Early in-hospital Re-ischemia and/or Re-infarction following thrombolytics and non-thrombolytics therapy for myocardial infarction

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Abstract: Objective: To compare the incidence of early in-hospital recurrent ischemia and/or reinfarction (fatal or nonfatal) in patients receiving thrombolytic therapy for ST segment myocardial infarction (STEMI) and those who did not receive thrombolysis, and to assess the clinical risk factors for reischemia and /or reinfarction in both groups. **Methods:** 285 consecutive patients presenting with STEMI were enrolled, and divided into two groups, whether refused primary percutaneous coronary intervention (PCI) and being eligible candidates for thrombolytic therapy in the first group, and those who were not the candidate to thrombolytic therapy in the second group. Eighteen clinical variables were assessed to identify the predictors of early in-hospital (pre-discharge) reischemia and/or reinfarction in both groups. **Results:** Thrombolytic therapy was given to 159 patients, while 126 (44.2%) patients were treated conservatively. Re-ischemia was diagnosed in 30 patients (19 in thrombolytic versus 11 in non thrombolytic candidates), while reinfarction was diagnosed in twelve patients (8 in thrombolytic versus 4 in non thrombolytic candidates). Five of the reinfarction events were fatal. The episodes occurred within 4.71±3.6 days in thrombolytic cases versus 5.85±2.5 days in the non thrombolytic cases (P=0.263). Anti-thrombotic and anti-ischemic medications were used equally in both groups (P=0.002 and P>0.05 respectively). However there was a significant higher rate of Beta-blockers usage among thrombolytic candidates than non thrombolytic candidates (P=0.002). Thrombolytic candidates were relatively younger than non thrombolytic candidates (P=0.001). **Conclusion:** Despite of conventional medical treatment including thrombolytic, anti-thrombotic and anti-ischemic therapy some survivors of MI were subjected to re-ischemia and/or reinfarction events during early in-hospital follow up. The incidence is slightly higher in patients who received thrombolytic therapy compared to those who did not, but statistically not significant.

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1. Introduction:

Although early thrombolysis results in reperfusion in a large proportion of occluded coronary arteries, it does not remove the thrombogenic stimulus i.e. the ruptured plaque. This leaves the patients with unstable endothelial lesion at risk of having recurrent ischemia and even fatal or nonfatal re-infarction. Reinfarction is one of the determinants of cardiac mortality after acute myocardial infarction (MI)[1-3]. Most previous studies have been focusing on the incidence of recurrent ischemia and reinfarction after hospital discharge in patients who received thrombolytic therapy for acute myocardial infarction. In hospital recurrent myocardial ischemia after thrombolytic therapy was frequent and had been recognized for years as a strong predictor of both reinfarction and death.

This prospective study was designed to compare the incidence of early in-hospital (pre-discharge) recurrent ischemia and/or reinfarction (fatal or non-fatal) in the patients who received thrombolytic therapy for acute myocardial infarction and those who did not.

Methods: This study was conducted prospectively at the Cardiology Department of Erciyes University (Kayseri–Turkey). A group of 285 consecutive adult patients, age of 18 – 75 years with MI were admitted to CCU and divided into two groups: those who (refused primary intervention) were candidate for thrombolytic therapy and those who were not candidates. Thrombolytic candidates (n = 159) received Streptokinase or recombinant tissue-plasminogen (rt-pA), whereas, non thrombolytic candidates (n = 126) were treated conservatively.

The risk and benefits of primary intervention versus thrombolytic therapy were explained in details to all patients with ST segments elevation myocardial infarction (STEMI), if refused intervention, thrombolytic therapy was administered immediately and the patient was enrolled for observation.

Post admission, all patients with no a history of Aspirin intolerance received Aspirin (dose range 100

– 300 mg / day), oral beta-adrenergic blocking therapy was initiated if no contraindication, intravenous Nitroglycerin was given for 24 - 48 hours (excluding patients with RV myocardial infarction or hypotension) followed by oral nitrate and Statins. ACE-inhibitors and other medications (diuretics, Ca channel blockers, Digoxin ... ect) were prescribed at the discretion of the attending physician during hospital follow-up. A set of eighteen demographic and historical variables were recorded to analyze the relationship among these different clinical variables with both recurrent ischemia and re-infarction (fatal or nonfatal) from the time of admission to pre-discharge in both groups. These variables include, gender, age, weight, height, lipid profile, Diabetes mellitus, Hypertension, tobacco use (non, smoker, Ex-smoker), peak CK, peak CK-MB, prior myocardial infarction and family history of MI.

