ORIGINAL ARTICLE

Impact of an Evaluation System of Times to Reperfusion in ST-segment Elevation Acute Myocardial Infarction

Impacto de un sistema de evaluación de tiempos a la reperfusión en infarto agudo de miocardio con elevación del ST

ALFONSINA CANDIELLO[1,2], FERNANDO COHEN[3], LEANDRO LASAVE[4], LORENA VILLAGRA[5,6], GUILLERMO MULINARIS[7], CESAR RODRIGO ZONI[8], ALEJANDRO GARCÍA ESCUDERO[9], RUBÉN KEVORKIAN[10], IGNACIO M. CIGALINI[1,11], PEDRO ZANGRONIZ[12]. REPRESENTING THE PARTICIPATING CENTERS OF THE STENT-SAVE A LIFE! ARGENTINA INITIATIVE

ABSTRACT

Background: Treatment of patients with ST-elevation myocardial infarction (STEMI) is time-dependent; therefore centers with primary percutaneous coronary intervention (pPCI) capability should be organized to achieve rapid reperfusion.
Objectives: The aim of this study was to assess the impact of a systematic evaluation of reperfusion times with periodic feedback of results in reducing delays to treatment.
Methods: This was an observational, prospective study conducted in 46 centers with 24/7 pPCI capability participating in the Stent-Save a Life! Argentina Initiative. Patients with STEMI who underwent pPCI within 12 hours from the onset of symptoms were included from March 2016 to February 2019. The population was divided into three consecutive stages lasting one year each since the inclusion of each center in the Stent-Save a Life! Initiative.
Results: A total of 3,492 patients were included (1st year: 1,482, 2nd year: 1,166, 3rd year: 844). There was a significant reduction in door-to-balloon (DTB) time (68, 60 and 50 min; p <0.0001), regardless of the type of first medical contact (FMC), and of the time from FMC to reperfusion (115, 112 and 98 min; p <0.0001), without differences in time from the onset of symptoms to FMC or total ischemic time (TIT). In addition, patients with FMC in centers without PCI capability who were referred for pPCI also evidenced a significant reduction of TIT (274, 260 and 235 min; p <0.001).
Conclusion: The implementation of a DTB program in centers with pPCI capability resulted in a significant reduction of treatment times.

Key words: Acute myocardial infarction – Reperfusion – Angioplasty - Time-to-treatment.

RESUMEN

Introducción: El tratamiento del infarto con supradesnivel del ST (IAMCEST) es tiempo-dependiente por lo que los centros con angioplastia primaria (ATCp) deben estar organizados para asegurar una rápida reperfusión.
Objetivos: Evaluar el impacto de un sistema de evaluación sistemática de los tiempos de reperfusión y feedback de resultados en la reducción de las demoras.
Material y métodos: Estudio observacional, prospectivo realizado en 46 centros con ATCp 24/7 de la Iniciativa Stent-Save a Life! Argentina. Se incluyeron pacientes con IAMCEST sometidos a ATCp < 12 hs del inicio de los síntomas desde marzo/2016 a febrero/2019. La población se dividió en tres etapas consecutivas de 1 año cada una desde la inclusión de cada centro.
Resultados: Se incluyeron 3492 pacientes consecutivos (1 año: 1482, 2 año: 1166 y 3 año: 844). Se observó una reducción significativa del tiempo puerta-balón (TPB) (68, 60 y 50 min; p<0,0001), independientemente de cual fuera el PCM, y del tiempo desde el primer contacto médico (PCM) al balón (115, 112 y 98 min; p<0,0001), sin diferencias en el tiempo desde el inicio de los síntomas al PCM ni en el tiempo total de isquemia (TTI). Asimismo, aquellos pacientes que tuvieron su PCM en centros sin hemodinamia y fueron derivados para realización de ATCp se observó además una disminución del TTI (274, 260 y 235; p<0.001).
Conclusiones: La implementación de un TPB en centros con ATCp permitió reducir los tiempos al tratamiento.

Palabras clave: Infarto agudo del miocardio - Reperfusión – Angioplastia - Tiempo de tratamiento.

