Acute coronary syndromes in Latin America: lessons from the ACCESS registry

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Síndromes coronarios agudos en Latinoamérica: lecciones aprendidas del registro ACCESS

Introducción: se desconocen las características, la evolución y el tratamiento de pacientes latinoamericanos con síndromes coronarios agudos (SCA).
Métodos: registro internacional multicéntrico y prospectivo para evaluar riesgo, terapéutica y evolución en SCA. Punto primario: toda causa de mortalidad durante el primer año y mortalidad a 30 días. Ingresaron pacientes con síntomas de isquemia coronaria aguda en las primeras 24 horas del inicio de los síntomas y evidencia electrocardiográfica de isquemia. El diagnóstico final requirió pruebas invasivas o no invasivas.
Resultados: entre el 2007 y 2008 se ingresaron en ocho países latinoamericanos 4436 pacientes, 2562 con angina inestable o infarto sin elevación del ST y 2374 con infarto con elevación del ST. Al ingreso tuvieron síntomas agudos 79 y 90 %, respectivamente. Ambos grupos tuvieron retraso entre el inicio de síntomas y el ingreso hospitalario. En infarto y elevación del ST se observó baja accesibilidad a reperfusión farmacológica (29 %) y mecánica (32 %). Al ingreso en ambos el porcentaje de tratamiento basado en evidencia fue bajo. Las complicaciones hospitalarias fueron la insuficiencia cardiaca (angina inestable e infarto sin elevación del ST 10 % y el infarto con elevación del ST 20 %) e isquemia recurrente (8 y 11 %). La mortalidad a 30 días fue 2 % y a un año 8 %.
Conclusiones: el registro ACCESS ofrece información contemporánea sobre el espectro de pacientes, el manejo hospitalario y la evolución clínica subsecuente.

Palabras clave	Keywords
Síndrome coronario agudo	Acute coronary syndrome
Infarto del miocardio	Myocardial infarction
Angina inestable	Unstable angina
Isquemia miocárdica	Ischemic heart disease

Worldwide, acute coronary syndromes (ACS) are estimated to be the leading cause of death and loss of disability-adjusted life years in both developing and developed countries.[1,2] Current knowledge on therapeutic and mortality trends is derived largely from randomized controlled clinical trials,[3-5] registries[2,6] and practice guidelines.[7,8] However, in both clinical models Latin American (LA) population has been underrepresented and evidence to demonstrate whether current recommendations[7,8] reduce mortality and improve outcomes is limited.[9] The multinational prospective ACCESS registry[10] provides a unique opportunity to assess current clinical practices and subsequent outcomes in patients hospitalized for an ACS in developing countries. The registry data will help to identify — in every day clinical practice — whether current knowledge is being applied appropriately and potential areas where educational efforts are necessary to improve adherence to evidence-based guidelines.

Methods

Study design

A detailed description of the study design has been previously published.[10] Briefly, ACCESS is a prospective, observational, multinational registry of patients hospitalized for an acute coronary event. The study was designed to evaluate risk stratification, current management and one-year outcomes in 19 countries, in LA, Africa, and Middle East. Medical practices dictated by current clinical guidelines in acute and post-discharge settings, interventional and non-interventional strategies, and clinical outcomes will be

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Abstract

Background: Evidence of the clinical characteristics, treatment and outcomes among Latin American (LA) patients with acute coronary syndromes (ACS) is scarce.

Methods: ACCESS, international prospective multicenter registry to evaluate risk stratification, management and outcomes in ACS (unstable angina or non-ST elevation myocardial infarction [UA/NSTEMI] or ST elevation myocardial infarction [STEMI]) in developing countries. Primary endpoint: all-cause death at 1 year; all-cause mortality within 30 days was also recorded, Patients with acute ischemic symptoms within 24 hours of symptoms onset and electrocardiographic evidence of ischemia were enrolled. Coronary artery disease was proved by positive invasive or non-invasive tests.

