

Introduction

Since the groundbreaking findings by DeWood et al. (1), showed that acute myocardial infarction is caused by vascular occlusion from a thrombus attached to a ruptured plaque (2,3), the treatment of this condition has definitely entered the era of reperfusion therapy. Today, thrombolysis is a cornerstone of acute treatment and aims at lysis of capillary thrombi and the reduction of blood viscosity.

In contrast to more systematic investigations in Göttingen and Berlin, early attempts by Chazov et al. using intracoronary lysis with streptokinase did not attract any attention (4,5). However, the existence of catheter laboratories at that time was small. Moreover, the time delay until execution was an inevitable drawback of intracoronary lysis, the more so as the rapid progression of myocardial necrosis was proven experimentally (6). Therefore, it was only logical to test the effects of lysis in uncomplicated and easy-to-conduct “systemic” applications. Even during the dose-finding studies, Schröder et al. suggested that in order to further optimise the time gain with i.v. lysis, treatment could be initiated pre-hospitally in the patient’s home by the emergency services (7).

The fundamental breakthrough of intravenous thrombolysis using streptokinase was achieved in the randomised, placebo-controlled GISSI study (8), comprising approximately 12,000 patients, where the time dependency of therapeutic success was impressively demonstrated. At the same time, this study also noted the high rate of re-infarctions, which is the Achilles heel of thrombolysis. In the ISIS-2 study, the combination of aspirin and streptokinase showed a mortality reduction of 47% (9). This additional gain was partly explained by the blockade of platelet aggregation, which is a possible source of re-occlusion. Even aspirin monotherapy led to a mortality reduction of approximately 24% (9). Since then aspirin has become standard in infarct therapy. In contrast, during the first major thrombolysis studies, heparin was rarely and not systematically investigated; instead, it was used both subcutaneously and intravenously for the prevention of re-occlusions.

The next major advance in reperfusion therapy for myocardial infarction was the recombinant technology production of the tissue plasminogen activator, t-PA. In angiography-controlled studies, where alternative thrombolytic agents

such as APSAC and urokinase were also tested, t-PA showed a significantly higher rate of reperfusion compared to streptokinase. The GUSTO-1 study compared streptokinase with t-PA in 41,000 patients and resulted in a clinically significant superiority of t-PA, albeit at the cost of a slightly elevated rate of intracranial haemorrhage, especially in elderly patients (10). The use of heparin with t-PA proved to be effective in preventing re-occlusions (11). Finally, t-PA became the gold standard of reperfusion therapy after Neuhaus et al. described an effective modified dosing scheme (12).

Although the time dependency of the effect of thrombolysis was the major driving force behind the introduction of intravenous lytic therapy, the option of the earliest possible pre-hospital lysis was widely postulated and discussed, but its potential was only investigated in a number of small and one larger study. The big EMIP-study (13) was also prematurely stopped due to lack of sponsorship. However, in general these studies proved the principal rationales of pre-hospital lysis were safe and showed a trend towards its use. Even so, this beneficial trend was first statistically proven in a meta-analysis (14). One possible reason for the lack of widespread interest in early pre-hospital thrombolysis could have been that cardiologists at that time were turning their focus to interventional catheterisation of an infarct, as an increasing number of hospitals were investing in cath labs. After a cautious start (15), rapid technological development took place, which enabled broad use of this method. From early on, balloon dilation was used in combination with thrombolysis (16-19), because angiography showed that lysis did not lead in all patients to an early, complete and sustained re-opening of infarcted vessels. However, these investigations had lots of complications and the results were discouraging.

The further development of coronary intervention was characterised by rapid technological progress (e.g. stents), the development of efficient adjuvant therapies (Gp IIb/IIIa receptor blockers, thienopyridines, alternative anti-thrombins) and extensive establishment of interventional centres. Comparative investigations of primary interventions with relatively late in-hospital thrombolysis appeared to prove the superiority of primary intervention in all circumstances (20). Only one study – the CAPTIM study, conducted in France – compared pre-hospital lysis (with the possibility of additional interventions following “liberal” criteria) with primary intervention (PPCI). This study showed that pre-hospital lysis (PHT) was equivalent to PPCI, and in patients treated within 120 minutes after symptom onset, PHT tended to show a lower 90-day mortality rate (21,22).

The development of injectable bolus thrombolytics with a longer half-life provided substantial additional potential for the future of lytic therapy. This easy-to-use method is especially valuable for pre-hospital use. Meanwhile, clopidogrel was also successfully applied in lytic therapy in addition to aspirin (23). Alternative antithrombins, such as enoxaparin, also contributed to significant improvements in the outcomes of lysis in ST-elevation myocardial infarction (STEMI) (24). Once again, the rationale of the combination of lysis and inter-

vention was considered in the course of technological advances. The concept of “facilitated PCI”, which is defined as immediate intervention after lytic therapy, did not turn out to be beneficial overall, although interestingly, it showed very good results after pre-hospital lysis (25,26). Conversely, the concept of a “pharmacoinvasive approach”, consisting of, above all, pre-hospital lysis with a time-delayed angiography and possible PCI, has turned out to be a promising strategy in some studies (27,28).

This book is intended to provide the rationale for the use of pre-hospital lysis, PPCI and combination strategies, taking into consideration the current guidelines, which were developed and refined using clinical and scientific experience collected over decades. Further chapters deal with practical considerations (e.g. adjunctive therapy), the procedures for specific patients groups, the organisation of networks of emergency medical services, hospitals with and without cath labs, and the comparison of various emergency systems with different levels of staff and equipment.

The aim of this book is to provide the interested reader with a current overview of the role of pre-hospital lysis as a primary reperfusion strategy within the scope of a general management of ST-elevation myocardial infarction. The authors hope to encourage the staff responsible within the emergency services to exploit the often unutilised potential of pre-hospital thrombolysis to benefit patients.

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