National Survey of ST-Segment Elevation Acute Myocardial Infarction in Argentina (ARGEN-IAM-ST)

Encuesta nacional de infarto agudo de miocardio con elevación del ST en la República Argentina (ARGENT-IAM-ST)

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ABSTRACT

Background: ST-segment elevation acute myocardial infarction (STEMI) is one of the most challenging pathologies for the health system; therefore, it is necessary to have a registry with suitably accurate information to adopt public policies and guidelines adjusted to national needs. The Argentine Society of Cardiology (SAC) and the Argentine Federation of Cardiology (FAC) are carrying out a national registry (ARGEN-IAM-ST) that aims to comprise the “universe” of STEMI treatment.

Objective: The purpose of this study was to evaluate, as broadly as possible, clinical aspects, delays, treatment strategies and outcomes, as well as eventual barriers that need improvement in STEMI care.

Methods: The study included 1,759 patients in 247 centers throughout the country between March and December 2015.

Results: Among all patients, 83.5% received reperfusion treatment, and in 78.3% of cases, this was performed by primary angioplasty. Thirty-seven per cent of patients were admitted from another institution, but only 16% of them received fibrinolytic therapy prior to referral. Door-to-needle time was ≤30 minutes in only 25% of patients receiving fibrinolytic agents and door-to-balloon time was ≤90 minutes in 47.7% of patients treated with angioplasty. In-hospital mortality was 8.8%.

Conclusions: These data allow delineating a map of acute myocardial infarction in Argentina. Delays in treatment are important and there are aspects to correct. These data suggest the need to implement corrective strategies, such as the application of medical education programs, supportive health policies, considering regional characteristics and on-site cost/benefit of reperfusion strategies, which might help to shorten time to reperfusion, both for thrombolytic therapy as for primary angioplasty.

Key words: Myocardial Infarction - Registries - Epidemiology - Reperfusion - Primary Angioplasty

RESUMEN

Introducción: El infarto agudo de miocardio con elevación del segmento ST (IAMCEST) es una de las patologías que más desafíos le impone al sistema de salud, por lo que es necesario contar con un registro con la suficiente solidez de información que permita adoptar políticas públicas y guías ajustadas a las necesidades nacionales. La Sociedad Argentina de Cardiología (SAC) y la Federación Argentina de Cardiología (FAC) se encuentran llevando a cabo un registro nacional (ARGEN-IAM-ST) que intenta llegar al “universo” de la atención del IAMCEST.

Objetivo: Relevar a nivel nacional, en la forma más amplia posible, aspectos de la clínica, demoras y esquemas de tratamiento y resultados, así como las eventuales barreras a ser mejoradas en la atención del IAMCEST.

Material y métodos: Se incluyeron 1.759 pacientes en 247 centros de todo el país entre marzo y diciembre de 2015.

Resultados: El 83,5% de los pacientes recibieron tratamiento de reperfusión, el cual en el 78,3% de los casos se realizó mediante angioplastia primaria. El 37% de los pacientes ingresaron derivados de otra institución, pero solo el 16% de ellos recibieron fibrinolíticos antes de la derivación. Solo el 25% de los pacientes que recibieron fibrinolíticos tuvieron un tiempo puerta-aguja ≤30 minutos y el 47,7% de los pacientes tratados con angioplastia tuvieron una puerta-balón ≤90 minutos. La mortalidad intrahospitalaria fue del 8,8%.

Conclusiones: Estos datos permiten delinear un mapa de la realidad del infarto agudo de miocardio en la Argentina. Las demoras al tratamiento son importantes y existen puntos a corregir. Estos datos sugieren la necesidad de implementar estrategias correctivas tales como instrumentar programas de educación médica, políticas sanitarias coadyuvantes, considerar las características regionales y el costo/beneficio en terreno de las estrategias de reperfusión, las cuales podrían colaborar en acortar los tiempos a la reperfusión, tanto para los trombolíticos como para la angioplastia primaria.

