ORIGINAL ARTICLE

CME

Patients with ST-Segment Elevation Acute Myocardial Infarction Transferred to Centers with Percutaneous Coronary Intervention Capabilities. National Survey of ST-Segment Elevation Acute Myocardial Infarction in Argentina (ARGEN-IAM-ST)

Pacientes con infarto agudo de miocardio con elevación del ST trasladados a centros con hemodinamia. Encuesta Nacional de Infarto Agudo de Miocardio con Elevación del ST en la República Argentina (ARGEN-IAM-ST)

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ABSTRACT

Background: In Argentina, the use of primary percutaneous coronary intervention as a reperfusion strategy in ST-segment elevation acute myocardial infarction (STEMI) patients has progressively increased based on formal or informal patient transfer networks. The use and time delays produced by patient transfer have not been universally explored in our country.
Objective: The aim of this study was to evaluate the frequency of STEMI patient transfer to centers with percutaneous coronary intervention capabilities, the reperfusion strategy adopted (primary percutaneous coronary intervention, thrombolytic therapy, rescue percutaneous coronary intervention or pharmacoinvasive strategy) and the system delays.
Methods: A prospective, observational, multicenter study was conducted in 247 centers in all the Argentine provinces. A total of 1,661 patients with STEMI lasting <36 hours were included in the study from March to December 2015.
Results: Mean age was 61±11.9 years and 77.6% were men. The average prevalence of patient transfer from other centers for reperfusion therapy was 37% (95% CI: 34.80-39.44) nationwide. The overall use of reperfusion therapy was lower in patients transferred than in those treated in situ [80% vs. 86% (OR: 0.65; 95% CI: 0.50-0.84; p <0.001)]. Considering only those patients treated with reperfusion strategies, the use of primary percutaneous coronary intervention was lower in patients transferred [71% vs. 83% (OR: 0.51; 95% CI: 0.39-0.67)], while the use of thrombolytic therapy was higher [29% vs. 17% (OR: 1.92; 95% CI: 1.48-2.50)] (p <0.001). Rescue percutaneous coronary intervention was performed in 41 patients transferred versus 12 patients treated in the center of the first medical contact, while pharmacoinvasive treatment was used in only 12 patients, 6 of them transferred from another center. Total ischemic time from onset of symptoms to primary percutaneous coronary intervention was 350 minutes (IQR 25-75: 235-650) in patients transferred and 245 minutes (IQR 25-75:170-450) in those treated in the center of the first medical contact (p <0.001). Door-to-balloon time was 85 minutes (IQR 25-75: 50-153) vs. 95 minutes (IQR 25-75: 62-150) in patients transferred and not transferred, respectively (p=0.01). In patients transferred, the symptom-to-needle time in patients treated with thrombolysis before referral was 165 minutes and in those transferred for percutaneous coronary intervention the symptom-to-balloon time was 350 minutes, with a difference of 185 minutes. The delay between the access to thrombolysis in situ and transfer for percutaneous coronary intervention was 140 minutes.
Conclusions: In our country, one out of three STEMI patients is transferred to another center for reperfusion therapy. Patients transferred are less likely to receive reperfusion therapy and to undergo primary percutaneous coronary intervention. The time difference between patients who received thrombolysis before being transferred and the waiting time to undergo primary percutaneous coronary intervention was >2 hours. The use of pharmacoinvasive treatment was very low. The availability of resources in the participating centers indicate that a better articulation of patient transfer networks could improve the time delays to treatment and reduce STEMI-related morbidity and mortality in Argentina.

