Time to and Use of Reperfusion Therapy in a Health Care Network

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ABSTRACT

Background
Time delays to reperfusion therapy in the acute phase of myocardial infarction are associated with lower treatment efficacy. Shortening these delays requires recognizing the specific time components in each system of care.

Objectives
The aim of this study was to analyze the use of reperfusion therapy and the time components of its implementation in a network of public hospitals.

Methods
Patients with acute coronary syndromes admitted to the coronary care unit of the Hospital El Cruce were included in an observational, prospective study. Patients with acute myocardial infarction were included for the description of time intervals.

Results
During the study period, 327 patients with acute myocardial infarction were hospitalized. Reperfusion therapy was administered to 63.6% of patients (65.9% were treated with fibrinolytics and 34.1% underwent primary percutaneous intervention). Time to consultation was 60 minutes (interquartile range: 30 to 180 minutes). Door-to-needle time was 75 minutes (45 to 121 minutes). The time from the first electrocardiogram to balloon inflation in patients transferred for primary percutaneous coronary intervention was 240 minutes (154 to 390 minutes) and was longer in patients transferred from hospitals outside the network (p < 0.016).

Conclusions
The use of reperfusion therapy is suboptimal, with prolonged time delays in the health care system. Both aspects have been considered in a network-based myocardial infarction care protocol and this study constitutes a baseline for the evaluation of future results.

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INTRODUCTION
Ischemic heart disease is the leading cause of mortality worldwide. (1) In patients with ST-segment elevation acute myocardial infarction (AMI) reperfusion therapy with fibrinolytic agents or primary percutaneous coronary intervention (PCI) has proved to reduce mortality. (2, 3)The magnitude of the benefit achieved with reperfusion therapy has an inverse correlation with the time interval between the onset of AMI symptoms and treatment implementation. (4, 5) The advantage of PCI over fibrinolytic therapy (FT) depends on the time required to initiate treatment; thus, both methods are equivalent in terms of mortality when delays related to implementation of

fibrinolysis or balloon inflation exceed 120 minutes. (6, 7)

The time interval from the onset of AMI to treatment has two components: one before presentation and another initiating when the patient contacts with the health care system. (8) Shortening time to presentation by means of community education campaigns has shown a modest effect in clinical trial evaluations. (9-11) On the other hand, reduction of health care system delays requires recognizing which specific components of the system should be intervened. (8) Some of the strategies analyzed, as prehospital thrombolysis, which decrease the time to reperfusion therapy and mortality, are not applicable in our environment. (12) The characteristics of each health care system demand specific strategies to reduce time delays in the treatment of AMI.

The Hospital El Cruce is a high complexity medical center, equipped with highly advanced technology, which belongs to a collaborative network of medium-complexity hospitals working together for the care of different diseases. The goal of the present study was to analyze the components of the time intervals of an AMI system of care in this network of public hospitals, as the first-step of a group of interventions aimed at improving the coordination of the system and shortening the times to reperfusion.

METHODS
Patients
This prospective, observational study included consecutive patients with ST-segment elevation AMI transferred from other centers to the coronary care unit of the Hospital El Cruce from April 24, 2009 to December 31, 2011. Patients consulting directly to our emergency department were excluded from the study.

Health care network
The Hospital El Cruce is a high-complexity public hospital belonging to a collaborative network of medium-complexity hospitals from the south of the Greater Buenos Aires. The following medium-complexity hospitals are part of the network: Evita Pueblo (Berazategui), Mi Pueblo (Florencio Varela), Dr. Arturo Oñativia (Rafael Calzada), Dr. Eduardo Oller (San Francisco Solano), Dr. Isidoro Iriarte (Quilmes) y Dr. Lucio Meléndez (Adrogué). These hospitals do not have cardiologists incorporated to the emergency department.

Our hospital also receives patients transferred from other centers nationwide. As time intervals may be longer in patients transferred from centers not belonging to the network due to geographical issues, for the purpose of the study patients were divided into two groups: network vs. no network.

