Primary coronary angioplasty in acute myocardial infarction: is it possible to prevent postinfarction cardiac rupture?

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Background. **Cardiac rupture is a leading cause of death among patients hospitalized for acute myocardial infarction (AMI). The aim of our retrospective study was to evaluate the impact of primary coronary angioplasty (PTCA) on this not common but usually fatal complication.**

Methods. **Since January 1998 PTCA has been the routine treatment for AMI patients in our Institution monitored during the first 12 hours from symptom onset. The AMI patients hospitalized between January 1998 and December 1999 (Group A) were retrospectively compared to those observed between January 1996 and December 1997 (Group B, historical control group), mainly treated with systemic thrombolysis. Patients hospitalized after 12 hours of symptom onset were excluded from the study. Data were analyzed on an intention-to-treat design.**

Results. **Group A consisted of 204 patients (148 males, 56 females, mean age 67 ± 11 years), 165 (81%) of whom underwent coronary angiography. Group B consisted of 185 patients (123 males, 62 females, mean age 71 ± 12 years), 78 (42%) of whom were treated with thrombolysis and 33 (18%) with PTCA. The groups did not differ as regards the time delay before hospital entry, Killip class at admission and site of AMI. Fourteen patients (6.8%) of Group A and 20 (10.8%) of Group B died in the Cardiology Division. No deaths due to cardiac rupture were observed among the 165 Group A patients, nor among the 33 Group B patients treated with PTCA. Cardiac rupture was the cause of death for 1 out of 14 (7%) patients in Group A, and for 8 out of 20 (40%) patients in Group B ($p < 0.02$ Group A vs Group B). Nine Group A patients and 11 Group B patients died because of cardiogenic shock.**

Conclusions. **A lower cardiac rupture incidence was observed among Group A patients in comparison to those of Group B. Thus our data, although not randomized, suggest the ability of primary PTCA in preventing post-AMI cardiac rupture.**

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Spontaneous cardiac rupture, either internal or external[1,2], is a not fairly frequent but very severe complication of acute myocardial infarction (AMI)[3,4]. Although several therapeutical interventions, such as beta-blockers[5,6], nitrates[7], ACE-inhibitors[6] and early thrombolysis[8,9] have been advocated to reduce the risk of rupture following an AMI, the incidence of this complication has not been reduced over the last few decades[4,10-12], while its prevalence among the causes of in-hospital death has increased[13,14]. Thus, postinfarction cardiac rupture still represents a crucial clinical problem. Among the risk factors for cardiac rupture[15,16], the persistent occlusion of the infarct-related artery plays a pivotal role[17]. Although primary coronary angioplasty (PTCA) is considered the most efficacious therapeutic tool currently available for the recanalization of the infarct-related artery[18-22], its role in preventing postinfarction cardiac rupture has not been adequately investigated until now. From these observations, we retrospectively assessed the cardiac rupture incidence in a cohort of AMI patients mainly treated with primary PTCA and in a historical control group mainly treated with systemic thrombolysis, in order to compare the impact of the different reperfusion strategies on this serious complication.

Methods

Patients. The criteria for inclusion in the study were: 1) AMI at hospital admission[23] with ST segment elevation Ž 1 mm in at

least 2 limb leads and/or Ž 2 mm in at least 2 chest leads[24]; 2) hospitalization within 12 hours of symptom onset[25]. Patients with left bundle branch block or with permanent pacemaker were excluded from the study, due to the inability to evaluate the ST segment. The AMI location was defined as anterior, inferior, lateral or multiple according to the criteria suggested by the GISSI study[26]. Patients observed between January 1998 and December 1999 were defined as Group A (routine reperfusion treatment: PTCA), and were retrospectively compared to those observed between January 1996 and December 1997 (Group B, historical control group), when the routine treatment consisted of systemic thrombolysis.

