Implementation of reperfusion therapy in acute myocardial infarction. A policy statement from the European Society of Cardiology

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Summary Reperfusion therapy in ST-segment elevation myocardial infarction (STEMI) is the most important component of treatment, as it strongly influences short- and long-term patient outcome. The main objective of healthcare providers should be to achieve at least 75% of reperfusion therapy applied to patients suffering from STEMI in a timely manner, and preferably within the first 3 h after onset of symptoms.

Establishing networks of reperfusion at regional and national level, implying close collaboration between all the actors involved in reperfusion therapy, namely hospitals, departments of cardiology, PCI centres, emergency medical systems (EMS), (para)medically staffed ambulances, private cardiologists, primary care physicians, etc., is a key issue. All forms of reperfusion, depending on local facilities, need to be available to patients. Protocols must be written and agreed for the strategy of reperfusion to be applied within a network. Early diagnosis of STEMI is essential and is best achieved by rapid ECG recording and interpretation at first medical contact, wherever this contact takes place (hospital or ambulance). Tele-transmission of ECG for immediate interpretation by experienced cardiologists is an alternative.

Primary PCI is the preferred reperfusion option if it can be performed by experienced staff within 90 min after first medical contact. Thrombolytic treatment, administered if possible in the pre-hospital setting, is a valid option if PCI cannot be performed in a timely manner, particularly within the first 3 h following onset of symptoms. Thrombolysis is not the end of the reperfusion therapy. Rescue PCI must be performed in the case of thrombolysis failure. Next-day PCI after successful thrombolysis has been proven efficacious.

Quality control is important for monitoring the efficacy of networks of reperfusion. All elements that influence time to reperfusion must be taken into account, particularly transfer delays, in-hospital delays, and door-to-balloon or door-to-needle times. The rate of reperfusion achieved must also be taken into consideration.

Professional organizations such as the European Society of Cardiology (ESC) have the responsibility to impart this message to the cardiology community, and inform politicians and health authorities about the best possible strategy to achieve reperfusion therapy.

Reperfusion therapy in the acute phase of STEMI has been shown to be the most important component of the treatment, and when applied in a timely manner, can favourably influence short- and long-term patient outcome. Various strategies of reperfusion are available to the clinician, namely thrombolytic treatment, percutaneous coronary intervention (PCI), or a combination of both. Both thrombolytic therapy and PCI have been shown to improve outcome, although the efficacy and safety of their combination is still a matter of considerable debate.

Data from several large registries have shown that reperfusion therapy is insufficiently implemented in many countries. A large proportion of patients with STEMI do not receive any reperfusion therapy, for a wide variety of reasons, despite its availability and the absence of any contraindication. Lack of reperfusion is an independent predictor of death in the short- and long-term, as shown by almost

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all registries. In addition, for patients who do have access to reperfusion, pre-, or in-hospital delays can stall the onset of therapy, thereby influencing the outcome.

In this context, the ESC decided to review the *status quo* of reperfusion strategies—both pharmacological and mechanical reperfusion, taking into account existing guidelines, and data from registries, with the two-fold final aim of identifying obstacles to reperfusion, and proposing solutions for optimizing access to reperfusion.

Objectives of the meeting

For this purpose, a policy conference was organized over two half-days, on Friday 24 and Saturday 25 June 2005 at the European Heart House, headquarters of the ESC in Sophia Antipolis, France. (The Policy Conference was supported by an unrestricted educational grant from Eli Lilly Critical Care Europe.) Key opinion leaders involved in reperfusion therapy at the acute phase of STEMI, including the authors of existing guidelines,[1–3] renowned experts in reperfusion therapy from throughout Europe, representatives of National Societies of Cardiology, and representatives of the ESC Working Groups involved in reperfusion (WG#10 Interventional Cardiology and WG#27 Acute Cardiac Care), and also from the United States came together. (The list of scientific faculty and participants can be found in Appendix 1.)

Existing guidelines for the management of STEMI were reviewed, and areas where the guidelines need to be implemented more thoroughly were identified. Data from registries, surveys, and meta-analyses were reviewed, as well as data from recent clinical randomized trials that have been made public since the guidelines were written. The differences between clinical randomized trials and real life data from registries, and the factors that contribute to the success or failure of reperfusion were highlighted. The outcome of patients who undergo reperfusion therapy was discussed in the light of the various reperfusion methods available, and the current practices in relation to each form of reperfusion were described. In an overview of the current status of reperfusion therapy in Europe, specific cases of particular interest, based on concrete experiences, were analysed.

