Program of Coronary Angioplasty in Acute Myocardial Infarction in the Region of Murcia (Spain): APRIMUR Registry

Pilar Carrillo, Ramón López-Palop, Eduardo Pinar, Íñigo Lozano, Rocío Cortés, Daniel Saura, Josefa González, Francisco Picó and Mariano Valdés

Servicio de Cardiología. Hospital Universitario Virgen de la Arrixaca. Murcia.

Introduction and objectives. The geographic characteristic and healthcare facilities of the region of Murcia, Spain, are enough to assure that coronary angioplasty can be carried out in acute myocardial infarction according to current guidelines. The development of a regional program for coronary intervention in acute myocardial infarction may increase the number of patients who would benefit from reperfusion therapy in general and primary angioplasty in particular.

Material and methods. The program was initiated in April 2000 and had four steps: 1) Establishment of primary angioplasty as the treatment of choice of acute myocardial infarction in the regional reference hospital. 2) Application of phase 1 to a second hospital located 10 kilometers away from the reference hospital. 3) Extension of phase 1 to the entire city of Murcia. 4) Provision of facilities for coronary angioplasty in acute myocardial infarction to all patients in the region.

Results. Between January 2000 and August 2001, 392 angioplasties were performed for acute myocardial infarction. Primary angioplasty was performed in 92% and 85% of the patients with an indication for reperfusion therapy in phase 1 and 2, respectively. The median delay (indication to beginning of procedure) was 25 and 35 minutes in phases 1 and 2, respectively. Total mortality was 11.5% (5.2% in patients without shock at admission).

Conclusions. The design of a regional program of primary angioplasty may increase the number of patients who receive reperfusion therapy in compliance with current recommendations for the treatment of acute myocardial infarction.

Key words: Myocardial infarction. Coronary angioplasty. Registries.

Proyecto de un plan de accesibilidad al intervencionismo coronario en el infarto agudo de miocardio en la Región de Murcia (España). Registro APRIMUR

Introducción y objetivos. La Región de Murcia posee las características geográficas y la infraestructura suficiente para asegurar el empleo de la angioplastia coronaria en el infarto agudo de miocardio en los casos indicados según las vigentes guías de actuación. La elaboración de un plan regional de intervencionismo coronario en el infarto agudo de miocardio podría aumentar el número de pacientes beneficiados del tratamiento de reperfusión en general, y de la angioplastia primaria en particular.

Material y métodos. El plan iniciado en abril de 2000 consta de 4 fases: 1) establecimiento de la angioplastia primaria como tratamiento de elección en el infarto en el hospital de referencia regional; 2) extensión de la fase 1 a un segundo hospital distante 10 km del hospital de referencia; 3) extensión de la fase 1 a toda la capital, y 4) facilitación al resto de la región de la angioplastia coronaria en el infarto agudo de miocardio.

Resultados. Entre enero de 2000 y agosto de 2001 se han realizado 392 angioplastias en el seno del infarto agudo de miocardio. El 92% y el 85% de los pacientes con indicación de tratamiento de reperfusión recibieron angioplastia primaria en los hospitales implicados en las fases 1 y 2, respectivamente, con una mediana de retraso (indicación-inicio de angioplastia primaria) de 25 y 35 min, respectivamente. La mortalidad total fue del 11.5% (5.2% en los pacientes sin shock al ingreso).

Conclusiones. La elaboración de un plan regional y la utilización de la angioplastia primaria pueden aumentar el número de pacientes que reciba tratamiento de reperfusión, aproximándose a las actuales recomendaciones terapéuticas en el infarto agudo de miocardio.

Palabras clave: Infarto de miocardio. Angioplastia coronaria. Registros.
perfusion treatment, by either primary thrombolysis or angioplasty, is the most effective way to improve the short and long-term survival of these patients. The benefits that derive from applying reperfusion treatments are greater when the procedures are performed early and diminish to the point of disappearance when intervention is delayed, although primary angioplasty could extend the time since onset of the symptoms of AMI in which patients can benefit from reperfusion treatment. Primary angioplasty has recently shown better results than thrombolysis in terms of reducing short and long-term mortality and salvaging myocardium. The use of angioplasty also extends the benefits of the reperfusion to patients in which thrombolysis is contraindicated.

