Reperfusion Therapy Starts in the Ambulance

Freek W.A. Verheugt, MD

Reperfusion therapy for ST-elevation acute coronary syndromes aims at early and complete recanalization of the infarct-related artery in order to salvage myocardium and improve both early and late clinical outcomes. The benefit rises exponentially the earlier therapy is initiated. The highest number of lives saved is within the first hour after symptom onset: the “golden hour.” The exponential form of the curve relating mortality to time-to-reperfusion has major implications for the timing of treatment. The impact of delay in time-to-treatment lessens as the duration of ischemia lengthens. Consequently, reducing delays will have a much more positive return in patients presenting early for those presenting late. These considerations have provided a strong incentive for the initiation of very early reperfusion therapy.

The optimal site for initiation of reperfusion strategies is the patient’s home or place where the infarction occurs. Prehospital diagnosis and treatment has been performed since 1985, when Gotsman applied prehospital fibrinolytic therapy with streptokinase in Jerusalem, Israel. This strategy has proven to be feasible, relatively safe, and efficacious. The time gain with prehospital fibrinolysis is ≈1 hour and results in 15% relative risk reduction of early mortality. Later, this form of therapy spread over the world, including the United States, where in the Seattle and Boston areas a time gain of at least 30 minutes could be reached. The major component of time gain in prehospital triage is bypassing emergency departments of hospitals, where door-to-needle easily exceeds 30 minutes, the upper limit mandated in the guidelines. An absolute prerequisite for prehospital triage is proper ECG diagnosis of ST-elevation acute myocardial infarction by ambulance personnel. This can be done by telephone transmission of the ambulance ECG for judgment by a hospital cardiologist or by computer diagnosis. Both methods are equally reliable and not inferior to hospital diagnosis of ST-elevation acute myocardial infarction. Prehospital diagnosis and triage of ST-elevation acute myocardial infarction is not only applicable to early start of fibrinolytic therapy but can also be used for adjunctive and efficacious therapies like aspirin, (low-molecular-weight) heparin, clopidogrel, and/or glycoprotein IIb/IIIa antagonists. Finally, the ambulance is the almost ideal place for triage for primary coronary angioplasty for ST-elevation acute myocardial infarction. Prehospital diagnosis followed by direct transfer to a hospital with percutaneous coronary intervention (PCI) facilities reduces time-to-treatment with at least 1 hour in Denmark. This may also be attractive in the United States, where nearly 80% of the adult population lives within 1 hour of driving time from a PCI center.

Prehospital triage, treatment, and prompt transfer to tertiary care hospitals require an elaborate system of well-trained ambulance personnel, a single dispatch system, and regional collaboration of cardiology hospitals. Whether nurses are entitled to diagnose and treat patients with acute myocardial infarction in an ambulance environment differs from country to country. Training personnel and installing equipment in ambulances in large areas are expensive but seem cost-effective. The establishment of an ambulance system to improve time delays in the treatment of ST-elevation acute myocardial infarction pays off medically, as well.