Finally, break-out sessions were held for a brainstorming by participants on four different topics to come up with concrete proposals on: (i) ways to improve reperfusion in Europe; (ii) identification of barriers to reperfusion in Europe; (iii) how the ESC and its National Societies can best collaborate to improve implementation of guidelines; (iv) definition of quality control.

The current manuscript presents the proceedings of this Policy Conference. The writing and review process are described in Appendix I.

Reperfusion therapy: critical review of the evidence

The ESC as well as the American College of Cardiology/ American Heart Association (ACC/AHA) have published guidelines for the management of ACS with ST-elevation.[1,3] In addition, the management of STEMI is also addressed in the guidelines on PCIs by the ESC.[2] There are only minor differences between the guidelines that partly relate to different publication dates in this rapidly moving field. A review of the three currently available guidelines led to the discussion of a certain number of key points.

Diagnosis of STEMI

There is general consensus with respect to the diagnosis of STEMI. The electrocardiogram is an obligatory tool in identifying patients with STEMI, who should receive reperfusion treatment. In all ACS patients, a 12-lead ECG should be recorded and interpreted as quickly as possible after first medical contact, and ideally within a maximum of 10 min. Accordingly, the ambulances should be equipped with appropriate ECG recorders and with medical or paramedical staff trained in interpreting ECG recordings. Teletransmission of ECG recordings for final validation by a cardiologist is an alternative solution. ST-segment elevation at the J-point with the cut-off points ≥ 0.2 mV in V1 through V3 and ≥ 0.1 mV in other leads are considered as diagnostic, as well as presumably new left bundle branch block. Some patients without typical ST-elevation may develop extensive myocardial necrosis as diagnosed by biomarkers, but the therapeutic management in this case is different from STEMI.

Reperfusion therapy

In patients with suspected acute coronary syndromes, reperfusion therapy is indicated in case of ST-segment elevation or new left bundle-branch block, and measures to initiate this treatment must be taken without delay. Fibrinolysis has for more than 20 years been the standard treatment preserving left ventricular function and resulting in improved survival.[4] Mechanical reperfusion techniques were introduced more than 15 years ago, initially for cases where contraindications precluded the use of fibrinolytics or as rescue tool after failed fibrinolysis.[2] Primary PCI has been improved considerably during the last decade making this approach safer and more successful. The introduction of stents and glycoprotein IIb/IIIa antagonists have been milestones, resulting in mechanical reperfusion therapy being advocated as routine care based on meta-analyses of several randomized trials.[5]

The treatment algorithms of all three guidelines are very similar. All advocate reperfusion therapy for all patients with STEMI within 12 h after onset of symptoms. Beyond 12 h after onset of symptoms, there is no evidence that either form of reperfusion therapy is useful. For patients with contraindications to fibrinolytics and those in cardiogenic shock mechanical reperfusion is the preferred treatment, even if this results in longer transport times. Primary PCI is recommended by the ESC as the preferred therapeutic reperfusion strategy for all patients with STEMI, when it can be performed within 90 min after first medical contact. First medical contact must be understood to mean the exact time when the firm diagnosis of STEMI has been established by ECG, be it in the pre-hospital setting, in the emergency room, or in the coronary care unit. The recommendations from the ACC/AHA Practice Guidelines Task Force are practically identical. However, for patients presenting within 3 h after onset of symptoms, there is no expression of preference for lysis vs. primary PCI in the ACC/AHA and also in the ESC PCI guidelines.[1,2] The 90 min

time delay is based on meta-analyses of clinical randomized trials, performed in a highly experienced medical environment, and comparing primary PCI and thrombolysis. These trials demonstrated that the benefit of primary PCI with respect to death, re-infarction, or stroke is optimal within this time window.[5,6] However, more recent reports have shown that PCI remained superior to fibrinolysis even with a time window up to 110 min, rather than the traditionally admitted 90 min.[6] In these meta-analyses, when transfer to a tertiary hospital is needed, there remains an advantage for primary PCI, although the benefit in terms of mortality is not significant and influenced by the length of additional delay related to transport. Only combined endpoints such as death + MI or recurrence of events reached statistical significance.[5,7] More recent data shows, however, that primary PCI offers a major advantage over thrombolytic treatment in high-risk patients as defined by the TIMI risk score.[8] The transfer time in the trials, however, was quite short and certainly shorter than what is observed in the real world setting, making extrapolation of the results of these randomized trials to everyday life difficult.