Key words: Myocardial Infarction - Angioplasty – Fibrinolytics

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RESUMEN

Introducción: En la Argentina se ha incrementado progresivamente el uso de angioplastia primaria como estrategia de reperfusión en los pacientes con infarto agudo de miocardio y elevación del segmento ST (IAMCEST) sobre la base de redes formales o informales de derivación. No se han explorado en forma universal en nuestro país la funcionalidad y las demoras generadas por las derivaciones.
Objetivos: Evaluar la frecuencia con que los pacientes con IAMCEST son derivados a centros con hemodinamia, la estrategia de reperfusión adoptada (angioplastia primaria, terapéutica trombolítica, angioplastia de rescate y farmacoinvasiva) y las demoras en el sistema.
Material y métodos: Estudio prospectivo, observacional, multicéntrico, llevado a cabo en 247 centros de todas las provincias de la República Argentina. Desde marzo a diciembre de 2015 se incluyeron 1.661 pacientes con diagnóstico de IAMCEST de hasta 36 horas de evolución.
Resultados: La edad promedio de los pacientes fue de 61 ± 11,9 años y el 77,6% eran de sexo masculino. La prevalencia promedio de derivación de todo el país desde otros centros para realizar tratamiento de reperfusión fue del 37% (IC 95% 34,80-39,44). Comparando los pacientes derivados con los tratados *in situ*, la aplicación global de tratamientos de reperfusión fue menor en los derivados [80% vs. 86% (OR 0,65; IC 95% 0,50-0,84; p < 0,001)]. Considerando solo los tratados con estrategias de reperfusión, en los derivados se utilizó menos angioplastia primaria [71% vs. 83% (OR 0,51; IC 95% 0,39-0,67)] y mayor aplicación de trombolíticos [29% vs. 17% (OR 1,92; IC 95% 1,48-2,50)] (p < 0,001). La angioplastia de rescate se realizó en 41 pacientes derivados *versus* 12 pacientes tratados en el primer centro de contacto y el tratamiento farmacoinvasivo en solo 12 pacientes, de los cuales 6 eran derivados de otro centro. El tiempo total de isquemia desde el comienzo de los síntomas hasta la realización de la angioplastia primaria fue de 350 minutos (RIC 25-75: 235-650) para los pacientes derivados y de 245 minutos (RIC 25/75: 170-450) para los pacientes tratados en el centro de primera consulta (p < 0,001). El tiempo puerta-balón fue de 85 minutos (RIC 25/75: 50-153) versus 95 minutos (RIC 25/75: 62-150) en los derivados y los no derivados, respectivamente (p = 0,01). En los pacientes derivados, el tiempo síntoma-aguja en los tratados con trombolíticos previo a la derivación fue de 165 minutos y en los derivados a angioplastia primaria, el tiempo síntoma-balón fue de 350 minutos, una diferencia de 185 minutos. La demora entre el acceso a la trombólisis in situ y la angioplastia derivada fue de 140 minutos.
Conclusiones: En nuestro país, uno de cada tres pacientes con IAMCEST es derivado a otro centro para realizar tratamiento de reperfusión miocárdica. Los pacientes derivados tienen menos probabilidad de recibir tratamiento de reperfusión y menor utilización de angioplastia primaria. La diferencia de tiempo entre los pacientes que recibieron trombólisis previa a la derivación y la espera para realizar una angioplastia primaria supera las dos horas. El tratamiento farmacoinvasivo fue mínimo. La disponibilidad de recursos en los centros participantes indica que una mejor articulación de las redes de derivación podría mejorar los tiempos de acceso al tratamiento y disminuir la morbimortalidad del IAMCEST en la Argentina.

Palabras clave: Infarto del miocardio - Angioplastia - Fibrinolíticos

Abbreviations

BPCI	Percutaneous coronary intervention	**STEMI**	ST-segment elevation myocardial infarction
FAC	Argentine Federation of Cardiology	**SAC**	Argentine Society of Cardiology
MI	Myocardial infarction	**TNK**	Tenecteplase

INTRODUCTION

Cardiovascular diseases are the most frequent causes of death, disability and loss of working capacity in adults worldwide and in our country. (1-3) Treatment of severe conditions, as acute coronary syndromes and heart failure, is currently supported by scientific studies and allows significant reductions in disability and mortality. (4) The access to diagnostic and therapeutic strategies demands an adequate coordination of the health care system and far exceeds the role of the specialists. ST-segment elevation myocardial infarction (STEMI) is one of the most challenging problems for the health care system. The early diagnosis permits the implementation of strategies for myocardial reperfusion, either using fibrinolysis or primary percutaneous coronary intervention (PCI), with proven efficacy to reduce mortality. Multiple barriers prevent people from receiving an adequate treatment. The absence of coordinated networks facilitating the rapid transfer of patients to centers with PCI capabilities produce delays that reduce the relative advantage of this procedure, which is currently considered the strategy with the best outcomes. (5) In Argentina, over 80% of STEMI patients receive reperfusion therapy. (6, 8) This number might seem high, but its application in the real world and particularly the time delays are not what would be expected. For example, in a registry of the hospitals of the city of Buenos Aires, less than 3% of the patients transferred for primary PCI arrive with an adequate time window. (9) The Argentine Society of Cardiology (SAC) and the Argentine Federation of Cardiology (FAC) have developed the National Survey of ST-Segment Elevation Myocardial Infarction (ARGEN-IAM-ST) to gather information about the time delays and the type of STEMI treatments at the national level. The particular aim of this presentation was to determine the prevalence of patients with acute myocardial infarction (AMI) that were transferred to centers with PCI capabilities in our country and to establish whether these patients were treated in due time and form according to national and international recommendations, either in terms of referral for PCI or using a pharmacoinvasive strategy..

METHODS

A nationwide multicenter, prospective and observational registry was performed inviting coronary care units and general intensive care units admitting patients with acute cardiovascular conditions, independently of the complexity of the institution.

