ORIGINAL ARTICLE

Annual Incidence and Lethality of Acute Myocardial Infarction in the City of San Carlos de Bariloche. The REGIBAR Study

Incidencia anual y letalidad del infarto agudo de miocardio en la Ciudad de San Carlos de Bariloche. Estudio REGIBAR

MATÍAS E. CALANDRELLI[1], MARIO CAMINOS[2], JORGE L. BOCIAN[1], MARÍA E. SAAVEDRA[3], MARÍA E. ZGAIB[4], ANTONIO BAZÁN[5], DANIEL J. ABRIATA[2], MARISA PAROLA[4], JORGE GRILLI[2], MARIANO TREVISAN[1]

ABSTRACT

Background: The incidence and lethality of myocardial infarction in Argentina were estimated by extrapolating data from hospital records and death certificates.
Objective: The aim of this study was to assess the annual incidence and lethality of cases presenting a first spontaneous acute myocardial infarction in the city of San Carlos de Bariloche.
Methods: A prospective registry was carried out during one year of all spontaneous fatal and non-fatal acute myocardial infarctions in stable residents of the city, following the World Health Organization-MONICA protocol. Based on the 112,887 inhabitants of the city of San Carlos de Bariloche, according to the 2010 Census, hospitalized cases were registered in all the health centers; fatal out-of-hospital cases through verbal autopsies and non-fatal ones in doctor's offices.
Results: One hundred and forty-four cases of acute myocardial infarction were registered (age 71.1 years, 63.5% men) with an annual incidence of 128 per 100,000 inhabitants. The annual rate of acute myocardial infarction standardized by age (35 to 64 years) was 119 per 100,000 inhabitants, corresponding to 173 men and 44 women. Among the 61 fatal out-of-hospital infarctions, 16 were possible fatal acute myocardial infarctions and 45 unclassifiable deaths (included according to the MONICA criteria). Overall mortality was 46.5%, 9% corresponding to hospitalized patients and 91% to non-hospitalized cases.
Conclusions: According to the MONICA project criteria, the annual incidence of acute myocardial infarction in San Carlos de Bariloche was 128 per 100,000 inhabitants. More than 40% of cases did not reach admission to a health center. Overall mortality due to acute myocardial infarction was 46.2%, with more than 90% of deaths occurring before hospital admission.

Key words: Myocardial infarction - Incidence - Epidemiology – Myocardial ischemia - Mortality

RESUMEN

Introducción: La incidencia y la letalidad del infarto de miocardio en la Argentina se estimaron extrapolando datos de registros hospitalarios y certificados de defunción.
Objetivo: Determinar la incidencia anual y la letalidad del primer infarto agudo de miocardio espontáneo en la ciudad de San Carlos de Bariloche, Argentina.
Material y métodos: Se realizó un registro prospectivo durante un año de todos los casos de infarto agudo de miocardio espontáneo, fatales y no fatales en residentes estables de la ciudad, siguiendo el protocolo OMS-MONICA. Sobre la base de la población de San Carlos de Bariloche, 112.887 habitantes, según el Censo Nacional de 2010, los casos internados se registraron en todos los centros de salud; los extrahospitalarios fatales, a través de autopsias verbales y los no fatales, en consultorios.
Resultados: Se registraron 144 casos de infarto agudo de miocardio (edad 71,1 años, 63,5% varones) con una incidencia anual de 128 cada 100.000 habitantes. La tasa de infarto agudo de miocardio anual estandarizada por edad (35 a 64 años) fue de 119 cada 100.000 habitantes, 173 varones y 44 mujeres. De los 61 infartos fatales extrahospitalarios, 16 fueron infarto agudo de miocardio fatal posible, y 45 muertes inclasificables (incluidos según criterios MONICA). La mortalidad global fue 46,5%, el 9% pertenecían a casos hospitalizados y el 91%, a casos fatales no hospitalizados.
Conclusiones: De acuerdo con los criterios del proyecto MONICA, la incidencia anual de infarto agudo de miocardio en San Carlos de Bariloche fue 128 cada 100.000 habitantes. Más del 40% de los casos no llegaron a ingresar a un centro de salud. La mortalidad global por infarto agudo de miocardio fue 46,2%, de los cuales más del 90 % de los decesos ocurrieron antes de ingresar al hospital.