During hospital stay patients were monitored for recurrent ischemia and/or reinfarction. Recurrent ischemia was defined in any patient who developed symptoms compatible with myocardial ischemia and associated with new ECG changes such as ST-segment depression, elevation or T wave changes (inversion / pseudo-normalization).

Reinfarction was defined as recurrent anginal chest discomfort lasting for more than 20 minutes after resolution of symptoms of index myocardial infarction, associated with new or worse ST-segment re-elevation and new rise in creatinine kinase (CK) and MB fraction (CK-MB). Patients were candidate for thrombolytic therapy if they presented with symptoms of acute MI for 20 minutes to 24 hours accompanied by ST segment elevation ≥ 0.1 mv in at least two contiguous leads or if there was ST-segment depression in the precordial leads (V1 through V4) consistent with posterior MI, and refused primary coronary intervention and had none of the other criteria of contraindications for thrombolytic therapy as shown in Table 1.

Due to misinterpretation of electrocardiogram (ECG) during follow-up, patients with left bundle branch block (LBBB) or ventricular pacing were excluded.

Table 1: Criteria for non-thrombolytic therapy:

No.	Clinical criteria
1	Suspected pregnancy
2	Recent major trauma or stroke (last 6 months)
3	Major surgery within two weeks
4	Recent internal bleeding
5	Structural brain disease (including tumor or vascular malformation)
6	Uncontrolled hypertension (> 190 / 110 mmHg in several measurements, not lower with anti hypertensive therapy)
7	Other serious disease of other organs systems (cancer ….. ect)

Statistical analysis was done using SPSS Version 21, P values < 0.05 were considered statistically significant.

Results: A total of 285 patients (36 female, 249 male) were selected for this study. 159 patients (55.8%) with acute myocardial infarction (mean age 54±11 years) received thrombolytic therapy after refusing primary intervention and the remaining 126 patients (44.2 %) were treated conservatively (mean age 58 ± 12 years).

The baseline clinical characteristic variables of all patients were summarized in Table 2.

Table 2: Patients' clinical characteristics

Demographic data	Thrombolytics candidates (n=159)	Non-Thrombolytic candidates (n=126)	*P-value
Male (n, %)	142(89.3%)	107(84.9%)	0.268
Female (n, %)	17 (10.7%)	19(15.1%)	
Age (mean ± SD)	54 ± 11	58 ± 12	0.001
Weight (kg)	77 ± 18	75 ± 19	0.361
Height (cm)	167 ± 15	179 ± 14	0.109
Total Chol. (mg/dL)	169 ± 87	150 ± 80	0.069
TG (mg/dL)	123 ± 111	106 ± 85	0.164
HDL- Chol. (mg/dL)	45 ± 25	39 ± 27	0.192
LDL- Chol. (mg/dL)	101 ± 63	85 ± 62	0.027
Peak CK (IU/L)	2545 ± 183	1458 ± 173	0.033
Peak CK-MB (IU/L)	236 ± 24	178 ± 33	0.090
Non smoker (n,%)	28 (%17.6)	33 (%26.9)	
Smoker (n, %)	110 (%69.18)	72 (%57.14)	0.101
Ex-smoker (n, %)	21 (%13.2)	21 (%16.66)	0.102
DM (n, %)	29 (%18.23)	22 (%17.46)	0.865
Hypertension (n, %)	49 (%30.8 9)	40 (%31.74)	0.867
Old MI (n, %)	15 (%9.43)	10 (%7.9)	0.657
Family Hx. (n, %)	74 (%46.54)	57 (%45.23)	0.827

*χ^2 test

The number of female patients (12.6) was lower compared to male patients (87.4%), however there was no statistical significant difference between the two groups.

The non thrombolytic group was relatively older than thrombolytic candidates (P = 0.001). Statistically there were no significant differences between the two groups regarding weight, height, lipid profile, peak CK, peak CK-MB, tobacco use (none smokers, smokers, ex-smokers), diabetes mellitus, hypertension, prior myocardial infarction and family history (P>0.05). The various anti-ischemic, anti-thrombotic and statin medications were used equivalently between both groups (Table 3).