Palabras clave: Infarto del miocardio - Registros - Epidemiología - Reperfusión - Angioplastia primaria

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ATSAC – Full Member of the Argentine Society of Cardiology

1 Argentine Society of Cardiology

2 Argentine Federation of Cardiology
INTRODUCTION

Cardiovascular diseases are the most frequent cause of mortality worldwide including our country, as well as of impairment and loss of labor capacity in the adult population. (1-3) Treatment of several forms of serious diseases such as acute ischemic coronary artery disease and heart failure are now supported by scientific studies and can significantly reduce disability and mortality. (4) Access to diagnostic and therapeutic strategies requires adequate coordination of the health system, which far exceeds the role of specialists. Given the frequency of these diseases, information on their prevalence and treatment and on the different barriers that limit access to diagnosis and proper treatment is essential from the perspective of their modification. Both for basic knowledge as to assess the relevance and effectiveness of corrective measures, a registry of diseases with suitably accurate information is necessary to adopt public policies and guidelines adjusted to national needs.

Cardiovascular scientific societies, the Argentine Society of Cardiology (SAC) and the Argentine Federation of Cardiology (FAC), have a long history of registries and educational programs to improve cardiovascular care. (5-7) However, this task is limited to institutions with academic programs and probably it does not reach most of our population.

ST-segment elevation acute myocardial infarction (STEMI) is one of the most challenging pathologies for the health system. Early detection allows the adoption of myocardial reperfusion strategies either with fibrinolytics or with primary percutaneous transluminal coronary angioplasty (PTCA) of proven effectiveness in reducing mortality. Multiple barriers hinder appropriate treatment: delayed patient consultation, failure to perform or adequately interpret electrocardiograms, training of emergency physicians to adopt suitable reperfusion strategies, access to medications and absence of coordinated networks that would help the rapid referral to centers with greater treatment capacity. Knowledge of the general and local barriers would allow rapid implementation of corrective measures and the assessment of their impact over time.

Therefore, the SAC and FAC have developed the National Survey of ST-segment Elevation Acute Myocardial Infarction in Argentina (ARGEN-IAM-ST), that aims to evaluate, as broadly as possible and trying to comprise the “universe” of STEMI treatment in our country, clinical aspects, delays, treatment strategies and outcomes, as well as eventual barriers that need improvement.

METHODS

A prospective, multicenter, observational national registry was conducted inviting all cardiology and polyvalent intensive care units admitting patients with cardiovascular disease, regardless of the complexity of the center.

Inclusion criteria were:
- Patients admitted with suspected AMI and ST-segment elevation ≥1 mV in 2 limb leads or ≥2 mV in two contiguous precordial leads.
- Evolving AMI with new Q waves of less than 36 h evolution.
- Suspected inferoposterior AMI (horizontal ST-depression in V1 to V3 suggestive of acute circumflex coronary artery occlusion).
- Complete new or presumed new left bundle branch block
Patients with non–ST-segment elevation acute coronary syndrome or non–ST-segment elevation myocardial infarction and those with infarct evolution >36 hours were excluded.

All patients who met the inclusion criteria for at least 3 consecutive months in each center were registered. A pilot phase was carried out from November 2014 to March 2015 in selected centers, which was then extended all over the country until December 31, 2015.

Patient characteristics (age, gender, risk factors, history, comorbidities), clinical presentation (location of myocardial infarction, admission Killip and Kimbal, time of evolution), treatment employed (antiplatelet therapy, reperfusion, adjuvant treatment) and in-hospital clinical outcome (heart failure, post-infarction angina, shock, death) were recorded on admission and at 30 days. Delays for an effective treatment were obtained.

The following times and delays were considered:
1) Pain-consultation time: Time elapsed between the onset of symptoms suggestive of coronary ischemia and first medical contact.
2) Time to reperfusion: Time elapsed between hospital or private institution arrival and initiation of reperfusion treatment:
   a) In case of fibrinolytics:
      - Time window: Time interval in minutes from the onset of symptoms to treatment initiation.
      - Door-to-needle time: Time interval in minutes from the arrival at the institution to treatment initiation.
   b) In case of PTCA:
      - Time window: Time interval in minutes from onset of symptoms to PTCA initiation.
      - Door-to-balloon-time: Time interval in minutes from the arrival at the institution to balloon inflation.

A telephone contact or follow-up visit was carried out at 30 days by the local responsible physician at each center.

Internet-based data collection was done using an electronic format file specially designed by the FAC Center of Medical Teleinformatics (CETIFAC), which allowed online monitoring of the variables entered. Patient privacy was warranted as patient names or initials were not stored in the database. Patients were identified by a consecutive...
number per center. An informed consent was required for the 30-day follow-up period.

Statistical analysis
This is a cross-sectional, prospective, multi-center national study. Qualitative variables are presented as tables of frequencies and percentages with their confidence intervals. Mean ± standard deviation (SD) or median and interquartile range (IQR 25-75) were used for the analysis of quantitative variables according to their distribution.