The inclusion criteria were:

- Suspected acute MI and ST-segment elevation ≥ 1 mV in 2 limb leads or ≥ 2 mV in 2 contiguous precordial leads.
- AMI with presence of new Q waves for < 36 hours.
- Suspected posteroinferior MI (horizontal ST-segment depression from V1 to V3 suggestive of acute occlusion of the left circumflex artery).
- New or presumed new complete left bundle branch block.

In each center, the patients were consecutively included during a period of at least 3 months. A pilot phase was conducted between November 2014 and March 2015 in selected centers and was then extended nationwide until December 31, 2015.

The ARGEN-IAM-ST included 1,759 STEMI patients. For this sub-analysis, 98 patients were excluded due to incomplete data related with the transfer to other centers. This small group of patients (6%) had a homogeneous distribution that was proportional to the density of the population nationwide, and the frequency of reperfusion therapy was similar to that of the general population (94%), including two rescue PCIs and one pharmacoinvasive strategy. After excluding these patients, the cohort consisted of 1,661 patients. The following data were collected: patients' characteristics (age, sex, risk factors, history and comorbidities), clinical features (site of infarction, Killip and Kimball class at admission, time from symptom onset), treatment (antiplatelet drugs, reperfusion therapy, coadjuvant treatment) and in-hospital outcome (heart failure, postinfarction angina, shock and death), as previously published in detail. (10) We focused on the detailed information of the delays to achieve an effective treatment. Of importance, in the case of patients transferred, patient delay (from symptom onset to admission) was recorded in both institutions. Data were collected through the web using an electronic worksheet especially designed by the Centro de Teleinformática Médica de FAC (CETIFAC) which allowed online monitoring of the variables entered. Patients' names or initials were not stored in the database to ensure privacy. The patients were identified by a correlative number by center.

Statistical analysis

A cross-sectional, multicenter and prospective study was performed nationwide. Qualitative variables are presented as frequency tables and percentages with their corresponding confidence intervals. Quantitative variables are expressed as mean ± standard deviation (SD), or median and interquartile range (IQR 25-75), according to their distribution.

Discrete variables were analyzed using contingency tables, and for continuous variables, the t test or the Kruskall-Wallis test for unmatched data or the analysis of variance (ANOVA) were used, as applicable. A p value <0.05 was considered statistically significant. In Figure 1, the percentages were rounded. The analysis was performed using Epi-Info 7.2 and Stata/SE v13.0™ software packages.

Ethical considerations

The protocol design was evaluated and approved by the Bioethics Committee of the Argentine Society of Cardiology, and was subjected to evaluations of the local committees, depending on the local regulations and institutional policies. The protocol was registered in ClinicalTrials.gov with the number NCT2458885.

RESULTS

Overall, 247 centers (Appendix) nationwide participated in the registry (43% public institutions and 57% private centers); 56.3% were coronary care units and 57.6% were centers with PCI capabilities.

This analysis included a total of 1,661 patients, with 616 (37%) referred from other centers. The distribution of patients transferred from other centers by province is described in Table 1. The province of Mendoza (15%) and the Autonomous City of Buenos Aires (19%) stand out with the lowest transfer rate, while the provinces of Río Negro (60%), Entre Ríos (59%), San Luis (55%), La Rioja (54%) and Tucumán (49%) had the highest transfer rates. Moreover, the transfer rate of the province of Buenos Aires, which has high population density, is above the average general rate (44%).

The characteristics of the population are summarized in Table 2. The patients transferred from other centers were younger (mean age 59.94±12.15 years vs. 62.05±11.71 years, p<0.001), had lower prevalence of previous PCI and higher incidence of anterior wall myocardial infarction. There were no differences in the Killip and Kimball class at admission.

Reperfusion therapy

The prevalence of reperfusion therapy in patients transferred was lower compared with patients treated in the first center or in situ, particularly due to a lower use of primary PCI (Figure 1). The overall use of reperfusion therapy was lower in patients transferred than in those treated in situ (80% vs. 86%, OR 0.65; 95% CI, 0.50-0.84; p <0.001). When only those patients treated with reperfusion strategies were analyzed, the use of primary PCI was lower in patients transferred, 71% vs. 83%, (OR 0.51; 95% CI: 0.39-0.67) while the use of thrombolytic therapy was higher, 29% vs. 17% (OR 1.92; 95% CI, 1.48-2.50, p <0.001). Of the 141/616 patients transferred that received thrombolytic therapy (23%), 96/141 (68%) were treated before referral. Overall, only 96/616 of the patients transferred (16%) underwent thrombolysis before being transferred.