Results: Between 2007 and 2008, 4436 patients with ACS (2562 UA/NSTEMI and 2374 STEMI) from eight LA countries. On admission, acute symptoms were identified in 79% and 90%, respectively. Both groups had a long delay from symptom onset to hospital arrival. Low access to pharmacological (29%) and mechanical reperfusion (32%) were observed. At admission, rates of evidence-based treatment were low in all groups. The most common in-hospital complications were heart failure (10% UA/NSTEMI and 20% STEMI) and recurrent ischemia (8% and 11%). Mortality at 30 days was 2% and 8% at 1 year.

Conclusion: ACCESS registry provides contemporary information of patients with ACS in LA and their hospital management and subsequent clinical outcomes.

analyzed for patients admitted to hospitals with or without access to interventional cardiology facilities.

Study setting and site selection

Potential researchers and sites were identified from the spectrum of clinical settings in which ACS patients are treated, and included different types of institution (public, private, teaching), location, number of ACS patients treated, and services offered (interventional or non-interventional). The affiliated researchers in each country provided a list of centers that represented their country as completely as possible, from which the trial manager generated a random list of study investigators.

Evaluations and clinical outcomes

A standardized case-report form[10] was used to record data prospectively, at hospital admission, at discharge, and at 6 ± 1 month and at 12 ± 1 month follow-up. Data were collected during follow-up visits or by telephone calls to the patient or a third party (e.g. relative/friend, or family physician). Patient data collected at baseline included demographics, medical history, risk factors, results of physical examination, cardiac biomarkers concentrations, ankle-brachial index, Killip class, use of chronic medical treatments, and health insurance status. Data collected at discharge from hospital included discharge status and diagnosis, hospital management, cardiac biomarkers concentrations, and occurrence of events in hospital. Follow-up data included clinical outcomes occurring after discharge, as well as those leading to rehospitalization, and treatments initiated since discharge or previous follow-up.

Data quality control was performed by trained personnel at ≥10% of sites chosen randomly in each country. All case-report forms were monitored for source documentation and accuracy. Data-request forms were generated automatically in response to queries and were resolved by the site investigators.

Study population

Patients with a suspected ACS with electrocardiographic evidence of ischemia and proven ischemic heart disease at discharge were included. Patients with an acute coronary event secondary to a comorbidity (e.g. anemia, heart failure, trauma, etcetera), and those participating in a clinical trial were not eligible for inclusion in the study.

Study outcomes

The primary endpoint was all-cause death at one-year. Secondary endpoints in the same period were cardiovascular death, non-fatal stroke and non-fatal myocardial infarction. The combined endpoint was comprised of cardiovascular death, stroke, or myocardial infarction[11] (for ischemic events) and bleeding complications. All-cause death at 30 days was also recorded.

Statistical analysis

Analyses were performed at the 5% significance level, using 2-sided tests or 2-sided confidence intervals (CI). Analyses were conducted in the overall population and in ACS subgroups. Continuous data are described using descriptive statistics: mean, standard deviation, median, 25th percentile (Q1) and 75th percentile (Q3), minimum, and maximum. Categorical data are summarized using counts and percentages (the denominator for calculating percentages is the number of non-missing observations). Logistic regression on the outcome event rates (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, combined endpoint) was performed to test the impact

of covariates (patient characteristics, risk factors, physician characteristic, Killip class, cardiac biomarkers and patient socioeconomic profile). Kaplan-Meier survival methods were used for time-to-event endpoints from hospital arrival. A multivariable proportional hazards model was used for prognostic analyses, with data given as odds ratios (ORs) and 95% CIs. Data were analyzed with the SAS package, release 9.1.3 (SAS Institute, Cary, NC).

Results

Between January 2007 and January 2008, 5115 consecutive patients from eight countries in LA (Argentina, Brazil, Colombia, Dominican Republic, Ecuador, Guatemala, Mexico, and Venezuela) were enrolled in the multinational ACCESS registry. At discharge, 4936 had evidence of ischemic heart disease, 2562 with UA/NSTEMI and 2374 with STEMI. Patients were enrolled by 215 investigators: 62% were cardiologists, 17% were interventional cardiologists, 11% were internists, 4% were hospital physicians and 7% were other physicians. Mexico had the highest number of participating investigators (96) and enrolled the greatest number of patients (2113, 18%). Colombia enrolled 730 patients (7%), Venezuela 621 (5%), Brazil 578 (5%), Ecuador 314 (2.6%), Guatemala 291 (2%), Argentina 276 (2%) and Dominican Republic 132 (1.1%).

