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ACUTE CORONARY SYNDROME

Network models for large cities: the European experience

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Optimal treatment for ST segment elevation myocardial infarction (STEMI) has largely been defined and recently published in guidelines of the international societies of cardiology.1,2 Both reperfusion strategies—primary percutaneous coronary intervention (pPCI) and thrombolytic therapy (TT)—dramatically improve clinical outcome compared to conservative treatment strategies if offered with short time delay from symptom onset. Unfortunately, 25–30% of patients with acute STEMI are still not reperfused at all, even though they are seen by physicians within 12 h of symptom onset, due to lack of organised, around the clock, 24 h care. Even in existing but not optimised networks, reperfusion strategies are offered after unacceptably long time delays in real world settings as demonstrated by the Euro Heart acute coronary syndrome survey,3 the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse outcomes with Early Implementation of the ACC/AHA Guidelines (CRUSADE) initiative,4 and the Global Registry of Acute Coronary Events (GRACE),8 respectively. Very few patients receive all the guideline indicated treatments promptly.6 Reasons for this are: the long delay until patients call medical services for ongoing chest pain (patient delay); long transfer times of patients seen by emergency medical systems (EMS), especially the inter-hospital transfer (transportation delay); and the delay which occurs within PCI capable hospitals if the personnel is not sufficiently trained, if the annual caseload is low, or if the patient is not directly transferred to the catheter laboratory and time is lost in emergency rooms or coronary care units (in-hospital delay).7

This unfavourable situation can be improved by building up and optimising systems of care (STEMI networks), in which EMS, non-PCI capable hospitals, and hospitals with PCI facilities cooperate closely with the goal to reduce total ischaemic time, offer pPCI to the majority of patients within the recommended time, and use prehospital TT in the ambulance or in-hospital TT in non-PCI hospitals with immediate transfer of the treated patients to a PCI centre. Accordingly, the organisation of networks is also part of the recent European Society of Cardiology (ESC) guidelines3 and has, wherever organised, led not only to a reduced total ischaemic time but also to a significantly higher number of patients receiving any reperfusion therapy based on guideline recommendations. As a consequence, subsequent improvements in outcomes are reflected by the decrease in short and long term mortality, fewer new cases of heart failure, and fewer recurrent myocardial infarctions, respectively.5

THE IMPACT OF TIME DELAYS
Systems of care need to consider not only delays from first medical contact (FMC) to treatment,7 9 10 but also the entire delay from symptom onset to reperfusion—the “total ischaemic time” (fig 1). As described by others, only 11% of patients could be randomised within the first hour after onset of symptoms and only 15% of patients referred for pPCI were treated within 2 h of pain onset.10–12 Large scale registries have demonstrated similar delays. In the GRACE registry, time from symptom onset to FMC was 104–120 min, with an additional “door-to-treatment” time of 35 min for fibrinolytic therapy and 73 min for pPCI. For both fibrinolytic treatment and pPCI, longer delays until reperfusion were associated with raised 6 month mortality.10 Therefore, much of the delay before reperfusion occurs before FMC (patient delay), and “door to balloon time” accounts for only about a third of the delay between symptom onset and reperfusion treatment.5

Patient related delays in initiating treatment for STEMI are mainly influenced by individual characteristics including age, sex, infarct location, character of pain, and the presence or absence of prior myocardial infarction.7 13 14 Time trends do not indicate that there have been substantial changes in patient related delay over time.

Several public initiatives have been performed in order to shorten the patient’s decision time and accordingly also total ischaemic time. The American Heart Association launched Mission Lifeline,15 a community based initiative aimed at quickly activating the appropriate chain of events critical to opening an occluded infarct related artery. In Northern France (in the region of Lille), patient related delay could be reduced by repeated media campaigns offering information about characteristic symptoms, importance of time, and a unique emergency call number for chest pain.16 The two main aims of this campaign were to encourage people to call the French emergency number (number 15) directly and as quickly as possible after noticing the first moment of a potential coronary symptom, and to encourage the general practitioners to “prescribe calling 15 directly for any chest pain”. The impact of this campaign has been the increased number of successful prehospital interventions for ACS patients and the reduction of delay of onset of pain to treatment in the case of prehospital TT from 4.45 h down to 1.58 h in 2 years.
In Vienna the public campaign “Schach-dem-Herztod” ("give check to cardiac death") led to a significant reduction of patient delay until FMC, which, together with the organisation of a local network of care, further decreased in-hospital mortality in patients with acute STEMI. Unfortunately, such campaigns have only a temporary beneficial effect with respect to reducing patient related delays if not performed repeatedly. One of the main factors of success for this kind of campaign is the evaluation and constant monitoring of the results. The campaign has to be maintained over time, so the message must be simple, easy to understand and to reproduce, and inexpensive: “Please in case of chest pain – call us!”

