ORIGINAL ARTICLE

Cardiogenic Shock in the Setting of Acute Coronary Syndromes in Argentina: Results from the ARGEN SHOCK 2 Registry

Shock cardiogénico en el contexto de los síndromes coronarios agudos en Argentina: resultados del Registro ARGEN SHOCK 2

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ABSTRACT

Background: Cardiogenic shock (CS) is a life-threatening complication of acute myocardial infarction (AMI) and constitutes one of the leading causes of death.
Objective: The aim of this study was to investigate the clinical characteristics, treatment strategies, hospital outcome and 30-day mortality of CS in Argentina.
Methods: We conducted a prospective, and multicenter registry of patients with acute coronary syndromes (ACS) with and without ST-segment elevation complicated with CS that were hospitalized in 23 centers in Argentina for 14 months (between August 1, 2021, and September 30, 2022).
Results: The cohort was made up of 114 patients; median age was 64 years (58-73) and 72% were women; 76.3% corresponded to ST-segment elevation ACS, 12.3% to non-ST-segment elevation ACS, 7% had right ventricular infarction and 4.4% had mechanical complications. In 66.6% of cases CS was present on admission. Revascularization: 91.1%, use of inotropic agents: 98.2%, mechanical ventilation (MV): 59.6%, Swan-Ganz catheter: 33.3%, intra-aortic balloon pump: 30.1%. Overall in-hospital mortality was 60.5%, with no differences between ACS with or without ST-segment elevation, and was 62.6% at 30 days.
Conclusion: Morbidity and mortality of CS are high despite the high rate of reperfusion therapy used.

Key words: Cardiogenic Shock- Acute Coronary Syndromes- Registry

RESUMEN

El shock cardiogénico (SC) es una complicación grave del infarto agudo de miocardio (IAM) y constituye una de sus principales causas de muerte.
Objetivos: Conocer las características clínicas, estrategias de tratamiento, evolución intrahospitalaria y mortalidad a 30 días del SC en Argentina.
Material y métodos: Se trata de un registro prospectivo, multicéntrico, de pacientes internados con SC en el contexto de los síndromes coronarios agudos (SCA) con y sin elevación del segmento ST durante 14 meses (1 de agosto 2021 al 30 de septiembre 2022) en 23 centros de Argentina.
Resultados: Se incluyeron 114 pacientes, edad 64 (58-73) años, 72% hombres. El 76,3% de los casos corresponden a SCA con elevación del segmento ST, 12,3% a SCA sin elevación del segmento ST, el 7% a infarto de ventrículo derecho y el 4,4% a complicaciones mecánicas. El SC estuvo presente desde el ingreso en el 66,6% de los casos. Revascularización: 91,1%, uso de inotrópicos: 98,2%, asistencia respiratoria mecánica (ARM): 59,6%, SwanGanz: 33,3%, balón de contrapulsación intraaórtico: 30,1%. La mortalidad intrahospitalaria global fue 60,5%, sin diferencias entre los SCA con o sin elevación del segmento ST y a 30 días del 62,6%.
Conclusiones: La morbimortalidad del SC es muy elevada a pesar de la alta tasa de reperfusión empleada.

Palabras clave: Shock Cardiogénico- Síndromes Coronarios Agudos- Registro

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INTRODUCTION

Cardiogenic shock (CS) is an infrequent complication but remains the leading cause of death in patients hospitalized with acute myocardial infarction (AMI), (1) ranging from 40% to 55% depending on the populations analyzed. (2,3) In Argentina, the incidence of CS is 10%, and according to recent data from the ARGEN IAM ST Registry, CS mortality rate in the setting of ST-segment elevation MI is 57%. (4) Some recommendations of the guidelines for the treatment of CS in the setting of acute coronary syndromes have changed in recent years. (5) Moreover, as it has been more than 5 years since the first Argentine Registry of Cardiogenic Shock was published, (6) the Research Area of the Argentine Society of Cardiology (SAC) decided to carry out this study, the second National Registry of Cardiogenic Shock (ARGEN SHOCK), which was specially designed to determine the clinical characteristics, reperfusion strategies, treatments, in-hospital outcome and 30-day mortality of patients admitted to intensive care units with acute coronary syndromes (ACS) and CS on admission or who develop this complication during hospitalization.