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Address for reprints: Alfonsina Candiello – Av. Libertador 6302, CABA - CP: 1428 -E -mail: acandiello@icba.com.ar

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[1] Instituto Cardiovascular de Buenos Aires
[2] Director of the Stent-Save a Life! Argentina Initiative
[3] Hospital Italiano de Buenos Aires
[4] Instituto Cardiovascular de Rosario
[5] Sanatorio Pasteur, Catamarca
[6] Sanatorio Junín, Catamarca
[7] Hospital San Juan de Dios, La Plata.
[8] Instituto de Cardiología de Corrientes Juana F. Cabral, Corrientes
[9] Hospital General de Agudos Dr. Cosme Argerich
[10] Hospital Donación Francisco Santojanni
[11] Coordinator of the Stent-Save a Life! Argentina Initiative
[12] Hospital Provincial del Centenario

INTRODUCTION

Treatment of ST-segment myocardial infarction (STEMI) is time dependent, so delays in treatment implementation are essential for short and long-term prognosis of these patients. (1) Clinical guidelines recommend primary percutaneous coronary intervention (pPCI) within 90 minutes of first medical contact (FMC) in patients admitted to centers with PCI capability, arriving either by their own means or by ambulance after calling the medical emergency service (MES). In case patients spontaneously consult centers without cardiac cath lab and are transferred for pPCI, the time from FMC to balloon should not exceed 120 minutes (2, 3)

The door-to-balloon (DTB) time, defined as the time interval since the patient arrives to the center until the artery is reopened with PCI, is considered a measure of the quality of care for these centers and, according to guideline recommendations, this time should be as short as possible, with a maximum limit of 90 minutes. (4)

The Stent-Save a Life! (SSL) Initiative has the goal of reducing the morbidity and mortality of STEMI patients, ensuring their timely access to a reperfusion treatment of quality based on clinical guidelines.

In order to reduce the gap between recommendations and daily practice, centers with pPCI capability should be organized to guarantee a rapid diagnosis and reestablishment of flow in the culprit artery.

This poses a challenge for institutions as it requires the multidisciplinary and coordinated work of all the involved participants: administrative admission staff and emergency department, coronary or intensive care unit and cath lab physicians and nurses.

The systematic registry of times to reperfusion treatment of centers with pPCI capability and their continuous analysis represents the first step to evaluate their functioning and thus detect and correct the barriers preventing the timely treatment of these patients.

The aim of this work was to assess the impact of an evaluation and feedback system of times to reperfusion treatment in the reduction of delays in centers with pPCI capability participating in the SSL Argentina Initiative.

METHODS

This was an observational, prospective study performed in 46 centers with 24/7 pPCI capability in 11 provinces of Argentina and the Anonymous City of Buenos Aires , participating in the SSL Initiative. Centers, their coordinators and the participation requirements are detailed in the Appendix.

All STEMI patients within 12 hours of symptom onset undergoing pPCI were included in the analysis. The responsible staff of each center recorded patient data in a common database, including an anonymized photograph of the diagnostic ECG and the coronary angiography with guidewire insertion reporting the times in which they were obtained. The Appendix details the recorded variables.

Each center receives a monthly global report comparing in a blind fashion its DTB time with that of the other centers, together with an individual report describing the times to treatment according to FMC with suggestions to improve them.

The population was divided into three consecutive stages (S), lasting one year each from the inclusion of each center to the SSL Initiative: first year (S1, n=1,482), second year (S2, n=1,166) and third year (S3, n=844).

The following times were analyzed:

- Patient time (PT): from pain onset to FMC
- FMC-balloon time
- Pre-hospital time (PHT): from FMC to arrival at the center with pPCI capability (valid for patients arriving by ambulance to the center with pPCI)
- DTB time
- Total ischemic time (TIT): from pain onset to reperfusion of the culprit artery.

The proportion of patients with DTB time <60 and 90 min for the total population and the proportion of patients with FMC-balloon time <90 and 120 min (for those arriving by ambulance from their home and referred from other centers, respectively) was calculated.

Statistical analysis

Categorical variables were expressed as frequencies and/or proportions and were evaluated with the chi-square test or Fischer's exact test, as appropriate. Quantitative variables were subjected to normality tests including the Kolmogorov-Smirnoff test or the Shapiro-Wilk test, as appropriate, and histogram parameter measurements: asymmetry, kurtosis and QQ plots. Variables with normality criteria were expressed as mean±SD and non-normal variables as median and interquartile range.

In the analysis of the global population, the reperfusion times of multiple independent groups in each intervention stage were compared analyzing data distribution en each group with normality QQ plots and the homogeneity of variance with the Levene test. As the latter showed violation of the variance homogeneity assumption, the Kruskal-Wallis test was applied.