There is currently no evidence that facilitated PCI improves outcome. A recent meta-analysis showed no superiority of this strategy, but an increase in bleeding. It included 15 trials, with various regimens, upstream of PCI (GP IIb/IIIa inhibitors in seven, thrombolytics in five, and a combination of the two in three).[9] In the ASSENT 4-trial, recently reported at the annual congress of the ESC in Stockholm, upstream fibrinolysis followed by immediate systematic angiography and angioplasty was tested vs. primary PCI. An excess of events, both ischaemic events and death, was observed in the facilitated PCI arm, and therefore, upstream fibrinolysis cannot be recommended. However, it was shown in this study that patients who received thrombolytic treatment in ambulance fared better and had equally good evolution when compared with patients submitted to primary PCI. Upstream administration of GP IIb/IIIa inhibitors might have an influence, as shown in a meta-analysis of the trials that have used these compounds in the setting of primary PCI.[10] More recent meta-analyses show that pre-hospital administration of GP IIb/IIIa results in a higher rate of aborted infarction and leads to a strong trend for long-term mortality benefit in pre-treated patients.[11,12] This strategy is currently under investigation in a large clinical trial (FINESSE).[13] At this stage, it is unclear whether clopidogrel given in a pre-hospital setting can improve outcome. However, there is mounting evidence that clopidogrel, at a dose of 75 or 300 mg in patients less than 75 years old, makes it possible to reduce the rate of major adverse cardiac events in patients submitted to thrombolytic treatment,[14,14a] and subsequently submitted to PCI.[15]

The management of very early infarction (within the first 3 h after onset of symptoms) is still debated, because fibrinolysis may be at least as effective as primary PCI in achieving reperfusion in this situation.[16,17] Accordingly, the US guidelines differentiate the role of primary PCI for early (<3 h) infarction by preferring fibrinolysis when the expected door-to-balloon time minus the expected door-to-needle time is more than 60 min. There is some indication that in very early infarctions fibrinolysis may prevent the development of cardiogenic shock.[17] After 3 h following onset of symptoms, primary PCI is strongly favoured by all guidelines, as the benefit is greater than that obtained with thrombolytic therapy. However, if the expected delay for primary PCI far exceeds the current recommendations, then thrombolytic therapy should be initiated. The smaller benefit of thrombolysis >3 h after onset of symptoms must be balanced individually against the risk of intracranial bleeding (on average 1%).[5,7]

Pre-hospital thrombolysis can achieve shorter time delays (on average, 60 min) between onset of pain and thrombolytic treatment and results in improved outcome.[18,19] The CAPTIM trial did not show significant differences between pre-hospital thrombolysis and primary PCI.[20] A post hoc analysis showed that for patients managed within the first 2 h following onset of symptoms, both strategies did equally well.[17] In a French registry, 1-year survival was significantly better with pre-hospital thrombolysis when compared with in-hospital thrombolysis and primary PCI.[21] In the nationwide Swedish registry RIKS-HIA, 1-year mortality was equivalent in patients submitted to primary PCI when compared with those who underwent pre-hospital thrombolysis (unpublished data). If pre-hospital thrombolysis is available, it could be preferred over transfer for PCI if the expected delay from first medical contact to balloon is greater than 90 min, particularly if the patients present early after symptom onset (within 2–3 h).

If thrombolysis is chosen as the reperfusion strategy, whether pre-hospital or in-hospital, it must not be considered as the end of treatment. Lack of reperfusion calls for rescue PCI (see below). In patients in whom reperfusion is achieved with thrombolysis, there is no consensus as to whether they should subsequently be submitted to angiography and/or revascularization, and if so, when. After the GRACIA-1 study, which used composite endpoints, it was suggested that systematic angiography after thrombolysis, and PCI the next day, if appropriate, could be beneficial.[22] This approach is advocated in the ESC guidelines for PCIs.[2] However, this point remains debated. Ongoing trials comparing primary PCI with thrombolysis followed by either systematic angiography and angioplasty, or angiography restricted to cases without clear signs of reperfusion may help answer this question.[23] Transfer to a tertiary centre early after initiation of thrombolytic therapy is proposed as an alternative solution, at least for patients with high-risk features, in order not to delay rescue PCI in case thrombolysis is unsuccessful.