Coronary angioplasty. Starting from January 1997, and according to the policy of the Cardiology Department of the University of Florence (Italy), primary PTCA was available for reperfusion treatment of our AMI patients. PTCA was initially reserved for AMI patients with severe left ventricular dysfunction[27], while the routine AMI treatment was systemic thrombolysis. Since January 1998, following the availability of the catheterization laboratory and upon direct phone call of the dedicated staff working 24 hours a day, primary PTCA has become the routine reperfusion treatment of all our AMI patients. Patients under observation during the first 12 hours from symptom onset[28], after giving their informed consent, were transferred by a medicalized ambulance provided by the emergency service "118" phone number to the catheterization laboratory of the University of Florence, where they received an emergency coronary angiography followed, if necessary, by angioplasty of the infarct-related artery. Immediately after the procedure the patients returned to our Cardiology Division until acute phase completion. Before catheterization and in the absence of clinical contraindications, patients received aspirin, metoprolol and nitrates[25], while heparin and thrombolytics were not routinely administered. In patients with multivessel lesions the immediate treatment consisted of angioplasty of the infarct-related artery alone, with the exception of those with cardiogenic shock or left ventricular dysfunction[27]. PTCA was defined as successful whenever a TIMI 3 flow and a residual stenosis of < 20% were attained[29]. Furthermore, PTCA was almost routinely followed by stenting of the treated lesion[30], and in the case of no-reflow phenomenon it was followed by the administration of the monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor abciximab. Finally, PTCA was followed by heparin infusion (24 hours), associated with ticlopidine (2 months) and aspirin (indefinitely). Adjunctive maneuvers (intraaortic balloon pumping, temporary transvenous pacing) were performed as required.

In-hospital management. During the Coronary Care Unit stay the patients were directly observed, and the electrocardiogram was continuously monitored. Patients treated with PTCA received invasive arterial pressure monitoring for at least 24 hours, subsequently arterial pressure was evaluated at least every 3 hours. Systemic thrombolysis was performed with front-loaded recombinant tissue-type plasminogen activator (rt-PA)[31]. No patient received oral anticoagulation. After AMI, patients remained in the Cardiology Division until normalization of the cardiac enzyme blood levels, withdrawal of any infusive treatment and stabilization of the clinical status to allow active mobilization.

Diagnosis of cardiac rupture. Since 1991 in our Cardiology Division the diagnosis of cardiac rupture has been prospectively based upon the immediate echocardiographic evaluation (besides those at hospital admission and at the Cardiology Division discharge) in every case of sudden modification of the patients' clinical status: new-onset cardiac murmurs, severe chest pain, arterial hypotension not due to drug effect, shock, syncope, and cardiac arrest[12].

Echocardiograms were obtained employing commercially available ultrasound systems with 3.5 and 2.5 MHz probes (SIM 4000 2D, Esaote Biomedica, Florence, Italy). Images were obtained in the standard parasternal long and short axis, apical and subcostal 4-chamber views in the two-dimensional and M-mode techniques. The diagnosis of pericardial effusion was made only in the presence of a pericardial echo-free space without end-diastolic obliteration[32]. The amount of pericardial effusion was arbitrarily considered as moderate (< 10 mm separation between the pericardial layers) or severe (Ž 10 mm separation).

The diagnosis of cardiac rupture was considered whenever a sudden clinical worsening was associated with the echocardiographic detection of: 1) a new-onset, severe pericardial effusion with compression of right heart chambers (free wall rupture); 2) a new-onset left-to-right ventricular shunt (interventricular septum rupture); 3) a new-onset, massive mitral or tricuspid regurgitation with direct visualization of papillary muscle rupture. The diagnostic accuracy for heart rupture of a strategy based upon the association of predefined clinical and echocardiographic findings has been validated by previous studies[12,33,34].

Other definitions. The causes of death different from cardiac rupture were prospectively defined as follows:
• cardiogenic shock was defined as hypotension (systolic blood pressure < 90 mmHg) with symptoms/signs of systemic hypoperfusion, not due to drug effect and not responsive to volume expansion, associated with severe left ventricular dysfunction or hemodynamic findings of dominant right ventricular infarction[35], and without evidence of myocardial rupture;
• infarction recurrence was considered the mechanism of death whenever recurrent ischemic chest pain, with either ST segment or repeat creatine kinase elevation oc-

curred, subsequently leading to cardiac death, in the absence of cardiac rupture;
• ventricular arrhythmia was considered the primary mechanism of death whenever ventricular tachycardia or ventricular fibrillation occurred, leading to hemodynamic collapse and cardiopulmonary arrest, in the absence of preexisting pump failure and without evidence of cardiac rupture.

