

Acute Myocardial Infarction, a Public Health Care Issue

ALBERTO CACCAVO^{MTSAC, 1}

Address for offprints:

Dr. Alberto Caccavo
Alem 152 - (7540) Coronel Suárez
Pcia. de Buenos Aires
e-mail: acaccavo@infovia.com.ar

SUMMARY

Acute myocardial infarction (AMI) is an important cause of death in Argentina. At present, in-hospital mortality due to AMI is about 10%, at least in registry participating centers. Treatment is focused on achieving reperfusion of the occluded artery with either primary angioplasty or thrombolytic therapy. However, only a few hospitals have primary angioplasty facilities, and the indication of thrombolytic therapy is lower than recommended.

Thrombolytics, anticoagulant drugs and antiplatelet agents should be indicated promptly and broadly to reduce mortality.

The health care authorities, with the support of the scientific societies, should design a national program to achieve a substantial impact on mortality due to AMI.

This program should focus on three main issues:

1. A 12-lead electrocardiogram should be performed and interpreted as soon as possible in all patients with chest pain, including the use of pre-hospital emergency services. A centralized ECG reading with expert physicians may help those health care centers that lack qualified staff.
2. Rapid reperfusion with thrombolytic therapy and/or angioplasty. Bolus fibrinolytic drugs are simpler and more effective than streptokinase, yet, they are more expensive. It is very important to choose an easy-to-administer thrombolytic agent in primary care facilities.
3. The organization of a network to transfer the most severe patients to referral centers in fully equipped ambulances with trained staff. Possibly, 50% of AMI patients need to be transferred due to severe congestive heart failure, failed thrombolysis, or recurrent ischemia.

REV ARGENT CARDIOL 2010; 78:259-263.

Key words > Myocardial infarction – Mortality – Health policy

Abbreviations >	
ECG Electrocardiogram	TL Thrombolytic
AMI Acute Myocardial Infarction	TPA Tissue Plasminogen Activator
SK Streptokinase	

INTRODUCTION

Acute myocardial infarction (AMI) is an important cause of hospitalization and death in our country. (1-6)

Recent publications estimate that there are more than 30,000 hospitalizations per year in Argentina due to STEMI (ST-segment elevation myocardial infarction). (2)

At present, its treatment focuses on attempting early reperfusion following thrombotic occlusion of an artery. (7, 8)

While primary angioplasty is the chosen treatment for STEMI in our country and around the world, most acute care hospitals lack the possibility of performing it within 24 hours. Primary angioplasty is available in only 25% of the hospitals in the United States. (9) In our country, this percentage is probably lower.

Thrombolysis (TL) is the most common form of reperfusion therapy.

Mortality rate remains at around 10% for inpatients with STEMI, (1, 3-6), according to the information presented recently (10, 11) (Table 1). This is so at

least in the centers we have data from; however, global mortality rate may be higher, especially if one includes those who die before reaching hospital.

The fact that only half of the inpatients have access to reperfusion in the surveyed centers certainly affects this high mortality rate.

On the other hand, when correlating the estimates of infarction with TL sales –considering that our country uses streptokinase (SK) almost exclusively–, we notice that many of the infarctions do not receive reperfusion therapy. (12)

The aim of this article is to discuss behaviors and health policies that can reduce myocardial infarction mortality in the population.

DISCUSSION

Pre-hospital emergency services

The early stage of STEMI is a critical period, with high mortality rate. A pre-hospital emergency system plays a key role in diagnosis, triage, and therapeutics.

^{MTSAC} Full Member of the Argentine Society of Cardiology

¹ Hospital Municipal de Coronel Suárez - Clínica Coronel Suárez

Table 1. Mortality due to AMI in Argentina

• SAC Registry - 1987	11.9%
• SAC Registry - 1991	10.6%
• SAC Registry - 1996	9.9%
• SAC Registry - 2000	11.4%
• SAC Registry - 2003	10.1%
• SAC Registry - 2005	12.6%
• FAC Registry - 2002-2005	8%
• Coronel Suárez Registry - 1995-2005	9%
• Hospital Ramos Mejía Bs. As. - 1998-2007	12.4%
• Registro Epicardio [Epicardial Registry] - 2006-2008	7.2%

Ambulance service has a crucial role, so it should not be considered just a means of transport. Its equipment should include defibrillators, and, ideally, the use of remote ECG transmission systems. Pre-hospital thrombolysis is very attractive, mainly in large cities and/or long distances to hospital.

