ORIGINAL ARTICLE

A Prospective Multi-Center Registry of Patients Hospitalized for Non-ST Segment Elevation Acute Coronary Syndrome in High Complexity Centers. In-hospital and 6-month Outcomes (Buenos Aires I)

Registro multicéntrico prospectivo de pacientes hospitalizados por síndrome coronario agudo sin elevación del segmento ST en centros de alta complejidad. Resultados intrahospitalarios y evolución a 6 meses (Buenos Aires I)

JUAN P. COSTABEL , EZEQUIEL ZAIDEL, MIRZA RIVERO, IVÁN GÓMEZ, GONZALO PÉREZ, CRISTIAN M. GARMENDIA , ERNESTO DURONTO, JOSÉ BONORINO, ROSINA ARBUCCI, IGNACIO VACA. (ON BEHALF OF THE INVESTIGATORS OF THE BUENOS AIRES I REGISTRY).

ABSTRACT

Background: Non-ST elevation acute coronary syndrome (NSTE-ACS) management has evolved over the past years, based on new pharmacological agents and progress in revascularization techniques. The aim of this study was to analyze the current management of NSTE-ACS in high complexity centers of the city of Buenos Aires and the province of Buenos Aires.
Methods: Patients hospitalized in 21 centers with coronary care unit, 24-hour catheterization lab availability and cardiovascular surgery were prospectively enrolled in the study and followed up for 6 months after hospital discharge.
Results: The registry included 1,100 consecutive patients: 61% corresponded to non-ST-segment elevation myocardial infarction and 37.4% were unstable angina. Mean age was 65.4 ± 11.5 years and 77.2% were men; 27.6% had diabetes mellitus and 31.5% previous myocardial infarction. An early invasive management was used in 86.7% of cases with a median time to coronary angiography of 18 hours (IQR 7-27.7). During hospitalization, 5.2% of the patients presented reinfarction, 0.3% stroke and overall mortality was 2.7%. The rate of bleeding events ≥ BARC type 2 was 10.1%. At 6-month follow-up, the rates of reinfarction, ACS and overall mortality were 8.4%, 10.9% and 5.7%, respectively.
Conclusions: The registry demonstrated a predominantly invasive therapeutic approach in patients with NSTE-ACS treated in high complexity centers with low rates of in-hospital complications and during follow-up.

Key words: Acute coronary syndrome without ST segment elevation, myocardial infarction, coronary revascularization.

RESUMEN

Introducción: El manejo de los síndromes coronarios agudos (SCA) sin elevación del segmento ST (SCASEST) ha presentado cambios en los últimos años, basados en nuevos agentes farmacológicos y en el avance de las técnicas de revascularización coronaria. El objetivo de este estudio fue determinar cómo es el manejo de los SCASEST en la actualidad, en centros de alta complejidad de la ciudad de Buenos Aires y la provincia de Buenos Aires.
Métodos: Se registraron en forma prospectiva pacientes hospitalizados en 21 centros con servicio de unidad coronaria, hemodinamia disponible las 24 horas y cirugía cardíaca. Se realizó seguimiento a 6 meses del alta hospitalaria.
Resultados: Se incluyeron 1100 pacientes consecutivos; el 62,6% fue catalogado como infarto sin elevación del ST y, 37,4% como angina inestable. La edad media fue de 65,4 ± 11,5 años, con el 77,2% de sexo masculino. El 27,6% presentaba diabetes mellitus y el 31,5% infarto previo. El manejo inicial fue invasivo en el 86,7%, con una mediana de tiempo a la cinecoronariografía de 18 horas (RIC 7-27,7). En la evolución intrahospitalaria, la incidencia de nuevo infarto fue del 5,2%, el accidente cerebrovascular de 0,3% y la mortalidad total, 2,7%. La tasa de sangrado BARC ≥ 2 fue del 10,1%. En el seguimiento extrahospitalario a los 6 meses del alta hospitalaria, la tasa de infarto fue de 8,4%, SCA 10,9% y la mortalidad total de 5,7%.
Conclusiones: El registro evidenció un abordaje terapéutico predominantemente invasivo de los pacientes con SCASEST en los centros con alta complejidad, con baja prevalencia de complicaciones intrahospitalarias y en la evolución.