Transportation delay mainly depends on the priority of patient transfer. Transfer between hospitals of a “stabilised” patient with acute STEMI, who initially presented to a non-PCI centre, has in many regions a lower priority than primary transfer of a patient first seen by the ambulance team. The problem of primary or secondary inter-hospital transfer of patients with acute STEMI is one of the biggest hurdles in accelerating FMC-to-balloon times.

**OPTIMISING DIAGNOSIS AND TREATMENT**

While in some European countries ambulance teams include a physician who is responsible for triage of patients and interpretation of ECGs, in the majority of countries skilled and highly trained paramedic ambulance crews are in operation. For paramedics, ECG telemetry offers interpretation of high quality ECGs in a cardiac centre at distance, and rapid triage and transfer of the patient directly to the cardiac catheterisation facility. ECG telemetry also alerts the hospital staff and thus allows quicker organisation and a reduction of in-hospital delay within the PCI hospital. It would be desirable to bypass the emergency room in hospitals with pPCI facilities because this has been shown to minimise in-hospital delays. Although this practice is still widespread in many parts of Europe and elsewhere, there is no role for a two stage transfer of the patient, first to an emergency department of a non-interventional hospital, followed by transfer to an interventional centre for pPCI.

**STEMI NETWORKS IN PRACTICE**

**Vienna STEMI network**

The Vienna STEMI network has been organised and guided by cardiologists, but triage of patients is done in 60% of cases by physicians (in the majority non-cardiologists) of the Viennese Ambulance Systems. In 40% of cases the patients reach the emergency room in hospitals with pPCI facilities because this has been shown to minimise in-hospital delays. Although this practice is still widespread in many parts of Europe and elsewhere, there is no role for a two stage transfer of the patient, first to an emergency department of a non-interventional hospital, followed by transfer to an interventional centre for pPCI.
patients in whom the FMC-to-balloon time is expected to exceed 90–120 min, in-hospital TT is initiated before they are transferred. A special feature of the Vienna network is that during non-official catheter times (4 pm to 7 am from Monday to Saturday morning), by means of a rotation plan between the participating PCI centres, two active catheter laboratories are always available, while during the weekend only one PCI centre is available 24 h per day. The advantage of this system is that only highly experienced interventional cardiologists and well trained personnel are on duty during these official off-times of the catheter laboratories. During official catheter times (approximately 7 am to 4 pm from Monday to Friday), the closest PCI capable hospital is attended by ambulance cars. Helicopter transportation within the city of Vienna has no advantage and frequently prolongs the transportation delay.

In the first 2 years of the Vienna STEMI network, an increase in the proportion of patients receiving any reperfusion therapy (from 66% to 87%) and a decrease of non-reperfused patients (from 34% to 13%) was reported. As a consequence, during this 24 month period, in-hospital mortality of all registered STEMI patients, including patients who received reperfusion therapy and those who were not reperfused but had the same guideline recommended basic treatment as reperfused patients, decreased from 16% to 9.5% (p<0.01). The registry also showed that, whereas pPCI and TT demonstrated comparable in-hospital mortality when initiated within 2–3 h of symptom onset, pPCI was more effective than TT when performed between 3–12 h after symptom onset. One year mortality reflected a persistent beneficial effect of early pharmacological reperfusion in patients with STEMI of short duration (<2 h of symptom onset) as compared with pPCI (performed early or late) or pharmacological reperfusion in patients with infarction of >2 h duration. Moreover, it could also be demonstrated that since the network started, all different time delays were consecutively reduced over time, which led in turn to a consecutive reduction in in-hospital mortality. Most importantly, it could be shown that approximately 75% of patients with short duration of symptoms who were referred for pPCI, because an FMC-to-balloon time of <90–120 min was expected, were treated within the recently recommended 90–120 min. As shown in fig 2, patients treated in the catheterisation laboratory after this recommended time interval experienced a higher mortality, which was statistically significant in 8.3% of patients who received mechanical reperfusion later than 3 h after FMC.

In the medical dispatching centre an emergency doctor is online. After a short tele-triage, if the doctor online suspects an ACS he will send a mobile intensive care unit (MICU) linked to the SAMU. By law the MICU staff comprise a senior emergency doctor (ED), a specially trained nurse, and a BLS certified ambulance driver. Seven MICUs in the Lille area can be alerted 24 h a day and are fully equipped for cardiac and coronary emergencies. The diagnosis is done at the scene by the ED, following clinical examination and an ECG. Finally, the decision to initiate a certain reperfusion strategy is made by the ED at the scene. Strategies of reperfusion and other acute treatment are correlated with the recent ESC guidelines.