Several works have demonstrated it is helpful in achieving a significant mortality reduction, especially when this treatment is started within 2 hours. (13-17)

In the recent Guidelines of the Argentine Society of Cardiology, pre-hospital thrombolysis is included as a Class I recommendation, with the use of a fibrin-specific bolus thrombolytic agent, if primary angioplasty cannot be performed within 90 minutes in high-risk infarctions. (18)

Reperfusion therapy

Primary angioplasty is the ideal treatment for AMI patients. In the case of hospitals lacking the means to perform it, patients should be referred for primary angioplasty if it can be performed within 2 hours of patient's arrival. In the case of infarction with high risk for ischemia and low risk for bleeding, the transfer window is reduced to 90 minutes. (19)

When these therapeutic transfer windows cannot be achieved, the treatment of choice is thrombolysis.

In our country, many fewer patients than those who require it receive TL. (12) Its causes are multiple.

According to the available records, a considerable number of patients does not receive treatment due to late arrival and/or delayed diagnosis.

Other cases probably relate to the fear of cerebral hemorrhage, especially in the elderly. However, thrombolytic therapy in patients > 75 years of age offers clear benefits, since mortality rate without reperfusion is very high in this group. (20)

When the infarction occurred several hours ago, efficacy of pharmacological reperfusion is lower; nevertheless, if this were the only therapy available, it could be used in patients with clear evidence of evolving ischemia.

Which thrombolytic agent to use?

The debate about the benefits and disadvantages of fibrin-specific TL includes the efficacy (mortality reduction), the risk (increase of intra-cerebral hemorrhage), and the difference in cost, which has been an important determinant factor for the use of SK in our country. (21)

The GUSTO-1 trial showed an absolute mortality reduction in patients treated with TPA versus SK -6.3% vs 7.3% , which was considered enough to include TPA as first choice therapy in the American guidelines; however, this led to a significant increase of hemorrhagic strokes (about 40%). (22)

In a registry of our own population –with all the limitations a retrospective registry may have–, it seems that there is a trend towards lower mortality with fibrin-specific TL, although not statistically significant. (23)

Anyway, a center that does not offer angioplasty should have at least a small stock of fibrin-specific TL to use in patients with a contraindication to streptokinase, who are the ones who received it at some point in their lives. (24)

These more powerful lytic drugs may also be used in patients with extensive infarctions and low risk for bleeding: patients who are young, normotensive, with no history of cerebro-vascular disease and no low weight.

The current recommendation included in the 2008 European Guidelines is about fibrin-specific TL. (19)

The 2009 Guidelines of the Chilean Society of Cardiology about the treatment of AMI recommend the use of tenecteplase as chosen thrombolytic agent to replace streptokinase, because of its enhanced lytic efficacy and its easy of use in bolus. (25)

However, more important than choosing the thrombolytic agent at this moment, in our country, is administering it within the therapeutic window in all the patients who reach hospital with STEMI.

What to do after thrombolytics?

Hospitals in which angioplasty is not available should be part of a network with tertiary care hospitals to allow for the transfer of some of the patients after having received thrombolytic therapy; this requires a health organization that includes an efficient transfer service and a network for referrals –even to different subsectors– with a central coordination.

In our country, we have little information about transfer of patients with AMI in progress. A very recent publication addresses this issue in the context of the city of Buenos Aires. (26) It is difficult to know if this experience of transfers with no major complications can be repeated within the country, where transfer times are considerably longer.

Today, unstable patients with shock and also patients with ineffective thrombolysis are considered clear indications of immediate transfer after TL.

Pharmacological thrombolysis evolution should be assessed in the patient's bedside with clinical symptoms and ECG findings. (27, 28) When ST segment elevation did not lower more than 50% in the worst derivation, there is a strong indication of rescue angioplasty in large infarctions, and, if possible, within 12 hours. (29, 30) However, even without firm data, we believe that it is still difficult to perform rescue angioplasty in our country, due to lack of coordination among sectors and inadequate transfer system.

Other groups that require immediate angiography include patients with suspected coronary reocclusion, hemodynamic instability, or severe heart failure.