Palabras clave: Síndrome coronario agudo - Infarto de miocardio sin elevación del ST - Revascularización miocárdica - Intervención coronaria percutánea - Estudios de seguimiento

Rev Argent Cardiol 2020;88:299-307. http://dx.doi.org/10.7775/rac.v88.i4.18501

Address for reprints: Dr. Juan Pablo Costabel - Av. del Libertador 6302 – (C1428) CABA, Argentina - e-mail: jpcostabel@icba.com.ar – Phone: +54 11 4787-7500

INTRODUCTION

Non-ST elevation acute coronary syndromes (NSTE-ACS) include unstable angina (UA) and non-ST-segment elevation acute myocardial infarctions (NSTEMI). Beyond these two terms, these clinical presentations represent a wide variety of conditions from the point of view of diagnosis, treatment and prognosis, which share common underlying pathophysiological mechanisms. (1)

In the early 21st century, several randomized studies and clinical trials have provided new treatments and interventional strategies for NSTE-ACS. However, there is currently limited information available about how these therapies are incorporated into clinical practice, with scarce information about the magnitude, prognosis, and optimal management of patients with ACS in our population. (2)

In Argentina, the information available on the treatment of ACS comes from registries developed by the Argentine Society of Cardiology (SCAR) in 2011 and the Argentine Council of Cardiology Residents (CONAREC XVII), which collected information from patients treated during 2010. (3, 4) This valuable information, however, was recorded many years ago. Furthermore, it is important to know both in-hospital and out-of-hospital outcomes, since none of the two studies provided information about the follow-up of the patients included.

Therefore, we developed the BUENOS AIRES I registry with the aim of collecting information about the current situation in the management of NSTE-ACS in high complexity centers in the city of Buenos Aires (CABA) and the province of Buenos Aires (PBA), including in-hospital and 6-month follow-up outcomes.

METHODS

BUENOS AIRES I was a prospective multicenter observational registry, which was carried out in medical centers of CABA and PBA. The registry was designed and conducted by the Emergency and Cardiovascular Critical Care Council of the Argentine Society of Cardiology and included patients between December 2017 and July 2018.

The participating centers of CABA and PBA included in the registry were affiliated to the Argentine Society of Cardiology (SAC) and fulfilled the following requirements: they had coronary care unit, 24-hour catheterization lab availability and cardiovascular surgery capabilities.

Patients were followed up for 6 months after hospital discharge, using data collected from the clinical record and supplemented with information obtained by telephone contact within 14 days from hospital discharge. Presence of cardiovascular events, medication used and adherence to the treatment prescribed were recorded.

The inclusion criteria were: patients >18 years with primary NSTE-ACS who signed the informed consent form. The only exclusion criterion was follow-up impossibility.

Cardiovascular risk factors and relevant clinical history data were obtained through anamnesis on hospital admission. The following variables were recorded: history of hypertension, diabetes mellitus, dyslipidemia and smoking habits (current or former active or passive smoker), family history of early cardiovascular disease, sedentary lifestyle, relevant medical history, usual pharmacological treatment and history of cardiovascular disease [acute myocardial infarction (AMI), percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABGS)].

Characteristics of ACS: the information related with the ACS was obtained from the medical record, considering:

A) Type of ACS: UA or NSTEMI.
B) Killip and Kimball (KK) class at admission and during hospitalization.
C) Electrocardiographic (ECG) changes: transient ST-segment elevation; ST-segment depression, changes in T wave, Q waves associated with changes in ST-segment or T wave, left bundle branch block (LBBB), pacemaker rhythm or absence of acute ischemic changes.
D) Treatment implemented: type of anticoagulation, P2Y12 receptor inhibitors (P2Y12i) used and time of prescription.
E) Cardiovascular complications: recurrent angina, refractory angina, postinfarction angina, reinfarction, PCI-related AMI, heart failure, electrical complications (atrial fibrillation, non-sustained ventricular tachycardia, sustained ventricular tachycardia, high-grade atrioventricular block, ventricular fibrillation or other rhythms of cardiac arrest), mechanical complications (ventricular septal rupture, acute mitral regurgitation or free wall rupture), need for ventricular assist device or temporary pacemaker implantation and in-hospital mortality.
F) Other complications: ischemic or hemorrhagic stroke, transient ischemic attack (TIA), acute kidney failure, bleeding event according to the Bleeding Academic Research Consortium (BARC), need for mechanical ventilation. (5)
G) Treatment on hospital discharge: antiplatelet therapy (aspirin, clopidogrel, prasugrel or ticagrelor), oral anticoagulation, beta-blockers (BB), angiotensin converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), statins, ezetimibe and aldosterone antagonists.
H) Blood pressure on hospital admission and discharge.
I) Heart rate on hospital admission and discharge.
J) Findings on coronary angiography: procedure-related complications, use of glycoprotein IIb/IIIa inhibitors (GPI), time from hospital admission to coronary angiography, premedication with P2Y12i.
K) Length of hospital stay.

Statistical analysis

All the statistical calculations were performed using IBM SPSS 25.0 software package (for Mac iOS). Continuous variables were expressed as mean ± standard deviation, or median and interquartile range, according to their distribution, Normality of variable distribution was assessed using the Kolmogorov-Smirnov test or the Shapiro-Wilk test, as applicable. The chi-square test or Fisher's exact test was used to compare categorical variables and continuous variables were analyzed using Student's t test or the Mann-Whitney test according to their distribution. Survival was evaluated with the log rank test and was represented with Kaplan-Meier curves.

