Which is the best reperfusion strategy for patients with high-risk myocardial infarction?

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Systemic thrombolysis and primary percutaneous coronary intervention (PCI) are both effective treatments for acute ST-elevation myocardial infarction. Several randomized trials have shown that primary PCI is superior to thrombolytic therapy in acute myocardial infarction (AMI). Despite these findings, thrombolytic therapy remains an acceptable alternative for most patients, yet it may not be ideal for higher-risk AMI patients. Advanced age, diabetes mellitus, anterior infarction, severe tachycardia, shock and comorbidities are associated with early mortality rates ranging from 10 to 58% in patients treated with thrombolytic agents.

This review will examine the data comparing primary PCI and systemic thrombolysis in the different clinical conditions which identify patients at high risk in the setting of AMI.

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Introduction

Systemic thrombolysis and primary percutaneous coronary intervention (PCI) are both effective treatments for acute ST-elevation myocardial infarction (STEMI). Several randomized comparisons have shown that primary PCI is superior to thrombolytic therapy in achieving reperfusion and reducing mortality[1-3] in acute myocardial infarction (AMI). Despite these findings, thrombolytic therapy remains the mainstay of therapy for AMI, partly due to the fact that the majority of hospitals lack of PCI capabilities.

Although trials and registries suggest substantial benefit for routine primary angioplasty in some settings[1-4], whether routine use for all patients would be worthwhile is controversial for several reasons. Firstly, modeling experiments suggest that even relatively small, high-risk subgroups may be critically influential in determining the overall outcome of a clinical trial[5]. Secondly, most patients with AMI have excellent outcomes with thrombolytic therapy, and the marginal benefits of primary angioplasty in these patients may be modest, even in the best settings, and may be outweighed by the adverse impact of delaying reperfusion on account of the transport to an angioplasty-capable center. Therefore, although thrombolytic therapy remains an acceptable alternative for most patients, it may not be ideal for higher-risk patients. Advanced age, diabetes mellitus, anterior infarction, shock, and comorbidities are associated with early mortality rates ranging from 10 to 58% in patients treated with thrombolytic agents[6].

A recent study[7], using a validated logistic regression model in order to estimate the distribution of mortality risk in a community-based sample of 1058 patients, suggested that high-risk populations with AMI are much more likely to benefit from primary angioplasty than low-risk populations.

This review will examine the data comparing primary PCI and systemic thrombolysis in the different clinical conditions which identify patients at high risk in the setting of AMI.

Advanced age

In the last decades the number of elderly patients being treated for symptomatic coronary artery disease has been steadily increasing[8-10]. Patients > 75 years of age comprise 36% of all patients with AMI and 60% of all deaths from myocardial infarction, 9-fold higher than younger patients[11-17].

Reperfusion therapy, including thrombolytic therapy and primary angioplasty, is underutilized in eligible elderly patients with AMI. This is especially true in high-risk patients, like elderly patients with large anterior myocardial infarction complicated

by heart failure and hypotension, who have the most to gain from aggressive therapy[18].

Although older patients, who received thrombolytic therapy or primary angioplasty, had a lower mortality at 1 year compared with those who did not receive a reperfusion strategy, only those treated with primary angioplasty had better survival at 30 days[19,20]. For this reason, the effectiveness of thrombolytic therapy in elderly patients has recently been questioned[21,22], based also on data from the Medicare Cooperative Cardiovascular Project registry[23]. The FTT (Fibrinolytic Therapy Trialists) performed a meta-analysis of nine randomized, placebo-controlled studies of the use of thrombolytic therapy in 5754 patients aged ≥ 75 years with AMI[24]. The initial meta-analysis showed a non-significant reduction in mortality at 35-day follow-up in patients treated with thrombolytic therapy vs placebo (24.3 vs 25.3%). On the other hand, a more recent meta-analysis of FTT data, cited by White[19] and by Estess and Topol[25] showed that among patients aged ≥ 75 years with AMI, mortality at 35-day follow-up was significantly reduced: from 29% on placebo to 26% on thrombolytic therapy (p = 0.03). On the contrary, three observational studies[20,23,26] have suggested that the use of thrombolytic therapy in patients > 75 years with AMI may be associated with adverse outcomes.