Demographic and characteristics at clinical presentation

In both ACS groups, patients were in their sixth decade of life and were more likely to be male, of LA origin, with overweight and with clinical indicators of cardiovascular disease and poor outcome (Table I). Compared with STEMI patients, those with UA/NSTEMI had a greater prevalence of hypertension and dyslipidemia and were more likely to have had a prior myocardial infarction, angina, ventricular dysfunction and to have had a prior PCI or CABG. Patients with STEMI had a higher rate of smoking; prevalence of diabetes was similar in both groups. Patients' socioeconomic profiles, including education level, location of residence, and distance from hospital, employment status, disability and health insurance coverage are detailed in Table II.

Reperfusion therapy

Most patients had acute ischemic symptoms on admission, late arrival after onset symptoms and clinical stability (Table I). Among patients with STEMI a significant number arrived outside of time window for optimal time of reperfusion (45%) and only 29% were submitted to thrombolysis. Percutaneous coronary intervention performed within 24 hours of admission was infrequent (Table I). Streptokinase was the most commonly used fibrinolytic drug, followed by tenecteplase, alteplase and reteplase. Thrombolysis was used in 3% of UA/NSTEMI patients (Table I). The most frequently used antithrombin adjunctive treatments were the low-molecular-weight heparin, enoxaparin (46%) and unfractionated heparin (28%); glycoprotein IIb/IIIa inhibitors were used in 7%.

In-hospital and at discharge pharmacological treatments

There was an upward trend to use aspirin, clopidogrel, low-molecular-weight heparin, statins, beta-blockers, nitrates and angiotensin-converting enzyme inhibitors in UA/NSTEMI and STEMI patients compared with RENASICA II registry.[9]

In-hospital clopidogrel and enoxaparin loading doses were underused (Table III). Overall, most frequent in-hospital and at discharge treatments were aspirin (92%) followed by statins (90%), clopidogrel (85%), and beta-blockers (72%), in both UA/NSTEMI and STEMI patients. As expected, the use of ticlopidine, oral anticoagulation and other antithrombotics was infrequent in both groups. Detailed pharmacological treatments are shown in Tables III and IV.

Interventions and procedures

The overall rate of angiography during index hospitalization was 67% in UA/NSTEMI patients and 62% in STEMI patients. Mechanical revascularization plus a stent were used in a high percentage of patients (93%) who underwent PCI. CABG was considered in 7% UA/NSTEMI patients and 4% STEMI patients. Transthoracic echocardiograms were performed in 67% and 70% of patients, respectively, and ejection fraction was obtained over 70% in both groups. The exercise test was underused (9% overall).

In-hospital cardiovascular adverse events and bleeding complications

The most frequent adverse events were left ventricular dysfunction and recurrent ischemia. Patients with STEMI (2374) had a higher incidence and more severe left ventricular dysfunction compared with UA/NSTEMI (2562) (20% vs. 10%), recurrent ischemia (11% vs 8%) cardiogenic shock (8% vs. 2%), atrioventricular block (7% vs. 2%), cardiac arrest (6% vs. 2%) and ventricular arrhythmias (5% vs. 2%).