A type I error <5% (two-tailed p value <0.05) was considered statistically significant.

We calculated a sample size of 1,100 patients with NSTE-ACS diagnosis. The expected incidence of combined ischemic events and of bleeding events was 7% and 6%, respectively.

Ethical considerations

All patients gave their informed consent before participating in the study. Patients were clearly informed about the aim of the study and the mechanisms used to protect their identity to ensure the confidentiality of the data provided. They were informed that their participation was voluntary, that they could refuse to participate in the study without any consequences or differences in their medical care, and that they had the right to withdraw their consent at any time.

During the evaluation process for inclusion in the study, the investigator provided verbal explanation to the patient about the information included in the informed consent and answered all his/her questions regarding the study. The consent was submitted for institutional review board approval, which is under the regulations of the Central Review Board. The investigators implemented measures to protect the confidentiality of all the information according to the Argentine personal data protection law 25,326, so the identity of the patients and all their personal data would remain anonymous, and only the researchers and the members of the teaching and research and ethics on research committee would have access to this data, if required. The study was conducted following national ethical standards (law 3301 of the city of Buenos Aires, National Law for Good Clinical Practice in Research on Human Subjects, and the Declaration of Helsinki, among others).

RESULTS

A total of 1,100 patients with mean age of 65.4 ± 11.5 years and 77.2% men were included in the study. The prevalence of hypertension was 74.6%; 27.6% of the patients had diabetes mellitus, 60.1% had dyslipidemia and 21.8% were active smokers (Table 1 and Figure 1).

A history of AMI, PCI, CABGS and stroke was reported by 31.5%, 32.8%, 11% and 5.7% of the patients, respectively. Bleeding events were reported in 1.7% of cases (Table 2).

Before hospital admission, 51.9% of the patients were on aspirin treatment; 19.2% were receiving P2Y12i; 39.3% statins (8.4% high-intensity statins) and 6.7% anticoagulant therapy.

On admission, the mean GRACE score was 133.8 ± 52.1 and the mean CRUSADE score 24.3 ± 13.9. Among the total number of NSTE-ACS, 62.6% was classified as NSTEMI and 37.4% as UA. The hemodynamic state was classified as KK A in 93.3% of patients, B in 4.9%, C in 1.7% and D in 0.1%.

An invasive strategy was used in 86.7% of the cases. During hospitalization, 91.5% of the patients underwent conventional coronary angiography (CA); 62.1% required PCI and 14.4% CABGS.

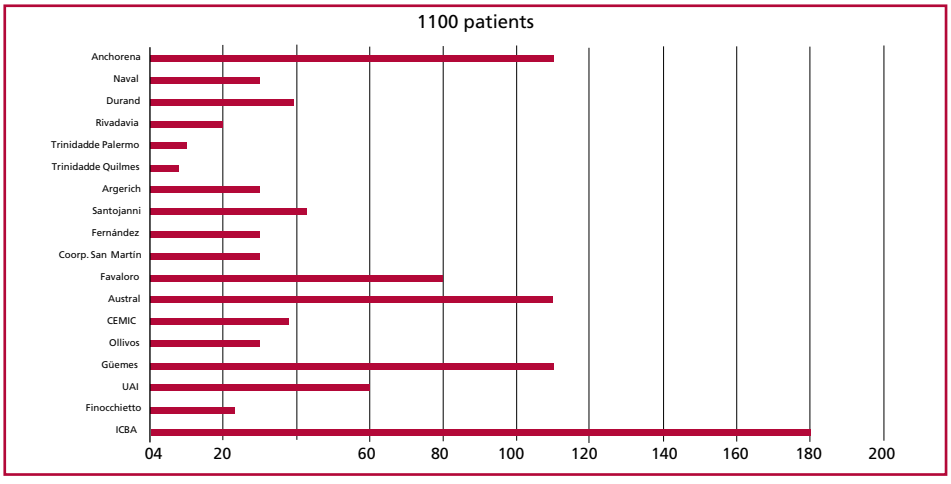
Median time to CA was 18 hours (IQR 7-27.7) and 65.4% received pretreatment with a P2Y12i. Of the pre-treated patients, 83.6% received clopidogrel, 14.5% ticagrelor, and 1.9% prasugrel. A GPI was used

Table 1. Baseline population characteristics n = 1,100

Variable	Value
Age, years, mean ± SD	65.4 ± 11.5
Male gender, n (%)	849 (77.2%)
Hypertension, n (%)	821 (74.6%)
Dyslipidemia, n (%)	661 (60.1%)
Diabetes, n (%)	304 (27.6%)
Smoking habits, n (%)	240 (21.8%)
Family history, n (%)	282 (25.6%)
Obesity, n (%)	184 (16.7%)
Chronic kidney failure, n (%)	223 (21.0%)
Previous cardiovascular events	
AMI, n (%)	347 (31.5%)
PCI, n (%)	361 (32.8%)
CABGS, n (%)	121 (11.0%)
AF, n (%)	75 (6.8%)
PVD, n (%)	70 (6.4%)
Stroke/TIA, n (%)	63 (5.7%)
Bleeding, n (%)	19 (1.7%)
Cancer, n (%)	36 (3.3%)

SD: Standard deviation. AMI: Acute myocardial infarction. PCI: Percutaneous coronary intervention. CABGS: Coronary artery bypass graft surgery. AF: Atrial fibrillation. PVD; Peripheral vascular disease. TIA: Transient ischemic attack.