Primary coronary angioplasty is an alternative tool to accomplish reperfusion of the infarct-related vessel with a lower risk of intracerebral hemorrhage, when compared with thrombolytic therapy[1,2,24,27]. In a pooled analysis of three randomized studies of primary angioplasty vs thrombolysis in elderly patients (> 70 years), angioplasty was more effective[28]. Furthermore, the high incidence of comorbidity and contraindications to thrombolytic therapy makes primary PCI an attractive reperfusion modality in this AMI patient group.

On the other hand, PCIs carry an increased procedural risk in older patients when compared with those of younger age[29] and the place of primary coronary angioplasty in elderly patients with AMI has not yet been determined in a randomized comparison as most studies recruited only few elderly patients. Recently, a prospective randomized trial[30] comparing primary coronary angioplasty with intravenous streptokinase therapy in ≥ 76 years AMI patients with no contraindications to thrombolytic therapy did not demonstrate any benefit with regard to 30-day survival (relative risk-RR 4.0, 95% confidence interval-CI 0.9 to 24.6, p = 0.04): conversely, the incidence of the predefined composite endpoint of death, recurrent infarction and stroke after 30 days was significantly lower in the angioplasty-treated patient group (RR 4.3, 95% CI 1.2 to 20.0, p = 0.01). The long-term follow-up data showed a statistically significant benefit with regard to survival after 1 year (RR 3.4, 95% CI 1.0 to 13.5, p = 0.03) and the combined clinical endpoint of death, recurrent AMI or stroke (RR 5.2, 95% CI 1.7 to 18.1, p = 0.001) of angioplasty treatment over thrombolytic therapy. Previously, Zijlstra et al.[31] randomized 395 patients (mean age 60 years) with AMI to treatment with PCI or streptokinase therapy. At 5-year follow-up, mortality was 13% in the PCI group vs 24% in the streptokinase group (a 46% significant reduction by primary angioplasty). Non-fatal reinfarction occurred in 6% of the PCI group vs 22% of the streptokinase group (a 73% significant reduction by PCI). In the Cooperative Cardiovascular Project[32], a retrospective cohort study showed that 18 645 patients with AMI (mean age 73 years) were treated with thrombolytic therapy and 2038 (mean age 73 years) were treated with primary PCI. The 30-day mortality was 8.7% in patients treated with PCI vs 11.9% in patients treated with thrombolytic therapy (p = 0.001). The 1-year mortality was 14.4% in patients treated with PCI vs 17.6% in patients treated with thrombolytic therapy (p = 0.001). Finally, Aversano et al.[33] randomized 451 thrombolytic-eligible patients (mean age 64 years) with AMI to PCI or thrombolytic therapy in 11 community hospitals without on-site cardiac surgery. At 6-week follow-up, the primary endpoint of death, recurrent myocardial infarction, and stroke was 10.7% in the PCI-treated group vs 17.7% in the thrombolytic therapy group (p = 0.03).

A paucity of data exists regarding the outcome after primary PCI of the specific subset of very elderly patients (≥ 80 years), with the only published study being that of Laster et al.[34]. These investigators reviewed the cumulative experience of primary PCI (mean time to reperfusion of 4.3 ± 2.8 hours) in 55 patients (mean age 83.3 ± 2.3 years) over a period of 13 years. Overall, the 30-day mortality rate was 16%. The mortality rate was 67% for patients with cardiogenic shock on presentation and 10% for patients without cardiogenic shock. The 1-year actuarial survival rate was 67%. These data seem to be confirmed by the observational data of centers performing systematic primary angioplasty in Italy. A single center registry of 55 octogenarian and older patients treated with primary PCI in Florence reported a 30-day mortality of 16% including patients with cardiogenic shock at presentation and 4% in those without cardiogenic shock[35]; a recent extension of the registry, including 342 patients > 75 years, reported a 30-day mortality of 15% including shock patients.

Nowadays, tenecteplase seems to be the best available candidate for thrombolytic therapy in elderly patients. The ASSENT-2 (Assessment of the Safety and Efficacy of a New Thrombolytic) trial[36], in patients > 75 years, showed a lower incidence of intracranial hemorrhage in patients treated with tenecteplase compared to alteplase (1.7 vs 2.6%), and also a trend toward lower mortality (17.4 vs 19.3%, p = 0.286). Due to its higher fibrin specificity, tenecteplase was also associated with lower non-intracranial bleeding[36]. Furthermore, in terms of lytic efficacy, tenecteplase is at least as effective as alteplase in angiographic studies[37,38].