Analysis of discrete variables was done using contingency tables and that of continuous variables with Student’s t-test or the Kruskall Wallis test for unpaired data or analysis of variance (ANOVA) as appropriate. A p value <0.05 was considered significant. The analysis was performed with Epidata 7.2 and Stata/SE v13.0™.

Ethical considerations
The protocol was evaluated and approved by the Bioethics committee of the Argentine Society of Cardiology and, depending on local regulations and institutional policies, was submitted to evaluation by local committees. The protocol was registered in ClinicalTrials.gov with the number NCT2458885.

RESULTS
Two hundred and forty seven centers nationwide participated in the study (43% public and 57% private centers), among which 56.3% were exclusive coronary care units and 57.6% were centers with primary PTCA capacity. The distribution of centers and population per province is detailed in Table 1.

A total of 1,759 patients (mean age 61±12 years, 78% male) were included in the study. Most patients were admitted with ST-segment elevation, only 25 patients with left bundle branch block and 11 patients with ST-segment depression in leads V1 to V3 due to suspicion of circumflex coronary artery occlusion. Population characteristics are summarized in Table 2.

A high prevalence of unidentified dyslipidemia (18%) and, to a lesser extent, hypertension (6.5%) and diabetes (5%) was observed. About 10% of patients had history of coronary heart disease and almost one out of three infarcted patients was previously taking aspirin.

Infarct location was anterior in 43.9% of cases and inferior in 44.3%. On admission, 446 patients (25.4%) presented some sign of heart failure while the prevalence of cardiogenic shock was 8.4%.

Reperfusion treatment
In 83.5% of cases, patients (n=1,469) received reperfusion treatment. In 78.3% of cases, patients (n=1,150) were treated with PTCA, while 319 patients (21.7%)...
were reperfused with thrombolytics. Rescue PTCA was performed in 55 patients (17.2%) treated with thrombolytic therapy and only 13 patients (4.1%) received a pharmaco-invasive strategy. The thrombolytic drug of choice was streptokinase (94%), and alteplase (3%) and reteplase (3%) were used in the remaining patients. Although 37% of patients were admitted from another institution, only 16% of them received thrombolytic therapy prior to referral. The primary success of PTCA was 94.5%, and 94% of the patients had stent implantation, most of them metallic (61%). The infarction culprit vessels were: the anterior descending (46%), right coronary (34%), circumflex (14%), diagonal (3%) and left coronary trunk (2%) arteries and venous bridges (1%).

In 290 patients (16.5%), reperfusion treatment was not performed mainly due to late presentation. The reasons are detailed in Table 3.

**Delays**

The delay from onset of symptoms to admission was 170 minutes (IQR 25-75: 75-420) in the overall population. When patients were referred from another institution, the delay was greater: 245 minutes (IQR 25-75: 120-540), while the delay in those who consulted directly was almost 2 hours less: 135 (IQR 25-75: 65-300) (p <0.001). Two-thirds of subjects entered within 6 hours of symptom onset (see Table 4 in Supplementary material). In those treated with primary PTCA at the first contact center (721 patients), only 32% entered within 3 hours of symptom onset.

The door-to-balloon time of patients who under-
went primary PTCA was 95 minutes (IQR 25-75: 60-167), while the total time window between the onset of symptoms and balloon inflation was 300 minutes (IQR 25-75: 180-570). Only 47.7% of patients had a door-to-balloon time <90 minutes (Figure 1).

Among the 721 patients who consulted at a center with PTCA availability, 60% who arrived by ambulance had a time window and a door-to-balloon time higher than the 40% who came by their own means: 262 versus 220 minutes (p=0.01) and 107 versus 90 minutes (p=0.001), respectively. Moreover, the door-to-balloon time in those who consulted directly at a center with hemodynamic availability was somewhat higher than in referred patients: 95 minutes (IQR 25-75: 62-150) versus 85 minutes (IQR 25-75: 50-153) p=0.01, respectively. In the referred patients, the time window between the onset of symptoms and balloon inflation was much higher: 350 minutes (IQR 25-75: 235-650) versus 245 minutes (25-75: 170-450) in non-referred patients.