In addition a segmented analysis was performed to compare the reperfusion times in each stage among multiple independent groups, according to the type of FMC.

SPSS 2.2 (SPSS, IBM Corporation, Armonk, New York) software package was used for the statistical analysis.

Ethical considerations

All patients signed the informed consent of each participating institution.

RESULTS

A total of 3,492 patients with STEMI within 12 hours of symptom onset who were transferred or directly admitted to centers with pPCI capability were prospectively included from March 2016 to February 2019.

Mean age was 60.8±11 years, and 81% of patients were men. The remaining baseline characteristics are detailed in Table 1.

Analysis of reperfusion times in the global population

Throughout the participation time, the overall population evidenced a statistically significant reduction in

DTB time and in FMC-balloon time, without differences in TIT (Table 2).

This reduction in DTB time resulted in a significant increase of the proportion of patients with DTB time <90 min (S1: 70%, S2: 76% and S3: 83%; p<0.001) and even <60 min (S1: 43%, S2: 51%, and S3: 62%; p<0.001).

The PT time, as well as the time to FMC did not change throughout the stages in the global population.

Analysis of times according to first medical contact

In the global population, DTB time according to FMC was significantly lower in the group of patients arriving by ambulance either from centers without PCI capability or from home compared with patients who consulted spontaneously [38 min (24-62) vs. 50 min (34-74) vs. 81 min (60-112), respectively; p <0.001].

Table 1. Basline population characteristics

	Global (n= 3,492)
Age (mean ± SD	60,8 (±11.4)
Male gender	2,836 (81.2%)
Cardiovascular risk factors	
Hypertension	2,298 (65.8%)
Dyslipidemia	1,530 (43.8%)
Smoking	1,521 (43.6%)
Diabetes	735 (21.1%)
Obesity	804 (23%)
Cardiovascular history	
Coronary angioplasty	473 (13.6%)
Coronary artery bypass graft surgery	68 (2%)
Acute myocardial infarction	458 (13.1%)
Stroke	109 (3.1%)
Peripheral vascular disease	192 (5.5%)
Atrial fibrillation	88 (2.5%)
Other non-cardiovascular history	
Chronic obstructive pulmonary disease	122 (3.5%)
Chronic renal failure	110 (3.2%)
Killip & Kimball on admission	
- A	2,787 (79.8%)
- B	389 (11.1%)
- C	48 (1.4%)
- D	268 (7.7%)

First medical contact in centers with PCI capability

Among the total population, 46.2% (n=1,613) consulted spontaneously centers with PCI capability. A significant reduction in DTB time was observed throughout time, without changes in TIT (Figure 1).

Simultaneously, the proportion of patients with DTB time <90 min (S1: 53%, S2: 63% and S3: 67%; p<0.001) and <60 min (S1: 22%, S2: 28% and S3: 30%; p=0.005) increased significantly.

First medical contact in medical emergency service

In 18.9% of cases (n=661) patients called the MES to request medical assistance. A significant reduction in FMC-balloon time was observed throughout time [S1: 123 min (93-158), S2: 121 min (94-163), and S3: 107 min (85-148); p=0.046]. This reduction was at the expense of a decrease in DTB time, without modifications in PHT, or in TIT (Figure 2).

This resulted in a significant increase in the proportion of patients with DTB time < 90 min (S1: 86%, S2: 81%, and S3: 92%; p<0.014) and <60 min (S1: 57%, S2: 59% and S3: 79%; p <0.001).

There were no changes in the proportion of center preactivation throughout time (S1:35%, S2: 35% and S3: 38%; p=0.70).

The proportion of patients with FMC-balloon time <90 min increased throughout time, but was not statistically significant (S1: 22%, S2: 22% and S3: 31%; p=0.056).

First medical contact in centers without pPCI capability

Patients transferred to the center with PCI capability from centers without cardiac cath lab (39%, n=1,218) presented a significant reduction of the FMC-balloon time throughout the study stages, at the expense of a significant reduction both in PHT as in DTB time (Figure 3).