More than 75% of patients suffering chest pain will call the SAMU <2 h after onset of pain. The first ECG performed is considered as the FMC. If the delay between FMC and the catheterisation laboratory is <120 min, direct PCI will be chosen. All patients will receive aspirin, clopidogrel (600 mg loading dose), unfractionated heparin (UHF), and a glycoprotein IIb/IIIa inhibitor for those <75 years of age. For young patients and large infarcts the delay considered is 90 min. STEMI patients taken in charge by the SAMU with direct access to catheter facilities represent 74% of all patients.

Conversely, 24% of patients cannot reach the catheter laboratory within the recommended time. For those patients, and only if onset of pain to FMC is <2 h, prehospital pharmacologic reperfusion therapy will be initiated with enoxaparin, clopidogrel (500 mg for patients <75 years and 75 mg for patients >75 years) and aspirin. All patients will then be transferred to a cardiac ICU with catheter facilities (five such units are open 24 h a day). Twenty-seven per cent of the thrombolised patients will need a rescue PCI and 75% will have an angigram within the first 24 h. All STEMI patients are admitted by convention to the cardiac ICU and never pass through the emergency room.

**Paris system of care**

The system of emergency care is the same in Paris as in the rest of France, and is based upon the SAMU system, with primary PCI being considered the default strategy for STEMI patients, as many catheterisation laboratories in the Paris region have PCI capability around the clock. The results achieved have been investigated in the French registry on Acute ST-elevation and non ST-elevation myocardial infarction (FAST-MI). Of note, however, only 33% of the patients with confirmed ST elevation/left bundle branch block myocardial infarction call the SAMU for assistance directly, confirming insufficient awareness of the population of the appropriate steps to take in the case of prolonged chest pain. In total, 55% of the patients are transported by the SAMU.

Use of the SAMU system leads to shortened time to reperfusion (median time from first call to reperfusion 110 min in SAMU transported patients vs 154 min for the other pathways), and more patients receiving reperfusion therapy (77% vs 59%). Overall, half of the patients are treated with primary

**Lille experience**

Lille is an urban area of 1 200 000 inhabitants. The network is based on the French SAMU system. All patients suffering chest pain must call number 15, which is the number of the medical dispatching centre located in the emergency department of Lille University Hospital. The call to the SAMU can be made by the patient, family, or the general practitioner.
PCI and 18% receive intravenous TT (13% prehospital). Of note, all patients treated with intravenous TT underwent subsequent coronary angiography, with 83% having a PCI. The number of intervening parties before hospital admission is crucial as regards time to reperfusion, use of reperfusion therapy, and early mortality, respectively. Median time from call to reperfusion is 115 min when only one party is involved, 130 min when two parties are involved, and 156 min for three parties or more; reperfusion therapy was used in 76.5% of the patients when only one party was involved, compared with 59% for two or more. Thirty day mortality was 2.9%, 6.3%, and 10.0% for one, two, and three or more parties involved before hospital admission, respectively.

The data shown for European cities are in accordance with findings from the Mayo Clinic network, which used a similar decision tree for patients with acute STEMI but extended the radius of action into rural areas up to 150 miles from the PCI centre. Patients within the city limits were directly transferred to the PCI centre, and patients coming from far away with onset of pain to FMC of 3 h were directly transferred for pPCI (only receiving pain relief as well as aspirin, clopidogrel and heparin in the recommended doses). In contrast, patients transferred over distance with pain onset >3 h were directly transferred for pPCI (only receiving pain relief as well as aspirin, clopidogrel and heparin in the recommended doses). In contrast, patients transferred over distance with pain onset >3 h until FMC of 3 h were directly transferred to the PCI centre, but received only rescue PCI when signs of failure of TT were evident. The latter group showed the lowest mortality rates compared to both pPCI groups.

All networks and registries show the importance of early reperfusion, particularly in patients with short onset of pain. They demonstrate furthermore the need for an early diagnostic angiogram and, if appropriate, PCI with or without stenting in all patients who received successful TT in order to optimise the clinical outcome. The role of coronary angiography and PCI after thrombolytic treatment has been assessed in both randomised trials and registries. The REACT trial has shown that rescue angioplasty in patients without signs of reperfusion was superior to conventional medical treatment or re-administration of thrombolytic agents. Recently, the CARESS-in-AMI trial extended this concept by showing that a policy of systematic angiography/PCI after initial TT was superior to a conventional strategy including rescue PCI, and further support for this strategy has come from the Canadian TRANSFER-AMI trial. In the French FAST-MI registry, 96% of the patients who received thrombolysis underwent subsequent coronary angiography, most of them within the first 24 h, and 84% had coronary interventions. Mortality was higher in the patients who did not undergo PCI after thrombolysis; in those who had coronary interventions, mortality was the lowest for rescue PCI when it was performed soon after administration of TT; in contrast, in patients who underwent systematic PCI (not for failed reperfusion nor for recurrent symptoms), mortality tended to be higher when the procedure was performed early—that is, <2 h after administration of thrombolytic treatment. Overall, the FAST-MI registry showed that early and 1 year mortality in patients receiving a pharmaco-invasive strategy was similar to that in patients treated with primary PCI.