In patients who received thrombolitics, the door-to-needle time was 50 minutes (IQR 25-75: 30-90). Only 80 patients (25%) had a door-to-needle time ≤30 minutes. The total time window from onset of symptoms to thrombolytic infusion was 170 minutes (IQR 25-75: 97-296). In 70% of cases reperfusion criteria was positive, and 23.5% received PTCA after fibrinolitics.

The treating physicians considered there were reperfusion treatment delays in 948 patients (64.5%), 66.1% in primary PTCA and 58.9% in the use of thrombolitics (p<0.001). Among the reasons (see Table 5 in Supplementary material) the delay in patient consultation and the need to refer to another center to perform PTCA are shown as the most important.

### Table 3. Reasons for non-reperfusion (n=290; 16.5%)

<table>
<thead>
<tr>
<th>Reason</th>
<th>n</th>
<th>%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late presentation</td>
<td>72</td>
<td>24.8</td>
<td>19.9-30.2</td>
</tr>
<tr>
<td>Decision NOT to perform angioplasty</td>
<td>25</td>
<td>8.6</td>
<td>5.7-12.5</td>
</tr>
<tr>
<td>Doubtful ECG</td>
<td>19</td>
<td>6.6</td>
<td>4.0-10.0</td>
</tr>
<tr>
<td>Small infarction</td>
<td>13</td>
<td>4.5</td>
<td>2.4-7.5</td>
</tr>
<tr>
<td>Unavailable angioplasty</td>
<td>12</td>
<td>4.1</td>
<td>2.2-7.1</td>
</tr>
<tr>
<td>Thrombolytic contraindication</td>
<td>10</td>
<td>3.5</td>
<td>1.7-6.3</td>
</tr>
<tr>
<td>Old age</td>
<td>4</td>
<td>1.4</td>
<td>0.4-3.5</td>
</tr>
<tr>
<td>Patient’s refusal</td>
<td>2</td>
<td>0.7</td>
<td>0.1-2.5</td>
</tr>
<tr>
<td>Unavailable thrombolitics</td>
<td>2</td>
<td>0.7</td>
<td>0.1-2.5</td>
</tr>
<tr>
<td>Other reasons (deaths; normal coronary arteries, technical failure and others)</td>
<td>71</td>
<td>24.5</td>
<td>19.6-29.9</td>
</tr>
<tr>
<td>No data</td>
<td>61</td>
<td>21.0</td>
<td>16.3-25.7</td>
</tr>
</tbody>
</table>

ECG: Electrocardiogram

Fig. 1. Percentage of patients treated with primary transluminal coronary angioplasty (PTCA), in situ or referred to centers with angioplasty, according to door-to-balloon time.
Taking into account the time windows of patients in whom delays were considered and comparing them with those in whom no delays were denoted, up to almost 2 hours of time could be saved (see Table 6 in Supplementary material).

The medical treatment indicated both in admission and discharge is summarized in Supplementary material (Table 7). In 99% of cases aspirin was administered and clopidogrel was the most used antiplatelet agent in patients treated with PTCA (79%). In those who received fibrinolytic treatment, double antiplatelet therapy was used in 97.2% of cases.

In-hospital outcome and 30-day follow-up
The use of procedures during hospitalization was relatively low: 43 patients (2.4%) required Swan Ganz catheter, 31 (1.8%) intra-aortic balloon counterpulsation, 57 (3.2%) transient pacemaker, 141 (8%) mechanical ventilation and 13 patients (0.7%) myocardial revascularization surgery.

In-hospital mortality was 8.81% (n=155), mostly due to cardiac causes (84.5%). Mortality of patients admitted with cardiogenic shock was 59.9%, while patients in Killip and Kimball I presented 1.75% mortality (Figure 2). The events that occurred during hospitalization are detailed in Supplementary material (Table 8). Atrial fibrillation was associated with an increased incidence of stroke: 5.4% versus 0.5% [OR: 12.0 (95% CI 3.5-41); p <0.001]. Among the 68 patients (3.8%) who presented with hemorrhages, 45% were associated with arterial punctures, but were all minimal or minor. Among major bleedings, 2 were intracranial, 4 gastrointestinal and 2 unspecified. Median hospital stay was 5 days (IQR 25-75: 4-7), stay in the coronary care unit 4 days (IQR 25-75: 3-5) and in the general ward 2 days (IQR 25/75: 0-3).

The 30-day follow-up period was completed in 941 patients, among which 5 patients died (0.53%), 82 patients (8.7%) were re-hospitalized and 33 PTCA and 19 revascularization surgeries were performed.