Rescue PCI was used in 53 patients, in 41 patients transferred, and in 12 patients treated in situ, while pharmacoinvasive treatment was used in 6 patients transferred and in 6 treated in situ.

The primary success of PCI was similar in patients treated in situ and in those transferred (94.36% vs. 95.06%) with no differences in the distribution of the type of stent used: bare metal stent or drug eluting stent in 68% and 28% of the patients transferred vs. 63% and 30% of the patients treated in situ, respectively. The left anterior descending coronary artery was the culprit vessel in patients referred from another center (47.71% vs. 42.51%, p=0.06).

Province	Transferred from another center (n=616) n	%	Not transferred (n=1,045) n	%	Total
Buenos Aires	164	43.97	209	56.03	373
CABA	101	19.20	425	80.80	526
Catamarca	19	44.19	24	55.81	43
Chaco	1	20.00	4	80.00	5
Chubut	1	33.33	2	66.67	3
Córdoba	46	46.46	53	53.54	99
Corrientes	17	33.33	34	66.67	51
Entre Ríos	26	59.09	18	40.91	44
Formosa	1	100.00	0	0.00	1
Jujuy	3	27.27	8	72.73	11
La Pampa	7	77.78	2	22.22	9
La Rioja	15	53.57	13	46.43	28
Mendoza	5	14.71	29	85.29	34
Misiones	4	44.44	5	55.56	9
Neuquén	6	100.00	0	0.00	6
Río Negro	33	60.00	22	40.00	55
Salta	4	30.77	9	69.23	13
San Juan	18	40.91	26	59.09	44
San Luis	12	54.55	10	45.45	22
Santiago del Estero	5	50.00	5	50.00	10
Santa Cruz	2	18.18	9	81.82	11
Santa Fe	72	45.28	87	54.72	159
Tierra del Fuego	5	41.67	7	58.33	12
Tucumán	49	52.69	44	47.31	93
Total	616	37.09	1.045	62.91	1661

Table 1. Distribution of patients transferred by provinces

Reperfusion therapy was not used in 274 patients (16.5%), with a higher rate of non-reperfusion among patients transferred (Figure 1). The reasons of non-reperfusion in patients transferred and not transferred were similar, except for a lower prevalence of small infarctions among patients transferred (Table 3).

Time delays

The time from symptom onset to admission was 170 minutes (IQR 25-75: 75-420) in the overall population, and was higher when patients were transferred from other institutions: 245 minutes (IQR 25-75: 120-540). For patients treated in situ, the delay was almost 2 hours lower: 135 minutes [(IQR 25-75: 65-300, p <0.001)]. Less than half of the patients transferred from other institutions were admitted within 3 hours of symptom onset (41.56% vs. 62.97%, OR 0.41, 95% CI, 0.34-0.51, p <0.001) (Table 4).

In patients undergoing primary PCI in the center of the first medical contact and with PCI capabilities, door-to-balloon time was 95 minutes (IQR 25-75: 62-150) and 85 minutes (IQR 25-75: 50-153, p=0.01) in patients transferred from other centers. The time window from symptom onset to balloon inflation was 350 minutes (IQR 25-75: 235-650) in patients transferred and 245 minutes (IQR 25-75: 170-450) in those treated in situ (p <0.001). The waiting time to start treatment in situ and/or in the transfer is around 2 hours. As shown in Figure 2, in patients transferred, time to thrombolysis before referral was 165 minutes and time to primary PCI was 350 minutes. The difference in time delays to the possible use of thrombolysis before referral versus PCI can be analyzed in two ways: a) by comparing the time delays from symptom onset to thrombolysis in situ (165 minutes) with the time delay to PCI (350 minutes), with a difference of 185 minutes, >3 hours (see Figure 2); b) by comparing the time delays from arrival at the institution to thrombolysis in situ (60 minutes) with the sum of the time delay to transfer (115 minutes) plus the door-to-balloon time (85 minutes), a total of 200 minutes. Thus, this difference was of 140 minutes, >2 hours.

Table 2. Baseline characteristics of the population included in the study (n = 1,661)