Fig. 1. Patients included by center



in 1.4% of the patients undergoing PCI. The radial access was used in 76.3% of cases, and a drug-eluting stent (DES) was implanted in 79.6% of patients. Among the patients treated with a P2Y12i, 24.2% received the medication on the catheterization laboratory (51.1% clopidogrel, 43.4% ticagrelor, and 5.5% prasugrel).

Mean length of hospital stay was 3 days (2-6). During hospitalization, 5.2% of the patients presented reinfarction, 1.2% refractory angina, 2% postinfarction angina and 8.2% developed clinically relevant heart failure. The incidence of stroke/TIA was 0.3% and the presence of arrhythmias was low, with an incidence of 4.9% atrial fibrillation and 1.4% ventricular tachycardia. In-hospital mortality was 2.7% and was due to cardiovascular causes in 1.8% of cases (Table 3).

Of the total number of patients analyzed, 20.9% presented bleeding events during hospitalization with an incidence of 4.9% events ≥ BARC type 3 (Table 3).

On hospital discharge, 95% of the patients were receiving aspirin, 9.2% anticoagulant therapy, 91% statins, 58.4% ACEI/ARB and 73% BB, and 78.3% were discharged with P2Y12i: 73.5% with clopidogrel, 23.1% with ticagrelor and 3.4% with prasugrel.

Follow-up after 6 months was achieved in 88.3% of patients (n = 971). All-cause mortality was 5.7% and cardiovascular mortality 3.5% (Figure 2).

The individual analysis of events showed that 8.4% of patients presented reinfarction, 10.9% ACS and 17.5% of the patients included in the registry required CABGS (Table 4 and Figure 3).

Bleeding ≥BARC type 2 was present in 13.6% of the patients.

The simplified Morisky-Green Medication Adherence Scale used to evaluate adherence to treatment revealed that 60.9% of the patients classified as "adherent", with a score of 4 points.

DISCUSSION

BUENOS AIRES I is a multicenter registry that provides the possibility of analyzing updated real-world information about the treatment strategies implemented and the associated clinical complications of NSTE-ACS patients in high complexity centers in the city of Buenos Aires and the province of Buenos Aires. The invasive approach of NSTE-ACS in these centers has been the primary strategy in 86.7% of patients with a median time to CA of 18 hours. Considering that 37.4% were UA corresponding to the intermediate risk category of the GRACE score suggests that the invasive strategy was a decision made by the medical team rather than an inevitable need due to the potential ischemic risk of the patient. Our population presented high burden of comorbidities and history of coronary revascularization, which may have influenced on the decision to perform an anatomical test rather than functional testing. When the results of this registry were compared with those of international registries, we found that the invasive strategy was more common in our registry. In the Swedish SCAAR registry (NSTE-ACS n=15,442), the rate of coronary angiography as initial management of patients with NSTE-ACS was 62.9%, with 65.8% of NSTEMI similar to our registry, while in the Danish registry

Table 2. Index event and treatment received n = 1,100

Variables	Value
Type of event	
Unstable angina, n (%)	411 (37.4%)
NSTEMI, n (%)	689 (62.6%)
Risk scores	
GRACE, mean ± SD	133.83 ± 52.1
CRUSADE, mean ± SD	24.31 ± 13.9
Treatment received	
Early invasive strategy, n (%)	953 (86.7%)
Coronary angiography, n (%)	1,006 (91.5%)
Radial access, n (%)	768/1,006 (76.3%)
PCI, n (%)	625/1,006 (62.1%)
DES, n (%)	498/625 (79.6%)
Use of GPI, n (%)	9/625 (1.4%)
Pretreatment with P2Y12i, n (%)	658/1,006 (65.4%)
Time to CA, hours (median ± IQR)	18 (7-27.7)
CABGS requirement, n (%)	157/1,100 (14.4 %)
Time to CABGS, hours, median (IQR)	120 (96-192)

SD: Standard deviation NSTEMI: Non-ST-segment elevation myocardial infarction. PCI: Percutaneous coronary intervention. DES: Drug eluting stent. GPI: Glycoprotein IIb/IIIa inhibitor. P2Y12i: P2Y12 inhibitor. CA: Coronary angiography. CABGS: Coronary artery bypass graft surgery. IQR: Interquartile range