Finally, even with more limited evidence, the European Society of Cardiology recommends possible angiography and angioplasty before hospital discharge in patients who had successful thrombolysis. (19) The TRANSFER-AMI trial, which was published recently, also advocates in that sense; it achieved a reduction of recurrent ischemia as a result of early transfer of patients after TL, but with no decrease in mortality. (31)

About this issue, the recent Argentine consensus concluded that indication for angiography after thrombolysis is limited to rescue angioplasty, post-infarction angina, and heart failure, so it is not recommended in all patients after thrombolysis. (18)

Concomitant therapy

The centers that lack the means to perform primary angioplasty should make sure of using all accepted antithrombotic resources, even at the risk of increased bleeding events. In this regard, all patients treated or not with TL should receive anticoagulation and platelet antiaggregation therapy. If the thrombolytic therapy was SK, fondaparín, enoxaparín, or non-fractionated heparin can be used for anticoagulation, the first one showing apparent advantage of reduced bleeding. (19)

If the thrombolytic agent was fibrin-specific, enoxaparín is the accepted drug, and if this is not available, non-fractionated heparin should be used.

All patients should receive dual antiplatelet therapy, whether or not they have received TL, and clopidogrel should be used with loading dose in patients < 75 years of age, whereas clopidogrel for patients > 75 does not include loading dose. (19)

Health care regionalization

The creation of a regional network of hospitals with different levels of care is very important. This is clearly highlighted in the recent update of the ACC/AHA Guidelines, where the development of this kind of system in each community is considered a Class I recommendation. (32)

This network and the use of appropriate communication allow for direct transfer of patients from the ambulance to the cath service in cases of primary angioplasty, which skips the emergency room and hospitalization steps. These behaviors may result beneficial. (33)

Health policies in myocardial infarction

The design of appropriate public health policies is the most important factor to reduce mortality due to AMI.

Probably, the closest example of Chile may be useful to us.

The AUGE plan (Spanish initials for Universal Access with Explicit Guarantees in Health) came into force in Chile on July 1, 2005. (34)

As regards AMI, the plan ensured completion of an electrocardiogram (ECG) with central interpretation for all patients with chest pain, and rapid administration of TL, in addition to other measures such as adjuvant medication, coronary angiography, and angioplasty.

Its results were recently published for the first time (35) (Table 2).

In a group of ten (10) participating hospitals there was a significant mortality reduction –from 12% to 8.6%– from the pre-AUGE (2001-2005) to the post-AUGE (2005-2006) periods.

This was the result of a 50-60.5% increase in thrombolysis, and also due to improved primary and rescue angioplasty, and to better drug therapy.

This experience may be applied in our country with a comprehensive plan for the treatment of AMI, which –as in the case of Chile– should include the following:

- ECG should be performed as soon as possible, and remote interpretation should be available when it is not possible at the local level.
- Early administration of TL in the first hospital that receives the patient, when primary angioplasty is

Table 2. AUGE Plan from Chile

Period	01/01/2001 to 01/30/2005	07/01/2005 to 12/31/2006	p
Patients	2,623	924	
Mortality	12%	8.6%	< 0.003
Use of thrombolytic agents	50%	60.5%	< 0.001
Primary angioplasty	2.3%	7.3%	< 0.001
Rescue angioplasty	4%	7%	< 0.001

Data from quote 35.

not performed in that hospital. In the case of small centers with little experience in TL, bolus thrombolytic therapy seems to be a good choice due to its simplicity, but the difference in cost with the SK will surely make it difficult to implement.

- A global network of public and private providers that allows for the transfer to tertiary-care centers, at least of the most severe patients. This should be part of a previous planning, and should not be decided upon emergency. Fully equipped ambulances with trained professionals are required.
- Finally, the application of approved drugs to all patients, including aspirin, clopidogrel, and anti-coagulants. Within the anticoagulants, fondaparín and enoxaparín have the advantage of being easy to use.

CONCLUSIONS

Most STEMI patients are treated in hospitals that do not have the means to perform angioplasty. To optimize their treatment, we must resort to the early and extensive use of thrombolytic agents. It is necessary to organize a network so that all the primary care centers are related to some tertiary care provider and have an efficient transfer system.

We must be aware of the reality in our country through extensive records that include the largest possible number of primary care centers which, in general, have not been reviewed.

We must use all the accepted therapies, including the recent additions to the guidelines for the use of antithrombotic and antiplatelet therapies.

Anyway, the greatest effect on mortality due to myocardial infarction can only be achieved by means of public policies that coordinate the diagnosis and treatment through a network of providers, supervised by health care authorities and with the broad participation of scientific societies.

RESUMEN

El infarto agudo de miocardio, un problema de salud pública

El infarto agudo de miocardio (IAM) es una causa importante de muerte en la Argentina. La mortalidad intrahospitalaria del IAM en la actualidad es de aproximadamente el 10%, al menos en los centros que participan en registros.