Rescue PCI after failed thrombolysis has remained a matter of constant debate over the last two decades. The REACT randomized trial addressed this issue, comparing three strategies after failed thrombolysis (defined by <50% ST resolution at 90 min after treatment initiation); namely conservative therapy, repeat thrombolysis, and rescue PCI.[24] The last strategy appeared superior in all respects, including overall mortality at 6 months (HR: 0.48 when compared with the other two strategies). In real practice, the definition of failed thrombolysis remains an issue. Disappearance of pain is misleading as this can be achieved by analgesic drugs. ST resolution is probably the best indicator, but the extent of ST resolution that predicts full reperfusion (50 vs. 70% ST resolution) is still debated. Also, the point in time after delivery of thrombolysis at which the efficacy of thrombolytic therapy should be

assessed is also debated (45, 60, or 90 min following onset of infusion).

Networks for STEMI

Primary PCI can only be established as a routine treatment option, when a reliable interventional program with experienced staff is available on 7 days/24 h basis. The US guidelines give precise recommendations on the qualifications of the operator and the catheterization lab. Lack of in-house cardiac surgery does not preclude primary PCI. In this context, the question of case loads of catheterization laboratories and their impact on the results of primary PCI has been addressed. Data from a US database showed that caseload had no influence on outcome of primary PCI for acute MI, contrary to many reports published in the past.[25–27] Data from a comprehensive PCI registry carried out in the greater Paris area provides useful information. It would appear that in-hospital mortality in patients with primary PCI for acute myocardial infarction was higher (8.5 vs. 6.75%) in centres, which performed <400 interventions (both elective and urgent) per year. There is persistent controversy about whether or not low volume centres should continue to perform primary PCI, and about whether new centres should be opened to cover so-called 'unmet medical needs'.

Currently, the majority of patients will first be seen in hospitals that are not capable of performing primary PCI on routine basis. Therefore, networks between primary and tertiary hospitals have to be built up, requiring good cooperation and a clear care pathway agreed between referring centres and the catheterization site. The first question is whether the required time constraints can be met in the network, bearing in mind that the relative risk of death after adjustment for baseline factors is 1.08 for every additional 30 min delay.[28] This includes the time for decision-making regarding transfer and the door-to-balloon time in the tertiary hospital. In remote areas, fibrinolysis may be a better choice, if helicopter services are not available. Ideally, the decision for primary PCI should be made at the location where the patient is seen first. Untoward events during transport are rare (~1%). The catheterization personnel should always be available and should be notified as early as possible to prepare the laboratory. Valuable time—up to 60 min according to some reports—can be saved if the ambulance can ship the patient directly from the patient's home to the catheterization laboratory, bypassing the ICU/CCU. The physician performing the procedure should be present to receive all information and start immediately. A door-to-balloon time of 30 min is achievable in a well set-up network when the PCI service is alerted of the patient's arrival by ambulance staff. If the patient reports directly to the emergency department of a hospital with catheterization facilities, the time to set-up the lab should be less than 60 min.

Lessons learned from registries

The same messages arise from registries and surveys carried out in Europe and in the USA. First, patients seen in routine clinical practice differ significantly from those selected for participation in clinical trials as they are older, more often female, have a more severe cardiac condition, and more often suffer from concomitant diseases. In the national Swedish registry of consecutive patients with acute coronary syndromes involving around 20 000 patients annually, the mean age of the patients was 71 years in males and 76 years in females when compared with a mean age of ~65 years in randomized controlled trials. In this registry, 35% of patients presented with STEMI. Strong determinants for the hospital and long-term mortality were increasing age (doubling of mortality with every decade), and co-morbidities such as diabetes and renal failure.

