killip score than those given thrombolysis [Table 1]. The proportion of ST segment elevation patients referred for primary PCI among those given reperfusion therapy increased steadily from 14% in 1997 to 68% in 2002 [Figure 1]. The onset of pain to hospital arrival times for patients referred for thrombolysis or PCI was 181 ± 286 minutes and 225 ± 275 minutes, respectively. Door to treatment times among patients referred for thrombolysis or PCI were 54 ± 42 and 117 ± 77 minutes, respectively (*P* < 0.00001). Examination of temporal trends revealed that the door to needle time in patients given thrombolysis remained almost unchanged during the study period at around 54 minutes. In contrast, the door to balloon time has progressively and substantially decreased, from 175 ± 164 minutes in 1997 to 96 ± 52 in 2002 (*P* < 0.05) [Figure 2]. Door to needle time was longer in females than in males (63 ± 45 vs. 52 ± 41 minutes, respectively,

P = 0.01). In contrast, the door to balloon time for females and males was not statistically different (111 ± 42 and 119 ± 23 minutes, respectively, not significant). The comparison of patients treated during daytime vs. nighttime revealed that door to needle time was unaffected (53 ± 37 vs. 54 ± 46 minutes, respectively, $P <$ NS) but door to balloon time was shorter during daytime than during nighttime (109 ± 92 vs. 131 ± 61 minutes, respectively, P 0.005) [Figure 3A]. The progressive decrease in door to balloon time was observed over the years both during daytime and during nighttime [Figure 3B].

Discussion

The use of thrombolytic agents for reperfusion of occluded coronary arteries in ST-segment elevation acute MI is well established. Early, complete and sustained restoration of blood flow reduces infarct size and improves ventricular function and survival. During recent years primary angioplasty has emerged as the reperfusion modality of choice, but it requires an expert team and is heavily dependent, as is pharmacologic reperfusion, on minimizing the time delays to treatment [10].

There are little published data on the "real life" situation in Israel in terms of time delays to reperfusion and recent temporal trends in reperfusion. Examination of these trends is important to assess whether the growing use of primary PCI has been accompanied by sufficient attention to minimizing time delays to treatment in consecutive, unselected patients.

We found a steady increase in the proportion of patients referred for primary angioplasty rather than thrombolysis, and this modality is currently used in most patients presenting to our center with ST-elevation MI. Preliminary data from the Israeli nationwide ACSIS survey conducted during 2000 and 2002 suggest that this trend parallels that found in the country as a whole. This survey found that the proportion of patients referred for primary PCI among those given reperfusion therapy increased from 20% in 2000 to 43% in 2002 [11,12]. The increase in the utilization of primary PCI can probably be explained by increased familiarity with the modality, by the accumulating evidence pointing to the superiority of primary angioplasty over thrombolysis, and by improvements in technique and adjunctive medications [13–16].

The time from symptom onset to coronary reperfusion comprises three intervals: from symptom onset to admission, from admission to initiation of reperfusion therapy, and from the latter to arterial recanalization. We found that the first time interval was 44 minutes longer in patients referred for PCI, probably reflecting selection of relatively late arriving patients for PCI. The second interval reflects the system's response, efficiency and expertise. In patients given pharmacologic reperfusion, the third interval depends on the patient's response to thrombolysis. Typically, only about 25–30% of patients achieve normal epicardial flow within 90 minutes after initiation of streptokinase thrombolysis. With primary PCI the third interval is usually brief.

Our data indicate a considerable and significant decline in the door to balloon time from 175 ± 164 minutes in 1997 to 96 ± 52 minutes in 2002, such that the additional delay involved in PCI compared to thrombolysis is now about 45 minutes. This encouraging finding probably reflects efforts made over the years to minimize time delays. It is also conceivable that as experience with the procedure grew and primary PCI became routine, the decision process became shorter. Another two recently published registries reported similar time delays: the Euro Heart Survey and the Global Registry of Acute Coronary Events (GRACE) found median time delays from arrival in the emergency department to first balloon inflation of 93 and 111 minutes, respectively [17,18].

We observed longer door to balloon times during nighttime as compared to daytime. The time delay during nighttime exceeds the desired standard mentioned above. Nevertheless, a progressive trend toward shortening of the time delay during nighttime was also noted [Figure 3B]. We observed a significantly longer time to needle in women as compared to men, a finding that corresponds with previous studies [19]. For patients undergoing primary PCI we found no significant gender difference, which is in contrast to ACSIS 2002 which found a significantly shorter time delay for primary PCI in men (83 and 127 minutes respectively).

The observed door to needle delay in patients given thrombolysis, while substantially exceeding the recommended 30 minutes, is very similar to that observed in "real life" in other registries [10,20]. This delay is in contrast with controlled clinical trials in which much shorter delays to treatment were achieved [21–23]. Nationwide data from Israel in 2002 indicate similar delays to thrombolysis (a median door to needle delay of 54 minutes for men and 53 minutes for women) [12]. In contrast, the recently published European Heart Survey of acute coronary syndromes reported a median delay of only 40 minutes from arrival in the emergency department to initiation of fibrinolytic therapy [17]. This observation underscores the need to maintain efforts to minimize time delays to reperfusion in this country. A quality improvement project performed in our institution during 1995–1996 achieved a significant reduction in the door to needle time from 62 ± 33 to 48 ± 19 minutes, primarily due to decreasing door to decision and decision to drug times. [24]. We and others [25] believe that the arbitrary goal of 30 minutes for door to needle time is appropriate for the simple, straightforward patient. On the other hand, when there is a need for consultation or when it is unclear whether to administer thrombolytic therapy or perform primary angioplasty (e.g., when the catheterization laboratory is not immediately available), a door to needle delay of 45–60 minutes is still acceptable.