DISCUSSION
The national STEMI survey has so far been the largest survey in our country with the inclusion of more than 1,700 patients. In average, 22% of centers of all Argentine provinces participated in the study, reaching in some cases 100% of those registered in the National Ministry of Health. (8) The levels of complexity are varied and more than 40% do not have primary PTCA availability.

Although cases were recruited from all provinces, the majority (82%) were from the seven provinces with the largest population.

The data obtained allow delineating a map of infarction reality in Argentina, which shows a reperfusion rate higher than 80%, a high use of primary PTCA and an overall mortality of 8.8%. These data are similar to the last published records of more selected centers and with cardiology residencies. (6, 9) Mortality, while somewhat higher than that of some international registries, such as the French registry, (10) is similar to that of public registries of that country (11) and somewhat lower than that of American records. (12)

This registry also allows the identification of barriers for the access to proper timely treatments. Although more than 70% of patients consult at less than 6 hours of symptom onset, the number of those who receive treatment with door-to-balloon and door-to-needle times according to the recommendations are far from adequate.

Forty percent of patients are transferred to high complexity centers, but only 2% receive a pharmacoinvasive reperfusion strategy and only 5% rescue

Fig. 2. Mortality according to Killip and Kimball (KK) on admission.
PTCA. Studies that analyzed the strategy of using thrombolytics at the referral site versus transfer for primary PTCA did not show benefit when the time of symptom evolution was less than 3 hours; the transfer was beneficial with longer times especially in the incidence of reinfarction and stroke. (13-15) However, the door-to-balloon times of these studies were very low and very difficult to transmit to real life; therefore, considering these data, a large number of patients could benefit from the use of fibrinolytics prior to transfer.

The pharmaco-invasive strategy did not show significant differences with primary PTCA and could have an excess of bleeding and stroke with fibrinolytics; (16, 17) it may be considered as a valid strategy when primary PTCA is not available, especially in low complexity centers. Probably, lack of tenecteplase availability, of simpler and safer administration in IV bolus, is one of the reasons of underutilization of this strategy.

In more than 60% of infarctions, physicians detect delays in treatment, mainly attributed to deferral in patient consultation and the need to refer to another center for PTCA. This aspect could also be verified, since the time window for PTCA and thrombolytics was higher in this group. It is therefore necessary to work more actively in population information on the importance of early consultation and in the education and provision of adequate means for the diagnosis and early treatment at the consultation site, before the eventual referral to greater complexity centers.

The quality of care improvement of the cardiovascular patient, optimizing adherence to the standards of diagnosis and treatment, can be achieved through different pathways. One of them, already documented internationally, (18-22) is the institutions’ self-knowledge regarding their level of performance and the transmission of coordination measures, the generation of systematics, referral and care networks, diagnostic support systems such as telemedicine, and others that can be evaluated globally or regionally according to the problems detected. (23)

Networking will also allow the implementation of initiatives resulting in increased quality of care and the generation of epidemiological research projects that enhance patient care and outcomes. In short, to know in depth the problems and adopt measures to improve the quality of care and reduce morbidity and mortality.

Limitations

Although this is the most important registry performed in our country to date, in some regions the representativeness may be low since not all centers registered in the National Ministry of Health have participated in the survey. In addition, although an on-line database that allows a more complete follow-up of data loading was implemented, lack of resources has not allowed adequate monitoring to ensure data quality as well as of the non-inclusion of patients who died in emergency rooms, which could mean an underestimation of mortality.

Despite these limitations, the results obtained allow very clear information regarding the reality of STEMI diagnosis and treatment in our country.

The generation of a continuous registry, currently under way, will enable monitoring the policies and actions to be implemented based on these results.

CONCLUSIONS

These data allow delineating a map of the reality of AMI in Argentina, where the reperfusion rate is 84% and in-hospital mortality 8.81%.

Delays in treatment are important and there are issues to correct. Treatment delays are detected in 64.5% of cases, especially in the time of patient consultation and in referral to other centers. The detection of barriers and their correction could mean up to 2 hours of reduction in delays.

These data suggest the need of implementing corrective strategies, such as medical education programs, supporting health policies, considering regional characteristics and the cost/benefit of on-site of reperfusion strategies, which could help to shorten the time to reperfusion, both for thrombolytics as for primary PTCA.

Conflicts of interest

None declared. (See authors’ conflicts of interest forms in the website/Supplementary material).

REFERENCES

APPENDIX

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