The study was approved by the Ethics Committee of the Hospital El Cruce. Patients were not asked to sign an informed consent form due to the observational nature of the study.

Variables
A thorough clinical history was taken at admission and physical examination, lab tests, chest-X ray and electrocardiogram (ECG) were performed. The information for the registry was obtained from the results of these studies and from in-hospital outcome. The information about hours and dates

that were necessary to calculate the different time intervals was obtained from patients and their relatives, ECG records or hospital admission data, or was provided by referral physicians or physicians participating in patient transportation.

Data were recorded in a printed case report form and then incorporated to a database, both customized for the study. Follow-up was limited to the in-hospital period.

Time intervals
For the purpose of this study, the following time intervals were estimated:

Time-to-presentation: from the onset of symptoms to presentation.
- Time-to-ECG: from presentation to the first ECG.
- Time-to-reperfusion: from the first ECG to initiation of reperfusion therapy.
- Door-to-needle time: from presentation to initiation of FT.
- Door-to-balloon time: from hospital arrival to first balloon inflation.
- Total door-to-balloon time: from the first presentation at another center to first balloon inflation.
- Total time: from onset of symptoms to initiation of reperfusion therapy.

Time-to-presentation and time-to-ECG were calculated in all the patients. Time-to-reperfusion and total time were calculated in the patients who received FT or primary PCI. Door-to-needle time was calculated in the patients treated with FT and door-to-balloon time in those who received primary PCI.

Statistical analysis
Continuous variables are expressed as medians and interquartile ranges (IQR) and categorical variables as numbers and percentages.

The Mann-Whitney U test was used to compare the distribution of continuous variables across groups. A two-tailed p value < 0.05 was considered statistically significant. Calculations were performed using R software version 2.12.1 (The R Foundation for Statistical Software, Vienna, Austria)

RESULTS
During the study period, 1510 patients were admitted to the coronary care unit, 515 of whom had diagnosis of acute coronary syndrome (ACS) and 351 of ST-segment elevation AMI. Only 24 patients went directly to the hospital and were not included in the analysis. The remaining 327 patients constitute the study group: 256 (78.3%) were transferred from centers of the network and 71 (21.7%) from centers outside the network (Figure 1).

Table 1 shows the demographic characteristics, risk factors and personal history of the patients. Mean age was 55.6 years. Reperfusion therapy was delivered to 63.6% of patients (n = 208): 132 (63.5%) received onsite FT and 71 patients (34.1%) and 5 patients (2.4%) received primary PCI and FT, respectively, at the Hospital El Cruce.

Time intervals
Globally, median time-to-presentation was 60 minutes (IQR: 30 to 180 minutes) and time-to-ECG 15 minutes (IQR. 5 to 30 minutes), without significant differences

between patients from the network and those transferred from hospitals outside the network (Table 2).

In patients who received onsite FT, median time from the first ECG to treatment initiation was 45 minutes (IQR: 25 to 90 minutes) and door-to-needle time was 75 minutes (IQR: 45 to 120.8 minutes), without differences between network and no network patients (Table 2) (Figure 2).

In patients who did not receive onsite reperfusion therapy and underwent primary PCI, the time interval from the first ECG to balloon inflation was 240 minutes (IQR: 154-390), and was significantly lower in patients transferred from network hospitals versus no network hospitals (225.5 vs. 315 minutes; p = 0.016). Median door-to-balloon time in Hospital El Cruce was 62.5 minutes and was similar in both groups (p = 0.728).

Finally, time from onset of symptoms to reperfusion therapy (total time) was 180 minutes (IQR: 120-298.8) and 352.5 minutes (IQR: 240-607.5) in patients undergoing reperfusion therapy in the first hospital and in Hospital El Cruce, respectively. Consistent with time-to-reperfusion, this time interval was significantly shorter in patients transferred from network hospitals compared to those transferred from hospitals outside the network.