From the available data, it is not possible to conclude whether thrombolytic therapy is beneficial or

detrimental in patients > 75 years with AMI. However, the data favor the use of PCI, especially in high-risk elderly patients.

Diabetes mellitus

The prevalence of ischemic heart disease complicating diabetic syndromes is growing rapidly as is the prevalence of the syndrome itself.

Coronary atherosclerotic disease in diabetic patients differs in several aspects from coronary disease in non-diabetic patients. Endothelial dysfunction, platelet and coagulation abnormalities contribute to the accelerated atherosclerotic process and to the development of coronary thrombosis. Coronary specimens taken from diabetic patients exhibit a larger content of lipid-rich atheroma, a greater macrophage infiltration, and more thrombosis than tissue from patients without diabetes. These differences suggest a greater vulnerability for plaque disruption and coronary thrombosis in patients with diabetes mellitus than in the general population[39,40].

Hyperglycemia alone is associated with an increased risk of heart failure, cardiogenic shock, and death after AMI and is an independent prognostic factor for no-reflow, along with age, gender, absence of pre-infarction angina, complete occlusion of the culprit lesion, and anterior AMI[41].

Acute coronary syndromes, including AMI and sudden death, are indeed twice as frequent in diabetic than in non-diabetic coronary patients[40] and their management in this group of high-risk patients remains a difficult challenge.

In a major international trial involving more than 40 000 patients designed to evaluate four fibrinolytic strategies for the treatment of AMI, the 30-day mortality was 6.2% among patients without diabetes and 10.5% among patients with diabetes. Indeed, by pooling the data from several large fibrinolytic trials with a total of more than 80 000 patients, the 1-month mortality was increased by 1.7 times among diabetics[42]. Notably, mortality was highest among those treated with insulin. Undoubtedly less known is the fact that fibrinolysis saved 37 lives per 1000 patients with diabetes at 35 days, compared with 15 per 1000 patients without diabetes[24]. Thus, the absolute benefit is more than doubled for fibrinolytic therapy among diabetics.

Despite its tremendous benefit, patients with diabetes were less likely to receive fibrinolytic therapy[43], as evidenced in the SAVE (Survival and Ventricular Enlargement) study. In this trial, of the 2231 patients enrolled, fibrinolytic therapy was administered in 733 (32.9%).

Diabetic patients undergoing PCI exhibit similar angiographic success rates to non-diabetic patients, but show a trend toward higher in-hospital mortality rates, higher rates of urgent revascularization, and greater incidence of acute coronary occlusions. Diabetes is an independent predictor of clinical outcome, as the early and late mortality rates[44], with higher incidences of death, AMI and repeated revascularization at long-term follow-up, also after primary PCI.

Until now, the optimal strategy for coronary revascularization in diabetic patients remains to be determined. The addition of stent implantation to balloon angioplasty in diabetic patients is feasible with favorable procedural and in-hospital success rates. However, long-term outcomes after stenting remain worse because of a higher incidence of major adverse cardiac events and, above all, of restenosis rate as compared to non-diabetic patients[45]. The increased risk of restenosis after angioplasty and/or stenting in diabetic patients is primarily due to an exaggerated reactive intimal hyperplasia that causes increased late lumen loss and decreased vessel lumen area[46]. In a recent pooled analysis of several major recent stent trials, Cutlip et al.[47] found diabetes to be the strongest clinical predictor for restenosis, with almost 50% increased risk for target lesion revascularization at 1-year follow-up. Considering the higher rate of restenosis and the current prevalence of diabetes among patients who undergo PCI (e.g., a prevalence of 18 to 30% in most series), a simple calculation would show that 30 to 40% of the patients who sustain clinical restenosis and eventually undergo target vessel revascularization are those with diabetes mellitus[48]. Thus, the reduction of restenosis rate among diabetic patients will have a major favorable impact on the global outcome of catheter-based coronary interventions.

The liberal use of glycoprotein IIb/IIIa inhibitors favorably affects the results of PCI and stenting in diabetic patients. Pooled data from EPIC, EPILOG, and EPISTENT trials showed that abciximab decreases the 1-year mortality of diabetics to the rate observed in placebo-treated non-diabetic patients[49-51]. Subgroup analysis, however, suggests that clinical benefits may be not as sustained in diabetic patients as in the general population. Clearly, further investigations are needed to explain the interaction of glycoprotein IIb/IIIa inhibition and diabetes in patients undergoing PCI.