Variable	Transferred from another center (n=616)	Not transferred (n=1,045)	Odds ratio	95% CI	p
Age, years (mean±SD)	59.94±11.71	62.05±12.15	-	-	<0.001
Male sex, %	77.11	77.89	0.95	0.75-1.21	ns
Coronary risk factors.					
Hypertension, %	62.68	63.36	0.97	0.78-1.20	ns
Diabetes, %	21.13	21.23	0.99	0.76-1.28	ns
Dyslipidemia, %	52.26	50.95	1.05	0.83-1.33	ns
Current smoking, %	63.57	60.26	1.15	0.90-1.46	ns
Family history, %	29.80	28.45	1.06	0.83-1.36	ns
History of coronary artery disease					
Previous AMI, %	8.41	10.95	0.74	0.52-1.06	ns
Stable chronic angina, %	4.93	3.83	1.30	0.78-2.14	ns
Previous PCI, %	7.03	11.52	0.58	0.39-0.84	< 0.01
Previous CABGS, %	2.46	1.51	1.64	0.78-3.43	ns
Other diseases					
Heart failure, %	2.28	2.11	1.08	0.53-2.17	ns
COPD, %	3.52	4.66	0.74	0.43-1.27	ns
Chronic kydney failure, %	2.65	2.32	1.14	0.59-2.21	ns
History of stroke, %	3.00	4.41	0.67	0.37-1.18	ns
Previous use of aspirin, %	21.22	22.15	0.94	0.73-1.22	ns
Site of infarction					
Anterior wall, %	48.86	41.15	1.36	1.11-1.66	<0.001
Killip and Kimball class at admission					
I, %	73.21	74.93	0.91	0.72-1.14	ns
II, %	15.58	14.74	0.93	0.70-1.23	ns
III, %	2.44	2.20	1.10	0.57-2.14	ns
IV, %	8.77	8.13	1.08	0.75-1.55	ns

SD: Standard deviation. AMI: Acute myocardial infarction. PCI: Percutaneous coronary intervention. CABGS: Coronary artery bypass graft surgery. COPD: Chronic obstructive pulmonary disease.

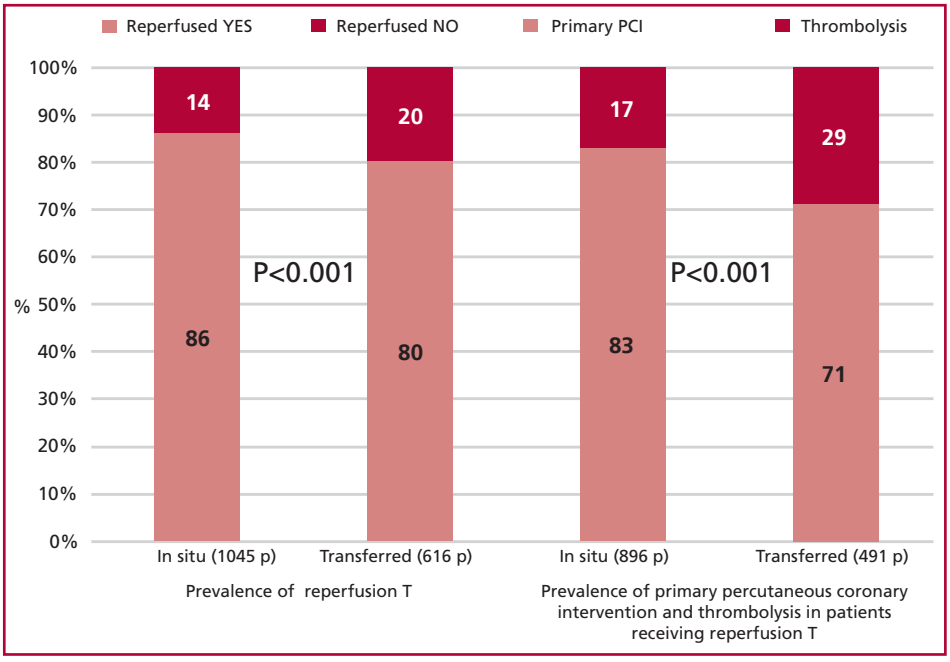

Fig. 1. Prevalence and type of reperfusion therapy in patients treated in the center of the first medical contact (in situ) or transferred from other centers. T.: Treatment

	Transferred from another center (n=125) %	Not transferred (n=149) %	Odds ratio	95% CI	p
Late presentation	26.4	24.83	1.08	0.63-1.87	ns
Decision not to perform PCI	9.60	8.72	1.11	0.48-2.53	ns
Uncertain electrocardiogram	8.80	5.37	1.70	0.66-4.36	ns
Small infarction	1.60	6.71	0.22	0.04-1.05	0.05
Lack of PCI capabilities	4.80	3.36	1.45	0.43-4.87	ns
Contraindications for thrombolysis	1.60	4.03	0.38	0.07-1.95	ns
Old age	1.60	1.34	1.19	0.16-8.60	ns
Patient refusal	0.80	0.67	1.19	0.07-19.2	ns
Lack of thrombolytic drugs	0.80	0.67	1.19	0.07-19.2	ns
Other reasons (death, normal coronary arteries, technical issues)	26.4	22.15	1.26	0.72-2.19	ns

PCI: Percutaneous coronary intervention.