Statistical analysis. Continuous data are described as mean ± 1 SD. Differences between continuous data were assessed with the unpaired Student's t-test. Discontinuous variables were compared by the χ^2 test or the Fisher's exact test, when appropriate. A p value of < 0.05 was considered statistically significant. The data were analyzed on an intention-to-treat design.

Results

Patients enrolled. Between January 1998 and December 1999, 241 AMI patients with ST segment elevation, of whom 204 (85%) during the first 12 hours from symptom onset (Group A: 148 males, 56 females, mean age 67 ± 11 years), were observed. Between January 1996 and December 1997, the patients observed were respectively 250 and 185 (74%, Group B: 123 males, 62 females, mean age 71 ± 12 years). The main demographic and clinical characteristics of patients are reported in table I.

Table I. Main demographic and clinical characteristics of patients (absolute numbers).

	Group A (n=204)	Group B (n=185)	p
Demographic characteristics			
> 65 years	125	131	NS
Females	56	62	NS
Clinical characteristics			
Diabetes	37	42	NS
Hypertension	73	64	NS
Angina	67	55	NS
Previous infarction	25	20	NS
Site of infarction			
Anterior	70	57	NS
Inferior	69	62	NS
Lateral	12	13	NS
Multiple	53	53	NS
Latency* (hours)	5 ± 3	5 ± 3	NS
Killip class at admission			
1 + 2	178	162	NS
3 + 4	26	23	NS
Reperfusion treatment			
Systemic thrombolysis	11	78	< 0.001
Primary PTCA	165	33	< 0.001
Neither reperfusion strategy	28	74	< 0.001
Other treatments			
Beta-blockers	47	42	NS
ACE-inhibitors	90	80	NS
Nitrates	140	138	NS
Cardiac rupture	1	8	< 0.02

PTCA = coronary angioplasty. * time elapsed from symptom onset to hospital admission.

Reperfusion treatment. Out of the 204 Group A patients, 165 (81%) underwent immediate coronary angiography; 158 (77%) of them underwent immediate PTCA of the infarct-related artery, while 7 were not treated due to anatomical contraindications. Seventy-four patients had single-vessel and 88 two- or three-vessel disease; of the remaining 3 patients 1 had a left main artery disease and 2 were actually free from occlusive lesions. Out of the 158 PTCA performed, 148 (94%) were successful. In a further 4 patients a TIMI 2 flow was obtained. The procedure was followed by stent implantation in 131 patients (83%), and by abciximab administration in 67 (42%). The mean transfer time to the catheterization laboratory was 66 ± 16 min (median time 60 min). Of the remaining 39 Group A patients not submitted to coronary angiography (due to refusal of PTCA, or because not transferable), 11 (5%) were treated with systemic thrombolysis, whereas the remaining 28 (14%) were excluded from any reperfusion treatment owing to contraindications to thrombolysis.

Of the 185 Group B patients, 78 (42%) received systemic thrombolysis and 33 (18%) primary PTCA. Among the remaining 74 patients (40%), 63 were not treated due to contraindications to systemic thrombolysis (intraaortic balloon pumping or central vein puncture: 22 patients; cardiopulmonary resuscitation maneuvers: 8 patients; other medical contraindications: 33 patients) while PTCA was not available; the remaining 11 patients were not treated because, at the Coronary Care Unit entry, they were considered borderline as regards to the latency of admission. Thus, 86% Group A patients and 60% Group B patients actually underwent a reperfusion treatment.

Clinical course. Fourteen (6.8%) Group A patients died before being discharged from the Cardiology Division. One death (due to ventricular fibrillation) occurred during the transfer to the catheterization laboratory. Of the 165 patients who received coronary angiography 6 deaths (3.6%) were observed. In Group B patients, 20 (10.8%) died before discharge: 7 out of 20 deaths occurred among the 78 patients treated with systemic thrombolysis (9%), 2 among those treated with PTCA (6%), and 11 among the 74 not treated with any reperfusion strategy (14.9%). The causes of death are reported in table II. The mean length of stay in the Cardiology Division (Group A + Group B) was 5 ± 4 days (range 1-27).