In conclusion, whether stents and glycoprotein IIb/IIIa inhibitors will modify these features is still controversial. Treatment advances such as improvements in interventional techniques, gene therapy and drug-eluting stents may substantially modify this scenario in the near future.

Renal insufficiency

Cardiovascular diseases are the leading cause of death among patients with renal insufficiency (RI). Patients with varying degrees of renal failure make up an increasing percentage of the population undergoing PCI[52]. Unfortunately, the management of AMI in this

subset of patients is particularly problematic. Although the existence of RI in patients undergoing PCI in the non-AMI setting is associated with a poor prognosis[52], the outcomes of primary PCI in patients with AMI and RI have not been well characterized since such patients are typically excluded from clinical trials[53,54].

Several observational series have found that patients with a baseline creatinine level > 1.5 mg/dl who undergo PCI experience a significantly lower procedural success rate, and at least a 5-fold increase in major in-hospital adverse events, and a nearly 4 times higher mortality rate on long-term follow-up than patients with a baseline creatinine level < 1.5 mg/dl. In a large retrospective analysis of patients undergoing elective PCI, RI was found to have a negative prognostic impact, similar to that of diabetes mellitus, on cardiovascular morbidity and mortality[55].

A recent study by Sadeghi et al.[56] demonstrated that, in patients undergoing primary PCI for AMI, the presence of RI at baseline was associated with a striking increase in short-term and late mortality, similar to the excess risk of anterior vs non-anterior myocardial infarction location. Despite the association of RI with multiple high-risk features known to affect the prognosis of patients after primary angioplasty, RI was one of the strongest independent predictors of diminished survival, especially in the early phase of post-AMI. The presence of baseline RI was also strongly associated with a significant increase in major hemorrhagic complications and the need for blood product transfusion as well as severe restenosis and infarct-related artery reocclusion.

Nonetheless, the impact of baseline RI on mortality was independent of age, sex, medication use, and other covariates when evaluated in a multivariable model. Unique metabolic abnormalities of chronic RI, including insulin resistance, dyslipidemia, homocysteinemia, hyperuricemia, and increased atherosclerotic, thrombotic, and oxidative stress[57-61], may contribute to the independent excess cardiovascular risk in these patients. In addition, the procedural success rate was lower in patients with RI owing to a higher rate of periprocedural complications, which may have contributed to their worse long-term prognosis.

Radiocontrast toxicity may also contribute to clinical deterioration after primary PCI in AMI. Depending on the definition used, a contrast-induced nephropathy occurs in about 1 to 15% of a general PCI population and in 20 to 40% of patients with preexisting RI[62-64]. All attempts must be made to prevent contrast nephropathy, including adequate hydration[65], minimizing contrast use[64], use of low-osmolar contrast[66], and possible administration of N-acetylcysteine[67]. Patients with baseline RI warrant close surveillance and intensive medical management, including tight control of diabetes, hypertension, and dyslipidemia[57], dietary modification, and potentially frequent stress testing for early recognition of disease progression. Whether the incidence or prognostic implications of RI after fibrinolytic therapy are different from those after primary PCI also deserves further study. Novel approaches are required for patients with RI to favorably affect their otherwise poor prognosis.

Shock

The incidence of cardiogenic shock complicating AMI remains approximately 7 to 8%, according to the recent literature[68]. Retrospective studies suggest that early PCI may improve the outcome in patients with cardiogenic shock[69-72]. The randomized SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial[73] showed that a strategy of early revascularization, either with surgery or PCI as deemed appropriate by the treating cardiologist, increased the 1-year survival from 34 to 47% ($p = 0.025$) compared with initial aggressive medical therapy in 302 patients with shock due to left ventricular dysfunction complicating AMI. In this trial, the success rate of PCI was relatively low (76%) but consistent with previous retrospective shock studies[74], and not unexpected given that most patients had diffuse disease, occluded arteries, and were hemodynamically unstable. Stents were used in 34% of the patients, mainly to salvage a failed balloon PCI, and were largely first-generation devices implanted without the benefit of current adjunctive techniques. Similarly, glycoprotein IIb/IIIa inhibitor and thienopyridine use was infrequent but increased during the nearly 6-year trial period. Potentially, the increased use of stenting and adjunctive therapies that improve coronary blood flow might further extend the benefits of PCI[75-78].