It is important to know that 35–40% of patients primarily treated with pharmacological reperfusion are non-responders to therapy and need rescue PCI. Rescue should be offered as soon as possible after initiation of unsuccessful TT. This can only be afforded if patients after TT are immediately transferred to a PCI capable facility, where the success of TT is proven and rescue PCI can be offered timely.
Recurrent public information campaigns.
- One common number for patients with chest pain.
- ECG telemetry (especially when paramedics are on board ambulance vehicles).
- Bypass community hospitals.
- Re-transfer of patients to their home hospital after successful intervention.

Barriers in building up systems of care
- Low patient and public awareness of symptoms.
- Communication problems.
- Between hospital transfer.
- Bypass community hospitals.
- Promotion of use of prehospital thrombolysis.
- Reimbursement, funding and insurance policies.
- Regional legislation.

Other studies and registries—for example, the Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial, the USIC 2000 registry or the FAST registry—were also able to demonstrate a beneficial effect of TT, especially in patients with short onset of pain. In the Swedish RIKS-HIA registry, which is usually mentioned when arguments for pPCI and against TT are made, those patients with shortest times from pain onset to FMC had a favourable and similar outcome when TT was used. Furthermore, prehospital fibrinolytic therapy reduced symptom onset to treatment time by about 60 min compared with in-hospital fibrinolysis. If pPCI cannot be guaranteed within 120 min of FMC (within 90 min in patients with short onset of pain and anterior wall infarction), it is unethical to accept long time delay for transportation and in-hospital organisation for pPCI. Accordingly, most integrated systems of care (although this is not offered everywhere) would require prehospital TT, performed by well trained physicians or paramedics in the ambulance, as the “back up” for patients who would otherwise incur unacceptable delays to pPCI.

THE NEED FOR FURTHER INTEGRATED SYSTEMS OF CARE

Geographic considerations and distribution of pPCI centres mean that, for most countries in Europe, pPCI can only be provided for part of the population. Currently, 20–55% of patients with STEMI undergo pPCI, according to the Euro Heart Survey. Nevertheless, the feasibility of providing pPCI for the majority of the population has been established in several countries, such as the Czech Republic, Denmark, Germany, and Sweden, respectively. Moreover, not all patients referred for pPCI receive optimal mechanical reperfusion (that is, FMC-to-balloon time of <120 min, and PCI performed in an experienced centre by an experienced team). Even in urban locations with well developed systems of care, a minority of patients still require prehospital TT.

An integrated system of care should involve an emergency telephone response system (one emergency number for all patients with chest pain), the prehospital ambulance system, community hospitals without PCI facilities, and interventional centres. Although such integration presents substantial challenges, even within health care systems without competing financial interests, the feasibility of such systems has been established worldwide.

BARRIERS IN BUILDING UP SYSTEMS OF CARE

Common problems with building up systems of care to optimise STEMI treatment have been reported with respect to: patient and public awareness of symptoms and how to react when they occur; communication problems between ambulance transportation systems and catheterisation laboratories; financial barriers for staffing and training of EMS personnel (doctors, paramedics) and equipment of the ambulances; and availability of PCI facilities (round the clock staffing); improvement of in-hospital delays of pPCI facilities; reimbursement policies, funding and insurance policies; and regional legislation. Last but not least, physician and hospital capacity issues have to be re-evaluated when systems of care are organised. As shown by many examples, all these financial, regulatory and political barriers can be resolved and the implementation of networks for acute STEMI care is feasible, achievable, and affordable.

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Provenance and peer review: Commissioned; internally peer reviewed.

► Excellent update of the 2004 published STEMI guidelines of the American College of Cardiology/American Heart Association.


► Recently published new STEMI guidelines of the European Society of Cardiology indicating new components of organisation for the treatment of STEMI.


► The GRACE registry demonstrated that delay times have not improved tremendously despite better organised acute systems of care for STEMI treatment.


► Overview of optimising prehospital diagnosis and treatment strategies and basis for later modification of guidelines.


► Registry demonstrating that implementation of guidelines for STEMI treatment leads to fast improvement in hard clinical endpoints.


► Description of components of acute systems of care of STEMI in Europe.


► French registry confirming the important role of prehospital thrombolytic therapy in patients with acute STEMI in well established networks.


► Important paper demonstrating that even transfer over great distances to an active PCI centre is possible with excellent clinical outcome if patients with acute STEMI of short duration are pretreated with thrombolytic therapy.


► Swedish registry in STEMI patients demonstrating the benefit of primary PCI over thrombolytic therapy.


► Canadian STEMI registry demonstrating that field transportation is favoured over between hospital transfer.