DISCUSSION

The results show that in AMI patients admitted to public hospitals belonging to a collaborative network, most time delays occur after the first medical contact, that is, within the health care system. The information indicates that the longest delay occurs after taking the first ECG, which, together with the anamnesis, are sufficient to decide reperfusion therapy in most cases.

Previous studies have analyzed the impact of delays in the implementation of reperfusion strategies during the acute phase of AMI, demonstrating poorer
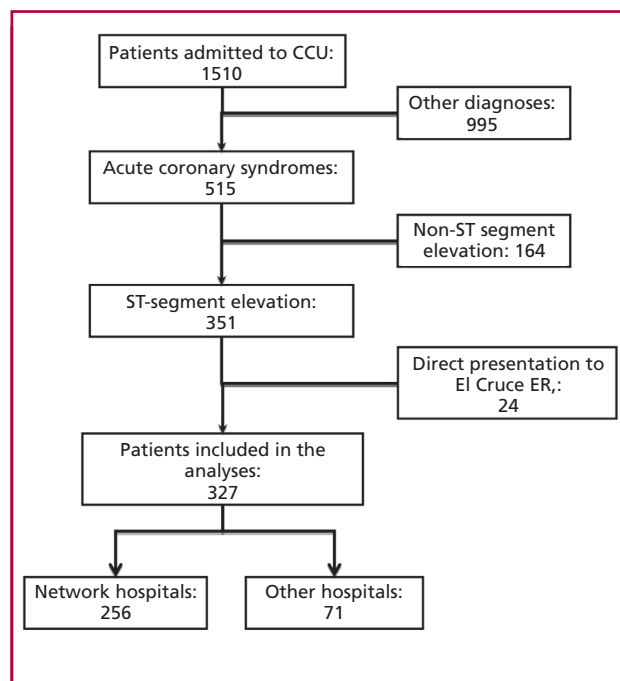

Fig. 1. Patient flow chart during the study period.

Table 1. Demographic characteristics, coronary risk factors and history of the study group.

Variables	All	Network	No network	p
n	327	256	71	-
Age, mean (SD)	55.6 (10.1)	55.5 (9.9)	56.3 (10.8)	0.565
Male gender, n (%)	272 (83.2)	217 (84.8)	55 (77.5)	0.146
BMI, mean (SD)	27.9 (7.7)	27.9 (8.1)	28.4 (6.2)	0.623
Diabetes, n (%)	45 (13.9)	32 (12.5)	13 (18.3)	0.209
Hypertension, n (%)	180 (55.0)	144 (56.2)	36 (50.7)	0.406
Dyslipidemia, n (%)	114 (34.9)	95 (37.1)	19 (26.8)	0.105
Smoking habits, n (%)	184 (56.3)	150 (58.6)	34 (47.9)	0.108
Previous myocardial infarction, n (%)	36 (11.0)	28 (10.9)	8 (11.3)	0.937
Chronic angina, n (%)	26 (8.0)	21 (8.2)	5 (7.0)	0.749
Previous PCI, n (%)	2 (0.6)	2 (0.6)	0 (0.0)	1.00**
Previous myocardial infarction, n (%)	164 (50.2)	130 (50.8)	34 (47.9)	0.666
Killip class > A, n (%)	86 (26.3)	61 (23.8)	25 (35.2)	0.054
Reperfusion, n (%)	208 (63.6)	170 (66.4)	38 (53.5)	0.046
FT, n (%)*	137 (65.9)	112 (43.8)	25 (35.2)	0.197
Primary PCI, n (%)*	71 (34.1)	58 (22.7)	13 (18.3)	0.432
Mortality, n (%)	15 (4.6)	9 (3.5)	6 (8.5)	0.104**

* Estimated on the total number of patients receiving reperfusion therapy.
** Fisher's exact test
   SD: Standard deviation. BMI: Body mass index. FT: Fibrinolytic therapy. PCI: percutaneous coronary intervention.