Table I Demographic characteristics of the patients

Variable	All ACS (*n* = 4936)		UA/NSTEMI (*n* = 2562)		STEMI (*n* = 2374)	
	n	%	*n*	%	*n*	%
Male sex	3489	71	1647	64	1842	78
Latin American race	3883	79	1961	77	1922	81
Ankle-brachial index	3429	83	1757	81	1672	85
Risk factors						
Smoking history	1676	34	696	27	980	42
Diabetes mellitus	1515	31	818	32	697	29
Hypertension	3082	62	1805	71	1277	54
Dyslipidemia	2215	45	1339	52	876	37
Medical history						
Myocardial infarction	1073	22	708	28	365	15
Angina	2047	42	1356	53	691	29
Heart failure	310	6	201	8	109	5
Stroke/transient ischemic attack	220	5	125	5	95	4
Peripheral artery disease	267	5	173	7	94	4
Percutaneous coronary intervention	653	13	475	19	178	8
Coronary artery bypass graft	247	5	215	8	32	1
Killip - Kimball class						
I	3918	81	2104	86	1814	77
II	638	13	264	11	374	16
III	192	4	76	3	116	5
IV	82	2	17	1	65	3
Reperfusion therapy						
Thrombolysis	762	15	64	3	698	29
Streptokinase	160	21	16	25	144	21
Tenecteplase	102	13	6	9	96	14
Alteplase	96	13	6	9	90	13
Reteplase	16	2	3	5	13	2
PCI on 1st day in-hospital	1208	25	458	18	750	32
PCI with stent 1st day in hospital	1120	93	422	92	698	29
Clinical characteristics						
Ischemic symptoms at admission	4155	84	2028	79	2127	90
Symptoms onset to hospital arrival < six hours	2520	51	1209	47	1311	55
	Mean ± SD		Mean ± SD		Mean ± SD	
Symptoms onset to hospital arrival (h)	28.3 + 281.1		37.6 + 382.0		18.2 + 81.5	
Diastolic blood pressure (mmHg)	75.6 + 13.6		76.8 + 13.4		74.4 + 13.7	
Heart rate (beats/min)	77.7 + 16.5		77.0 + 16.3		78.5 + 16.7	
Ejection fraction (%)	50.74 + 12.69		53.13 + 13.12		48.21 + 11.69	
Age (years)	62.1 + 12.3		63.7 + 11.9		60.3 + 12.5	
Height (cm)	165.3 + 9.1		164.6 + 9.4		166.1 + 8.8	
Weight (kg)	75.0 + 14.5		74.5 + 14.6		75.5 + 14.5	
Body mass index (kg/m²)	27.4 + 4.5		27.4 + 4.5		27.3 + 4.6	
Waist circumference (cm)						
Men	98.5 + 13.3		98.8 + 13.3		98.3 + 13.3	
Women	94.4 + 13.8		94.7 + 13.7		94.0 + 14.0	

ACS = acute coronary syndrome; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation

No differences were observed with atrial fibrillation (4% vs. 4%) and stroke or transient ischemic attack (1% vs. 1%). The incidence of bleeding complications was similar in UA/NSTEMI (109, 4%) and STEMI (101, 4%) patients; GUSTO classification grade I 33 and 23%, grade II 24 and 25% and grade III 43 and 53%. The rate of in-hospital mortality was 2%.

Mortality at one year

In this period, mortality rate was 8% and was attributed to acute coronary and cerebral events (Table V). In patients with UA/NSTEMI, stroke was the most frequent cause of death versus recurrent myocardial infarction in patients with STEMI (Table V).

Predictors of 1 and 12-month death

In a logistic regression analysis performed to assess the effect of independent variables on mortality while adjusting for potentially confounding factors in UA/NSTEMI and STEMI patients, mechanical complications, acute neurologic events, surgical revascularization and antithrombin treatment had relevance, but with wide confidence intervals at 30 days. In the analysis for predictors of death at 1 year, the same factors were identified for 30-day death, with the addition of age; the confidence intervals were wide again (Table VI). The Cox model confirmed these variables as independent predictors of death at 1 year. In this model, surgical revascularization (HR 2.64,