Paradoxically, in spite of the broad consensus regarding the indications for reperfusion treatment, national and international registries show that these procedures are used in less than 50% of the patients considered «ideal candidates» for this treatment. The figures are even lower for patients who are not considered «ideal candidates» for reperfusion treatment, although they meet the criteria for its application in current practice guidelines in AMI. The scant use of primary angioplasty as a reperfusion technique in Spain and other countries, despite being considered the best reperfusion treatment for AMI, is noteworthy.

Given the superiority of primary angioplasty as a reperfusion treatment in AMI and the large percentage of patients who do not receive reperfusion treatment in spite of eligibility, we decided to promote from our cardiology department a regional plan for AMI care based on facilitating access to the hemodynamics laboratory of potential beneficiaries of AMI interventions according to present practice guidelines.

Program objectives:

1. To extend reperfusion treatment to all patients eligible according to the AMI practice guidelines of the SEC and AHA/ACC.

2. To offer primary angioplasty as the treatment of choice in AMI.

3. To favor access to rescue angioplasty for patients in the region for which thrombolysis has not produced the desired result.

4. To establish a registry of interventionist activities in AMI and record the short and long-term results in the region of Murcia. This registry was named APRIMUR (Angioplastia PRImaria en la región de MURcia [Primary Angioplasty in the region of Murcia]).

We report here the design of the regional program and the preliminary results of its first year of operation.

MATERIAL AND METHODS

Population and area of application

The Region of Murcia is a single-province autonomous community with 1 115 068 inhabitants according to the Provincial Delegation of Statistics. Half of the population reside in Murcia, Cartagena, and Lorca, the three largest municipalities, which have 349 040, 175 628, and 69 930 inhabitants, respectively. The region has nine hospitals pertaining to the public healthcare system: three in the city of Murcia and six in different districts of the region. The capital, where the regional reference hospital is located, is situated in the geographic center of the region and connected by rail with seven of the eight remaining hospitals.

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<table>
<thead>
<tr>
<th>ABBREVIATIONS</th>
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<tr>
<td>AMI: acute myocardial infarction.</td>
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<td>LBBB: left bundle-branch block.</td>
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<td>AHA: American Heart Association.</td>
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<td>ACC: American College of Cardiology.</td>
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<td>SEC: Sociedad Española de Cardiología.</td>
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<td>ICU: intensive care unit.</td>
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Fig. 1. Distribution of the hospitals of the public health service in the Region of Murcia and their distance by highway from the regional reference hospital.
Transfer times by highway are less than 1 h in every case (Figure 1). Five of the eight hospitals in the community have coronary units, all of them integrated in the intensive care services. There is no coronary unit integrated in a cardiology department in the region (Table 1).

About 600 patients with acute transmural infarctions are hospitalized in the region every year, according to figures from hospital coronary units in the autonomous community.

### Infrastructure. Logistics

The regional reference hospital for hemodynamics and cardiac surgery is the Virgin de la Arrixaca University Hospital, located 7 km from the center of the city of Murcia. It has the only two hemodynamics laboratories that operate in the public healthcare system of Murcia. It is the only hospital with a cardiologist on call 24 h a day at the hospital and a hemodynamics teams that is continuously available. Its hemodynamics laboratory currently performs more than 1300 angioplasties a year and is staffed by 6 hemodynamics specialists who have complied with the requirements of the SEC and AHA/ACC for performing out scheduled and primary angioplasties in AMI.

Except during the workday, when telephone contact with the hemodynamics laboratory is direct, the hospital requesting the AMI intervention contacts the cardiologist on call of the regional reference hospital, who then alerts the hemodynamics team to come to the hospital. Patients are transferred by mobile ICU unit, generally belonging to the 061 emergency service. After the intervention the patient is transferred to the ICU of the reference hospital, unless the hemodynamics or clinical situation (electrical instability, the criterion of the hemodynamics specialist who performs the procedure, etc.) makes it inadvisable.

### Design of the AMI angioplasty program

Given the scant tradition of primary angioplasty in the Region of Murcia, the program was designed with phases in which the availability of effective percutaneous AMI interventions would be expanded progressively.

#### Phase 1

Establishment of primary angioplasty as the treatment of choice for AMI in patients hospitalized in the hospital where the hemodynamics laboratory is located (Virgin de la Arrixaca University Hospital). Date of onset: April 2000.