There was a significant higher rate of Beta-blockers usage among thrombolytic candidates than non thrombolytic candidates (P=0.002). We observed that previous MI was not associated with increased

rate of recurrent ischemia and/or reinfarction between the two groups during early in-hospital follow- up.

Table 3: Use of Anti-ischemia and Anti-thrombotic medications throughout the study:

Medications	Thrombolytic candidates (n, %)	Non-Thrombolytics Candidates (n, %)	*P- value
β- blocker	148 (%93.1)	102 (%80.95)	0.002
Ca- blocker	4 (%2.5)	5 (%3.9)	0.486
Nitrat	130 (%81.8)	107 (%84.9)	0.479
Aspirin	154 (%98.9)	115 (%91.3)	0.076
Heparin	157 (%98.8)	124 (%98.4)	0.814
ACE inhibitor	143 (%89.9)	114 (%90.5)	0.879
Statins	159 (100%)	126 (100%)	-

*χ^2 test

Despite the timing of reischemia or reinfarction between the two groups was clearly unpredictable, during our follow-up the mean time of recurrence of both events was within 5.85±2.5 days in the non thrombolytic candidates versus 4.71±3.6 days in the thrombolytic candidates, but with no statistical significant difference(P= 0.263).

Chest pain associated with ST-segment or T wave changes was diagnosed in 30 patients (10.5%) before hospital discharge, 19 in the thrombolytic and 11 in the non-thrombolytic group. Reinfarction was diagnosed in 12 (4.2 %) out of 285 patients, 8 in the thrombolytic group and 4 in the non thrombolytic group (Table 4 and Figure 1).

Table 4: Incidence of reischemia and reinfarction in the two groups:

Patient group (n=285)	Reischemia (n, %)	Reinfarction (n, %)	Recurrent reischemia + infarction
Thrombolytic candidates (n=159)	19(%11.95)	8 (%5.03)	27 (%16.98)
Nonthrombolytic candidates (n=126)	11 (%8.73)	4 (%3.17)	15 (%11.90)
*P value	0.440	0.967	0.244

*χ^2 test

Five of the re-infarction events were fatal, three events in the thrombolytic and two in the non thrombolytic group.

Twenty eight of the 42 patients who developed recurrent ischemia and/or reinfarction agreed to undergo coronary intervention while 14 patients refused the procedure. There were no major catastrophic bleeding complications (Gastrointestinal bleeding, intracranial bleeding...etc) seen among the thrombolytic candidates.

Streptokinase was given to 141 (88.7%) while t-pA was given to 25 (15.7%) patients. There were seven patients who had streptokinase on admission and due to STE re-MI and refusal of rescue angioplasty; they had been re-thrombolysed with t-pA.

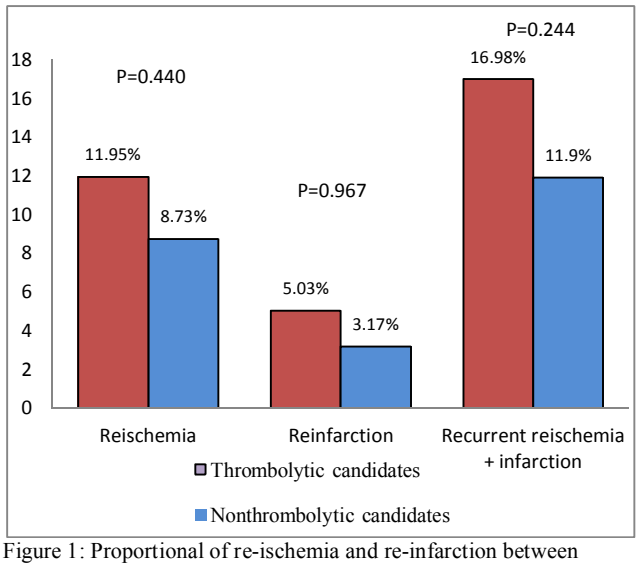

Figure 1: Proportional of re-ischemia and re-infarction between two groups

In contrast, our data showed relatively higher rates of recurrent ischemia and reinfarction in thrombolytic candidates at early in-hospital follow-up compared with non thrombolytic candidates, these differences were not statistically significant (P=0.044 and P=0.967 respectively).

Peak creatinine kinase level after reinfarction was lower compared with index myocardial infarction as a result of less myocardial necrosis post index infarction.