Cardiac rupture. One death was due to cardiac rupture among Group A patients, occurring in a female subject treated with systemic thrombolysis. No deaths were due to cardiac rupture among the 165 Group A patients, as

Table II. Causes of death during the Cardiology Division stay.

	Group A (n=204)	Group B (n=185)	p
Cardiogenic shock	9	11	NS
Cardiac rupture	1	8	0.04*
Arrhythmia	1	–	NS
Infarction recurrence	1	1	NS
Stroke	1	–	NS
Not cardiovascular	1	–	NS
Total	14 (6.8%)	20 (10.8%)	NS

* prevalence among the causes of death.

well as the 33 patients of Group B, treated with primary PTCA. In contrast, cardiac rupture was the cause of death for 8 out of 20 patients deceased in Group B. The rupture affected the free ventricular wall in 7 cases (including the single patient of Group A), and the interventricular septum in 2. A cardiac rupture occurred in 4 out of 89 (4.5%) patients treated with systemic thrombolysis (11 of Group A and 78 of Group B), and in 5 out of 102 (5%) not treated with any reperfusion strategy (28 of Group A and 74 of Group B). A necropsy was performed in 4 out of the 34 non-survivors, and the clinical-echocardiographic diagnosis (2 cardiac rupture; 2 cardiogenic shock, without cardiac rupture) was confirmed in all the cases. Both the septal and 3 out of 7 free wall ruptures occurred during the first hospital day, while 2 further free wall ruptures occurred during day 2, and the remaining during day 3. The septal ruptures caused a cardiogenic shock, rapidly leading to death. In only one patient was it possible to attempt intra-aortic balloon pumping, but without clinical stabilization lasting long enough to allow surgical repair. The free wall rupture caused sudden electromechanical dissociation in all the patients, and none survived despite the early diagnosis and the prompt pericardiocentesis[12].

Discussion

In spite of the progress achieved in the treatment of AMI, cardiac rupture still represents an unsolved clinical problem. In fact, although during the past few decades several therapeutical interventions such as beta-blockers[5,6], nitrates[7] ACE-inhibitors[6] and early thrombolysis[8,9] have been advocated to reduce the risk of rupture following an AMI, the incidence of this complication has remained almost unchanged[4,10-12] and at least 4 out of 100 patients hospitalized for an AMI actually die of cardiac rupture[4,6,10,12,33,34]. For these reasons, postinfarction cardiac rupture has been considered until recently a poorly preventable complication[3,36].

The main result of our retrospective study was the lower cardiac rupture incidence among patients in the PTCA group in comparison to those in the systemic thrombolysis group. Although not randomized, our groups were well comparable as regards the main demographic and clinical characteristics of the patients enrolled, as well as the treatment of the acute phase of the infarction, with the main exception of the reperfusion strategy applied to each group. Thus our data suggest that the different reperfusion strategies may be responsible for the effect observed.

The general consensus is that cardiac rupture is related to a complete, persistent thrombotic occlusion of the infarct-related artery[15-17,37,38] and to the consequent transmural necrosis[39,40], massive and spatially delimited[41], of the infarcted area, particularly in patients with poor collateral support. Thus, the widespread use of systemic thrombolysis would have been expected to cause a dramatic reduction of postinfarction cardiac rupture. Unfortunately, the clinical studies undertaken until now have shown that systemic thrombolysis is poorly efficacious in preventing this complication of AMI[8,9,42-45]. The main cause of this is the incomplete reperfusion of the infarcted area often allowed by thrombolysis[46,47]. Furthermore, the thrombolytic agents have been demonstrated to cause both the heart's interstitial collagen breakdown[48,49] and local hemorrhage of the infarcted area[50,51]. Finally, the several contraindications to thrombolysis allow the treatment to be administered only in a relatively small percentage of the AMI patients[24,26,31,52].