Table II Socioeconomic profile of the patients

Variable	All ACS (*n* = 4936)		UA/NSTEMI (*n* = 2562)		STEMI (*n* = 2374)	
	n	%	*n*	%	*n*	%
Education level						
College/University	1101	23	563	22	538	23
Primary education	1981	41	1045	41	936	40
Secondary/high school education	1410	29	711	28	699	30
No education	394	8	218	9	176	8
Place of living and circumstances						
Urban/suburban area	4285	89	2234	90	2051	89
Rural area	511	11	250	10	261	11
Living alone	525	11	250	10	275	12
Distance from home to hospital						
< 30 minutes drive	2310	47	1195	47	1115	47
≥ 30 minutes drive	2394	49	1231	49	1163	50
Within walking distance	180	4	108	4	72	3
Employment status						
Full time	1922	39	847	33	1075	46
Part time	608	12	291	11	317	13
Disability	110	2.2	62	2.4	48	2
Retired	1205	25	684	27	521	22
Not working/unemployed	1056	22	659	26	397	17
Not working due to illness	91	15	65	16	156	15
Health insurance coverage						
Governmental	2134	44	1053	41	1081	46
Private	1123	23	651	26	472	20
Governmental and private	263	5	148	6	115	5
Not covered by insurance	1372	28	689	27	683	29

ACS = acute coronary syndrome; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction

$p = 0.005$), an age of 70 years (HR 1.62, $p = 0.02$) and ankle-brachial index (HR 1.62, $p = 0.04$) were also predictive of death. The Kaplan-Meier primary curve for death at 1 year, overall and in ACS subgroups is shown in Figure 1.

Discussion

Rigorous and well-designed registries, such as ACCESS, provide important information about the management and outcomes of patients treated in everyday clinical practice and, as such, complement the findings from the rather narrower scope of randomized clinical trials.[12-14] These data from the LA cohort of the ACCESS registry population provide valuable information about the therapeutic approaches chosen and the quality of care given to LA patients presenting with an ACS, and can be used to detect similarities

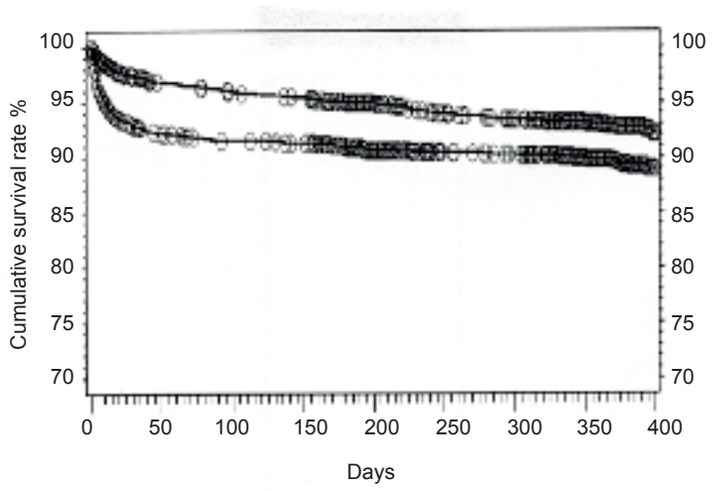

Figure 1 Kaplan-Meier primary curve for death at 1 year, overall and in acute coronary syndrome subgroups. Top line product limit estimate curve for UA/NSTEMI; bottom line product limit estimate curve for STEMI

Table III Pharmacological treatment during hospitalization

Drug	All ACS *n* = 4936		UA/NSTEMI *n* = 2562		STEMI *n* = 2374	
	n	%	*n*	%	n	%
Aspirin	4576	92	2362	92	2214	93
Clopidogrel (loading dose)	3023	61	1449	57	1574	66
Clopidogrel (maintenance)	4175	85	2091	82	2084	88
Ticlopidine	20	0.4	12	1	8	0.3
Other antiplatelet	27	1	18	1	9	0.4
Unfractionated heparin	1573	32	786	31	787	33
Enoxaparin (loading dose)	556	11	232	9	324	14
Enoxaparin (maintenance)	2804	57	1447	57	1357	58
Other LMWH*	335	7	176	7	159	7
Glycoprotein IIb/IIIa inhibitor	796	16	324	12	472	20
Bivalirudin	9	0.2	3	0.1	6	0.3
Fondaparinux	9	0.2	6	0.2	3	0.1
Other direct thrombin inhibitor	6	0.1	1	0	5	0.2
Other antithrombin	5	0.1	2	0.1	3	0.1
Warfarin or other vitamin K antagonist	113	2	53	2	60	3
Statin	4440	90	2281	89	2159	91
Beta blocker	3549	72	1871	73	1678	71
ACE inhibitor	3230	65	1551	61	1679	71
Nitrates/other anti-angina agent	3122	63	1635	64	1487	63
Calcium channel blocker	820	17	571	22	249	11
Angiotensin II receptor antagonist	669	14	459	18	210	9