Table 2. Delays in all the patients, network patients and no network patients

| Variables	All	Network	No network	p
n	327	256	71	-
Door- to-presentation time	60 (30 a 180)	70 (30 a 210)	60 (30 a 135)	0.571
Door- to-ECG time	15 (5 a 30)	15 (5 a 30)	15 (5.8 a 30)	0.780
Door- to- reperfusion time**	45 (25 a 90)	45 (25 a 82.5)	60 (27.5 a 93.5)	0.500
Door- to-needle time**	75 (45 a 120.8)	75 (45 a 139)	90 (45 a 105)	0.821
Total door- to-balloon time§	240 (154 a 390)	225.5 (153 a 352.5)	315 (252.5 a 1.169)	0.016
Door- to-balloon-time El Cruce#	62.5 (30 a 105)	65 (30 a 107)	60 (30 a 94.5)	0.728
Total time				
Onsite reperfusion	180 (120 a 298.8)	195 (120 a 300)	135 (112 a 222.5)	0.066
Rep. at El Cruce	352.5 (240 a 607.5)	315 (225.5 a 570)	440 (330 a 922.5)	0.045

* All values are expressed in minutes (median, interquartile range)
**Analysis based on 132 patients receiving onsite fibrinolysis (107 in network hospitals and 25 in hospitals outside the network).
§Analysis based on the 76 patients receiving reperfusion therapy at Hospital El Cruce. As only 5 patients received fibrinolytic agents, this analysis includes mostly door-to-balloon time.
Of the 76 patients undergoing reperfusion therapy at El Cruce, 5 received fibrinolysis; thus, this time delay is calculated on 71 patients with primary PCI.
Rep.: Reperfusion.
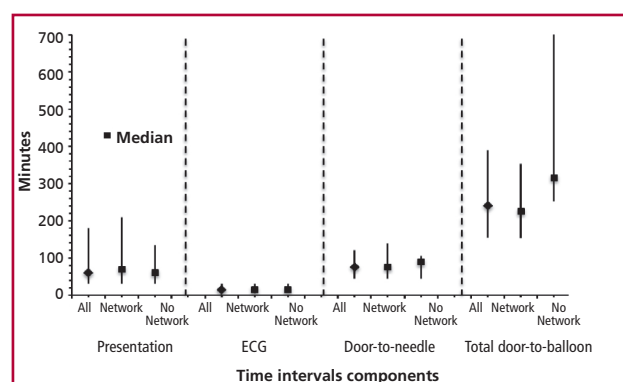
Fig. 2. Time intervals in the different stages and treatments.

outcomes for FT and primary PCI with longer delays between onset of symptoms and the initiation of thrombolysis or balloon inflation. (5, 6) The decision about the appropriate reperfusion strategy for each patient should take into account transfer delay, as the advantage of primary PCI over FT declines with delays > 90-120 minutes in most patients. (6, 7) In our study, delay to reperfusion was longer in patients receiving FT (door-to-needle time of 75 minutes, with less than 25% of patients achieving a time of 30 minutes recommended by the ACC/AHA guidelines) and also in those transferred for primary PCI. (13) In the latter group of patients, door-to-balloon time was adequate (median 62.5 minutes); however, the delay associated with the process of decision-making/transfer of patient produced excessive delays to reperfusion (240 minutes), according to the door-to-balloon time of 90-120 minutes recommended by guidelines. (13, 14)

Health care system delays in patients receiving onsite FT had two main components: time to first ECG (15 minutes) and a longer second component, from ECG to initiation of FT (45 minutes). Shortening these time intervals is a priority.

Several interventions have demonstrated significant reductions in the implementation of reperfusion strategies (15, 16) and our work group elaborated an ACS care protocol, with special focus on AMI treatment. Thus, these data provide a starting point upon which the ACS care protocol efficacy should be evaluated in the future.

As the longest delay is related to diagnosis and decision–making regarding FT indication, we have incorporated a telemedicine system to the network for Internet-based ECG transmission and with the possibility of consulting with cardiologists 24 hours a day, in order to shorten the delays and extend the use of reperfusion therapy in the network centers. In addition, we have scheduled training sessions for physicians on duty with whom patients make their first contact.