Secondly, registries show that implementation of reperfusion therapy is increasing throughout Europe and the United States. There is a clear link between reperfusion therapy and reduced 30-day mortality, favouring primary PCI over thrombolysis. Over 10 years, the rate of acute reperfusion was unchanged, but the proportion of primary angioplasty, and the use of adjunctive medical therapy significantly increased in the Swedish registry, and was associated with a 50% reduction of in-hospital and 30-day mortality. Data from the Euro Heart Survey on Acute Coronary Syndromes II, collected in 2004, demonstrated that currently 48% of patients with ACS present with STEMI, of whom 61% are submitted to reperfusion therapy (59% primary PCI; 41% thrombolysis). This is a 6% increase in primary PCI, since the first Euro Heart Survey on ACS in 2000 (55%). No reperfusion was undertaken in 39% of STEMI patients. It must be made clear that the data from this survey come from a collection of well-equipped and highly trained departments of Cardiology, and may not be representative of all of Europe. The same observations have been made in German registries started in 1992, and involving more than 64 000 patients. In the most recent ACOS registry, the reperfusion rate in the setting of STEMI was 73% (primary PCI 43%, thrombolysis 30%). Withholding reperfusion therapy was associated with nearly doubled hospital mortality. Patients undergoing primary PCI showed significantly lower hospital mortality than patients undergoing thrombolysis as acute reperfusion treatment. The rate of reperfusion increased over time, from 56% in 1994 to 73% in 2002, as did the prescription of adjunctive therapies, (anti-platelet agents, beta-blockers, statins, and ACE-inhibitors). This led to a significant reduction in mortality from 16.2% in 1994 to 9.9% in 2002, a relative risk reduction of 45%. The same observations have been made in the National Registries of Myocardial Infarctions (NRMI) in the United States, which have been collecting data since 1994. Reperfusion therapy increased from 64% to 72%, favouring primary PCI in 2004. Again, mortality decreased over time, reflecting better implementation of reperfusion therapy and adjunctive therapies. Door-to-needle time decreased from 62 min in 1990 to 35 min in 2004, but still in only 42% of the patients the door-to-needle time was below 30 min as recommended in the current guidelines.[29–32]

Thirdly, there are wide variations in clinical practice throughout Europe, not only between countries, but also between hospitals in the same country. It is probable that hospitals participating in registries do better than those that are not in a position to report on their management strategies and results. In the National Swedish Registry, clinical practice varied significantly, both with regard to

the patient characteristics and the choice of reperfusion therapy. Similar observations were made in the Euro Heart Survey on Acute Coronary Syndromes II, as well as in Germany, Spain and the USA.[33]

Finally, adherence to guidelines is variable but is improving and has led to better overall patient outcome. However, it would appear that there is a discrepancy between the initial risk of a given patient, and implementation of therapies; the lower risk patients benefiting more often from the most active treatments than their higher risk counterparts, particularly PCI and/or thrombolytic therapy.[34] It is clear that surveys and registries to monitor management of disease and outcome are part of a quality assurance programme and will help to implement guidelines into clinical practice and improve cardiac care in Europe.

Reperfusion therapy—review of practical organization with reference to specific experiences

A questionnaire about how reperfusion is organized was sent to the participants, and some key opinion leaders in Europe and the USA before the conference, to try to get an idea of how reperfusion is delivered in various settings. Responses to the questionnaire were based on figures found in national registries for some countries, and from best estimates for others. Twenty-three countries from western, eastern, central, northern Europe, and the Mediterranean basin were represented, as well as the USA.

According to this questionnaire, primary PCI is already the most widely applied type of reperfusion (39%), followed by lytic therapy (30%). The combined strategy, lytic therapy followed by PCI within the next 12 h, is applied in 7%. Administration of drugs before primary PCI is used in a minority of cases (4–6%), generally abciximab, and rarely combo-therapy of abciximab and half-dose lytics (1%). The rate of no reperfusion is 24%. Primary PCI facilities 24 h a day, 7 days-a-week are available in 65% of cases. In 19% of responding countries primary PCI is not available at all. Again, these figures may be optimistic, because they were collected in high volume, well-organized centres. When patients are admitted to a non-PCI hospital, the type of reperfusion is predominantly thrombolytic up to 6 h after symptom onset (63%). From 6 to 12 h, lytics and PCI are balanced, and beyond 12 h, primary PCI (32%) and no reperfusion (60%) are the most likely scenarios. Among reasons for not giving reperfusion therapy, late arrival (42%), contra-indications (15%), uncertain diagnosis (15%), and old age (11%) were the most common causes, which is in keeping with the Euro Heart survey on acute coronary syndromes II.

STEMI patients mostly reach the catheterization laboratory for primary PCI through the emergency room (48%), or through the CCU (30%), with only 22% going directly from the ambulance to the catheterization laboratory. Ambulances are equipped with defibrillator (automatic or manual); frequently equipped with 12-lead ECG (90%); ECG transmission (33%); intubation/ventilation set (90%). Lytics are rarely available in ambulances, with only 33% being equipped.