Table 3. In-hospital outcomes n = 1,100

Variables	Value
Ischemic events	
Reinfarction, n (%)	57 (5.2%)
Stroke/TIA, n (%)	3 (0.3%)
Stent thrombosis, n (%)	2/625 (0.3%)
Refractory angina, % (n)	13 (1.2%)
Postinfarction angina, n (%)	14/689 (2.0%)
Atrial fibrillation, n (%)	54 (4.9%)
Ventricular tachycardia, n (%)	15 (1.4%)
Heart failure, n (%)	90 (8.2%)
Cardiovascular mortality, % (n)	20 (1.8%)
All-cause mortality, n (%)	30 (2.7%)
Bleeding events	
No bleeding, n (%)	870 (79.9%)
BARC type 1, n (%)	110 (10.0%)
BARC type 2, n (%)	57 (5.2%)
BARC type 3, n (%)	40 (3.7%)
BARC type 4, n (%)	11 (1.0%)
BARC type 5, n (%)	2 (0.2%)

TIA: Transient ischemic attack. BARC: Bleeding Academic Research Consortium.

Fig. 2. Six-month evolution of all-cause mortality.

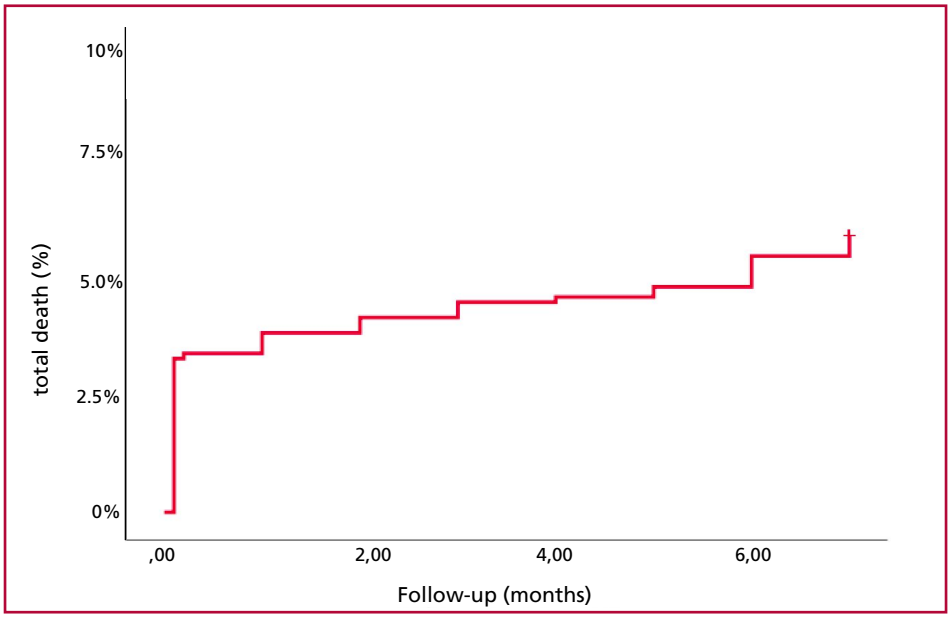


Table 4. 6-month outcome

Variables	Value
Ischemic events	
ACS, n (%)	105/963 (10.9%)
AMI, n (%)	81/963 (8.4)
New revascularization, n (%)	56/946 (5.9%)
CABGS, n (%)	166/946 (17.5%)
Stroke/TIA, n (%)	5/946 (0.5%)
Atrial fibrillation, n (%)	91/955 (9.5%)
Cardiovascular mortality, % (n)	34/966 (3.5%)
All-cause mortality, n (%)	55/971 (5.7%)
Bleeding events	
≥ BARC type 2	133/979 (13.6 %)

ACS: Acute coronary syndrome. AMI: Acute myocardial infarction. CABGS: Coronary artery bypass graft surgery. TIA: Transient ischemic attack. BARC: Bleeding Academic Research Consortium.

(NSTE-ACS n=170), an initial invasive management was observed in only 48% of cases (6-8).

Coronary artery bypass graft surgery was required in 14.4% of the cases due to anatomical complexity, a prevalence that was significantly higher than those reported by other studies or registries with similar populations. The French FAST-MI registry (n=1,941), reported that 10% of NSTEMI patients required CABGS, 4% of which were performed during the index hospitalization, while in the European cohort (Euro Heart Survey, n=5,367), only 5.4% of NSTE-ACS patients required CABGS. (7, 8)

The percentage of DES implantation was 79.6%, lower than that published in international registries which is close to 100%. Several studies have demonstrated the superiority of third-generation DES over bare metal stents (BMS), particularly associated with lower requirement for future revascularization and lower incidence of thrombosis during follow-up. The decision to implant BMS is probably due to costs and lack of availability of DES rather than a medical decision based on clinical considerations. We consider that the pre-established 15-month follow-up will provide evidence on whether this decision had any impact in terms of associated adverse clinical events. (9, 10)

Clopidogrel is still the antiplatelet agent most commonly indicated in our population, despite several clinical trials showing greater benefit with the use of ticagrelor and prasugrel in these patients. (11-13). The high percentage of clopigrel use (73.5%) in this registry does not seem to be linked to the bleeding risk of the patients included, since the CRUSADE score was relatively low (24.4 ± 13.9), and only 1.7% of the patients reported a history of bleeding events.