Delay to reperfusion in patients transferred for primary PCI was longer in our study than the one recommended by the guidelines, with the greatest component related to the decision-making process and patient transportation, as the door-to-balloon time at Hospital El Cruce was 62.5 minutes. (13, 14). This was due to the fact that transfer of patients includes doctor to doctor contact before transfer to the hospital and only after this has taken place, the catheterization laboratory alarm is activated. Telemedicine system and fast transport of patients might shorten this component.

The goal of implementing a system of care for AMI is to improve the access to the most efficient treatment for all the population seeking medical care. Although we have thoroughly described the composi-

tion of the different time intervals, the high percentage of patients (36.4%) who did not receive reperfusion therapy is a matter of concern. This percentage is consistent with some international registries. (17) In most of the cases where reperfusion was nor performed, we did not find any contraindication for onsite FT, and patient transfer for primary PCI resulted in such an additional and prolonged delay that the patients arrived at our center without criteria for acute reperfusion or were beyond the time window, constituting missed opportunities for reperfusion (this data will be reported soon). To optimize resources, we have designed a network protocol for acute myocardial infarction care. Figure 3 summarizes the strategy proposed for ST-segment elevation AMI. The severity of AMI and the estimation of delay are evaluated to decide whether to transfer the patient for primary PCI or perform onsite FT, and subsequent management. Similarly to time intervals, these data are also a baseline for the evaluation of protocol efficacy in terms of reperfusion.

A recent study, which included 145 patients with AMI treated in public hospitals of the City of Buenos Aires, indicated greater use of reperfusion therapy and shorter door-to-needle time and door-to-balloon time in transferred patients compared to our findings. (18) In the same study, door-to-balloon time of patients presenting to hospitals with PCI facilities was longer than that of Hospital El Cruce. The differences

between both studies might be related to differences in the participating centers (none of the medium-complexity hospitals belonging to our network has a cardiologist available at the emergency department 24 hours a day) geographical differences (the distances are greater in our network) and logistic differences (in our case, catheterization laboratory activation occurs at the moment of accepting the transfer of the patient; thus, door-to-balloon time was shorter while total time was longer).

Study Limitations
Some limitations should be mentioned to interpret the information. As the registry was performed at the hospital, only transferred patients were included and this might be a potential source of bias for the estimation of time intervals. Despite the possible bias, we were able to identify the components of the system time intervals in which an intervention is feasible. Delays were estimated by using information from different sources, which may not be consistent. (19) As the study focused on health care system delays, where in most cases the information retrieved from anamnesis can be verified with objective data from test, phone call or admission time registries, it is unlikely that this error had an effect on these delays. On the other hand, this source of error may have affected the estimation of time-to-presentation, which was shorter than the one reported by other studies. (9, 20)