The proportion of patients with DTB time <60 min (S1:63%, S2:75% and S3: 90%; p<0.001) and <90

Table 2. Time in minutes to treatment in the global population and according to participation stages. Data expressed as median and interquartile range

	Global (n=3,494)	Stage 1 (n=1,482)	Stage 12 (n=1,166)	Stage 3 (n=844)	P
PT	75 (35-160)	70 (35-150)	75 (30-158)	80 (40-170) 0	.129
DTB	61 (38-90)	68 (40-170)	60 (40-89)	50 (30-79)	<0.0001
FMC-Balloon	110 (75-166)	115 (80-117)	112 (73-165)	98 (71-150)	<0.0001
TIT	218 (147-326)	220 (150-335)	215 (147-320)	213 (140-315) 0	.616

PT: Patient time, DTB: Door-to-balloon time, FMC: First medical contact, TIT: Total ischemic time.

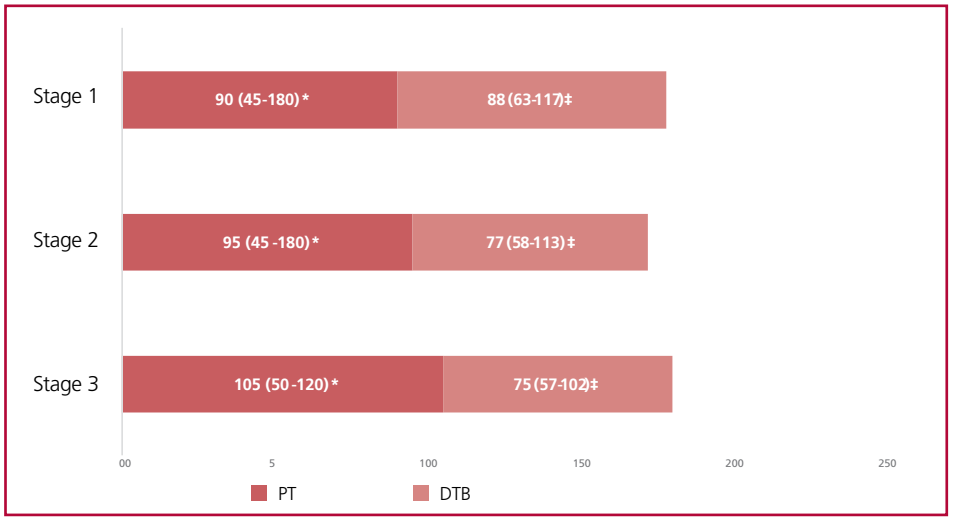


Fig. 1. First medical contact in centers with PCI capability. PT: Patient time, DTB: Door-to-balloon time

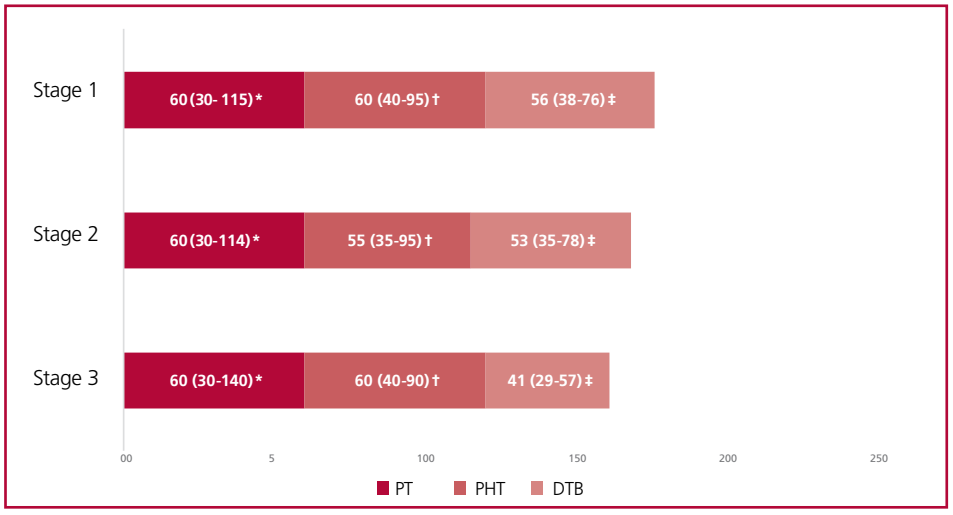


Fig. 2. First medical contact in medical emergency service. PT: Patient time, PHT: Pre-hospital time, DTB: Door-to-balloon time.

min (S1: 85%, S2: 91% and S3: 96%; p<0.001) also increased significantly.