METHODS

ARGEN SHOCK is a prospective, observational, and multicenter registry of consecutive patients with ACS complicated with CS conducted between August 1,2021, and September 30, 2022.

Cardiogenic shock was defined as systolic blood pressure (SBP) ≤ 90 mm Hg for at least 30 min or requirements of vasopressors or inotropic drugs to maintain a SBP ≥ 90 mm Hg, associated with clinical signs of hypoperfusion or pulmonary congestion.

Patients eligible for inclusion were > 18 years, admitted to coronary care units or multipurpose critical care units with ST-elevation ACS (STEACS) or non-ST-elevation ACS (non-STEACS) and with CS on admission or during hospitalization. Patients who developed mechanical complications were excluded for the analysis of mortality (n = 5).

Data were collected by the responsible investigators of the different centers in an ad hoc electronic worksheet designed on the RedCAP platform. In-hospital and 30-day events were analyzed.

The protocol was organized and conducted by the Research Area and the Council on Cardiovascular Emergency Care of the SAC. All the patients signed an informed consent form to be included. Follow-up at 30 days was reported by the principal investigators of the different participating centers.

Statistical analysis

The information obtained through RedCAP was exported to an Excel database and was analyzed using Epi-info 7 software package. Each variable was included in a frequency table. Continuous variables with normal distribution were presented as mean ± standard deviation, and those with non-normal distribution as median and interquartile range (IQR 25-75), and were compared using the Student's t test or the Wilcoxon rank sum test, as applicable. Discrete variables were expressed as percentages and were compared using the chi-square test with Yates correction or the Fisher's exact test, as applicable.

Contingency table analysis was used to compare the association or independence of the variables. The presence of associations or independent predictions between the different variables involved and mortality was analyzed using linear regression or multiple logistical regression analysis. Those variables with a p value <0.10 on univariate analysis were included in the different regression models. The value corresponding to each covariate was expressed as adjusted odds ratio (OR) with its corresponding 95% confidence interval. A two-tailed p value < 0.05 was considered statistically significant.

RESULTS

Fifty-four intensive care units from all over the country registered to participate in the registry: 17 from the city of Buenos Aires (CABA), 16 from the province of Buenos Aires (PBA) and the rest from other provinces of the country; 23 (10 in CABA, 4 in PBA and 9 in the rest of the country) included at least one patient. Of the participating centers, 74.5% were coronary care units, 18.2% were multipurpose units and 7.3% were intensive care units; 65.5 % of the centers had residents in cardiology. Doppler echocardiography was available in 98% of the centers and catheterization laboratory in 89%; 81.8% had cardiovascular surgery capabilities, 67.3% counted with intra-aortic balloon pump, 20% with extracorporeal membrane oxygenation (ECMO), 3.6% with Impella left ventricular assist device, and 23.6% with cardiac transplantation capabilities.

The registry included 114 patients with CS, 87 (76.3%) were STEACS and 14 (12.3%) non-STEACS, 5 had CS associated with mechanical complications and 8 had CS secondary to right ventricular (RV) infarction. Median age of the population was 64 years (58-73), 71.9% were men, 72.8% had hypertension, 35.1% had diabetes, 37.7% had dyslipidemia, and 35.1% were smokers. Almost all the patients (91.1%) underwent revascularization.

In 66.6% (74/114) of cases CS was present on admission. In the rest of the patients, 14,9% were admitted with Killip-Kimball class A, 13.2% with class B and 5.3% with class C, and 68.4% developed CS with 24 h.

Inotropic or vasoactive drugs were used in 98.2% of the patients (norepinephrine 86.6%, dopamine 20.5%, dobutamine 62.5% and levosimendan 11.6%); 59.6% required mechanical ventilation (MV). A Swan-Ganz catheter (SG) was inserted in 33.3% of the patients: 55.3% within the first day, 36.8% between 24 and 48 h and 7.9% after 48 h, and remained placed for a median time of 3 (2-4) days. The main indication for SG catheter was "treatment optimization" in 79%, for "diagnostic uncertainty" in 10.5% and as standard treatment of shock in the remaining 10.5%. Mortality rate in patients with a SG catheter inserted was 57.9%. There were no differences in the clinical characteristics and outcome of patients with or without insertion of a SG catheter.