#### Phase 2

Establishment of primary angioplasty as the treatment of choice for AMI in patients admitted to the second largest hospital in the city of Murcia (Hospital Morales Meseguer), located 10 km from the reference center. Date of onset: June 2000.

#### Phase 3

Establishment of primary angioplasty as the treatment of choice for AMI in patients in the city of Murcia. Incorporation of the third hospital of the city of Murcia (Hospital General Universitario).

#### Phase 4

To facilitate effective access to the rest of hospitals in the region to angioplasty for AMI (primary angioplasty, if indicated, and rescue angioplasty). Except in cases in which thrombolysis and rescue angioplasty are contraindicated, the use of primary angioplasty in each hospital is conditioned by the availability of the means to transfer patients in suitable circumstances within a reasonable time for the procedure to be effective (less than a hour between calling in the hemodynamics team and the patient’s arrival at the reference

### TABLE 1. Characteristics of the hospitals of the public health network of the Region of Murcia

<table>
<thead>
<tr>
<th>Hospital</th>
<th>No. of beds</th>
<th>Coronary Unit</th>
<th>Cardiology specialty</th>
<th>Cardiologist on call</th>
</tr>
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<tbody>
<tr>
<td>Virgen de la Arrixaca University Hospital (Murcia)</td>
<td>940</td>
<td>Yes</td>
<td>Yesa</td>
<td>Yes</td>
</tr>
<tr>
<td>Hospital Morales Meseguer (Murcia)</td>
<td>434</td>
<td>Yes</td>
<td>Yesb</td>
<td>No</td>
</tr>
<tr>
<td>Hospital General Universitario (Murcia)</td>
<td>80*</td>
<td>Yes</td>
<td>Yesb</td>
<td>No</td>
</tr>
<tr>
<td>Hospital Santa María del Rosell (Cartagena)</td>
<td>370</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Hospital de Los Arcos (San Javier)</td>
<td>95</td>
<td>No</td>
<td>Yesc</td>
<td>No</td>
</tr>
<tr>
<td>Hospital Rafael Méndez (Lorca)</td>
<td>224</td>
<td>Yes</td>
<td>Yesc</td>
<td>No</td>
</tr>
<tr>
<td>Hospital Comarcal del Noroeste (Caravaca)</td>
<td>105</td>
<td>No</td>
<td>Yesc</td>
<td>No</td>
</tr>
<tr>
<td>Hospital Virgen del Castillo (Yecla)</td>
<td>98</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Hospital Fundación de Cieza (Cieza)</td>
<td>110</td>
<td>No</td>
<td>No</td>
<td>No</td>
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</table>

*Independent from the Department of Internal Medicine. †Integrated as an independent section within the Department of Internal Medicine. ‡As an undifferentiated part of the Department of Internal Medicine. ‡Provisional data (hospital under construction).
hospital). Date of onset: for primary angioplasty in patients without an absolute contraindication, this date will be determined by the achievement of adequate transfer conditions.

For the development of different phases, agreements were made with the intensive care units of different hospitals, as well as with the management of the 061 Service, to ensure patient transfer between hospitals in program phases 1, 2 and 3.

**Design of the APRIMUR Registry**

The main objective of this prospective, observational registry is to serve as a quality control of the AMI interventions performed in the Region of Murcia.

The registry, which is centralized in the regional hemodynamics laboratory, began 1 January 2000 and collects baseline clinical information, procedure data, hospital outcome, and events in the first year of all patients referred to the hemodynamics laboratory for AMI.

The main use of the registry is to analyze hospital and one-year mortality of the patients who undergo these procedures.

**Registry inclusion criteria**

The patients referred to our laboratory for primary angioplasty or rescue angioplasty were included in the registry.

Patients who meet the following two criteria and have not undergone thrombolysis for the treatment of AMI are considered candidates for primary angioplasty:

- Symptoms compatible with myocardial ischemia lasting more than 30 min or persisting in spite of nitrate administration.
- ST-segment elevation of more than 1 mm in two or more contiguous electrocardiographic leads that persists for 30 min or more or after the administration of nitrates, or an undiagnostic electrocardiogram (ECG) showing complete left bundle-branch block (LBBB) or pacemaker rhythm.