Similarly, the proportion of patients with FMC-balloon time <120 min increased significantly (S1: 22%, S2: 26% and S3: 42%; p<0.001), reducing TIT in this group of patients [S1: 274 (193-397), S2: 260 (182-379) and S3: 235 (160-340); p<0.001].

Moreover, the proportion of center preactivation increased throughout time (S1: 62%, S2: 64% and S3: 83%; p <0.001).

Effect of center preactivation

In the group of patients arriving by ambulance to centers with pPCI capability (n=1,879) either from the street or from another referral center, the receiving center was notified of the patient's arrival in 57% of cases. This action significantly reduced the DTB time from 62 min (48-85) to 30 min (21-24); p <0.001.

DISCUSSION

The prognostic importance of the delay to reperfusion treatment in STEMI patients has been extensively demonstrated for more than a decade, evidencing a direct relationship of both DTB time and TIT with mortality. (5, 6)

Therefore, treatment of these patients should be considered as a care process, from symptom onset to reperfusion of the culprit artery, where survival depends on the quality of the whole process.

The recording and subsequent measurement of all the times to reperfusion treatment represents the first step for each center with PCI capability to know its reality.

The present study demonstrates that the implementation of a system to evaluate the times to reperfusion treatment, together with feedback of results to the participating centers, significantly improved the delays to treatment.

There is abundant evidence showing that the application of continuous evaluation systems of times to reperfusion treatment together with the generation of feedback mechanisms of results to all participat-

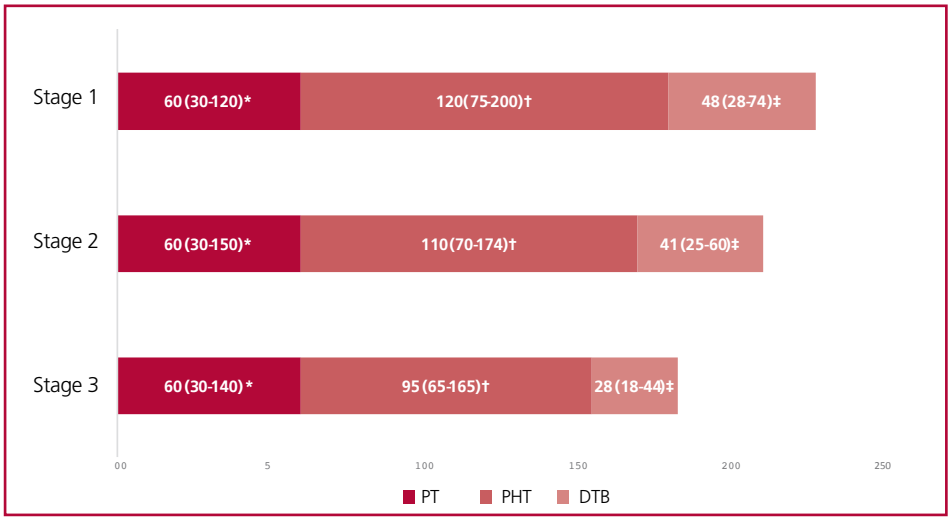


Fig. 3. First medical contact in centers without PCI capability. PT: Patient time, PHT: Pre-hospital time, DTB: Door-to-balloon time.

ing centers improves the quality of care, as it allows the implementation of strategies to shorten times to treatment, thus ensuring that patients are treated according to international standards. (7-10)

Already in 2005, Bradley et al. demonstrated that an efficient logistics together with real time feedback to the participating actors in the treatment of STEMI patients was associated with reduction of DTB time. (8)

Throughout the 3 years of work, a significant reduction was observed in DTB and FMC-balloon times, regardless of the type of FMC.

Every month the participating centers received together with the analysis of delays to treatment, suggestions with strategies to improve them.

The activation of the cath lab with a single call, the direct communication between on-call and interventional cardiologists (without need for inter-consultations) and the availability of the interventional cardiologist within 30 minutes of contact are some of the most effective strategies that allow reducing DTB time, and were recommended to the centers. In addition, periodic meetings of all the team were suggested to analyze the reports received as they allow the generation of ideas for improvement adapted to the reality of each center as well as the construction of a reperfusion culture. (8, 11)

The way in which patients arrive at centers with PCI is one of the factors most affecting DTB time. Arrival by ambulance reduces DTB time, as it avoids the waiting time in the emergency room, which in some centers without organization or triage may be excessive. (12, 13) If in addition the MES notifies the patient's arrival (preactivation), the DTB time is even further reduced as it allows the interventional cardiologist, in case he is not in the center, to arrive before or with the patient, the preparation of the cath lab and once the patient is in the center, his immediate transfer to the cath lab without going through the emergency room. (8, 14)

This explains the difference observed between the DTB time of patients consulting spontaneously the emergency department of centers with PCI capability and those who arrived by ambulance with and without preactivation.