ACS = acute coronary syndrome; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction; LMWH = low-molecular-weight heparin; ACE = angiotensin-converting enzyme

Table IV Pharmacological treatment at discharge

Drug	All ACS (*n* = 4936)		UA/NSTEMI (*n* = 2562)		STEMI (*n* = 2374)	
	n	%	*n*	%	*n*	%
Aspirin	4212	89	2215	89	1997	89
Clopidogrel (maintenance)	3811	80	1901	76	1910	85
Ticlopidine	10	0.2	7	0.3	3	0.1
Other antiplatelet	11	0.2	5	0.2	6	0.3
Warfarin or other vitamin K antagonist	102	2	48	2	54	2
Statins	4142	87	2172	87	1970	88
Beta blockers	3264	69	1742	69	1522	68
ACE inhibitors	2878	61	1411	56	1467	65
Nitrates / other anti-angina agents	1677	35	918	37	759	34
Calcium channel blockers	739	16	533	21	206	9
Angiotensin II receptor antagonists	671	14	458	18	213	10

ACS = acute coronary syndrome; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction; ACE = angiotensin-converting enzyme

and differences with other national and international registries.[2,6,9,15-25] In doing so, the ACCESS data provide the opportunity to identify key areas for improvement in the management of ACS patients in LA.

The management of ACS continues to undergo major changes, based on sound evidence derived from well-conducted clinical trials[3-5] and incorporated into practice guidelines.[7,8] Currently, the mortality rate is decreasing in developed countries due to a combination of factors including changes in socioeconomic status, reduction in prevalence of risk factors, application of results from clinical trials defining effective treatments, and the ability and infrastructure to translate these findings into clinical practice.[13] Currently, the best approach to define and apply effective therapies is likely to be high-quality clinical trials data combined with 'real-world' data from prospective registries.[13] However, in both models, the LA population has been underrepresented[15-25] and evidence showing whether current recommendations[2,3] reduce mortality and improve outcomes in this population is limited.[9]

Acute coronary syndromes incidence and risk factors

The ACCESS registry has generated a large volume of data on the incidence and relative frequency of ACS as a cause of hospital admission. Even though the most frequent ACS was UA/NSTEMI (in 52% of the population; 48% with STEMI), the ratio did not differ greatly from that reported in other registries.[6,21-25] The higher incidence of STEMI in Mexico (56%)[9] and in India (61%)[20] compared with developed countries (Table VII) could be attributed to cultural differences in the perceptions of disease, early access to care by insurance status (27% in USA vs. 4% in Mexico and in India),[2] social support and educational level. Although the incidence of diabetes reported previous in Mexican registries (42%[9] and 50%)[24] was lower in ACCESS (31%), its role in patients with STEMI and the association with extensive and severe coronary disease has to be considered.[2,9] In contrast, the demographic data in ACCESS were consistent with those in the INTERHEART study, also conducted in LA.[26] Considering the projected increase in life expectancy, obesity and sedentary behavior (33 million by 2030) in the LA population,[26] it will be mandatory to establish or increase the strength of secondary preventive efforts and apply even more strict targets for cardiovascular risk factors in an effort to improve primary and secondary prevention.[27,28]

Reperfusion and clinical profile

Mechanical and pharmacologic reperfusion in high-income and high-technology countries reduces mor-

Table V Causes of death: 1 year follow-up

Cause of death	All ACS (*n* = 409)		UA/NSTEMI (*n* = 173)		STEMI (*n* = 236)	
	n	%	*n*	%	*n*	%
Myocardial infarction	229	56	82	47	147	62
Stroke	18	4	11	6	7	3
Non-cardiovascular	45	11	20	12	25	11
Other cardiovascular, including sudden death of unknown cause	90	22	44	25	46	20
Unknown	27	7	16	9	11	5
Total mortality	409	8	173	7	236	10