Table 3. Reasons for non-reperfusion (n = 274)

Table 4. Distribution of patients by pre-established time intervals from the onset of symptoms to admission

Time to admission	Transferred from another center (n=616) %	Not transferred (n=1045) %
0-3	41.56	62.97
>3-6	21.43	15.79
>6-12	18.99	11.67
>12-24	11.20	5.55
>24-36	4.71	2.68
>36	2.11	1.34

In patients who received thrombolytic therapy, door-to-needle time was 50 minutes (IQR 25-75: 30-92.5) in the center of the first medical contact and 48 minutes (RIC 25-75: 30-90) in patients transferred; only 30% of the patients transferred and 26% of the patients treated in the center of the first medical contact had a door-to-needle time ≤30 minutes. The total time window from symptom onset to thrombolytic infusion was similar in both groups: 170 minutes (IQR 25-75: 100-300) in patients transferred and 180 minutes (IQR 25-75: 90-300) in those treated in the center. The patients transferred presented a lower proportion of reperfusion criteria compared with those treated in situ (63% vs. 78%, OR, 0.46; 95% CI, 0.27-0.77, p <0.001). In patients treated before being transferred, time from symptom onset to thrombolytic therapy was 165 minutes (IQR 25/75: 90-262), and the door-to-needle time was 60 minutes (IQR 25/75: 30-90) (see Figure 2).

Table 5 summarizes the medical treatment at admission. The use of clopidogrel and angiotensin-converting enzyme inhibitors was greater in the patients transferred from other centers.

In-hospital outcome

In-hospital mortality was similar in patients transferred from other institutions and in patients treated in situ (Table 6).

DISCUSSION

The national survey on STEMI has been the largest one conducted in Argentina so far. These results show that one third of myocardial infarctions require transfer for reperfusion therapy and that the time delays still remain inadequate, reflecting poor care coordination. The participation of centers nationwide has allowed an analysis by region on the prevalence of patient transfer. Forty percent of the participating centers lack primary PCI capabilities. (10)

Patients transferred were 35% less likely to receive reperfusion therapy and with lower quality of care, as the percentage of primary PCI was 47% lower. These findings are similar to those reported by Ting et al. (11) from the United States National Registry of Myocardial Infarction with 440,398 patients, in which they observed that longer delays from symptom onset to hospital presentation were associated with lower reperfusion therapy and greater mortality.

This registry has provided valuable information about the sequence of the strategies used: only 16% of the patients received thrombolytic therapy before being transferred. Overall, 6.7% underwent rescue PCI and only 1% received a pharmacoinvasive therapy. Time delay in treatment with primary PCI from symptom onset to balloon inflation was 350 minutes in patients transferred. The door-to-balloon time considering the first medical contact until primary PCI was 200 minutes, far above the national and international recommendations, and patients treated with thrombolytic therapy before being transferred also had a door-to-needle time that exceeded the one recommended (60 minutes).

The time delays observed demonstrate that the

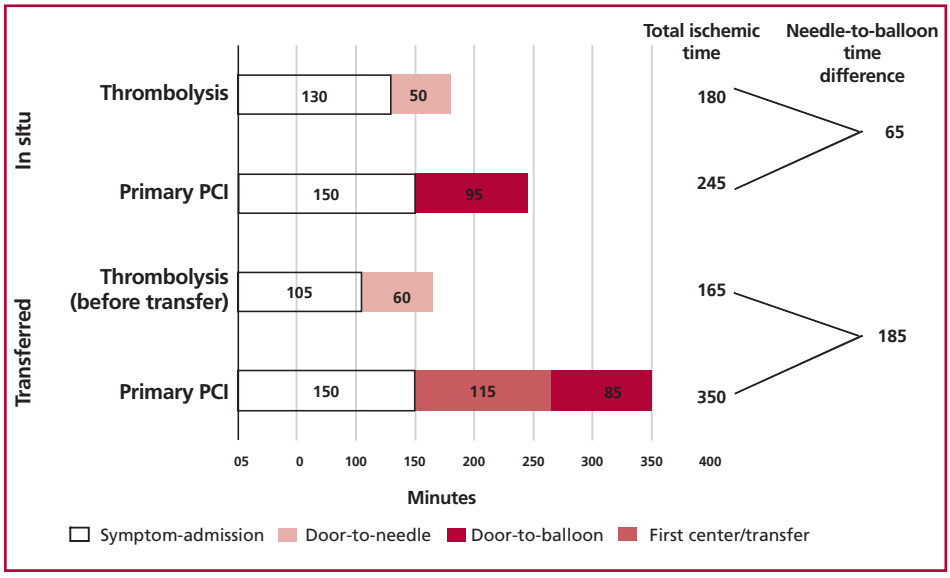

Fig. 2. Total ischemic time of patients in different therapeutic scenarios and institutional delays in patients treated in situ or transferred from other centers without PCI capabilities Time from the first medical contact to admission is the difference between the median total ischemic time and the median door-to-needle or door-to-balloon time. In the special case of patients transferred from other centers for primary percutaneous coronary intervention (PCI), the time to the first medical contact was considered the same (150 minutes) as in patients receiving primary PCI in situ.