Even though the FMC-balloon time was reduced in the global population, the impact of this reduction on TIT changed depending on the type of FMC.

For patients consulting spontaneously the emergency department of centers with PCI capability, the system time (ST), FMC-balloon time and DTB time are synonyms and in all cases should be <90 min, or even <60 min. (15)

In this group of patients, although the DTB time was significantly reduced, from 88 min in the first year to 75 min in the third year, 67% of patients achieved a DTB <90 min and only 30% a DTB time < 60 in the last stage. This result represents an opportunity for improvement, where the efforts should be focused in performing an adequate triage that ensures an ECG within 10 minutes of arrival to the center and a rapid activation and response of the cath lab.

For patients arriving by ambulance, the DTB time represents only a part of the ST or FMC-balloon time, as it also consists of PHT, so the generation of strategies to reduce both components are equally important.

Clinical guidelines recommend the regionalization of STEMI patients' treatment, where the diagnosis is performed at the pre-hospital stage and networks are established connecting hospitals with different levels of complexity by an efficient MES. This organization allows increasing the proportion of patients undergoing reperfusion, reducing the delays to treatment and hence morbidity and mortality. (16, 17)

In Argentina, most MES do not perform pre-hospital diagnosis; therefore, it is logical that in patients who called MES, the reduction in DTB time was not accompanied by a reduction in PHT. Consequently, the ST or FMC-balloon time and the proportion of patients with FMC-balloon time <90 min were not

modified.

To achieve the improvement of this time, MES should work coordinately with centers with PCI capability to perform a pre-hospital diagnosis and preactivate the center. (14)

This is a new opportunity for improvement that should be further analyzed.

There are few formal infarction networks, mainly due to the Argentine healthcare system.

Despite this drawback, in patients referred from centers without PCI capability, the reduction in DTB time was accompanied by a reduction in PHT and consequently of TIT.

The improvement in DTB time could be explained both by the better organization of centers as by the increase in the proportion of preactivation by referral centers.

In this study, 21.7% of centers are part of some type of formal or informal network, which implies a frequent contact with centers without PCI. Once the centers with PCI capability are organized, the integration and the coordinated work with MES and referral centers is easier, and allows the development of local improvement strategies.

Finally, this work focused on the organization of centers; thus, no actions directed to patients were performed in this stage of the program, resulting in a constant delay time from symptom onset to consultation during the three periods. We believe it is necessary to have an organized healthcare system that responds efficiently to the demands before developing campaigns of conscientization aimed at the population with the purpose of educating about symptoms suggestive of infarction and the importance of a timely consultation through MES. Therefore, there is still a great deal of work to do.

Limitations

The present work only sought to evaluate the impact of an evaluation process with feedback in centers with pPCI capability on the delays to reperfusion treatment of patients with STEMI. Therefore, its repercussion in in-hospital events or follow-up was not assessed.

CONCLUSION

The evaluation of times to reperfusion treatment and the monthly feedback of results allowed the in-door organization of centers, achieving a significant reduction in the door-to-balloon time independently from the site of first medical contact. Certainly, this represents the first step to provide a fast response at the moment of the network integration of ambulance systems and referral centers.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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APPENDIX

Centers participating in the Stent-Save a Life! Argentina Initiative and their coordinators ordered by province