In order to prevent cardiac rupture primary PTCA offers, in comparison to systemic thrombolysis, several theoretical advantages, first of all the greater probability of immediate recanalization of the infarct-related artery together with both a lower residual stenosis and a lower reocclusion risk[18-22]. Furthermore, PTCA is not associated with any direct hemorrhagic effect[53] and can be performed even in patients with clinical contraindications to systemic thrombolysis. Finally, the time window for PTCA seems wider than that observed for systemic thrombolysis[54].

The impact of PTCA on postinfarction cardiac rupture, although appealing, has not been adequately investigated until now. In fact, the main clinical studies of head-to-head comparison between PTCA and systemic thrombolysis[18-20,55-58], as well as the overviews on primary PTCA for AMI[21,59] did not analyze the causes of in-hospital death among the patients enrolled. A low cardiac rupture incidence has however been reported (generally as an incidental finding) in few clinical series of AMI patients treated with direct PTCA by tertiary centers with interventional cardiology facilities[22,60-62]. Therefore, these data include non-consecutive AMI patients, and largely referred for PTCA based on specific clinical indications, first of all hemodynamic instability[27], and thus more prone to die of circulatory failure from cardiogenic shock. In fact, a proportion of early deaths due to pump failure higher than that observed in the thrombolytic trials have been reported in these studies[22,61,62].

Moreover, in these studies the causes of death were defined retrospectively[61] and based on clinical criteria only[62], and this could have lead to an underestimation

of the number of cardiac ruptures[63,64].

To the best of our knowledge, until now only one study[65] specifically addressed the possible role of primary PTCA in preventing cardiac rupture, but concerning only the interventricular septum and the papillary ruptures which represent a minority of postinfarction cardiac ruptures[10,12].

Thus the present study is the first to suggest that, if applied to a "real world" AMI patient population, a PTCA-based reperfusion strategy might allow, in comparison to conventional thrombolytic treatment[31], a significant reduction of the global incidence of postinfarction cardiac ruptures.

Limitations of the study. The main limitation of the study is the retrospective design: in fact our patients were not randomly assigned to primary PTCA or to thrombolytic treatment. Thus, our results should be supported by a prospective, randomized clinical trial testing primary PTCA vs some novel thrombolytic strategy.

Furthermore, the reduced cardiac rupture incidence is a specific effect of primary PTCA, therefore a logical consequence would have been the reduction of the in-hospital mortality of PTCA-treated patients in comparison to those submitted to conventional reperfusion treatment. In our series mortality among Group A (6.8%) was actually lower in comparison to Group B (10.8%), but our data cannot bring about any definite conclusion on that owing to the retrospective design (and, secondarily, to the inadequate statistic power) of the study.

No papillary ruptures were observed among our patients: thus our data do not give any further information about the suggested ability of PTCA to prevent this particular form of cardiac rupture[65].

Finally, our data are relative to "conventional" systemic thrombolysis[31], and cannot be extrapolated to the more recent protocols of administration of the thrombolytic drugs[66], neither to any "combination" reperfusion therapy of AMI[67].