Palabras clave: Infarto del miocardio – Incidencia – Epidemiologia - Cardiopatía isquémica – Mortalidad

[1] Sanatorio San Carlos, San Carlos de Bariloche, Argentina.
[2] Hospital Privado Regional, San Carlos de Bariloche.
[3] Hospital Zonal Bariloche Dr. Ramón Carrillo. San Carlos de Bariloche.
[4] Distrito SAC San Carlos de Bariloche.
[5] Sanatorio del Sol, San Carlos de Bariloche.

Abbreviations

AMI	Acute myocardial infarction		**WHO**	World Health Organization
INDEC	National Institute of Statistics and Censuses			

INTRODUCTION

Cardiovascular diseases are the leading cause of death in Argentina. In 2013, 28.8% out of 326,197 deaths were attributed to circulatory system diseases, according to data from the National Institute of Statistics and Censuses (INDEC) obtained from death certificates. Within the spectrum of cardiovascular diseases, acute myocardial infarction (AMI) is the most aggressive manifestation and the second cause of death as an individual entity. (1) Knowing the incidence of AMI has not only scientific and epidemiological interest, but also represents vital information for public health planning.

In our country, multiple hospital registries of AMI have been performed in the last 25 years providing valid and useful information on the clinical characteristics of patients admitted to hospital, the procedures used and the prognosis, (2-4) but they do not reflect the incidence rates.

In Argentina, the annual rate of AMI has been estimated in 41.9 per 10,000 inhabitants and adjusted to other type of classic infarctions this has been extended to 55.9 per 10,000. (5-6) However, these values were obtained from the extrapolation of data from a retrospective registry of consecutive cases of ST-segment elevation AMI admitted to the two health centers of the city of Coronel Suarez. (6)

The experience of the MONICA project showed that two thirds of the deaths due to AMI occur before admission to a health center, so a significant number of cases would not be found in hospital records. (7) Also, another percentage of individuals do not consult and survive the AMI, which is only detected in subsequent medical controls.

Population studies are significantly more complicated to carry out than hospital registries. It is necessary to put together a complex multidisciplinary organizational framework that involves not only intensive care physicians, forensic doctors, cardiologists and general practitioners, but also relatives, death witnesses and civil registry personnel. Only thus can true rates of AMI incidence and mortality be established.

The methodology of AMI population registries was suggested by WHO more than 30 years ago. The MONICA project was the tool that allowed developing these objectives in 38 cities of 21 countries since 1985. (7) The study combined information from hospital medical records with death certificates and forensic records. However, no country in Latin America participated in this multinational work.

The city of San Carlos de Bariloche, located in the province of Río Negro, has four inpatient centers in the city (a public hospital and 3 private clinics that have the capacity to admit patients with AMI in intensive care units.

Therefore, the objective of this work was to determine the annual incidence and lethality of spontaneous AMI in residents of the city of San Carlos de Bariloche.

METHODS

A prospective registry of all consecutive cases of spontaneous fatal and nonfatal AMI was performed during the period comprised between 0 AM of June 1, 2014 and 11.59 PM. of May 31, 2015 (365 days). Patients over 18 years of age living during the last 6 months in the city of San Carlos de Bariloche who had a spontaneous, fatal or non-fatal AMI were included in the study. We excluded all cases with AMI in non-residents of the city (tourists and patients referred from other cities), those with repeat AMI during the study period and those in whom a non-spontaneous AMI was determined (type 2, 3, 4 or 5 of the Universal Definition of Myocardial Infarction). (8)

The case sources were hospitalized patients and out-of-hospital cases:

Hospitalized patients: Case detection was made in the intensive care units, where in the event of a suspected acute ischemic syndrome the investigator had to be contacted (called "hot pursuit" in the MONICA project). (7) The case was registered, and at the end of hospitalization it had to be recorded as non-AMI, definitive or probable AMI (see section "definition of infarction").