The difference in antiplatelet agent cost may have played a determining role in choosing this treatment, along with the fact that most patients received pretreatment with P2Y12i, which cannot be used with prasugrel. The Swedish SCAAR registry identified ticagrelor as the most widely used antiplatelet agent in more than 95% of cases, with a rate of clopidogrel use <20%. These data correlate with the observations of the French FAST-MI registry, where the use of ticagrelor in NSTEMI patients was predominant (44%). (7)

The prevalence of in-hospital complications was low compared with those reported by other international series. In the SCAAR registry, the prevalence of bleeding events in patients undergoing PCI was 4%, while the Euro Heart Survey cohort showed a similar prevalence of heart failure (12.7% vs. 8.2%), with a lower number of bleeding events ≥ BARC type 3 (0.9% vs. 4.9%). (14, 15)

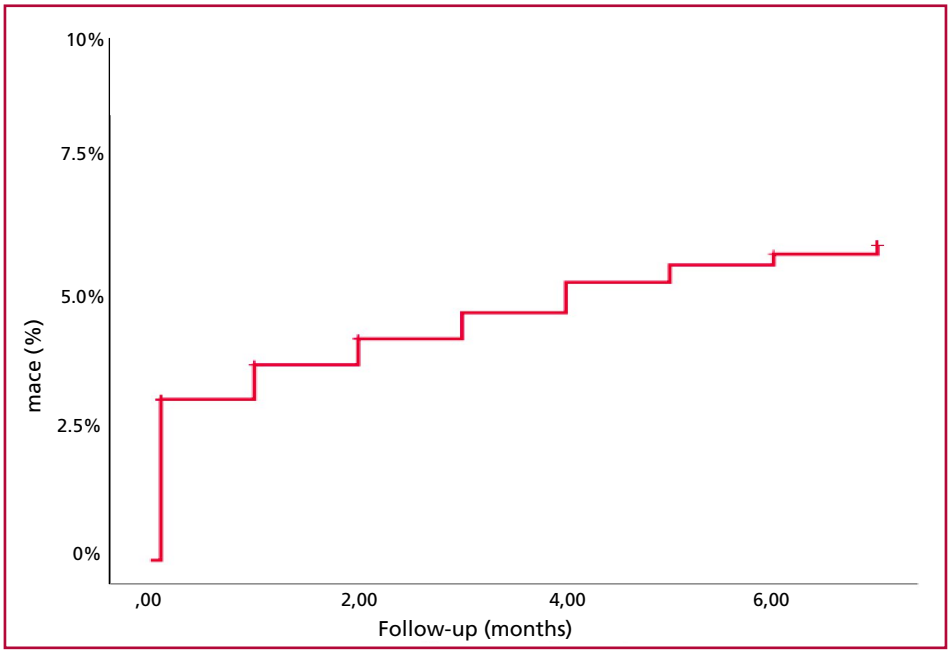


Fig. 2. Six-month evolution of combined ischemic events (MACE: myocardial infarction, ACS, stroke and cardiovascular mortality).

At 6 months, cardiovascular mortality was low, compared with other similar population cohorts. All-cause mortality was 5.7% in the BUENOS AIRES I registry, with cardiovascular mortality of 3.5%. In a cohort study based on a US metropolitan population (n=2,539 NSTEMI), mortality at 3 months was 12.6%. It is important to note that this study showed a shorter length of hospital stay compared with this registry (6 days vs. 3 days), and a lower prevalence of invasive treatment (33.1% vs. 86.7%), which could partially explain the results shown in the American registry. Perhaps the outcome at 15 months will provide a better perspective about long-term adverse clinical events. (15)

Study limitations

The participating centers were chosen because they are tertiary care centers belonging to an urban conglomerate with common demographic and geographic characteristics. The results of this registry cannot be extrapolated to healthcare practice outside this geographical area or to less complexity centers in the same region, although they will be useful to evaluate changes in the management of NSTE-ACS over time, as long as this survey can be repeated in the future.

CONCLUSIONS

The BUENOS AIRES I multicenter registry demonstrated a predominantly invasive therapeutic approach in patients with NSTE-ACS treated in high complexity centers of CABA and PBA, with low rates of in-hospital complications and good results at the 6-month follow-up

Conflicts of interest

None declared.