Discussion:

The efficacy of thrombolytic therapy for acute myocardial infarction was initially established in large placebo-controlled trials, in which death was the primary end point [4-6]. Other benefits included recovery of left ventricular function, preventing of left ventricular aneurysm formation, cardiac rupture, and enhanced electrical stability.

Those benefits precisely manifested in patients treated ≤ 6 hours after the onset chest pain [5,7] and was almost certainly beneficial in some patients treated later [5,8].

However, the risk of reocclusion of MI related artery post thrombolytic therapy causing recurrent ischemia and /or reinfarction remains high in the range of 20-30 % for reischemia and 5 % for reinfarction [9].

In our study the early reischemia or reinfarction in the two groups occurred before coronary angiography was performed. Reiner et al identified those neither quantitative nor qualitative

angiographic variables early (90 minutes) after onset of symptoms could predict reocclusion [10].

The present series illustrates that more than 50 % of patients with re-ischemia do not have accompanying ECG changes [11]; but the risk of re-infarction increased by concurrent ECG changes [12].

We still agree with others that angina pectoris remains a clinical diagnosis based on the characteristic of symptoms. Our findings however re-strengthen the value of careful clinical evaluation and immediate ECG recording once MI patients complain of chest discomfort during in-hospital follow-up.

Large trials reported 2 % to 6 % incidence of re-infarction after thrombolysis of acute myocardial infarction, for example; 4% in GUSTO-I,[13] 4 % in ASSENT-II,[14] 4.2 % in GUSTO-III [15] and 6 % in TMAI-II B. [16]

The incidence of reischemia in-hospital after thrombolysis as defined by symptoms and dynamic ECG changes was 18 % in TAMI series [16], 20 % as reported by Amadeo Betiru and his group and interestingly was 8 % when the definition includes only ECG changes[11]. Silva and colleagues [17] found early reischemia defined by spontaneous chest pain and ST segment and / or T wave changes to be present in 35 (8 %) of 453 patients after thrombolysis.

This wide variation in the rates of reischemia after thrombolysis therapy might be explained by differences in both the clinical characteristics of study patients and the diagnosis criteria used. In our study, the incidence of reischemia (11.95 %) and reinfarction (5.03 %) in thrombolytic candidates (n = 159) was consistent with the 8 – 18 % rate of reischemia and the 2– 6 % rate of re-infarction reported before in previous studies after thrombolysis[18].

Data concerning the rate of re-infarction during early hospital follow-up in patients without thrombolytic therapy is limited, whereas, GISSI-2 reported incidence of 2 % [7].

Nevertheless, the incidence of clinical re-infarction (fatal or nonfatal) observed in our non-thrombolytic candidates was relatively low (3.17%), and with no significant difference compared with incidence of re-infarction in thrombolytic candidates (P = 0.967).

Therefore the role of heparin and Aspirin became standard medications in reducing reischemia and reinfarction [19].

Such benefits also were noticed in patients who received immediately intravenous beta-blockers (Metoprolol) upon admission followed by oral administration in the absence of contraindication during short term [20-23] as well as long-term follow-up.

Thus Heparin and anti-platelets were used equally in both groups (P > 0.05). Increasing use of beta-blockers among our thrombolytic candidates is not surprising, because these candidates were more eligible to intravenous dosage of this agent in emergency department (pre-thrombolysis) compared with non thrombolytic candidates (P = 0.02).

Many studies found same parameters like previous angina, a history of myocardial infarction could be a marker of re-infarction on longer follow-up, but not during immediate hospitalization. [24-27]

History of hypertension and diabetes mellitus were associated with higher incidence of re-infarction in some studies but absent in others. [28]

Considering our small number of patients, we did not observe significant differences between diabetic and non-diabetic patients in the incidence of re-ischemia and / or reinfarction in two groups.

Nevertheless coronary collateral vessels development is poorer in patients with diabetes than in patients without diabetes mellitus as shown angiographycally by Abaci and colleagues. [29]

Current smoking is found to be associated with low risk of re-infarction in short-term follow-up, [30] whereas on long term continuing cigarette smoking after myocardial infarction was found to be the only independent risk factor other than left ventricular end-systolic volume to influence subsequent survival [31].

It is possible that cessation of smoking during hospitalization have immediate effects on reserving some of the adverse effect of smoking, such as, endothelial dysfunction, vasoconstriction or an increased thrombogenicity [32]. While continuing smoking lead to severe endothelial dysfunction and hypercoagulability which as major mediators in pathophysiology of reischemia and subsequent reinfarction after index infarction.