The window of indication for primary angioplasty is the 12 h period beginning from the onset of symptoms, unless the symptoms or signs of myocardial ischemia persist.

The candidates for rescue angioplasty are patients who meet the above criteria and have received thrombolysis without having observed indirect signs of reperfusion 90 min after the administration of the thrombolysis. Angioplasties in which thrombolysis has been performed in the 12 h preceding the intervention are not considered primary.

All patients will be included in the registry according to the principle of intention to treat. All patients for which the hemodynamics laboratory is called in to perform a primary or rescue angioplasty will be included, whether or not the procedure is performed.

**Data collection. Definition of variables**

The data are collected prospectively. The medical history of the patient and characteristics of the AMI are obtained on arrival to the hemodynamics laboratory. The data related with the procedure are collected upon completion of the procedure by the physicians who intervene. The hospital outcome is obtained from the medical records of the patient after discharge to home. The one-month follow-up is conducted by an interview in the outpatient office. The follow-ups at 6 months and one year of the patients who do not return to the office for the one-month appointment are made by telephone. The collection of data and follow-up of patients who meet the inclusion criteria but do not undergo primary angioplasty are carried out prospectively in a similar way by means of the medical record, obtaining the same data, with the logical exception of those related with the intervention. The registry of the Hospital Virgin de la Arrixaca will be used to analyze retrospectively each year the medical records of the patients hospitalized with a diagnosis of AMI to determine whether or not they met criteria for inclusion in the program.

Two grant holders, one physician, and one nurse are in charge of collecting data from the registry under the supervision of a member of the regional hemodynamics laboratory.

The procedure was considered successful when a TIMI III flow was obtained in the artery responsible for AMI at the end of the procedure without major complications in the hemodynamics laboratory (death or cerebrovascular accident). The presence of cardiogenic shock at the time of admission was considered if the patient presented an invasive blood pressure <90 mm Hg with signs of peripheral hypoperfusion (cold sweating, pallor of skin and mucous membranes, obnubilation, etc.) in the absence of triggering drugs.

**Statistical analysis**

The APRIMUR Registry has the statistical design of a prospective observational study. Qualitative variables are expressed as percentages and quantitative variables are expressed as the mean and standard deviation. The time variables are expressed as medians (25th-75th percentile) because they did not meet normality criteria.
PRELIMINARY RESULTS

From 1 January 2000 to 31 August 2001, 392 patients were referred to our laboratory for primary angioplasty or rescue angioplasty (231 from 1 January to 31 August 2001). From the overall group of patients, 355 (90.6%) were referred for primary angioplasty.

From the beginning of phase 1 of the program (1-4-2000), primary angioplasty was indicated for 201 patients who were hospitalized in the hospital where the hemodynamics laboratory is located, which represents 92% of the patients who were hospitalized in this center with AMI and an indication for reperfusion treatment. The reasons why primary angioplasty was not performed in the remaining 16 patients were:

a) occupation of the hemodynamics team with another AMI, 2 patients (1%);
b) refusal of the patient to undergo catheterization, 1 patient (0.5%);
c) very poor baseline situation of the patient before AMI, 8 patients (4%); d) unfavorable coronary anatomy, 2 patients (1%), and e) criterion of responsible physician, 3 patients (1.5%). Six of these 16 patients (3%) underwent thrombolysis.

From the beginning of phase 2 (1-6-2000), primary angioplasty has been indicated in 84 patients, who represent 85% of the patients hospitalized in the Hospital Morales Meseguer of the city of Murcia with meet AMI criteria and have an indication for reperfusion treatment. The causes for not indicating primary angioplasty in the 10 remaining patients were: a) unavailability of a mobile ICU for transfer in 2 cases (2%); b) occupation of the hemodynamics team with another case of AMI in 2 cases (2%), and c) criterion of the responsible physician in the 6 remaining cases (6%).

Phases 3 and 4 are in their initial stage, so that, currently, the indication for primary angioplasty in the other centers in the region depends on the criterion of the attending physician guided by the characteristics of presentation of the AMI, presence of contraindications for thrombolysis, and availability of a mobile ICU to transfer the patients in a reasonable time. In Figure 2 is shown the origin of the patients for primary and rescue angioplasty. On six occasions, the 061 emergency service directly contacted the hemodynamics laboratory and transferred the patient without previous admission to the reference hospital. The delay in carrying out the examination from the onset of symptoms and from the moment the indication is established is shown in Table 2. Patients from all the hospitals outside the capital had a median delay of more than one hour from the moment the indication for primary angioplasty was established to its performance.
and in most cases more than 90 min. On the contrary, the times for the hospitals in the city of Murcia were similar to those recorded in the reference hospital. The growth of monthly activity in relation to the previous year (1999) is shown in Figure 3.