Table 5. Adjuvant treatment at admission

	Transferred from another center (n=616) %	Not transferred (n=1,045) %	Odds ratio	95% CI	p
Aspirin	99.00	98.74	1.26	0.47-3.34	ns
Clopidogrel	86.46	73.65	2.28	1.73-3.01	<0.001
Prasugrel	8.35	11.68	0.68	0.47-1.00	<0.05
Ticagrelor	10.61	21.62	0.43	0.31-0.59	<0.001
GPIIb/IIIa inhibitors	6.84	8.82	0.75	0.50-1.14	ns
UFH anticoagulant	26.30	26.51	0.98	0.78-1.24	ns
LMWH anticoagulant	25.00	24.21	1.04	0.82-1.31	ns
Bivalirudin	4.68	3.76	1.25	0.72-2.17	ns
Intravenous nitroglycerin	63.47	68.73	0.79	0.63-0.98	<0.05
Oral nitrates	2.88	4.41	0.64	0.36-1.13	ns
Beta blockers	64.37	57.61	1.32	1.07-1.64	<0.01
ACEIs	58.59	50.91	1.36	1.10-1.68	0.001
ARBs	5.72	5.70	1.00	0.62-1.60	ns
Calcium channel blockers	2.37	1.59	1.49	0.68-3.26	ns
Statins	91.61	91.51	1.01	0.70-1.46	ns
Diuretics	24.71	20.38	1.28	0.99-1.65	0.05
Aldosterone antagonists	14.01	11.89	1.20	0.87-1.66	ns
Insulin	18.00	16.26	1.13	0.84-1.50	ns
Oral hypoglycemic drugs	4.72	3.27	1.46	0.84-2.54	ns
Antiarrhythmic drugs	6.69	7.59	0.87	0.56-1.34	ns
Vitamin K antagonists	2.36	1.37	1.73	0.77-3.90	ns
Dopamine	8.53	9.41	0.89	0.61-1.31	ns
Dobutamine	6.86	4.45	1.58	0.98-2.53	0.05
Norepinephrine	10.47	9.95	1.05	0.73-1.51	ns
Levosimendan	1.39	1.26	1.08	0.42-2.85	ns
Milrinone	0.79	0.80	0.98	0.28-3.38	ns

GP IIb/IIIa: Glycoprotein IIb/IIIa. UFH: Unfractionated heparin. LMWH: Low-molecular-weight heparin. ACEIs: Angiotensin-converting enzyme inhibitors. ARBs: Angiotensin II receptor blockers.

In-hospital events	Transferred from another center (n=616) %	Not transferred (n=1,045) %	Odds ratio	95% CI	p
Overall mortality	8.28	9.00	0.91	0.63-1.30	ns
Cardiovascular mortality	6.66	7.94	0.82	0.56-1.21	ns
Postinfarction angina	2.92	2.20	1.33	0.71-2.49	ns
Reinfarction	1.46	1.91	0.75	0.34-1.67	ns
Percutaneous coronary intervention	0.32	0.86	0.37	0.08-1.74	ns
Atrial fibrillation	5.03	4.02	1.26	0.78-2.03	ns
Cardiac arrest	8.60	11.67	0.71	0.50-0.99	0.05
Bleeding	4.70	3.25	1.46	0.89-2.43	ns
Minor	3.08	1.72	1.81	0.94-3.48	ns
Moderate	0.97	1.24	0.78	0.29-2.06	ns
Major	0.65	0.29	2.27	0.50-10.1	ns
Heart failure	26.78	25.07	1.09	0.87-1.37	ns
Cardiogenic shock	10.06	8.71	1.17	0.83-1.63	ns
Mechanical complications	1.46	0.95	1.53	0.62-3.79	ns
Ventricular septal defect	0.49	0.10	5.10	0.53-49.2	ns
Mitral regurgitation	0.81	0.29	2.84	0.67-11.9	ns
External cardiac rupture	0.16	0.48	0.33	0.03-2.90	ns

Table 6. In-hospital events

difference between access to thrombolysis versus PCI in patients transferred ranged from 140 to 185 minutes depending on the measurement criterion, very prolonged in both cases. Several publications (12-14) have demonstrated that the advantage of PCI is lost with a needle-to-balloon time >2 hours.