In our study we did not find an association between smoking and recurrent ischemia and / or infarction. This might be linked again to the same fact of small sample size.

Most studies of thrombolysis reported advanced age as a strong predictor of re-infarction and death both in-hospital and on 6 months follow-up. [32,33]

With possible exception of the relatively advanced age noticed in non-thrombolytic candidates as compared to the thrombolytic candidates (P = 0.001), the proportion of other risk factors that we analyzed were similar in two groups (P > 0.05).

Hospital mortality rate in our thrombolytic candidates was 1.9 % which compares favorably with previously reported 3.7 % to 7.4 % post-thrombolytic treatment mortality rate [34].

In conclusion, we support pooled results from prior studies that showed higher incidence of re-

infarction in patients underwent thrombolysis for myocardial infarction compared with who did not, but we did not find statistically significant difference between the two groups.

For a better care and survival in patients suffering from myocardial infarction we agree with others that further large studies with randomization should be done to assess the outcome of early re-vascularization, either PCI (Percutaneous Coronary Intervention) or CABAG, use of newer thrombolytic, oral / iv anti-platelets and new antithrombin medications in prevention and treatment of re-ischemia and / or re-infarction during short and long term follow up.

References:

1. Moss AJ, Benhorin J. Prognosis and management after a first myocardial infarction. N Engl J Med 1990; 322; 743-5.
2. Gilpin E, Ricou F, Dittrich H, Nicod P, Henning H, Ross Jr. Factors associated with recurrent myocardial infarction within one year after a cute myocardial infarction. Am Heart J 1991; 121: 454-65.
3. Benhorin J, Moss AJ. Dakes D. Prognostic significance of non-fatal myocardial infarction. J Am Coll Cardial 1990; 15: 253-8.
4. Kennedy JW, Ritchie, David KB, Stadium ML, Manyarda C, Fritz Jk. The Western Washington randomized trial of intracoronary streptokinas in acute myocardial infarction. N Eng J Med 1985; 312: 1073-8.
5. ISIS-2 (Second international study of infarct survival) Collaborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 Cases of suspected acute myocardial infarction: ISIS-2. Lancet 1988; 2: 349-60.
6. 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.
7. Gruppo italiano per lo studio della streptokinase nell'infarto Miocardico (GISSI), Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986; 1: 397-402
8. White HD. Thrombolytic therapy for patients with myocardial infarction presenting after six hours. Lancet 1992¸340: 221-2.
9. Richard C, Becker MD, Worcester Mass. Recurrent myocardial ischemia following thrombolytic therapy: guidelines for practicing clinicians. Am Heart J 1992; 124:183-93.
10. Reiner JS, Lundergan CF, van den Brand M, Boland J, Thomson MA, Machecourt J, et al. Early angiography cannot predict post thrombolytic coronary reocclusion: observations from the GUSTO angiographic study. Global Utilization of streptokinase and t-PA For Occluded Coronary Arteries. J Am Coll Cardiol 1994; 24: 1439-44.
11. Betriu A, Califf RM, Bosch X, Guerci A, Stebbins AL, Barbagelata NA, Aylward PE, et al. Recurrent ischemia after thrombolysis: Importance of associated clinical findings. GUSTO-I Investigators. Global Utilization of Streptokinase and t-PA [tissue-plasminogen activator] for occluded coronary arteries. J Am Coll Cardial 1998; 31: 94-102.
12. Bosch X, Theroux P, Pelletier GB, Sanz G, Roy D, Waters D. Clinical and angiographic features and prognostic significance or early post infarction angina with and without electrocardiographic signs of transient ischemia. Am J Med 1991; 91: 493-501.
13. The Gusto Investigators. An international randomized trial comparing four thrombolysis strategies for acute myocardial infarction. N Engl J Med 1993; 329: 673-82.
14. Van De Werf F, Adgey J, Ardissino D, Armsrtong PW, Aylward P, Barbash G, Betriu A, Assessment of the safety and efficacy of a New Thrombolytic (ASSENT-2) Investigators. Single-bolus tenecteplase compared with front loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomized trial. Lancet. 1999; 354: 716-22.
15. The GUSTO-III investigators. A comparison of reteplase with alteplase for acute myocardial infarction. N Engl J Med 1997; 337: 1118-23
16. Chesebro JH, knatterud G, Roberts R, Berer J, Cohen LS, Dalen J, et al. Thrombolysis in Myocardial infarction (TIMI) Trial, phase I-Acomparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987; 76: 142-54.
17. Silva P. Galli M. Campolo AL. Prognostic Significance of early İschemia after acute myocardial infarction in Low risk patients IRES (İschemic Residua) Study Group. Am J Cardiol 1993; 71: 1142-7.
18. Barbagelata A, Granger CB, Topol EJ, Worley SJ, Kereiakes DJ, George BS, Ohman EM, et al. Frequency, significance and cost of recurrent ischemia after thrombolytic therapy for acute myocardial infarction. Am J Cardiol 1995; 76: 1007-13.