Intra-aortic balloon pump (IABP) was used in

30.1% of cases and ECMO in 4 patients (who also required IABP); IABP remained placed for a median time of 2 (1-4) days. The complications associated with IABP occurred in 29.4% of the patients and included fever in 4 patients, acute lower limb ischemia in 3, and thrombocytopenia in 3. There were no cases of sepsis. In patients with IABP support, mortality was 67.6% (23/34 patients).

Patients receiving IABP were younger [60.5 years (56-66) vs. 65 (60-76.5), p < 0.01]; most of them were men (85.3% vs. 67.1%, p = 0.02) and had more requirement of MV (73.5% vs. 53.1%, p = 0.02). There were no significant differences in mortality according to the use of IABP: 67.6% vs 57%, p = 0.14.

The main events during hospitalization are presented in Table 1.

The incidence of bleeding events was 8.7%. A total of 12.3% of patients required transfusions: < 2 units in 21.4%, between 2 and 4 in 42.9% and > 4 in 35.7%.

In 92 patients without mechanical complications undergoing coronary angiography, significant one-vessel disease was observed in 19.6% of the cases, two-vessel disease in 33.7% and three-vessel-disease in 46.7%. In patients with more than one-vessel disease, 69.9% underwent culprit-only percutaneous coronary intervention (PCI), and 30.1% underwent multivessel intervention. The procedure was successful in 84% of the cases.

Overall, in-hospital mortality was 60.5% (53% within the first 48 h) and was due to persistent shock (62.3%), mechanical complications (11.6%), arrhythmias (11.6%), infections (7.3%) and others (7.2%).

After excluding those patients with mechanical complications, univariate analysis revealed that age, history of AMI, arrhythmias, absence of RV involvement and STEACS were associated with greater mortality (Table 2). On multivariate analysis, a history of AMI remained as an independent predictor (OR 4.58, 95% CI 1.09-19.22; p = 0.037).

Mortality at 30 days was 62.6%.

Patients with STEACS (n = 87) had a median age of 64 (RIC 58-74) years, 71.3% were men, 32.2% had diabetes, 40.2% had dyslipidemia, 34.5% smoked, and 16.1% had a history of previous infarction; 80.9% of STEACS were anterior wall infarctions. Median time from symptoms to admission was 360 (140 - 1080) minutes and 94.2% were managed with a reperfusion strategy: 83.8% received primary PCI and 9.7% received thrombolytic therapy (streptokinase in 81.8%). In 82.2% of the cases undergoing PCI the procedure was successful, with a median (IQR) door-to-balloon-time of 115 (60-180) minutes. In-hospital and 30-day mortality of STEACS was 64.4% and 65.5%, respectively. Mortality rate was 62.2% in patients reperfused and 100% in those without reperfusion (p = 0.051). Coronary angiography showed 2-3 vessel disease in 81.1% of the cases and revascularization of non-culprit stenoses were performed in 28.3% of the patients.

DISCUSSION

Cardiogenic shock is the most life-threatening complication of MI and remains the leading cause of MI-related mortality. Historically, the incidence of CS was 5 to 15%, but has been decreasing worldwide across the years. (7-9). This is not the situation in our environment, where mortality remains between 8% and 10%. (1,4)

As in other contemporary registries, STEACS was the most common cause of cardiogenic shock. (10) Although in our population the prevalence of men was higher than that of women, the proportion of women affected was greater compared with populations with ACS and without shock, as in many registries available. (3,4,7,11,12) The age of our patients with shock is like that of international registries. (4)

In the setting of an ACS, CS may be present since hospital admission or may develop during hospitalization, but most cases occur within the first 24 hours; (3,4) in our registry, 66.6% of patients had CS since admission, similar to other experiences. (3,13)

Adequate reperfusion in AMI decreases overall mortality and the incidence of shock by limiting the size of the myocardium involved; (14,15) likewise, its use in the setting of CS also decreases mortality, as demonstrated in the SHOCK trial.(13) Therefore, all the clinical practice guidelines strongly recommend emergency revascularization in patients with shock, independently of the time since infarction occurred. (16-18) In our study, reperfusion rate was close to 90%, as observed in experiences in more developed countries. The prevalence of severe multivessel disease in the setting of CS ranges from 60% to 78%, (4,19) similar to that found in our study. As in the ReNa Shock registry, (20) culprit-only revascularization was the strategy most used, following current guidelines.