Fig. 3. Network algorithm for the management of patients with acute myocardial infarction.
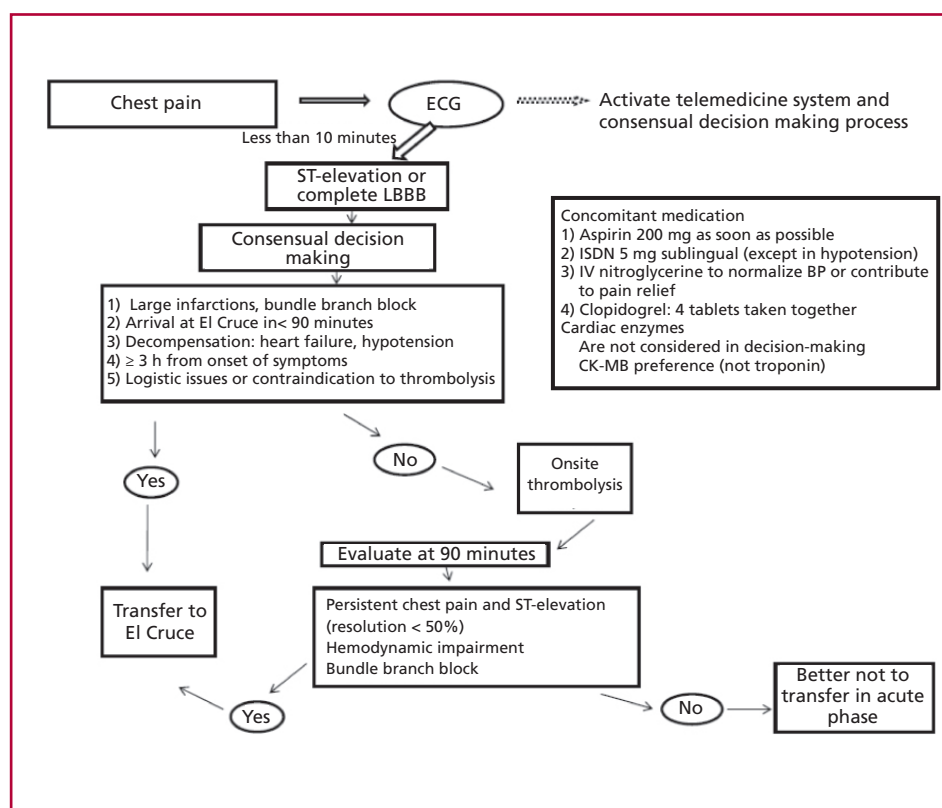
CONCLUSIONS

Our study reflects treatment results of ST-segment elevation AMI using a novel modality for the health care system in our country: a network of medium-complexity hospitals associated with a high-complexity hospital with PCI capability. In this primary stage, we conclude that the use of reperfusion therapy in AMI is suboptimal and that most of the delays in the implementation of reperfusion occur in the health care system. Both aspects might be modified, and a protocol has been developed to improve the situation with the participation of all the hospitals of the network and the authorities of the health care network. The effects of the protocol on these parameters will be evaluated in the future.

RESUMEN

Tiempos y utilización de terapia de reperfusión en un sistema de atención en red

Introducción
Las demoras en el tratamiento de reperfusión durante la fase aguda del infarto de miocardio se asocian con menor eficacia del tratamiento y su reducción exige el reconocimiento de los componentes específicos de los tiempos dentro de cada sistema de atención.

Objetivos
Analizar el uso de terapia de reperfusión y los componentes de los tiempos en su implementación en una red de hospitales públicos.

Material y métodos
Estudio observacional, prospectivo, de pacientes ingresados con diagnósticos de síndromes coronarios agudos en la Unidad Coronaria del Hospital El Cruce. Para la descripción de los intervalos de tiempo se incluyeron pacientes con infarto agudo de miocardio.

Resultados
Durante el período de estudio se internaron 327 pacientes con infarto agudo de miocardio. El 63,6% de los pacientes recibieron terapia de reperfusión (65,9% fibrinolíticos, 34,1% angioplastia primaria). El tiempo a la consulta fue de 60 minutos (rango intercuartil: 30 a 180 minutos). El tiempo puerta-aguja fue de 75 minutos (45 a 121 minutos). El intervalo desde el primer electrocardiograma al inflado del balón en los pacientes derivados para angioplastia primaria fue de 240 minutos (154 a 390 minutos) y fue mayor en los pacientes derivados de hospitales no pertenecientes a la red (p < 0,016).

Conclusiones
El uso de terapia de reperfusión es subóptima y los retrasos dentro del sistema de salud son prolongados. Ambos aspectos se han contemplado en un protocolo de asistencia del infarto en red y este estudio constituye una línea de base para la evaluación de futuros resultados.

Palabras clave > Infarto de miocardio - Angioplastia coronaria - Fibrinolíticos - Registro

Conflicts of interest
None declared.

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ACUTE CORONARY SYNDROME CARE NETWORK

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