ACS = acute coronary syndrome; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction

tality and improves outcome in STEMI patients. However, whether these results are reproducible in low- and middle-income countries is unknown. An important finding was a lower access to pharmacologic (29%) and mechanical (32%) reperfusion strategies;[6,9,20-24] furthermore, while it is not possible to identify a clear explanation, clinical and socioeconomic profiles may also have important implications. On admission, socially productive patients had acute ischemic symptoms, clinical stability, longer time to treatment and low socioeconomic status ascertained by years of education.[29] These were relevant characteristics in both groups. Although, ACCESS was not specifically designed to identify whether longer time to treatment was related to low socioeconomic status, it is possible to provide some insight into the contributions of some factors and to speculate on other explanations, which link low socioeconomic status with delay to treatment and lower reperfusion strategies proportion. A low educational level could reduce the individual's capacity to obtain and understand basic health information and the services needed in order to make appropriate health decisions.[29]

To the best of our knowledge, the characteristics of LA patients hospitalized with an ACS has not been described in terms of their socioeconomic profile (including young sociality productive workers) educational level, life style, place of living and medical health coverage. Our present data demonstrate that a significant proportion of patients with STEMI fail to receive any form of reperfusion strategy (despite almost half of them reported to live at < 30 minutes driving from hospital) and it also highlights the need to improve quality of care.

Outcome

Despite the low access of reperfusion strategies reported in the study, rates of in-hospital and 1 year mortality were similar to those reported in developed countries (Table VII). This finding could be attributed to the "Hispanic paradox,"[2,30-36] to almost optimal compliance with evidence-based medications in-hospital[7,8] and the high rates of use of coronary angiography and stenting. However, left ventricular dysfunction was the most important major adverse cardiac event and the strongest mortality predictor, probably related to the long ischemia time and low access to reperfusion rate.

New strategies are needed to improve the care of STEMI patients: first, by increasing the use of evidence-based therapies, such as clopidogrel, enoxaparin (intravenous dose) and thrombolysis, as is done in several developed countries; second, by reducing the delay between symptom onset and hospital admission through patient and physician education. Stroke was an important predictor of death and its combination with an ACS in daily clinical practice is complex and a challenge in terms of reperfusion strategies and antithrombotic use.

The unexpected finding regarding antithrombin treatment as a mortality predictor may reflect potential confounding variables not included in the multivariable analysis; patients on prolonged antithrombin treatment also be sicker or have more comorbid conditions than those who were not included in the treatment. Similar results were observed in ACCESS global results.[10] The low frequency of in-hospital major adverse cardiac events, including bleeding complications, is in line with

Table VI Variables associated with death at 30 days and 12 months

Variable	Odds ratio	95 % confidence interval		*p*
Death at 30 days		Lower 95 % CI	Upper 95 % CI	
Cardiac arrest	81.1	21.0	313.0	< 0.0001
Cardiogenic shock	60.3	16.8	216.9	< 0.0001
Stroke/TIA	24.1	2.9	199.1	0.0031
CABG	8.6	2.0	36.2	0.0035
Death at 12 months				
Cardiac arrest	31.8	9.0	111.7	< 0.0001
Cardiogenic shock	28.0	9.4	83.0	< 0.0001
Stroke/TIA	11.8	2.2	62.7	0.0038
Recurrent ischemia	3.8	1.5	10.0	0.0058
Antithrombins during hospitalization/at discharge	3.1	1.2	8.0	0.0174
Age > 70 years old	2.5	1.2	5.1	0.0111

CI = confidence interval; TIA = transient ischemic attack; CABG = coronary artery bypass graft

center expertise and low rates of reperfusion. In addition, in-hospital mortality and bleeding complications rate in STEMI patients support the safety and efficacy of the combination of aspirin, plus clopidogrel and a low-molecular-weight heparin, enoxaparin. By comparison with unfractionated heparin, enoxaparin has a weaker affinity for endothelial cells, anti-inflammatory properties and favorable effects on Von Willebrand factor release and glycoprotein Ib/IX receptors. These factors are a key part in the pathogenesis of myocardial infarction and are all affected favorably by enoxaparin.[37]