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

REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, Windecker S, et al. Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. ESC Committee for Practice Guidelines. Third Universal Definition of Myocardial Infarction. Eur Heart J 2012;33:2551–67. https://doi.org/10.1093/eurheartj/ehs184

2. Fox KAA, Goodman SG, Anderson FA, Granger CB, Moscucci M, Flather MD, et al. From guidelines to clinical practice: The impact of hospital and geographical characteristics on temporal trends in the management of acute coronary syndromes - The Global Registry of Acute Coronary Events (GRACE). Eur Heart J 2003;24:1414–24. https://doi.org/10.1016/S0195-668X(03)00315-4

3. Aurelio MJG, Arazi HC, Higa C, Gómez Santa María HR, Mauro VM, Fernández H, et al. Infarto agudo de miocardio con supradesnivel persistente del segmento ST. Registro multicéntrico SCAR (síndromes coronarios agudos en Argentina) de la Sociedad Argentina de Cardiología. Rev Argent Cardiol 2014;82:259–67. https://doi.org/10.7775/rac.es.v82.i4.2169

4. Pérez GE, Costabel JP, González N, Zaidel E, Altamirano M, Schiavone M, et al. Infarto agudo de miocardio en la República Argentina. Registro CONAREC XVII. Rev Argent Cardiol 2013;81:390-9. https://doi.org/10.7775/rac.v81.i5.1391

5. Mehran R, Rao S V, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: A consensus report from the bleeding academic research consortium. Circulation2011;123:2736–47. https://doi.org/10.1161/CIRCULATIONAHA.110.009449

6. Alkhouli M, Alqahtani F, Tarabishy A, Sandhu G, Rihal CS. Incidence, Predictors, and Outcomes of Acute Ischemic Stroke Following Percutaneous Coronary Intervention. JACC Cardiovasc Interv 2019;12:1497–506. https://doi.org/10.1016/j.jcin.2019.04.015

7. Belle L, Cayla G, Cottin Y, Coste P, Khalife K, Labèque JN, et al. French Registry on Acute ST-elevation and non−ST-elevation Myocardial Infarction 2015 (FAST-MI 2015). Design and baseline data. Arch Cardiovasc Dis 2017 ;110:366–78. https://doi.org/10.1016/j.acvd.2017.05.001

8. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin: The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). Eur Heart J 2002;23:1190–201. https://doi.org/10.1053/euhj.2002.3193

9. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, Holmes DR, et al. 2014 AHA/ACC Guideline for the management of patients with non-st-elevation acute coronary syndromes: Execu-

tive summary: A report of the American college of cardiology/American heart association task force on practice guidelines. Circulation 2014;130: 2354–94. https://doi.org/10.1161/CIR.0000000000000133

10. Rossington JA, Brown OI, Hoye A. Systematic review and meta-analysis of optimal P2Y 12 blockade in dual antiplatelet therapy for patients with diabetes with acute coronary syndrome . Open Heart 2016;3:e000296. https://doi.org/10.1136/openhrt-2015-000296

11. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;361:1045–57. https://doi.org/10.1056/NEJMoa0904327

12. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al. Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes. N Engl J Med 2007;357:2001–15. https://doi.org/10.1056/NEJMoa0706482

13. Schüpke S, Neumann F-J, Menichelli M, Mayer K, Bernlochner I, Wöhrle J, et al. Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes. N Engl J Med 2019;381:1524-34. https://doi.org/10.1056/NEJMoa1908973

14. Damman P, Varenhorst C, Koul S, Eriksson P, Erlinge D, Lagerqvist B, et al. Treatment patterns and outcomes in patients undergoing percutaneous coronary intervention treated with prasugrel or clopidogrel (from the Swedish Coronary Angiography and Angioplasty Registry [SCAAR]). Am J Cardiol 2014;113:64–9. https://doi.org/10.1016/j.amjcard.2013.09.019

15. Darling CE, Fisher KA, McManus DD, Coles AH, Spencer FA, Gore JM, et al. Survival after hospital discharge for ST-segment elevation and non-ST-segment elevation acute myocardial infarction: A Population-based study. Clin Epidemiol 2013;5:229–36. https://doi.org/10.2147/CLEP.S45646

Participating centers and investigators in alphabetical order:

CEMIC: Mirza Rivero.
Clínica Olivos: Sebastián Nani y Gonzalo Pérez.
Clínica San Lucas: Martín Odone.
Clínica Zavala: Claudia Bruno.
Corporación San Martín: Fernando Guardiani.
Fundación Favaloro: Ernesto Duronto.
Hospital Argerich: Maximiliano Mascarello.
Hospital Austral: Jorge Bilbao, José Bonorino y Nicolás Torres.
Hospital de la Universidad Abierta Interamericana: Ricardo Levín e Ignacio Vaca.
Hospital Durán: Leandro Parrilla.
Hospital Fernández: Andrea Tufo Pereyra.
Hospital Naval: Sofía Binder.
Hospital Posadas: NataliaCarli.
Hospital Santojanni: Carlos Ruano.
ICBA: Juan P Costabel, Cristian M Garmendia, Rosina Arbucci y Roberto Campos.
Sanatorio Anchorena sede San Martín: Leandro Rodríguez.
Sanatorio Anchorena sede Recoleta: Paz Domínguez y Nicolás Lalor.
Sanatorio Finochietto: Miguel González y Guido Damianich.
Sanatorio Güemes: Ezequiel José Zaidel e Iván Gómez.
Sanatorio la Trinidad Palermo: Andrea Tufo Pereyra.
Sanatorio la Trinidad Quilmes: Christian Musante

Supplementary material

Definitions

- Stent thrombosis: thrombotic occlusion of a coronary stent documented by angiography.
- BARC bleeding definitions: (6) Bleeding Academic Research Consortium

- Type 0: No bleeding
- Type 2: Minimal bleeding, Bleeding that does not require additional treatments, does not prolong hospitalization or cause symptoms beyond bleeding.
- Type 2: Bleeding that fulfills Type 3, 4 or 5 criteria but requires diagnostic studies, treatment, or hospitalization.
- Type 3:

a) Overt bleeding plus hemoglobin drop of 3-5 g/dL, or any bleeding requiring transfusion.
b) Overt bleeding plus hemoglobin drop >5 g/dL; cardiac tamponade; bleeding requiring surgical intervention or vasoactive agents.
c) Intracranial or intraocular bleeding compromising vision.

- Type 4: Surgery-related bleeding. Intracranial bleeding within 48 hours of surgery. Reoperation for bleeding. Transfusion of >5 U packed red blood cells within the first 48 hours after surgery. Chest tube drainage >2000 mL in the first 24 hours after surgery.
- Type 5: Fatal bleeding,

- AMI: (7) Acute myocardial infarction.

a) Spontaneous AMI: rise and/or fall of high-sensitivity cardiac troponin T (hsTnT) levels with at least one value above the 99th percentile upper reference limit (URL) in two samples; associated with chest pain, imaging evidence of new regional wall motion abnormality, new ischemic ECG changes (ST-segment deviation, T wave changes, new Q wave or new LBBB) or identification of a coronary thrombus by coronary angiography.
b) PCI-related AMI: elevation of hsTnT levels >5 times the 99th percentile URL within 48 hours after the procedure in patients with previous normal baseline values or hsTnT increase >20% in patients with stable elevated or decreasing levels. In addition, the patient had to present associated chest pain for >20 minutes, or new ischemic ECG changes (ST-segment deviation, T wave changes, new Q wave or new LBBB) or coronary thrombus identified by coronary angiography or imaging evidence of new regional wall motion abnormality.
c) CABG-related AMI: elevation of hsTnT levels >10 times the 99th percentile URL within 48 hours after the procedure in patients with previous normal baseline values or hsTnT increase >20% in patients with stable elevated or decreasing levels. In addition, the patient had to present associated chest pain for >20 minutes, or new ischemic ECG changes (ST-segment deviation, T wave changes, new Q wave or new LBBB) or coronary occlusion in a native artery or graft identified by coronary angiography or imaging evidence of new regional wall motion abnormality.

* LBBB diagnosis: QRS >120 ms, dominant S wave in V1, wide and monophasic R wave in leads I, aVL, V5-V6,

absence of Q wave in leads I, V5-V6 and R wave peak time >60 ms in V5-V6.

* ECG signs of ischemia in the absence of LBBB:

- New ST segment elevation >0.1 mV in 2 or more contiguous leads, except V2-V3; where the following cutoff points apply: >0.2 mV in men >40 years, >0.25 mV in men <40 years, or >0.15 mV in women.
- New ST-segment depression or with decreasing slope >0.05 mV in 2 or more contiguous leads.
- T-wave inversion >0.1 mV in two or more contiguous leads.

• Nonfatal stroke

a) Ischemic stroke: new sudden neurological deficit lasting for more than 24 hours, without an alternative cause (tumors, infections, etc.), documented by computed tomography scan or magnetic resonance imaging.

b) Hemorrhagic stroke: evidence of blood in the central nervous system by imaging tests or lumbar puncture.

• Adherence to treatment. The simplified Morisky-Green Medication Adherence questionnaire was used to evaluate adherence to treatment. This instrument consists of four questions with dichotomous answers that reflect the behavior of the patient in relation to compliance with treatment. The advantage of this questionnaire over others is that it provides information on the reasons for not taking the prescribed medication and having been previously implemented in studies of adherence to medical treatment in the Argentine population. The patient will be considered adherent if he/she answers the questions as follows: No-Yes-No-No.