The baseline characteristics of the patients who underwent primary angioplasty are shown in Table 3. The mean age of the patients was 64±12 years, and 75% of the patients were men. Of the 154 patients referred from other centers, 124 returned to the intensive care unit of the referring hospital. The 30 remaining patients were hospitalized in the intensive care unit of our center because it was thought that the transfer could be harmful for the patient’s clinical situation.

In 23 patients, the lesion responsible for the infarction was not found (6.5%). In 44% (8 patients) of the cases of suspected AMI of indeterminate location with suggestive symptoms and LBBB in the ECG (18 patients), coronary lesions were not observed.

The data related with the procedure performed and the hospital evolution in terms of mortality are shown in Table 4. Angiographic success was achieved in 82% of the patients. The hospital mortality was 11.5% of the entire group of patients analyzed by intention to treat, 10.7% in those who reached the hemodynamics...
laboratory alive, and 5.2% in those that did not present cardiogenic shock at time of admission.

DISCUSSION

Need for a regional AMI intervention program. Justification of objectives

Extension of reperfusion treatment to all patients who have an indication

The first goal of the program is to comply with currently effective AMI practice guidelines in most of the patients. 14,15-17 Establishment of primary angioplasty as the treatment of choice in the hospitals involved in phases 1 and 2 of the program has made it possible to use reperfusion treatment in more than 95%, a figure much higher than has been reported in other registries published to date.

In Spain, it is not known what percentage of patients with AMI and an indication for reperfusion treatment receive such treatment when they come in contact with the healthcare system. Data from different national registries, none referring to the entire national population, report figures for reperfusion treatment of 34% to 43%, 9,12 although in most cases it is not possible to ascertain what percentage of the patients who were included had an indication for this treatment. In the GE-SIR study 11 of 521 patients under the age of 75 years hospitalized with transmural AMI, after excluding patients with a non-definitive electrocardiographic diagnosis and those seen in the emergency room after the accepted time for reperfusion, only 62% of the patients received thrombolytic treatment. Outside of Spain, in the U.S., the NRMI2 data (National Registry of Myocardial Infarction 2) indicate that among the patients who are «ideal candidates» for reperfusion treatment (with less than 6 h of evolution of the AMI), only 39.8% receive it. 19 Therefore, in spite of the theoretical availability of thrombolytic treatment and its easy applicability, less than half of the eligible patients receive it in clinical practice.

In contrast with the idea that primary angioplasty is theoretically less applicable, our data from the two centers participating in phases 1 and 2 of the regional program demonstrate that in certain conditions the use of primary angioplasty as the treatment of choice in AMI can bring routine clinical practice closer to the theoretical goal of making reperfusion treatment available to more of the patients who can benefit from it.

Extension of primary angioplasty as the treatment of choice in AMI

In spite of the fact that many studies have demonstrated the benefits of primary angioplasty compared to thrombolysis in the treatment of AMI, 4,5,8 this procedu-
ber of patients discharged alive or who died in 1990 with the diagnosis of AMI was 27 642, although it is considered that more than 50 000 new myocardial infarctions take place every year. In the RISCI registry (whose participating centers represent only 5385 of all the infarctions that occurred in Spain in 1999), thrombolysis was performed in 2364 patients, a figure that exceeds the number of primary angioplasties made in year 2000. In the U.S. 7% of the patients underwent primary angioplasty versus 21% of those that underwent thrombolysis in 1999. In the Region of Murcia only 18 interventionist procedures were performed for AMI in 1999 (Figure 3). The lack of sufficient infrastructure to effectively carry out AMI interventions is the most likely explanation of this discrepancy between the recommendations of scientific evidence and routine clinical practice. In our experience, keeping a team on call 24 h a day, 7 days a week, with no time constraints for performing primary angioplasty, and the expansion of the service as a result of concentrating all interventionist activity in the region in a single center, made it possible to perform primary angioplasty on almost all the patients with AMI who had an indication for reperfusion treatment in the hospitals integrated in phases 1 and 2.