When compared with the results of the Mexican RENASICA II study,[9] in both ACS groups the results demonstrated low marginal use on admission of dual antiplatelet treatment and a trend to more frequent use of the low-molecular-weight heparin, enoxaparin. At discharge, whether any non-significant differences observed could be attributed to drug contraindications or collateral effects is unknown. Our data also suggest that hospitals that perform invasive cardiac procedures may also have funding to support the use of these more expensive therapies. However, bivalirudin and fondaparinux were infrequently used (0.2%), which may reflect the lack of availability of these drugs at the time the study was conducted, or their high cost. The most commonly used fibrinolytic was streptokinase, again possibly reflecting its lower cost relative to newer fibrinolytic drugs.

Data coming from RENASICA registry recently added new evidence of patients presenting an ACS in México in terms of risk stratification.[38] This registry validated the utility of GRACE score in Mexican population. Lastly, the results of RENASICA III,[39] a prospective, multicenter registry on ACS to identify the outcome in tertiary and community hospitals, as well as therapeutic approaches to improve quality of care in Mexico, will be published soon.

A relevant question is whether the patients in ACCESS are representative of the general ACS populations in the participating countries. Compared with clinical trials, registries are less able to monitor the patient inclusion process and to ensure the enrollment of consecutive patients. Conversely, patients enrolled in observational studies are more representative of those treated in everyday clinical practice and are free of many of the exclusion criteria commonly applied in clinical trials. At any rate, the size of the current survey, comprising 4496 patients with the spectrum of ACS, makes it reasonable to assume that the patterns disclosed do indeed represent a true picture of the current clinical situation, in selected hospitals at least. The data presented will therefore provide insights into the practice of cardiology in different hospital settings in LA.

Table VII Incidence and mortality in developed and less developed countries

Registry/countries	Patients	Countries	STEMI	UA/NSTEMI	In-hospital mortality
	n		%	%	%
Developed countries					
CRUSADE	172,763	USA	-----	92 MI	5
GRACE	11,543	14	30	38 UA, 25 MI	3 UA, 6 MI
EURHEART	10,484	25	33	42 UA, 25 MI	2 NSTE,11 U
ENACT	3029	29	39	46 UA/MI	2 UA, 2 SACS
PRAIS – UK	1046	England	-----	29 STD	2
Less developed countries					
CREATE	20,468	India	61	39	4 UA/MI
RENASICA II	8098	Mexico	56	43	7 UA, 4 MI
ACCESS	4496	8 Latin America	48	52 UA/MI	2
Total	231,927				

STEMI = ST elevation myocardial infarction; UA/NSTEMI = unstable angina or non-ST elevation myocardial infarction; MI = myocardial infarction; UA = unstable angina; NSTE = non-ST elevation; SACS = suspected of acute coronary syndrome; STD = ST depression

Limitations

Since ACCESS was not a population-based epidemiological study, some bias may have been introduced through the selection of participating centers: limited monitoring visits; the exclusion of patients who died at home or in the emergency room; the absence of long-term follow-up; the high proportion of centers with expertise and revascularization facilities; the combining of data from different countries with variable economies and sources of funding; the lack of differentiation between major or minor bleeding; and absence of data on hospital facilities.

Lessons learned from ACCESS

This contemporary high-quality clinical prospective registry provides a unique opportunity to assess contemporary clinical practices and outcomes in wide spectrum of ACS patients treated in developing countries, and to contribute to an ongoing process of quality assurance, indicating areas where education to improve adherence to best practice is necessary. The ACCESS registry emerges as another source of information — among randomized clinical trials, guidelines and daily clinical practice — in patient populations treated in different healthcare systems, and establishes information that could help to better apply resources in the forthcoming future of ACS treatment in LA.

Conclusion

These results from ACCESS registry provide contemporary information on the spectrum of patients with ACS in countries in Latin America and on their hospital management and subsequent clinical outcomes. The findings identify areas for improvement in the quality of cardiovascular care.

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