Su tratamiento está orientado a la reperfusión de la arteria ocluida con angioplastia primaria o trombolíticos. Sin embargo, sólo un pequeño número de hospitales disponen de angioplastia primaria y reciben trombolíticos muchos menos pacientes que los que los requieren. Para lograr una reducción de la mortalidad se debe enfatizar la pronta y amplia utilización de trombolíticos, anticoagulantes y antiagregantes.

El logro de un impacto trascendente sobre la mortalidad del IAM requiere la formulación de un programa nacional dirigido por las autoridades sanitarias con el consenso de las sociedades científicas. Este programa debería concentrarse en al menos en tres puntos:

1. Realización rápida e interpretación del electrocardiograma en todos los pacientes con dolor torácico, que incluya la utilización de la emergencia prehospitalaria. Una central de lectura con médicos expertos puede asistir a los centros de salud que carezcan de personal capacitado.
2. Reperusión rápida con trombolíticos y/o angioplastia. En la elección del trombolítico deben balancearse la sencillez de los trombolíticos en bolo y su mayor éxito fibrinolítico versus el alto costo comparado con la estreptocinasa. El tema de facilitar su aplicación es muy importante cuando se piensa en administrar trombolíticos en centros de baja complejidad.
3. Estructuración de una red para derivar los casos más graves a centros de referencia en unidades equipadas y con personal entrenado. Es posible que el 50% de los IAM requieran derivación por insuficiencia cardíaca grave, fracaso de la trombólisis o isquemia recurrente.

Palabras clave > Infarto del miocardio - Mortalidad - Política sanitaria

BIBLIOGRAPHY

1. Caccavo A, Alvarez A, Bello FH, Ferrari AE, Carrique AM, Lasdica SA et al. Incidencia poblacional del infarto con elevación del ST o bloqueo de rama izquierda a lo largo de 11 años en una comunidad de la provincia de Buenos Aires. *Rev Argent Cardiol* 2007;75; 185-8.
2. Ferrante D, Tajer C. ¿Cuántos infartos hay en la Argentina? *Rev Argent Cardiol* 2007;75; 161-2.
3. Blanco P, Gagliardi J, Higa C, Dini A, Guetta J, Di Toro D, et al. Infarto agudo de miocardio. Resultados de la Encuesta SAC 2005 en la República Argentina. *Rev Argent Cardiol* 2007; 75:163-70.
4. Gagliardi J, Charask A, Higa C, Blanco P, Dini A, Tajer C y col. Infarto agudo de miocardio en la República Argentina. Análisis comparativo en los últimos 18 años. Resultados de las Encuestas SAC. *Rev Argent Cardiol* 2007; 75:171-8.
5. Zapata G. Registro Nacional de Infarto Agudo de Miocardio de la Federación Argentina de Cardiología. Etapa III. *Rev Fed Arg Cardiol* 2006; 35:130-2.
6. Zapata G. Tratamiento del infarto agudo de miocardio. Análisis de la evidencia de las dos últimas décadas. Registros de FAC y SAC. *Rev Fed Arg Cardiol* 2008; 37:91-3.
7. Consensos y Guías de la Federación Argentina de Cardiología. Guía de manejo de los Síndromes Coronarios Agudos (2003). Comité de Cardiopatía Isquémica. www.fac.org.ar
8. Consenso de Síndromes Coronarios Agudos. *Rev Argent Cardiol* 2005; 73(Supl 3):45- 62.
9. Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM; NRMI Investigators. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. *Circulation* 2005; 111:761-7.
10. Goicoechea RF, Principiato M, Bruno Mule MF, von Wulffen MA, Tomatti A, Carbajales J y col. Mortalidad del infarto agudo de