The SHOCK trial also suggested a lack of benefit for early revascularization in patients ≥ 75 years of age. However, the numbers were small, with only 12 PCI patients ≥ 75 years of age.

Although PCI tended to be successful less often in elderly patients, successful PCI seems to be associated with increased survival. Dzavik et al.[79] reported higher survival rates for the 17% of patients ≥ 75 years of age in the SHOCK registry who were clinically selected to undergo early revascularization compared with those with late or no revascularization.

Further trials are needed to assess the impact of modern, innovative technologies and pharmacological treatment[80] in this high-risk subgroup of patients. However, at the moment, the prognosis of patients with AMI and cardiogenic shock remains extremely guarded.

Anterior wall myocardial infarction

Some prospective randomized trials have established the superiority of primary PCI over fibrinolytic

treatment even in patients with anterior wall AMI. These excellent PCI results are also duplicated in smaller hospitals where there may be delays in getting the cardiac catheterization team to the laboratory, as demonstrated by a recent study[81] aimed to compare the outcome of patients with anterior wall myocardial infarction, without cardiogenic shock on admission, treated with primary PCI or thrombolytic therapy. The data of all patients with myocardial infarction hospitalized in coronary care units operating in Israel during three consecutive national surveys were analyzed[81]. A total of 1038 patients with anterior wall myocardial infarction were treated by reperfusion (886 received thrombolytic therapy, 152 primary PCI). Overall, the outcome of patients treated using primary PCI was better compared to patients treated with thrombolysis, with a 68% RR reduction of 30-day mortality (mortality at 30 days: 2 vs 6.3%, p = 0.04). A subanalysis of patients according to age showed that the beneficial effect of primary PCI on mortality was mainly clustered among the younger AMI patients.

Late presentation

The benefits of intravenous thrombolysis appear to be dependent on the time elapsed between symptom onset and initiation of treatment[24], and when treatment is established in the first 2 hours, survival increases dramatically[82]. In this respect, it is noteworthy that the ability of certain thrombolytic agents to recanalize the infarct-related artery appears to decrease with time[83,84]. Prehospital thrombolysis appears safe and effective and is associated with a substantial gain in time to treatment[85]. The CAPTIM (Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction) trial[86] was set up to compare prehospital thrombolysis and primary PCI in patients with STEMI and did not demonstrate any difference in the combined endpoint of death, reinfarction, and disabling stroke at 30 days between the two groups.

Previous retrospective analyses of cohort and trial data have suggested that outcomes after primary PCI may be relatively independent of the time between symptom onset and reperfusion but are related to the time elapsed between admission and PCI[87,88]. Consistent with these data, Zijlstra et al.[89], in a pooled-analysis of several randomized trials comparing primary angioplasty and thrombolysis, found a direct relationship between time from symptom onset to treatment only in patients treated with thrombolysis, but not with primary angioplasty. A major limitation of these studies is that they did not stratify patients according to the risk of death.

Conversely, recent studies and clinical trials[90] suggest that time since symptom onset should be considered when one selects reperfusion therapy. A meta-analysis by De Luca et al.[91] showed that, in patients with STEMI treated with primary angioplasty, symptom-onset-to-balloon time, but not door-to-balloon time, was related to mortality, particularly in non-low-risk patients and a symptom-onset-to-balloon time > 4 hours was identified as an independent predictor of 1-year mortality. Consistent with these data, a previous study[92] found, in a population of 1332 patients undergoing primary angioplasty, a relationship between time delay and mortality in high-risk patients. A possible explanation for these findings is that the duration of coronary occlusion is a main determinant of the infarct size, as demonstrated in animal models[93,94]. Therefore, late reperfusion is expected to result in less myocardial salvage and higher mortality rate. Furthermore, a delay in reperfusion may be associated with an organized intracoronary thrombus in comparison with an early reperfusion, resulting in a higher incidence of distal embolization.

Transfer for primary percutaneous coronary intervention versus on-site thrombolysis

Observational studies reported few complications during transfer for primary PCI and no correlation between transfer distance and adverse outcomes[95]. Moreover, reported randomized trials have shown improved outcomes with transfer AMI patients for primary PCI[96,97].