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References

1. Normand J, Perrin A, Plauchu G, Froment R. Les ruptures pariétales et septales au cours des infarctus myocardiques. Arch Mal Coeur Vaiss 1965; 58: 1311-36.
2. Petrov K, Karalambev N, Toneva N, Vassilev C. Analyse de 153 cas de rupture du myocarde après l'infarctus aigu du myocarde. Arch Mal Coeur Vaiss 1977; 70: 691-7.
3. Bates RJ, Beutler S, Resnekov L, Anagnostopoulos E. Cardiac rupture - challenge in diagnosis and management. Am J Cardiol 1977; 40: 429-37.
4. Pollak H, Nobis H, Miczoch J. Frequency of left ventricular free wall rupture complicating acute myocardial infarction since the advent of thrombolysis. Am J Cardiol 1994; 74: 184-6.
5. ISIS-1 (First International Study of Infarct Survival) Collaborative Group. Mechanisms for the early mortality reduction produced by beta-blockade started early in acute myocardial infarction: ISIS-1. Lancet 1988; 1: 921-3.
6. Becker RC, Hochman JS, Cannon CP, et al. Fatal cardiac rupture among patients treated with thrombolytic agents and adjunctive thrombin antagonists: observations from the Thrombolysis and Thrombin Inhibition in Myocardial Infarction 9 Study. J Am Coll Cardiol 1999; 33: 479-87.
7. Pollak H, Mlczoch J. Effect of nitrates on the frequency of left ventricular free wall rupture complicating acute myocardial infarction: a case-controlled study. Am Heart J 1994; 128: 466-71.
8. Honan MB, Harrel FE, Reimer KA, et al. Cardiac rupture, mortality and the timing of thrombolytic therapy: a meta-analysis. J Am Coll Cardiol 1990; 16: 359-67.
9. Becker RC, Charlesworth A, Wilcox RG, et al. Cardiac rupture associated with thrombolytic therapy: impact of time to treatment in the Late Assessment of Thrombolytic Efficacy (LATE) study. J Am Coll Cardiol 1995; 25: 1063-8.
10. Dellborg M, Held P, Swedberg K, et al. Rupture of the myocardium. Occurrence and risk factors. Br Heart J 1985; 54: 11-6.
11. Reddy SG, Roberts WC. Frequency of rupture of the left ventricular free wall or ventricular septum among necropsy cases of fatal acute myocardial infarction since introduction of Coronary Care Units. Am J Cardiol 1989; 63: 906-11.
12. Bartoletti A, Mazzoni V, Casolo GC, Bini A. Rottura della parete libera del ventricolo sinistro in corso di infarto miocardico: incidenza, presentazione clinica, evoluzione. G Ital Cardiol 1993; 23: 1155-64.
13. Bellotto F, Stritoni P, Chioin R, et al. La rottura di cuore quale complicanza dell'infarto miocardico in fase acuta. Contributo casistico ed evoluzione clinica dei sopravvissuti. G Ital Cardiol 1985; 15: 1176-80.
14. Stevenson WG, Linssen GCM, Havenith MG, et al. The spectrum of death after myocardial infarction: a necropsy study. Am Heart J 1989; 118: 1182-8.
15. Oblath RW, Levinson DC, Griffith GC. Factors influencing rupture of the heart after myocardial infarction. JAMA 1952; 149: 1276-81.
16. Wessler S, Zoll PM, Schlesinger MJ. The pathogenesis of spontaneous cardiac rupture. Circulation 1952; 6: 334-51.
17. Cheriex EC, De Swart H, Dijkman LW, et al. Myocardial rupture after myocardial infarction is related to the perfusion status of the infarct-related coronary artery. Am Heart J 1995; 129: 644-50.
18. Grines GL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. N Engl J Med 1993; 328: 673-9.
19. Zijlstra F, Jan de Boer M, Hoorntje CA, et al. A comparison of immediate coronary angioplasty with intravenous streptokinase in acute myocardial infarction. N Engl J Med 1993; 328: 680-4.
20. Gibbons RJ, Holmes DR, Reeder GS, et al. Immediate angioplasty compared with the administration of a thrombolytic agent followed by conservative treatment for myocardial infarction. N Engl J Med 1993; 328: 685-91.
21. Weaver WD, Simes RJ, Betriu A, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. JAMA 1997; 278: 2093-8.
22. Antoniucci D, Bolognese L, Buonamici P, et al. Trattamento sistematico dell'infarto miocardico acuto con angioplastica primaria. Risultati clinici e angiografici precoci e a sei mesi. G Ital Cardiol 1999; 29: 1413-21.
23. WHO. Task Force on Standardization of Clinical Nomenclature: nomenclature and criteria for diagnosis of ischemic