There are many examples of well-established networks of reperfusion in Europe. Nationwide networks of reperfusion have been established in Denmark and the Czech Republic,

based on experience derived from multicentre trials.[35–37] Reperfusion therapy is organized involving all the hospitals in a pre-defined area, coordinated by one or several PCI centres, who welcome all patients, regardless of their age, origin, or referring hospital. In four reported experiences (Czech Republic, Denmark, Italy, and Poland), the vast majority of patients suffering from STEMI are submitted to PCI. Thrombolytic treatment is still recommended in some of these countries, but only for patients who present <3 h after onset of symptoms, and who cannot reach a hospital within 90 min following first medical contact. Facilitated primary PCI using various regimens, including combo-therapy, is used in only one network, in patients <75 years old. Above this age, it is known that there is an increased risk of intracranial bleeds.[38]

It is worth mentioning that based on the GRACIA-1 and -2 studies, alternative strategies have been developed in Spain, where 30 centres of cardiology (including three in Portugal) work with a common protocol.[22] Patients with first medical contact less than 3 h after onset of pain are submitted to immediate lysis, followed by PCI the next day. For patients presenting more than 3 h following onset of symptoms, if PCI is not available within 90 min, then patients are submitted to thrombolytic treatment followed by PCI within 12 h after onset of symptoms. If PCI is available within 90 min, then patients are transferred for primary PCI, with or without early initiation of GP IIb/IIIa inhibitors. As yet, this strategy has not been validated.

Transfers are a main component of a reperfusion strategy in these experiences. The distance of the transfer is about 55 km on average in Denmark for example, but reached >100 km, and up to 150 km in countries like the Czech Republic and Poland. This clearly means that the transfer delay for patients suffering from STEMI is far beyond the 90-min maximum time delay recommended in the guidelines between first medical contact and arrival at the catheterization laboratory. Depending on the country and experience, the transfer time can vary from 120 to 180 min. It is understood that this transfer delay is counted from the initial medical contact to the catheterization laboratory, and 30 min have to be added from arrival in the catheterization laboratory to first inflation. These transfer times are a significant deviation from what is recommended in the guidelines. The dilemma with current recommended times not being met in many cases in daily practice has prompted some countries to modify the time window between first medical contact to balloon inflation to 120 min in their national guidelines[39] (H.R. Andersen, personal communication). The situation in the United States is no different. A recent report has shown that the median total door-to-balloon time was 180 min in transferred patients.[30] This total time was measured from the time of arrival at the initial hospital to the time of balloon inflation at the PCI centre.

Since the outset of their experience, most of the networks report that they have managed to reduce the delay (particularly by bypassing the emergency room and/or CCU), which led to a significant reduction in mortality. In this regard, the experience of Vienna is particularly instructive. In this large city, strict implementation of the ESC guidelines for the management of STEMI was put in place. A network of hospitals with catheterization facilities offer primary PCI on a round-the-clock basis. A differential strategy is used,

based on delay from onset of symptoms, first medical contact, and predicted transfer time. Most patients are submitted to primary PCI (the rate increased from 16 to 60%), but patients presenting within 2 h following onset of symptoms, and patients with a long transfer time are submitted to thrombolytic treatment. This has led to a reduction in mortality from 16 to 9.5%, including patients who are not submitted to any reperfusion for whatever reason, and mortality has been reduced to only 8% in reperfused patients, and to a low of 2% in patients <75 old without signs of shock. Interestingly, the rate of non-reperfused patients was reduced from 34 to 13%.[40]

The volume of activity of PCI centres remains a subject of debate. It is clear that the higher the volume of (primary) PCIs per centre and per operator, the better the outcome for the patient. PCI centres that perform more than 200 cases per year do better than those with a lower volume of activity. Centres who perform >500 cases per year do better than centres with fewer interventions. Given the large disparities that exist in Europe as regards PCI facilities, it is hard to reach a consensus on a definition of high-volume centre. However, it is universally acknowledged that the higher the volume of activity, the better. More than 200 PCIs per year, and more than 75 PCIs per operator is considered to be the minimum (but somewhat liberal) requirement for a centre to perform primary PCI.