Acilitating access to rescue angioplasty of patients in the region who undergo thrombolysis without obtaining the expected result

From 15% to 50% of the patients, depending on the series and thrombolytic used, do not present indirect signs of reperfusion after intravenous administration of the thrombolytic drug. In certain subgroups of these patients, a rescue angioplasty can re-establish bloodflow and improve the prognosis if performed promptly. By improving patient transfer mechanisms and planning practice guidelines, it is possible to intervene effectively in such patients, who usually experience long delays because the time spent waiting for the thrombolytic to act is compounded by the time required to decide on a second form of reperfusion treatment. The time required to transfer patients from hospitals distant to the reference hospital (Table 2) is far from optimal. One of the aims of this program is to improve action in these patients, although the scant number of patients from distant hospitals, who may be patients highly selected with regard to the characteristics of AMI presentation and a worse hemodynamic situation, at present precludes drawing conclusions.

Establish a registry of interventionist activity in AMI and its short and long-term results in the Region of Murcia

The main objective of creating and maintaining a prospective registry of interventionist activity in AMI is quality control, especially when treatment is carried out in patients of which more than 50% are referred from other hospitals. The APRIMUR Registry complements the registry of our service for coronary interventionist activity in general. The second objective of the registry is to know the results of primary angioplasty in a clinical context, especially in centers where it has been established as the treatment of choice for AMI. The knowledge that clinical trials generally exclude patients at highest risk is, in our opinion, very important to understanding the results of the practical application of primary angioplasty to existing practice guidelines.

Preliminary results

As has been commented, the results of the first year of our program demonstrate that the application of primary angioplasty can yield better reperfusion results than the mean obtained with thrombolysis in most registries published to date. The median delay observed in the three hospitals of the capital (Table 2) is less than 40 min from the moment that the reperfusion indication is established at the beginning of angioplasty. This delay is clearly shorter than the time lapse from randomization to angioplasty reported in previous clinical trials, although it is longer in patients coming from other hospitals in the region.

The mortality observed in the series is clearly superior to that observed in previous clinical trials of primary angioplasty. This difference can probably be explained, as commented, by the selection of the most favorable patients in randomized studies, accentuated by the selection of patients at greater risk in hospitals distant from the reference center. Accordingly, the treated population has a higher percentage of shock at the time of admission and an older mean age than those included in previous clinical trials. As a result of the continuation of the regional program in upcoming months, we should obtain more trustworthy data on the results of this procedure and its applicability in centers distant from the hospital where the hemodynamics laboratory is located.

LIMITATIONS

The full operation of this program, especially the last two phases, will require the collaboration of health authorities and the coordination of all the groups involved to obtain an effective diagnosis and treatment of patients. As the distance from the reference hospital increases, so do the possibilities of failure in the chain from the onset of AMI to the restoration of blood flow in the artery responsible for infarction. In order to obtain the desired results, problems inherent to the transfer of patients and the logical increase in the work load of the reference center will have to be solved.
The PRIMUR Registry is exhaustive with respect to interventionalist activity in AMI in the public healthcare system of the Region of Murcia. In order to collect all the activity of the region, the activity carried out at two private laboratories would have to be included. However, the small number of AMI procedures performed at these centers (less than 3 in the year 2000) indicates that their exclusion from the overall analysis of results in the region is not very influential.

Since the main objective of this article is to present this regional project, which is in its initial phases, the available results have been analyzed in detail. As the development of the program advances, these analyses will reflect still better the results obtained.

CONCLUSIONS

The program for improving accessibility to coronary interventions for AMI in the Region of Murcia tries to bring the therapeutic procedures that have been demonstrated to produce that greatest benefits in the treatment of the AMI into routine use: reperfusion treatment, particularly primary angioplasty. The use of primary angioplasty as the treatment of choice for AMI can increase the percentage of patients who receive reperfusion treatment, thus coming closer to following the recommendations made in practice guidelines. The parallel development of a registry of the interventions for AMI performed and their results (APRIMUR Registry) provides the necessary quality control for the program and makes it possible to evaluate the consequences of generalizing the use of primary angioplasty as reperfusion treatment for AMI.

REFERENCES