Out-of-hospital cases:

Fatal: A systematic review was made in the Civil Registry of all deaths in the city during the study period. Persons deceased within the hospital setting and in whom there was a clearly non-cardiovascular diagnosis (trauma, suicide, neoplasms, etc.) were discarded. In all other cases a verbal autopsy was carried out to determine the cause of death. Briefly, this consists of a printed survey where the personal medical history and previous symptoms are documented to guide the cause of death and classify the event, as was done in the PRISMA study. (9) A nursing graduate with experience in epidemiological studies was trained to conduct the surveys, interviewing certifying physicians, witnesses, relatives, general practitioners and treating cardiologists. In turn, two investigators had to independently classify the cause of death. If the two investigators agreed on the diagnosis, that cause was considered. In case of disagreement, an Events Committee (DJA, JG) had to define the case.

Non-fatal: Cases with non-fatal AMI detected in the doctor's offices who had not been hospitalized or had not died and in whom, according to the investigator's criteria, the qualifying event had happened within the study period, were registered.

Instrument selection: The SCAR study survey (10) was used as basis for inpatients, modifying some variables according to the ARGEN-IAM-ST registry. (11) For the verbal autopsy, the PRISMA study model provided by the SAC's research area was used.

Definitions:

Following the MONICA project criteria, all the evaluated cases had to be finally classified in one of the following:

Non fatal cases

1) Definitive non-fatal AMI (NF1). The type 1 definition of the Universal Classification of Myocardial Infarction (8) was used: Detection of troponin elevation with at least one value above the 99th percentile upper reference limit (URL), together with evidence of myocardial ischemia and at least one of the following:
- Symptoms of ischemia.
- New ECG changes suggesting ischemia (ST-T changes or new left bundle branch block (LBBB).
- Development of pathological Q waves in the electrocardiogram.
- Imaging evidence of new loss of viable myocardium or new regional motility disorders.
- Identification of an intracoronary thrombus by angiography or autopsy.
2) Possible non-fatal AMI (NF2): Non-fatal cases that do not meet the previous definition due to missing criteria.
3) Non AMI (NF3): Non-fatal case that does not meet the requirements for the previous categories.

Fatal cases

1) Definitive fatal AMI (F1)
- In case of prior AMI diagnosed according to the previous definition, or
- Evidence of acute infarction or recent coronary thrombosis at an autopsy.
2) Possible fatal AMI (F2)
- Symptoms suggestive of AMI (precordial pain, dyspnea) in the last 72 hours before death.
- In the absence of previous symptoms, history of previous coronary event.
3) Non-coronary death (F3): In the presence of another clear cause of death.
4) Unclassifiable death (F4): In the absence of any of the above, including sudden death (less than 1 hour of symptoms prior to death).

To determine the annual incidence of AMI, the cases contemplated in NF1 + F1 + F2 + F4 were used.

Control strategies: A first pilot study carried out in August 2013 verified a significant underreporting of cases; therefore, a control strategy with troponin dosages was incorporated. All elevated troponin assessments in the laboratories of the city institutions were collected every 15 days and the cases were cross-compared with those entered into the registry. A second pilot study conducted in November 2013 showed better results in patient registration.

The cases detected by this method had to be reported to the corresponding center investigators, who had to define if the case not admitted (with elevated troponin) effectively corresponded to an undetected infarction ("cold pursuit" according to the MONICA denomination), (7) or if there was another cause for elevated troponin (dialysis, heart failure, lung embolism, etc.). If the center investigator could not determine the etiology of troponin elevation, the Events Committee (DJA, JG) had to define the case.