Table 1. In-hospital events and 30-day mortality

Event	n (%)
PIA/ReMI	4 (3.5%)
Arrhythmias	43 (37.7)
AF	15 (13.1)
VT/VF	18 (15.8)
ECV	15 (13.1)
AVB	10 (8.8)
Temporary pacing	9 (7.9)
Fever	24 (21)
Dialysis	9 (7.9)
Intra-aortic balloon pump	34 (30.1)
Heart transplantation	1 (0.88)
In-hospital mortality	69 (60.5)
30-day mortality	71 (62.6)

AF: atrial fibrillation; AVB: atrioventricular block; ECV: electric cardioversion; PIA: postinfarction angina; ReMI: reinfarction; VT/VF: ventricular tachycardia/ventricular fibrillation

Table 2. Univariate analysis for predictors of mortality Population: 109 patients (excluding the 5 patients with mechanical complications)

	Dead n= 64	Alive n= 45	p
Age, years, (median, IQR)	65 (59-76)	62 (56-68)	0.04
Male sex, (%)	71	71	0.46
Diabetes (%)	34	35	0.44
Hypertension (%)	72	73	0.43
Current smoker (%)	30	38	0.19
CKD (%)	4.7	0	0.09
Previous stroke (%)	3	0	0.17
Previous MI (%)	23.5	6.7	0.01
K-K class D on admission (%)	71.9	62.2	0.14
PIA/ReMI (%)	1.5	6.6	0.11
VF/VT (%)	20.3	11.1	0.12
AF (%)	9.4	15.5	0.17
ECV (%)	17.2	6.7	0.06
Failed PCI (%)	18.9	13.5	0.26
Time from symptoms onset at admission, min (median, IQR)	360 (120-1176)	360 (140-1080)	0.93
Anterior infarction (%)	48.4	57.8	0.17
STEACS (%)	87.5	68.9	0.01
RV involvement (%)	3.1	13.3	0.02
Reperfused (%)	90.5	93.3	0.31
Mutivessel disease (2 or greater), (%)	78.2	83.8	0.26

AF: atrial fibrillation; CKD: chronic kidney disease; ECV: electric cardioversion; IQR: interquartile range; K-K: Killip-Kimball; PCI: percutaneous coronary intervention; PIA: post-infarction angina; ReMI: reinfarction; RV: right ventricular; STEACS: ST-segment elevation acute coronary syndrome; VF: ventricular fibrillation; VT: ventricular tachycardia.

The use of IABP, a strategy not systematically recommended by the guidelines, (21-23) was 30.1%, like that of the ReNa SHOCK and other international registries (4,7), and its use did not imply differences in mortality. (24) The indication of other support devices was low, 3.5%, but higher than in the previous registry (2.4%).

Although some studies have reported a decline in mortality associated with CS throughout the years, (25, 26), it is still high, with figures between 40 and 60%. (10,18,19) Our overall in-hospital mortality was 60.5%, similar to that of the ReNa Shock (54%) registry and of the patients with CS in the ARGEN-IAM-ST registry (58%). (27)

The history of AMI was the only independent predictor of in-hospital mortality found in our study.

We found a 30-day mortality rate of 62.6%. Compared with international studies, mortality rate was 40.2% in the IABP-SHOCK II study (24) and 47.6% in the CULPRIT SHOCK study. (28) In our study, 30-day mortality is significantly higher than the one reported by the international literature (10) and even higher than that of patients in the SHOCK trial (51.5%) (13), which was conducted more than two decades ago. The differences found are not easy to interpret, since most of our patients were reperfused within a reasonable time course, comparable to that of other experiences. Unfortunately, this registry does not include the percentage of patients who developed cardiac arrest with successful cardiopulmonary resuscitation, because when the registry started, the new classification of the SCAI (29), which describes the significant adverse prognostic value of cardiac arrest, had not been validated yet. (30) Nevertheless, in a recent study by our group (in patients with ST-segment elevation myocardial infarction) we have found that the prevalence of cardiac arrest in the setting of CS is high (44.8%) and that patients presenting cardiac arrest and CS had a mortality rate of 79.3% compared with 39% in patients without cardiac arrest on admission. (31)

The disparity in the outcome of patients highlights the importance of updated local data since our reality (and probably that of the rest of Latin America) does not seem to be the same as in the United States or Europe. The Argentine Society of Cardiology is currently recruiting patients for the LATIN SHOCK registry (NCT:05246683), which will provide information on the situation in Latin America in this area for the first time.