heart disease. Circulation 1979; 59: 607-8.
24. GISSI-2. A factorial randomised trial of alteplase versus streptokinase and heparin versus no heparin among 12 490 patients with acute myocardial infarction. Lancet 1990; 336: 65-71.
25. 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 1996; 28: 1328-428.
26. GISSI. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986; 1: 397-402.
27. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography: executive summary and recommendations. Circulation 1999; 99: 2345-57.
28. Grines CL. Should thrombolysis or primary angioplasty be the treatment of choice for acute myocardial infarction? Primary angioplasty - the strategy of choice. N Engl J Med 1996; 335: 1313-6.
29. Chesebro JH, Knatterud G, Roberts R, et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Circulation 1987; 76: 142-54.
30. Antoniucci D, Santoro GM, Bolognese L, et al. A clinical trial comparing primary stenting of the infarct-related artery with optimal primary angioplasty for acute myocardial infarction. Results from the Florence Randomized Elective Stenting in acute Coronary Occlusions (FRESCO) trial. J Am Coll Cardiol 1998; 31: 1234-9.
31. The GUSTO Investigators. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. N Engl J Med 1993; 329: 673-82.
32. Galve E, Garcia-Del Castillo H, Evangelista A, et al. Pericardial effusion in the course of myocardial infarction: incidence, natural history and clinical relevance. Circulation 1985; 73: 294-9.
33. Lopez-Sendon J, Gonzalez A, Lopez de Sa E, et al. Diagnosis of subacute ventricular wall rupture after acute myocardial infarction: sensitivity and specificity of clinical, hemodynamic and echocardiographic criteria. J Am Coll Cardiol 1992; 19: 1145-53.
34. Purcaro A, Costantini C, Ciampani N, et al. Diagnostic criteria and management of subacute ventricular free wall rupture complicating acute myocardial infarction. Am J Cardiol 1997; 80: 397-405.
35. Hochman JS, Gersh BJ. Acute myocardial infarction: complications. In: Topol EJ, ed. Textbook of cardiovascular medicine. Philadelphia, PA: Lippincott-Raven, 1998: 437-80.
36. Thiene G. La rottura esterna dell'area necrotica in corso di infarto miocardico: rassegnazione o necessità di ripensamento? G Ital Cardiol 1985; 15: 334-5.
37. Krumbhaar EB, Crowell C. Spontaneous rupture of the heart: a clinical pathologic study based on 22 unpublished cases and 632 from the literature. Am J Med Sci 1925; 170: 828-56.
38. Lautsch EV, Lanks KW. Pathogenesis of cardiac rupture. Arch Pathol 1967; 84: 264-71.
39. London RE, London SB. Rupture of the heart. A critical analysis of 47 consecutive autopsy cases. Circulation 1965; 31: 202-8.
40. Naeim F, de la Maza LM, Robbins SL. Cardiac rupture during myocardial infarction. A review of 44 cases. Circulation 1972; 45: 1231-9.
41. Penther P, Hemon P, Blanc JJ, et al. Les ruptures du coeur à la phase aiguë de l'infarctus du myocarde. Arch Mal Coeur Vaiss 1975; 68: 711-8.
42. Yusuf S, Collins R, Peto R, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. Eur Heart J 1985; 6: 556-85.
43. Mauri F, De Biase AM, Franzosi MG, et al. Analisi delle cause di morte intraospedaliera. G Ital Cardiol 1987; 17: 37-44.
44. Becker RC, Gore JM, Lambrew C, et al. A composite view of cardiac rupture in the United States National Registry of Myocardial Infarction. J Am Coll Cardiol 1996; 27: 1321-6.
45. Verheugt FW. The early risk of thrombolytic therapy for acute myocardial infarction: incidence, mechanisms and possible prevention. J Cardiovasc Risk 1998; 5: 103-8.
46. Lincoff AM, Topol EJ. Illusion of reperfusion. Does anyone achieve optimal reperfusion during acute myocardial infarction? Circulation 1993; 88: 1361-74.
47. The GUSTO Angiographic Investigators. The effect of tissue plasminogen activator, streptokinase or both on coronary artery patency, ventricular function and survival after acute myocardial infarction. N Engl J Med 1993; 329: 1615-22.
48. Host NB, Stoltemberg NB, Jensen LT, Larsen OG, Aurup P. Effect on collagen metabolism of thrombolytic therapy with tissue-plasminogen activator. A randomized, placebo-controlled study. Eur J Clin Invest 1995; 25: 15-8.
49. Peuhkurinen K, Risteli L, Jounela A, Risteli J. Changes in interstitial collagen metabolism during acute myocardial infarction treated with streptokinase or tissue plasminogen activator. Am Heart J 1996; 131: 7-13.
50. Topol EJ, Herskowitz A, Hutchins GM. Massive hemorrhagic myocardial infarction after coronary thrombolysis. Am J Med 1986; 81: 339-43.
51. Renkin J, De Bruyne B, Benit E, Joris JM, Carlier M, Col J. Cardiac tamponade early after thrombolysis for acute myocardial infarction: a rare but not reported hemorrhagic complication. J Am Coll Cardiol 1991; 17: 280-5.
52. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction. Lancet 1988; ii: 349-60.
53. De Boer MJ, Hoorntje JCA, Ottervanger JD, et al. Immediate coronary angioplasty versus intravenous streptokinase in adult myocardial infarction: left ventricular ejection fraction, hospital mortality and reinfarction. J Am Coll Cardiol 1994; 23: 1004-8.
54. Nunn CM, O'Neill WW, Rothbaum D, et al. Long-term outcome after primary angioplasty: report from the Primary Angioplasty in Myocardial Infarction (PAMI-I) trial. J Am Coll Cardiol 1999; 33: 640-6.
55. Ribeiro EE, Silva LA, Carneiro R, et al. Randomized trial of direct coronary angioplasty versus intravenous streptokinase in acute myocardial infarction. J Am Coll Cardiol 1993; 22: 376-80.
56. Garcia E, Elizaga J, Perez-Castellano N, et al. Primary angioplasty versus systemic thrombolysis in anterior myocardial infarction. J Am Coll Cardiol 1999; 33: 605-11.
57. Danchin N, Vaur L, Genes N, et al. Treatment of acute myocardial infarction by primary coronary angioplasty or intravenous thrombolysis in the "real world": one-year results from a nationwide French survey. Circulation 1999; 99: 2639-44.
58. Berger AK, Schulman KA, Gersh BJ, et al. Primary coronary angioplasty vs thrombolysis for the management of acute myocardial infarction in elderly patients. JAMA 1999; 282: 341-8.
59. Michels KB, Yusuf S. Does PTCA in acute myocardial infarction affect mortality and reinfarction rates? A quantitative overview (meta-analysis) of the randomized clinical trials. Circulation 1995; 91: 476-85.
60. Rothbaum DA, Linnemeier TJ, Landin RJ, et al. Emergency percutaneous transluminal coronary angioplasty in acute myocardial infarction: a 3-year experience. J Am Coll Cardiol