The studies that evaluated thrombolysis in the center of the first medical contact versus transfer for primary PCI did not show benefit for PCI when the time from symptom onset was <3 hours; but patient transfer showed better outcomes with higher time delays, particularly in the incidence of reinfarction and stroke. (15-17) However, in these studies the door-to-balloon times were extremely low and very difficult to extrapolate to real life. Therefore, considering these data, an elevated number of patients could benefit from the use of fibrinolytic therapy before being transferred.

The pharmacoinvasive strategy did not show significant differences with primary PCI, and fibrinolysis could be associated with greater incidence of bleeding and stroke; (18, 19) therefore, it could be considered a valid strategy when primary PCI is not available, particularly in low complexity centers. Probably, the lack of availability of tenecteplase (TNK), a safe and easily administered drug as IV bolus, may explain the low utilization of this strategy. Recently, the STREAM study (20) evaluated the use of a pharmacoinvasive therapy with TNK in 1,892 patients and reported that the drug is safe despite a slightly increased risk of hemorrhagic stroke (<1%). This study randomized patients who were able to undergo primary PCI more than 60 minutes after the first medical contact and less than 3 hours after the onset of symptoms. The times between the first medical contact and TNK or primary PCI were 100 minutes and 178 minutes, respectively. There were no differences in the outcome of patients. Rescue PCI was required in on third of the patients (2.2 hours) whereas the rest of the patients underwent a pharmacoinvasive strategy within 24 hours (17 hours). In our population of patients transferred, the time delays are twice those published in this trial (165 and 350 minutes). As most patients seek medical care within 3 hours, they could benefit from a pharmacoinvasive strategy. Obviously, institutional and governmental programs are required to adopt the adequate strategies for the management of STEMI patients.

In Argentina, mortality due to STEMI is high, about 10%, and has not changed over the past years (6-10) compared with the 6% reported by recent registries. (11) The possible explanations are related to the small size or our surveys or the presence of diagnostic biases of other registries that could include less severe patients. The findings of the ARGEN-IAM-ST registry suggest that, despite the high rate of reperfusion strategies used, the door-to-needle time and the door-to-balloon time are much longer than expected, particularly in patients transferred, which could limit the benefits of reperfusion therapy and result in terms of greater mortality.

This registry is the first step to recognize that, in our country, STEMI patients transferred are not treated in due time and form. Evidently, we need

more active work in informing the population about the need of early consultation and in educating and providing the necessary tools for the early diagnosis and treatment in the place of the first medical contact before the eventual transfer to higher complexity centers.

A better quality of care of patients with cardiovascular disease can be achieved in different ways, optimizing the adherence to the standards of diagnosis and treatment. One of them has already been documented at the international level, (21-24) and includes the self-knowledge of the level of performance of the institutions and of the communication of coordinated measures, a single phone number for myocardial infarction, development of guideline-based protocols, transfer and care networks, telemedicine support system for diagnosis, and global or regional systems of care to optimize timeliness of reperfusion therapy.

The use of network systems will also allow the implementation of initiatives to increase the quality of care and generate epidemiological research projects to improve patients' care and outcomes. In conclusion, recognizing the problems and adopting measures to improve the quality of care and reduce morbidity and mortality.

Study limitations

Although this is the most important registry published in our country so far, the representation may be low in some regions as not all the centers registered in the National Ministry of Health have participated in the survey. Moreover, despite an online database was used, allowing for better follow-up of data loading, the quality of data could not be adequately monitored due to the lack of resources. The number of patients is low to determine differences in mortality or complications in the patients transferred.

We lack information about the exact time delay in the center of the first medical contact and if patient transfer was made using an organized network system. We assume that the time from symptom onset to the first medical contact in an institution without reperfusion capabilities is similar (150 minutes) to the time from symptom onset to medical contact in a center with reperfusion capabilities.

Despite these limitations, the results obtained provide very clear information about the need of establishing strategies to shorten the time delays due to patient transfer and improve treatment of STEMI patients in our country in centers without primary PCI capabilities.

CONCLUSIONS

These data outline the map of AMI reality in Argentina, as 37% of patients have their first medical contact in centers without primary PCI capabilities, and despite the delays in patient transfer, only 16% of the patients receive thrombolytic therapy before being transferred.

Patients transferred are 35% less likely to receive reperfusion therapy and of lower quality.

Time delays to primary PCI in patients transferred exceed 2 hours in the center of the first medical contact and/or waiting to be transferred; in addition, 3 hours could be saved if a pharmacoinvasive strategy were used. The detection of barriers, the use of TNK and the implementation of networks could improve survival of AMI.

The implementation of medical education and adjuvant health care policy programs, considering regional characteristics and the cost/benefit analysis in the setting of reperfusion strategies, could shorten the time delays to reperfusion, either for thrombolysis or primary PCI.

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Conflicts of interest

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

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