- **Buenos Aires:** Hospital Italiano de La Plata (Dr. Andrés Pascua, Dr. Agustín Hauqui), Hospital Español de La Plata (Dr. Diego Grinfeld, Dr. Sebastián Amicone), Instituto Médico Platense (Dr. Nicolás Nitti, Dr. Diego Rios), Sanatorio Argentino (Dr. Guillermo Cugat, Dr. Agustín Dettbarn), Hospital San Juan de Dios (Dr. Guillermo Mulinaris), Instituto de Diagnóstico (Dra. Elisabeth Marsiglio), Hospital San Martín (Dr. Nicolás Nitti, Dr. Dario Cavalie), Sanatorio Las Lomas (Dr. Pablo Stutzbach, Dr. Luciano Destefano), Sanatorio Anchorena San Martín (Dr. Gustavo Pedernera, Dr. Leandro Rodriguez)
- **Catamarca:** Sanatorio Pasteur (Dra. Lorena Villagra), Sanatorio Junín (Dra. Lorena Villagra)
- **Chaco:** Instituto Cordis (Dr. Eduardo Ferro Queirel)
- **Ciudad Autónoma de Buenos Aires:** Instituto Cardiovascular de Buenos Aires (Dr. Fernando Cura), Sanatorio Anchorena (Dr. Pablo Spaletra, Dr. Nicolás Lalor), Hospital Italiano de Buenos Aires (Dr. Daniel Berrocal, Dr. Fernando Cohen), Fundación Favaloro (Dr. Ernesto Duronto, Dr. Carlos Fava), Hospital Británico (Dr. Guillermo Migliaro), Hospital Alemán (Dr. Guillermo Migliaro), Hospital General de Agudos Dr. Juan A. Fernández (Dr. Pablo Perez Baliño, Dra. Verónica González), Hospital General de Agudos Dr. Cosme Argerich (Dr. Alejandro Escudero, Dra. Analia Alonso), Hospital General de Agudos Bernardino Rivadavia (Dr. Alfredo Hirschson Prado, Dr. Rodrigo Alderete), Sanatorio Güemes (Dr. Marcelo Bettinotti, Dr. Rodrigo Villarreal), Sanatorio de la Trinidad Palermo (Dr. Alejandro Palacios, Dra. María Daniela Coria), Clínica San Camilo (Dr. Aldo Rodríguez Saavedra, Dr. Sebastián Peralta), Hospital General de Agudos Francisco Santojanni (Dr. Rubén Kevorkian, Dra. Natacha Ruiz)
- **Córdoba:** Sanatorio Allende Cerro (Dr. Lucas Maldonado, Dr. Guillermo Pacheco)
- **Corrientes:** Instituto de Cardiología de Corrientes "Juana F. Cabral" (Dr. César Rodrigo Zoni)
- **Entre Ríos:** Sanatorio Garat (Dr. Federico Graziano), Hospital San Martín (Dr. Martín Hermida), Sanatorio San Lucas (Dr. Emiliano Luchessi)
- **Mendoza:** Hospital Central de Mendoza (Dr. Leonardo Ripa)
- **Santa Cruz:** Hospital Regional Río Gallegos (Dra. Corina Biagioni, Dr. Alejandro Cherro)
- **Santa Fe:** Hospital Provincial del Centenario (Dr. Pedro Zangroniz, Dr. Lucas Arias), Instituto Cardiovascular de Rosario (Dr. Aníbal Damonte, Dr. Leandro Lasave), Sanatorio Esperanza (Dr. Jorge Allín), Sanatorio Británico (Dr. Tomás Cuneo, Dr. Daniel Zanuttini), Sanatorio Nosti (Dr. Adrian Ingaramo, Dr. Eduardo Herrera), Sanatorio Plaza (Dr. Tomás Cuneo, Dr. Marcelo Menéndez), Hospital Provincial Dr. Jose M. Cullen (Dr. Rubén Retamar, Dr. Agustín Roude), Sanatorio Privado San Gerónimo (Dr. Oscar Birollo), Hospital Privado de Rosario (Dra. María Belén Cigalini, Dr, Claudio Cigalini), Hospital Español (Dr. Daniel Paolantonio), Clínica de Nefrología, Urología y Enfermedades Cardiovasculares (Dr. Oscar Birollo)
- **Santiago del Estero:** Instituto de Cardiología (Dr. Santiago Coroleu), Clínica Yunes (Dr. Jorge Trejo, Dr. Emanuel Sarnago)
- **Tucumán:** Instituto de Cardiologia (Dr. Arturo Fernández Murga, Dr. Jose Cruzado)

Center requirements to participate in the Door-to-Balloon Program

1. Centers with 24/7pPCI capability.
2. Commitment to work to fulfill the objectives of the Stent Save a Life! Argentina Initiative.
3. Creation of a multidisciplinary working team that includes at least Emergency, Clinical Cardiology (CCU/ICU) and Interventional Cardiology Medical staff.
4. Development of a systematic care of patients with STEMI following clinical guidelines.
5. Mandatory recording of the times to reperfusion treatment on a common database.
6. Allow monitoring of the data entered.