Perhaps at some future time mortality may de-

crease if cardiogenic shock patients are managed with a much broader multidisciplinary approach, as is currently recommended. (32)

Limitations

The present registry represents the actual treatment of patients with CS in Argentina who were mostly recruited in high complexity centers with residents in cardiology; thus, these results cannot be extrapolated to patients with CS on admission or developed during hospitalization in other type of centers.

CONCLUSIONS

The characteristics of cardiogenic shock in Argentina do not differ much from other populations worldwide; however, mortality in our environment is very high (despite high reperfusion) and has remained stable over the last years.

Conflicts of interest

None declared.
   (See authors' conflict of interests forms on the web).

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Appendix

Center	Province	Responsible investigator
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Clínica Mayo	Córdoba	Eduardo Quinteros
Clínica Modelo Lanús	Buenos Aires	Diego Novielli
Clínica Modelo Quilmes	Buenos Aires	Adrián Hrabar
Clínica Pasteur	Neuquén	Esteban Frontera
Favaloro	CABA	Fabricio Procopio
HIGA Eva Perón	Buenos Aires	González María
Hospital Alberto Balestrini	Buenos Aires	Roger Benjamín Ugarte
Hospital Álvarez	CABA	
Hospital Cullen	Santa Fe	Perello Leonel
Hospital de Alta Complejidad El Cruce	Buenos Aires	Adamowski Mariano Alejandro
Hospital de Clínicas	CABA	Víctor Hugo López
Hospital Descentralizado Doctor Guillermo Rawson	San Juan	María Navarta
Hospital Domingo Funes	Córdoba	Ana Karina Rios
Hospital Dr Alberto Duhau	Buenos Aires	Mónica Couso
Hospital El Carmen	Mendoza	Di Milta José
Hospital Español de Mendoza	Mendoza	Valentina Rodríguez
Hospital Italiano de La Plata	Buenos Aires	Nahuel Monti
Hospital Italiano Regional del Sur	Buenos Aires	Verónica Heredia
Hospital Jaime Ferrer	Santa Fe	Pozzi Ercilio
Hospital Nacional de Clínicas Córdoba	Córdoba	Ana Karina Rios
Hospital polo sanitario	Buenos Aires	Galeano Damián
HOSPITAL PRIVADO DE ROSARIO	Santa Fe	Marcelo Mario Cardona
Hospital Santa Isabel de Hungría	Mendoza	VICTORIA HAEDO
Hospital Universitario Austral	Buenos Aires	José Bonorino
Htal Alemán	CABA	Omar Tupayachi
Htal Argerich	CABA	Julián Colla
Htal Milstein	CABA	Leonardi Mariela
Htal San Isidro	Buenos Aires	Miguel Ulloa
ICBA	CABA	Leonardo Seoane
Instituto CV Cabral	Corrientes	Stella Macin
Sagrado Corazón	CABA	Diego Costa
San Roque	Salta	Marina Singh
Sanatorio Adventista del Plata	Entre Rios	Ramiro Ayala
Sanatorio Allende Cerro	Córdoba	Florencia Melgarejo
Sanatorio Allende Nueva Córdoba	Córdoba	Juan Pablo Ricarte Bratti
Sanatorio Anchorena	CABA	Raffaeli Alesis
Sanatorio Anchorena San Martin	Buenos Aires	Juan Souto
Sanatorio Dr. Julio Méndez	CABA	Benjamín Pérez Carrillo
Sanatorio Finochietto	CABA	Crippa Diego
Sanatorio Güemes	CABA	Joaquín Perea
Sanatorio Itoiz	Buenos Aires	Moglioni Nicolas
Sanatorio Lavalle	Jujuy	Néstor Singh
Sanatorio Pasteur	Catamarca	María Pía Marturano
Sanatorio Santa Fe	Santa Fe	Filippon Brenda
Santa Isabel	CABA	Yanina Castillo Costa
Santojanni	CABA	Gabriela Velasco
Trinidad Ramos Mejía	Buenos Aires	Esteban Romeo
Trinidad San Isidro	Buenos Aires	Miguel Ulloa