In this issue of Circulation, the STEMI Registry Group from Vienna, Austria, report on the buildup of a proper ambulance system for triage and diagnosis of ST-elevation acute myocardial infarction together with a regional rotational on-call system for PCI hospitals in a 1.8-million urban area. In >1000 patients, they found that the implementation of guidelines of early reperfusion therapy of acute ST-elevation myocardial infarction markedly improved over the years the system is active. This resulted in a drop in mortality and an increase in the use of primary angioplasty over a short period of time. Interestingly, they also compared prehospital fibrinolytic therapy and primary angioplasty with regard to mortality in relation to time-to-treatment. In addition, these investigators found that in the first 2 hours of symptom onset, there is no difference in mortality, whereas in patients presenting later angioplasty is superior in outcome. This corroborates well with the randomized Primary Angioplasty in Patients Transferred From General Community Hospitals to Specialized PTCA Units With or Without Emergency Thrombolysis (PRAUGE-2) and Comparison of Angioplasty and Prehospital Thrombolysis in acute Myocardial Infarction (CAPTIM) trials, as well as the French USIC and German PREMIR registry (Table). It seems that with an elaborate ambulance system, early treatment of ST-elevation myocardial infarction results in a low hospital mortality irrespective of the type of reperfusion strategy used. This is of great importance because in many parts of the world early primary PCI is still an illusion, whereas ambulances can reach patients quickly and start reperfusion therapy with fibrinolysis followed by transfer to a tertiary care facility where PCI can be performed, if necessary. Such a strategy is essentially...
different from lytic-facilitated primary PCI in all patients, which treatment proved to be ineffective and unsafe.16 Because rescue angioplasty after failed fibrinolysis improves clinical outcome significantly,17 a strategy of lyse first, stent later, if needed, may be attractive18 but has not been evaluated in a large trial. In the United Kingdom, the Rapid Early Action for Coronary Treatment (REACT-2) trial has been designed, in which 1440 patients will be randomized in the ambulance to primary PCI or prehospital lytic therapy plus transfer to a PCI center, where in case of <50% resolution of the ST-elevation rescue PCI is mandated. This study design is more stringent than that of the CAPTIM trial, in which patients were randomized in the ambulance to immediate transfer for primary PCI or to prehospital fibrinolytic therapy with transfer to a PCI center for a liberal but not standardized rescue strategy. In CAPTIM, rescue angioplasty was done in 26% of patients, whereas after early fibrinolysis 40% to 50% would have been expected. Until the results of the larger trials are available, the best prehospital reperfusion strategy is still unknown.

In the meantime, effort should be made to lift the early management of patients with ST-elevation myocardial infarction from the emergency department to the ambulance because this saves at least 30 to 60 minutes in time to proper treatment. Initiatives to shorten door-to-balloon time in hospitals are necessary, but more time can be gained in patients with ST-elevation myocardial infarction by direct hospital notification from the ambulance.2,3 In case of prehospital fibrinolysis, early notification of the catheterization laboratory is possible directly from the ambulance to prepare for rescue PCI, if necessary. Also in primary angioplasty, direct catheterization laboratory notification from the ambulance leads to shorter time-to-treatment by bypassing emergency departments.19 Finally, ambulance personnel should be highly trained to triage, diagnose, and treat myocardial infarction in the ambulance. Nurses can be trained for that purpose and are not necessarily less competent than physicians. In the Viennese ambulance system, physicians are on the ambulances, which seems optimal for diagnosis and treatment according to the guidelines. However, in the large Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT-3 PLUS) trial, it was shown that nurses triage and treat patients 15 minutes faster than physicians in the ambulance.20 Physicians on the ambulance are not always cardiologists or cardiology fellows but often emergency physicians. Nurses apparently treat patients faster because of computer diagnosis and lack of telephone transmission of the ECG to the hospital. Each strategy to shorten time delay in the treatment of ST-elevation acute myocardial infarction is welcome. The best step thus far is the use of ambulances in the early triage, diagnosis, and treatment of patients who present with chest pain and ST-elevation on their first ECG.

**Mortality in Studies Comparing Prehospital Fibrinolysis to Primary PCI in ST-Elevation Myocardial Infarction**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Year</th>
<th>Prehospital Fibrinolysis</th>
<th>Primary PCI</th>
<th>Follow-Up</th>
</tr>
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<tr>
<td>CAPTIM13</td>
<td>840</td>
<td>2002</td>
<td>3.8%</td>
<td>4.8%</td>
<td>30 days</td>
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<td>USC14</td>
<td>614</td>
<td>2004</td>
<td>3.3%</td>
<td>6.7%</td>
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<tr>
<td>PREMIR15</td>
<td>1449</td>
<td>2006</td>
<td>5.5%</td>
<td>4.4%</td>
<td>Hospital</td>
</tr>
</tbody>
</table>

**Disclosures**

None.

**References**


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