19. Theroux P, Ouimet H, Mc Cans J, Latour JG, Joly P, Levy G, Pelletier E, et al. Aspirin, heparin or both to treat acute binstable angina. N Engl J Med 1988; 319: 1105-11.
20. The Beta-Blocker Pooling Project (BBPP): subgroup findings from randomized trials in post infarction patients. The Beta-Blocker Pooling Project Research Group. Eur Heart J. 1988; 9: 8-16.
21. The TIMI Study Group. Comparison of invasive and Conservative Strategies after treatment with intravenous tissue plasminogen activator in acute myocardial infarction: results of the Thrombolysis in Myocardial infarction (TIMI) phase II trail. N Engl J Med 1989; 320: 618-27.
22. Roberts R, Rogers WJ, Mueller HS, Lambrew CT, Diver DJ, Smith HC, et al. Immediate versus deferred beta-blockade following thrombolytic therapy in patients with acute myocardial infarction. Results of the Thrombolysis in Myocardial Infarction (TIMI)II-B Study. Circulation 1991;83:422-37
23. Rich MW. Therapy for acute myocardial infarction. Clin Geriatric Med 1996; 12:141-68
24. Birnbaum Y, Herz I, Sclarovsky S, Zlotikamien B, Chetrit A, Olmer L, Barbash GI. Admission Clinical and electrocardiographic characteristics predicting and increased risk for early reinfarction after thrombolytic therapy. Am Heart J 1998; 135: 805-12.
25. Gilpin E, Ricou F, Dittrich H, Nicod P, Henning H, Ross J. Factors associated with recurrent myocardial infarction within one year after acute myocardial infarction. Am Heart J 1991; 121: 457-65.
26. Kornowski R, Goldbourt U, Zion M. Mandelzweig L. Kaplinsky E, Levo Y, Behar S. Predictors and Long-term prognostic significance of recurrent infarction in the year after a first myocardial infarction. Am J Cardiol 1993; 72: 883-8.
27. Ulvenstam G, Aberg A, Pennert K, Vedin A, Wedel H, Wilhemsen L, et al. recurrent myocardial infarction,II: possibilities of prediction. Eur Heart J 1985; 6: 303-11.
28. Abbot RD, Donaue R, Kannel WB, Wilson PW. The impact of diabetes on survival following myocardial infarction in men vs. woman: the Framingham Study. JAMA 1988; 260: 3456-60
29. Abacı A, Oguzhan A, Kahraman S, Eryol NK, Unal S, Arinc H, Ergin A. Effects of diabetes mellitus on formation of coronary collateral vessels. Circulation 1999; 99:2239-42.
30. Rivers JT, White HD, Cross DB, Williams BF, Norris RM. Reinfarction after thrombolytic therapy for acute myocardial infarction followed by conservative management: Incidence and effect of smoking. J Am Coll Cardiol 1990; 16: 340-8.
31. White HD, Norris RM, Brown MA, Brandt PWT, Whilock RML, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. Circulation 1987; 76: 44-51.
32. White HD. Lifting the smoke-screen: the enigma of better outcome in smokers after myocardial infarction. Am J Cardiol 1995; 75: 278-9.
33. Stone GW, Grines CL, Browne KF, Marco J, Rothbaum D, O'Keefe J, et al. Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: the Primary Angioplasty in Myocardial Infarction (PAMI) trail. J Am Coll Cardiol. 1995; 25:370-7.
34. White HD, Rivers JT, Maslowski AH, Ormiston JA, Takayama M, Hart HH, et al. Effect of intravenous streptokinase as Compared with Late of tissue plasminogen activator on Left Ventricular function after first myocardial infarction. N. Eng. J Med 1989; 320: 817-21.

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