1987; 10: 264-72.
61. Kahn JK, O'Keefe JH, Rutheford BD, et al. Timing and mechanism of in-hospital and late death after primary coronary angioplasty during acute myocardial infarction. Am J Cardiol 1990; 66: 1045-8.
62. Brodie BR, Stuckey TD, Hansen CJ, et al. Timing and mechanism of death determined clinically after primary angioplasty for acute myocardial infarction. Am J Cardiol 1997; 79: 1586-91.
63. O'Rourke MF. Subacute heart rupture following myocardial infarction. Clinical features of a correctable condition. Lancet 1973; 21: 124-6.
64. Figueras J, Curòs A, Cortadellas J, Soler-Soler J. Reliability of electromechanical dissociation in the diagnosis of left ventricular free wall rupture in acute myocardial infarction. Am Heart J 1996; 131: 861-4.
65. Kinn JW, O'Neill WW, Benzuly KH, et al. Primary angioplasty reduces risk of myocardial rupture compared to thrombolysis for acute myocardial infarction. Cathet Cardiovasc Diagn 1997; 42: 151-7.
66. Antman EM, Giugliano RP, Gibson M, et al, for the TIMI 14 Investigators. Abciximab facilitates the rate and extent of thrombolysis. Results of the Thrombolysis in Myocardial Infarction (TIMI) 14 Trial. Circulation 1999; 99: 2720-32.
67. Ross AM, Coyne KS, Reiner JS, et al. A randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute myocardial infarction: the PACT trial. PACT Investigators. Plasminogen-activator Angioplasty Compatibility Trial. J Am Coll Cardiol 1999; 34: 1954-62.