Messages to the cardiology community

Several clear messages arose out of this discussion and consensus was reached on the following points:

(i) The main objective is to achieve at least 75% of reperfusion therapy within the shortest possible time following onset of symptoms. This goal of 75% is certainly attainable, as already shown in certain countries and registries, particularly through strictly organized networks. Ideally, reperfusion should be initiated within the first 3 h following onset of symptoms, and a maximum of 90 min after first medical contact, if primary PCI is the chosen reperfusion strategy. This maximum time limit may be extended to 110 min in future guidelines.

(ii) Organization of networks of reperfusion at regional or national level is the key issue. This implies close collaboration among hospitals, EMS with medically or paramedically staffed ambulances, and preferably high-volume tertiary PCI centres, but also private practice cardiologists, primary care physicians and paramedics, where they are incorporated in the chain of treatment. Helicopters, if available, could also be used to collect patients in very remote areas. Practical organization of reperfusion through the network (e.g. establishing diagnosis, initiating therapy, transfer of patients when necessary) must be detailed, and the exact role of every participant in the network must be outlined and agreed.

(iii) Protocols must be written and agreed regarding the type of reperfusion to be offered to the patients. All forms of reperfusion, depending on local facilities, need to be available to patients; namely primary PCI, primary PCI after transfer, thrombolysis, pre-hospital thrombolysis. Facilitated PCI is not an option given the results from ASSENT-4, and as long as current clinical randomized trials are ongoing on this issue. Pre-hospital administration of drugs in case of PCI (if any) has to be limited to aspirin and heparin. However, there is mounting evidence that clopidogrel, at a dose of 75 or 300 mg in patients less than 75 years old, may be useful, whatever the type of reperfusion strategy chosen. Pre-hospital administration of abciximab may also be useful in patient triaged for primary PCI.

(iv) Every effort must be made to shorten delays. Early diagnosis of STEMI is essential for timely initiation of therapy. In all patients, ECG should be recorded within 10 min after first medical contact, wherever it is (home, ambulance, emergency room, CCU if the patient presents directly to the hospital), and immediately interpreted by trained physicians or paramedics, or transmitted to a tertiary centre for validation. That must be coordinated with the hospital where reperfusion therapy will be implemented to allow preparation of the patient and the catheterization laboratory during transfer. Direct access to the catheterization laboratory, bypassing both the emergency room and the CCU, is recommended if primary or rescue PCI are considered.

(v) Primary PCI is the preferred option for reperfusion therapy, provided it can be delivered by an experienced staff, preferably in a high-volume centre, within a reasonable time period following first medical contact. Every time delay must be taken into account to assess the time window between first medical contact and arrival at the catheterization laboratory, not only the transfer time but also door-to-balloon time. The definition of a high-volume centre is still debated, and should be defined according to local conditions. The most commonly acknowledged (but somewhat liberal) figures defining 'high-volume' in the medical literature are centres that perform more than 200 PCIs per year, and more than 75 PCIs per operator.

(vi) Thrombolytic treatment is a valid option if primary PCI cannot be delivered in a timely manner, particularly within the first 3 h after onset of symptoms. Pre-hospital thrombolysis must be preferred over in-hospital thrombolysis, if available. Thrombolysis is not the end of reperfusion therapy:

  (a) Lack of reperfusion after thrombolytic treatment warrants immediate transfer for angioplasty. No reperfusion must be based on clinical judgement. The extent of ST-segment resolution has to be assessed 45–90 min after onset of thrombolytic treatment.

  (b) Timing and need for systematic PCI after successful thrombolytic treatment remains a subject of debate. Systematic next day angiography is advocated by some, delayed elective angiography by others.

  (c) Some advocate transfer to a tertiary centre early after initiation of thrombolytic therapy, at least for patients with high-risk features, in order not to delay immediate reperfusion, in case thrombolysis is unsuccessful.

(vii) Information must be provided to physicians in charge of management of patients with STEMI, to help them

understand the need to shorten delays, and even sometimes, to abandon practices that can undermine access to reperfusion. In particular, owing to the pressure imposed by the reimbursement systems in place in some countries in Europe, based on diagnosis-related groups, some physicians may be perversely encouraged to keep STEMI patients in their local hospital, rather than transferring them to a tertiary centre, and losing resources for their own hospital.