- miocardio en un Hospital Público de la Ciudad Autónoma de Buenos Aires. *Rev Argent Cardiol* 2009; 77(Supl 2):168.
11. De Abreu M, Mariani J, Charask A, Swieszkowski S, Tevez J, Gagliardi J y col. Motivos de ingreso, procedimientos y pronóstico de 19.000 pacientes ingresados a Unidades de cuidados intensivos cardiovasculares en Argentina. 3 años del Registro Epicardio. *Rev Argent Cardiol* 2009; 77(Supl 2):147.
 12. Iglesias R. Infarto agudo de miocardio. Un problema epidemiológico mayor. *Rev Argent Cardiol* 2007; 75:327-8.
 13. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: a meta-analysis. *JAMA* 2000; 283:2686-92.
 14. Boersma H, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996; 348:771-5.
 15. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation* 2003; 108:2851-6.
 16. Danchin N, Coste P, Ferrières J, Steg PG, Cottin Y, Blanchard D, et al; FAST-MI Investigators. Comparison of thrombolysis followed by broad use of percutaneous coronary intervention with primary percutaneous coronary intervention for ST-segment-elevation acute myocardial infarction: data from the french registry on acute ST-elevation myocardial infarction (FAST-MI). *Circulation* 2008; 118:268-76.
 17. Kalla K, Christ G, Karnik R, Malzer R, Norman G, Prachar H, et al; Vienna STEMI Registry Group. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). *Circulation* 2006; 113:2398-405.
 18. Pomés Iparraguirre H. Consenso SCA con supradesnivel del ST. XXXV Congreso Argentino de Cardiología. Buenos Aires, 3 de octubre de 2009.
 19. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of The European Society Cardiology. *Eur Heart J* 2008; 29: 2909-45.
 20. White H. Thrombolytic therapy in the elderly. *Lancet* 2000; 356:2028-30.
 21. Tajer CD, Mauro V, Charask A. Tratamiento del infarto agudo de miocardio con elevación del segmento ST. In: Doval HC, Tajer CD. Evidencias en Cardiología V. Ed GEDIC; 2008. Cap 13, p. 343-9.
 22. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. The GUSTO Investigators. *N Engl J Med* 1993; 329:673-82.
 23. Caccavo A, Álvarez CA, Bello FH, Ferrari AE, Carrique AM, Lasdica SA y col. ¿Son iguales todos los trombolíticos? Análisis comparativo entre estreptoquinasa y trombolíticos fibrinoespecíficos en el infarto agudo de miocardio. *Rev Fed Arg Cardiol* 2009; 38:7-20.
 24. Squire IB, Lawley W, Fletcher S, Holme E, Hillis WS, Hewitt C, et al. Humoral and cellular responses up to 7.5 years after administration of streptokinase for acute myocardial infarction. *Eur Heart J* 1999; 20: 1245-52.
 25. Guarda E, Prieto JC, Sambueza P, et al. Guías 2009 de la Sociedad Chilena de Cardiología para el tratamiento del infarto agudo de miocardio con supradesnivel del ST. *Rev Chil Cardiol* 2009; 28:223-54.
 26. Riccitielli MA, Feldman M, García Escudero A, Szarfer J, Gigena G, Neme R y col. Riesgo en el traslado del IAM para efectuar angioplastia. *Rev Argent Cardiol* 2007; 75(Supl I):147.
 27. Verheugt FW, Gersh BJ, Armstrong PW. Aborted myocardial infarction: a new target for reperfusion therapy. *Eur Heart J* 2006; 27: 901-4.
 28. Pomés Iparraguirre H, Volman MS, Conti C, Callandrelli M, Grancelli HO, Garber V et al. Recanalización coronaria versus reperusión miocárdica en el infarto agudo de miocardio. Valor pronóstico del síndrome clínico de reperusión en pacientes con flujo TIMI 3 luego del tratamiento trombolítico. *Rev Argent Cardiol* 2000; 68:517-24.
 29. Gershlick AH, Stephens-Lloyd A, Hughes S, Abrams KR, Stevens SE, Uren NG, et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. *N Engl J Med* 2005; 353:2758-68.
 30. Wijeyesundera HC, Vijayaraghavan R, Nallamothu BK, Foody JM, Krumholz HM, Phillips CO, et al. Rescue angioplasty or repeat fibrinolysis after failed fibrinolytic therapy for ST-segment myocardial infarction: a meta-analysis of randomized trials. *J Am Coll Cardiol* 2007; 49:422-30.
 31. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med* 2009; 360:2705-18.
 32. Kushner FG, Hand M, Smith SC Jr, King SB 3rd, Anderson JL, Antman EM, et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2009; 54:2205-41.
 33. Rokos IC, Larson DM, Henry TD, Koenig WJ, Eckstein M, French WJ, et al. Rationale for establishing regional ST-elevation myocardial infarction receiving center (SRC) networks. *Am Heart J* 2006; 152:661-7.
 34. www.redsalud.gov.cl
 35. Nazzari NC, Campos TP, Corbalán HR, Lanús ZF. Impacto del plan AUGE en el tratamiento de pacientes con infarto agudo al miocardio con supradesnivel ST, en hospitales chilenos. *Rev Med Chile* 2008; 136:1234-9.