Statistical analysis

The following annual rates were calculated: a) Incidence: number of AMI per 100,000 inhabitants; b) Hospitalization: number of AMI cases who arrived alive to the hospital per 100,000 inhabitants; c) Mortality: cases of fatal AMI per 100,000 inhabitants; d) Lethality: proportion of fatal cases in the first 28 days among all patients with AMI, and e) In-hospital lethality: proportion of fatal cases among patients with AMI who arrived alive to the hospital.

Following the protocol suggested in the MONICA project, (12) the rates are standardized by age with the direct method using the world population as reference.

All the data was entered into specifically designed databases and expressed as percentages, mean and 95% confidence intervals.

Ethical considerations

The protocol was accepted by the Ethics Committee of the Hospital Zonal Bariloche "Ramón Carrillo" and all the admitted patients or relatives, depending on the case, signed an informed consent.

RESULTS

Hospitalized cases

One hundred and fourteen cases with AMI were registered in the hospital setting. Thirty-four patients were excluded: 5 were considered secondary AMI (type 2), one was a reinfarction and the other 28 were not residents of the city of San Carlos de Bariloche (9 were referred from neighboring districts and 19 were tourists). In only 2 cases, the center coordinator could not classify the event, requiring the decision of the Events Committee. Both were excluded, one was considered secondary to chemotherapy and in the other case myocarditis was suggested as the first diagnosis.

In this way, 80 patients with AMI were registered for the primary endpoint of the study (Table 1). In the admission ECG, 40 patients (50%) had ST-segment elevation, 3 (4%) had complete LBBB and 37 (46%) were considered without ST-segment elevation. Among the patients with ST-segment elevation or LBBB, only 24 (55.8%) received reperfusion treatment, in all cases fibrinolysis with streptokinase. The most common cause of non-reperfusion was late admission (> 12 h.) in 7/24 of cases (29%). In no case was primary angioplasty or coronary angiography (CA) evaluation performed on admission. Late CA was performed (after

Table 1. All AMI according to case source

	AMI Hospitalized (n=80)	AMI Doctor's office (n=3)	AMI Out-of-hospital (n=61)
Age (x̄, SD)	65.8±13.5	68±14.5	78.3±11.6
Mortality	6/80 (7.5%)	0/3 (0%)	61/61 (100%)

AMI: Acute myocardial infarction

24 hours) in 15 cases (18.8%), 9 of which underwent angioplasty and 5 received indication of myocardial revascularization surgery.

Out-of-hospital cases

Five hundred and nine deaths occurring during the study period were analyzed to establish out-of-hospital mortality (Table 2). A total of 313 in-hospital deaths and another 123 due to clear causes of non-cardiovascular mortality, of which cancer was the most frequent, were discarded. In the remaining 70 cases, a verbal autopsy was performed, establishing 16 possible fatal AMI and 45 unclassifiable deaths. In 18 cases, the cause of death was established by the Events Committee.

Three patients admitted from the doctor´s office, who had not been hospitalized and were diagnosed on an outpatient basis, were included.

Annual incidence of AMI

A total of 144 AMI cases were recorded in the year (Table 3). Mean age was 71.1 years and 63.5% were men. The population of the urban area of Bariloche according to the 2010 census was 112,887 inhabitants, so the annual crude incidence was 128 cases per 100,000 inhabitants. In 79% of cases it occurred in people over 64 years of age. It was greater for men than for women (160 and 94 cases per 100,000 inhabitants, respectively). The annual incidence of AMI standardized by age (35 to 64 years) was 111 per 100,000 inhabitants, 173 for men and 44 for women (Table 4).

Lethality and mortality

Lethality of hospitalized cases at 28 days was 7.5%. Considering also the non-hospitalized fatal cases, global lethality was 46.5% (Table 5). Among all AMI deaths, 91% corresponded to non-hospitalized fatal cases.

At the population level, the rate of mortality due to AMI (fatal AMI/100,000 inhabitants) was 59.4, which was higher for men than for women (69.8 and 48.6, respectively).

According to these data, 13.2% (95% CI 10.5-16.4) of all deaths in the city during the study period can be attributed to AMI.