(viii) Quality control is a key issue for monitoring the efficacy of a reperfusion network. To this end, indicators have to be defined, and registries have to be put in place to provide information about the proportion of patients who have access to reperfusion, the time delay from onset of symptoms to medical contact, transfer delay, in-hospital delays, door-to-balloon time, door-to-needle time, etc. Registries such as these should ideally also include patients who do not receive any reperfusion, and should document mortality at 30 days, and in the longer term as well if possible. Rates of prescription of recommended therapies during the in-hospital phase and at discharge should also be included. Feedback by benchmark reports should be part of the registries, as this is the strongest tool for encouraging the implementation of guidelines. Ideally, these registries should use the dataset as defined in the CARDS initiative.[41]

(ix) Public information campaigns should be considered, as most of the time delay between onset of symptoms and start of reperfusion therapy is the delay in patients seeking medical attention. The primary target of public information campaigns should be patients with known coronary artery disease, who need to understand that prolonged chest pain has a particular significance, and that they should act quickly. Information of primary care physicians is also needed.

(x) Informing politicians and health authorities about the need to organize networks of reperfusion therapy at regional and national level is of key importance. Human, financial, and material resources are an important part of health policy at national level, so physicians should strive to influence politicians and decision-makers at local and national level, to ensure that the treatment of infarction receives the attention it deserves. In the same way, informing health authorities at the level of the European Union is also a key issue. One symbolic and important gesture could be to propose wider use of the single, Europe-wide emergency call number, namely 1-1-2.

(xi) The ESC, with the help of its member National Societies, has to make every effort to ensure that the messages derived from this Policy Conference are relayed at national and regional level, in order to make sure that the proposed strategies and recommendations are implemented locally. The ESC and its members National Societies can organize individual meetings to this end.

Conclusion

After intense discussion among key opinion leaders of reperfusion therapy in STEMI, clear conclusions can be drawn. Ways to achieve reperfusion therapy are clearly described and are summarized in guidelines, but reperfusion therapy is insufficiently implemented, although there has been considerable improvement over the last 10–15 years in Europe. Further progress can be made if a few essential messages are delivered to the cardiology community. All types of reperfusion have to be available to patients suffering from STEMI, taking into account clinical factors, local resources, and geography, to make the ultimate choice of therapy for a given individual. Many obstacles still prevent reperfusion therapy from being implemented, or from being carried out in a timely manner in Europe. Organizing networks of reperfusion based on a clear common protocol, outlining diagnostic and therapeutic algorithms, can help to improve the rate of reperfusion therapy offered to patients. Mobilization of the cardiology community, with involvement of health authorities, can achieve this goal. The ESC, in taking the initiative of organizing this Policy Conference, can contribute to achieving these aims in a joint effort with its member National Societies.

Acknowledgements

Appendix I

The STEMI Implementation Programme was held on Friday 24 and Saturday 25 June 2005 at the European Heart House, headquarters of the ESC, in Sophia Antipolis, France. The members of the Organizing Committee were: J.-P. Bassand (France), G. Filippatos (Greece), S. Silber (Germany), M. Tubaro (Italy), F. Van de Werf (Belgium), F. Weidinger (Austria).

The scientific Faculty members were: H. R. Andersen (Denmark), E. Antman (USA), D. Antoniucci (Italy), H. R. Arntz (Germany), J.-P. Bassand (France), S. Behar (Israel), A. Betriu (Spain), H. Boudoulas (Greece), P. Clemmensen (Denmark), S. Dalby Kristensen (Denmark), N. Danchin (France), R. de Winter (Netherlands), C. Di Mario (UK), D. Dudek (Poland), F. Eberli (Switzerland), F. Fernandez-Aviles (Spain), G. Filippatos (Greece), K. Fox (UK), A. Gershlick (UK), A. Gitt (Germany), H. Gray (UK), C. Hamm (Germany), Y. Hasin (Israel), K. Huber (Austria), E. Keeley (USA), A. Lafont (France), M. Pfisterer (Switzerland), S. Savonitto (Italy), S. Silber (Germany), C. Stefanadis (Greece), C. Spaulding (France), M. Tendera (Poland), M. Tubaro (Italy), F. Van de Werf (Belgium), L. Wallentin (Sweden), F. Weidinger (Austria), P. Widimsky (Czech Republic), R. Wilcox (UK).

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The final version was reviewed by the members of the Organizing Committee, the Scientific Faculty, all speakers and chairpersons, plus S. Behar, A. Budaj, H. Bueno, C. Di Mario, Y. Hasin, K. Huber, S. Savonitto, G. Steg. The final article was submitted to the ESC Practice Guidelines Committee for approval, and was endorsed by the Board of the ESC.

The participants in the meeting are listed hereafter:

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