Conclusions

The present study demonstrates the evolution of reperfusion therapy during recent years and the gradual shift from thrombolysis to primary PCI in a large tertiary medical center. We found that door to needle times have remained remarkably stable during recent years, while the time required to perform primary PCI has progressively decreased. Given the mandatory delay between initiation of lysis and arterial reperfusion, it appears from our experience that PCI does not substantially delay arterial recanalization as compared to thrombolysis. The delays we observed in time to reperfusion, both for thrombolysis and for primary PCI, exceed current recommendations. Efforts should continue to minimize delays to reperfusion therapy with both modalities.

References

1. Zijlstra F, Hoorntje JC, de Boer MJ, et al. Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 1999;341(19):1413–19.
2. Grines CL, Westerhausen DR Jr, Grines LL, et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. *J Am Coll Cardiol* 2002;39(11):1713–19.
3. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13–20.
4. Widimsky P, Budesinsky T, Vorac D, 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(1):94–104.
5. Grines C, Patel A, Zijlstra F, Weaver WD, Granger C, Simes RJ. Primary coronary angioplasty compared with intravenous thrombolytic therapy for acute myocardial infarction: six-month follow up and analysis of individual patient data from randomized trials. *Am Heart J* 2003; 145(1):47–57.
6. Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999; 34(3):890–911.
7. Van de Werf F, Ardissino D, Betriu A, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. *Eur Heart J* 2003;24(1):28–66.
8. Cannon CP, Gibson CM, Lambrew CT, et al. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000;283(22):2941–7.
9. Berger PB, Bell MR, Holmes DR Jr, Gersh BJ, Hopfenspirger M, Gibbons R. Time to reperfusion with direct coronary angioplasty and thrombolytic therapy in acute myocardial infarction. *Am J Cardiol* 1994;73(4):231–6.
10. Tiefenbrunn AJ, Chandra NC, French WJ, Gore JM, Rogers WJ. Clinical experience with primary percutaneous transluminal coronary angioplasty compared with alteplase (recombinant tissue-type plasminogen activator) in patients with acute myocardial infarction: a report from the Second National Registry of Myocardial Infarction (NRMI-2). *J Am Coll Cardiol* 1998;31(6):1240–5.
11. Behar S, Battler A, Porath A, et al., for the Israel Heart and Internal Medicine Societies. A prospective national survey of management and clinical outcome of acute myocardial infarction in Israel, 2000. *IMAJ* 2003;5:249–54.
12. The Working Group on Intensive Cardiac Care of the Israel Heart Society. Israel Center for Disease Control PN, April 2003. (The Israel Society for the Prevention of Heart Attacks, the Israel Center for Disease Control of the Ministry of Health.). ACSIS 2002 (Acute Coronary Syndromes – Israel 2002), National Survey, February-March 2002, Preliminary Findings. 2003 April 2003. Report No. 230.
13. Schomig A, Kastrati A, Dirschinger J, et al. Coronary stenting plus platelet glycoprotein IIb/IIIa blockade compared with tissue plasminogen activator in acute myocardial infarction. *N Engl J Med* 2000; 343(6):385–91.
14. Loubeyre C, Morice MC, Lefevre T, Piechaud JF, Louvard Y, Dumas P. A randomized comparison of direct stenting with conventional stent implantation in selected patients with acute myocardial infarction. *J Am Coll Cardiol* 2002;39(1):15–21.
15. Montalescot G, Barragan P, Wittenberg O, et al. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. *N Engl J Med* 2001;344(25):1895–903.
16. Goldman L. Cost and quality of life: thrombolysis and primary angioplasty. *J Am Coll Cardiol* 1995;25(7 Suppl):38–41S.
17. Hasdai D, Behar S, Wallentin L, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J* 2002;23(15):1190–201.
18. Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol* 2002;90(4):358–63.
19. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. Assessment of the safety and efficacy of new thrombolytic investigators. *Lancet* 1999;354:716–22.
20. Every N WW, Parsons L, Martin JS, for the MITI Project Investigators. Direct PTCA vs thrombolysis: immediate and one year outcome and procedure utilization for the two treatment strategies [Abstract]. *Circulation* 1995;92(Suppl I):I–138.
21. Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. *N Engl J Med* 1993;328(10):673–9.
22. de Boer MJ, Hoorntje JC, Ottervanger JP, Reiffers S, Suryapranata H, Zijlstra F. Immediate coronary angioplasty versus intravenous streptokinase in acute myocardial infarction: left ventricular ejection fraction, hospital mortality and reinfarction. *J Am Coll Cardiol* 1994;23(5):1004–8.
23. Gibbons RJ, Holmes DR, Reeder GS, Bailey KR, Hopfenspirger MR, Gersh BJ. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. The Mayo Coronary Care Unit and Catheterization Laboratory Groups. *N Engl J Med* 1993;328(10):685–91.
24. Gilutz H, Battler A, Rabinowitz I, Snir Y, Porath A, Rabinowitz G. The "door-to-needle blitz" in acute myocardial infarction: the impact of a CQI project. *J Comm J Qual Improv* 1998;24(6):323–33.
25. Weaver WD. Time to thrombolytic treatment: factors affecting delay and their influence on outcome. *J Am Coll Cardiol* 1995;25(7 Suppl):3–9S.

Correspondence: Dr. D. Zahger, Dept. of Cardiology. Soroka University Medical Center, P.O. Box 151, Beer Sheva 84101, Israel.
Phone: (972-8) 640-3468
Fax: (972-8) 628-2112
email: dzahger@bgumail.bgu.ac.il