DISCUSSION

The methodology used in our work was that suggested by WHO, which included: multidisciplinary work organization, registration of all cases of infarction (fatal and non-fatal, with and without ST-segment elevation, in inpatients and outpatients), inclusion only of residents (minimum 6 months), one-year registry, data recording at presentation, outcome and treatment (for internal validity), use of informed consent, 28-day follow-up and control mechanisms to avoid under-registration. According to our knowledge, we have not been able to find a study of the incidence of AMI in Argentina that follows these guidelines.

Using this format, the crude annual incidence of spontaneous AMI in the city of Bariloche was 128 cases per 100,000 inhabitants. This number is higher than the one reported in other registries of our country, which is probably explained by the inclusion in our study not only of hospitalized or outpatient cases, but also of fatal AMI that did not reach the hospital (6, 13). If we exclude out-of-hospital cases, the incidence would have been 87.7 per 100,000, similar to the aforementioned reports.

The process of standardization by age allowed us to compare the incidence of AMI in our city with similar registries in other countries. Compared with the 37 study sites of the MONICA project (population between 35 and 64 years of age), Bariloche would be among the three sites with the lowest incidence. Two considerations are necessary in this comparison: first,

	Total deaths	Home	Verb. aut.	AMI
June	41	8	3	3
July	49	14	5	5
Aug	39	14	3	3
Sep	40	19	4	4
Oct	44	20	2	2
Nov	41	11	4	4
Dec	41	16	7	7
Jan	51	25	15	15
Feb	31	8	3	3
Mar	41	17	5	5
Apr	47	19	6	6
May	41	22	13	13
	506	193	70	70
		38.1%	36.3%	36.3%
Per month (average)	42.17	16.08	5.83	5.83

Table 2. Detail of all deaths per month

Verb. aut.: Verbal autopsy. AMI: Acute myocardial infarction

Table 3. All AMI per age and source of origin

POPULATION PER AGE GROUPS				IH AMI		Ambulat. AMI		OH AMI		Total AMI
Age Groups	Total	Male	Female	Male	Female	Male	Female	Male	Female	per age
95 years or more	44	38	6	0	1	0	0	0	0	1
90-94 years	188	127	61	1	0	0	0	0	0	1
85-89 years	565	343	222	2	5	0	0	0	0	7
80-84 years	1,064	675	389	3	1	0	1	0	0	5
75-79 years	1,624	957	667	7	3	0	0	0	0	10
70-74 years	2,253	1,266	987	3	5	0	1	0	0	9
65-69 years	3,142	1,719	1,423	10	3	0	0	0	0	13
60-64 years	4,384	2,301	2,083	8	2	0	0	0	0	10
55-59 years	5,456	2,838	2,618	8	1	0	0	0	0	9
50-54 years	6,409	3,316	3,093	6	2	1	0	0	0	9
45-49 years	6,967	3,625	3,342	4	1	0	0	0	0	5
40-44 years	7,095	3,690	3,405	1	0	0	0	0	0	1
35-39 years	8,218	4,186	4,032	1	1	0	0	0	0	2
30-34 years	9,340	4,824	4,516	1	0	0	0	0	0	1
25-29 years	9,138	4,562	4,576	0	0	0	0	0	0	0
20-24 years	9,134	4,404	4,730	0	0	0	0	0	0	0
15-19 years	10,822	5,357	5,465	0	0	0	0	0	0	0
10-14 years	9,787	4,712	5,075	0	0	0	0	0	0	0
5-9 years	8,375	4,064	4,311	0	0	0	0	0	0	0
0-4 years	8,882	4,326	4,556	0	0	0	0	0	0	0
Total	112,887	57,330	55.557	55	25	1	2	0	0	83

AMI: Acute myocardial infarction. IH AMI: In-hospital AMI. Ambul AMI: Ambulatory AMI. OH AMI: Out-of-hospital AMI