A recent trial[98] demonstrated that also patients with high-risk AMI at hospitals without PCI capabilities might have an improved outcome if transferred for emergency PCI rather than being treated with on-site thrombolytic therapy. This trial randomized 138 patients before the study ended (71 to transfer for PCI with a mean time of 52 min, and 67 to thrombolysis). At 30 days, a 38% reduction in major adverse cardiac events was observed for the transfer group; however, because of the inability to recruit the necessary sample size, this did not achieve statistical significance (8.4 vs 13.6%, p = 0.331). Considering that the number of patients enrolled is very small, these findings need to be confirmed in a large trial before any general recommendations can be made.

Conclusions

Collected data from the literature suggest that high-risk patients, especially when presenting precociously, have the greatest benefit from primary PCI when compared with thrombolysis. Therefore, an early identification of the high-risk group may allow most of the benefits identified in population-wide angioplasty trials. The possibility of transferring high-risk patients for primary PCI to a center with interventional facilities need to be ascertained.

Riassunto

La trombolisi e l'angioplastica primaria sono entrambi efficaci trattamenti in caso di infarto miocardico acuto (IMA) con sopraslivellamento del tratto ST.

Diversi studi randomizzati di controllo hanno tuttavia dimostrato come l'angioplastica primaria sia superiore al trattamento trombolitico in termini di riperfusione e mortalità. Malgrado ciò, la trombolisi rimane il trattamento più utilizzato in caso di IMA, perché la maggior parte degli ospedali non è provvisto di emodinamica. La trombolisi però, sebbene possa essere considerata un'alternativa accettabile per molti pazienti con IMA, può non costituire il trattamento ideale per i pazienti ad alto rischio. È noto infatti che l'età avanzata, il diabete, l'infarto anteriore, lo shock e le comorbilità sono condizioni che traggono un maggior beneficio dalla procedura di angioplastica primaria, mentre sono associate ad una mortalità che varia dal 10 al 58% in pazienti trattati con agenti trombolitici.

I pazienti con più di 75 anni costituiscono il 36% di tutti i pazienti con diagnosi di IMA e il 60% di tutti i decessi per infarto miocardico. È ormai documentato che la terapia riperfusiva, sia essa la trombolisi o l'angioplastica, è sottoutilizzata in pazienti anziani con IMA. Ciò è soprattutto vero per i pazienti ad alto rischio, come i pazienti anziani con infarto anteriore esteso complicato da scompenso cardiaco ed ipotensione, che potrebbero maggiormente avvantaggiarsi di una strategia terapeutica più aggressiva. Recenti studi hanno dimostrato che i pazienti anziani sottoposti a terapia riperfusiva hanno una migliore sopravvivenza ad 1 anno rispetto a quelli che non sono trattati ed in particolare che i pazienti anziani trattati con angioplastica primaria hanno una mortalità più bassa a 30 giorni rispetto a quelli trombolisati.

Le sindromi coronariche acute e la morte improvvisa sono 2 volte più frequenti in pazienti diabetici rispetto ai non diabetici. Il miglior trattamento riperfusivo per questo gruppo di pazienti ad alto rischio rimane ancora controverso ed occorre precisare che molti studi di comparazione tra angioplastica e fibrinolisi in corso di IMA in pazienti diabetici sono stati eseguiti senza l'utilizzo di stent o di inibitori della glicoproteina IIb/IIIa che potrebbero, in un prossimo futuro, essere determinanti.

Il trattamento dell'IMA per i pazienti con insufficienza renale è particolarmente problematico. Sebbene sia ormai chiaro che la presenza di insufficienza renale in caso di IMA sia associata ad una peggiore prognosi, gli outcome dell'angioplastica primaria in caso di insufficienza renale non sono stati ancora ben delineati in quanto spesso questi pazienti ad alto rischio sono esclusi dai grandi trial clinici.

Attualmente lo shock cardiogeno in corso di IMA costituisce un fattore prognostico negativo estremamente severo. Sebbene lo SHOCK trial abbia dimostrato i benefici di una precoce terapia invasiva in questo sottogruppo di pazienti, ulteriori studi sono necessari per confermare i favorevoli risultati dell'angioplastica primaria vs la terapia trombolitica.

Differente invece è il caso dell'IMA anteriore in cui diversi trial prospettici e studi *post-hoc* hanno ormai ampiamente dimostrato la superiorità dell'angioplastica primaria sulla fibrinolisi.

In conclusione, i dati della letteratura suggeriscono che i pazienti ad alto rischio con IMA, specialmente se si presentano precocemente in ospedale, hanno maggiori vantaggi, in termini di mortalità, quando sono trattati con angioplastica primaria.

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