Table 4. Infarction and lethality rates

Rate	Definition	Total	Male	Female
Crude incidence	AMI/100,000 inhab. (n)	127.6	160.5	93.6
Incidence standardized by age (35-64 years)	Total AMI/100,000 inhab. 35-64 years	111.8	173.22	43.55
Prehospital AMI lethality	Prehospital fatal AMI/total AMI (%, 95% CI)	42.4 (34.6-50.5)	39.1 (29.8-49.4)	48.1 (35.1-51.3)
In-hospital AMI lethality	IH fatal AMI/total IH AMI (%, 95% CI)	7.5 (3.5-15.4)	7.3 (2.9-17.3)	8.0 (2.2-25)
AMI lethality	Fatal AMI/total AMI (%, 95% CI)	46.5 (38.6-54.7)	43.5 (33.8-53.7)	51.9 (38.7-68.9)
Mortality rate	Fatal AMI×100,000/total inhab.	59.4	69.8	48.6
Proportion of deaths attributable to infarction	Fatal AMI/total deaths (%, 95% CI)	13.2 (10.5-16.4)	14.3 (10.7-18-9)	11.7 (8.2-16.5)
Hospitalization rate	AMI admitted alive to hospital / 100,000 inhab.	70.9	95.9	45

AMI: Acute myocardial infarction. IH: In-hospital.

it should be noted that in our population, 70% of cases occurred in people older than 64 years (which are excluded when adjusting by age), and second, there are multiple reports both in the US and Europe which confirm that the incidence of AMI has decreased in recent years, having even reached an average decline of approximately 3.5% per year, even higher than in the period between 1997 and 2007. (14-16).

The inclusion of unclassifiable deaths within the cases with AMI was performed according to WHO guidelines. In the 37 sites that participated in the MONICA project, the percentage of unclassifiable deaths relative to the total number of deaths due to infarction ranged between 1 and 46%, whereas in the present registry it was 73%. To a certain degree, the unclassifiable cases are less when there are autopsies that clarify the cause of death; in the MONICA project, 17% of fatal AMI were confirmed by autopsy, while in our study there were no cases diagnosed by forensic doctors.

The mechanism of control suggested by WHO to avoid under-registrations in hospitalized patients with AMI is to evaluate the codes of the discharge diagnoses, a strategy they called "cold pursuit". We assumed that this method would not be feasible in our setting and, after a first pilot study with an unacceptable number of unregistered AMI, we decided to incorporate the assessment of all cases with elevated troponins in the city during the study period. This allowed us to detect 1 additional case every 5 admitted from the intensive care units, which would not have been recorded without this control. In addition, these cases detected through troponin dosing were more frequently admitted during weekends, holidays and the month of January (data not shown).

Following WHO criteria, 13.2% of deaths in Bariloche are due to AMI. In 2015, according to the Vital Statistics of Río Negro (Provincial Department of Statistics), 3.97% of the 3,995 deaths at the provincial level were attributed to ischemic heart disease (I20-I25), and at the national level only 6.2% of all deaths was attributed to the same code, which appears to be lower than the data obtained in San Carlos de Bariloche. (1, 17) However, if we exclude from this study cases with unclassifiable deaths, only 4.3% of deaths in San Carlos de Bariloche would be ascribed to AMI, a figure closer to the provincial and national parameters.

Limitations

The MONICA project suggested that the population covered by each registry should have between 100 and 300 fatal cases due to coronary heart disease among males less than 65 years of age. (7) It has been estimated that this would represent a reference male population of at least 230.000 inhabitants. (18) Although the city of Bariloche does not have that number of events, it should be noted that in the MONICA project more than 90% of the participating sites had a population lower than the recommended one.

CONCLUSIONS

Considering the criteria of the MONICA project, the annual incidence of first acute myocardial infarction in the city of Bariloche was 128 per 100,000 inhabitants. More than 40% of cases do not reach admission to a health center. The overall mortality due to AMI was 46.2%, with more than 90% of deaths occurring before admission to hospital.

Conflicts of interest

None declared
(See author´s conflicts of interest forms on the web / Supplementary Material)

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