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Summary

EDITORIAL

I Confess That I Have Lived

Pablo Neruda. 1904-1973

Confieso que he vivido

Pablo Neruda. 1904-1973

RICARDO IGLESIAS[MTSAC]

After reading ReSCAR, (1) the interesting Registry on Acute Coronary Syndromes (ACS) carried out in centers of Argentina, a compendium of experiences gained in more than 40 years of treating and studying this clinical entity came to my mind.

Over these years, several randomized and observational studies have been conducted (the latter were pioneered by resident physicians through the CONAREC registries), with the aim of addressing the different types of ACS.

Despite the most specific diagnostic methods and advances in interventional and pharmacological therapies, my first thought is that every time I am dealing with a patient with ACS, I still have doubts about the optimal treatment.

ACSs are a group of clinical entities with a high prevalence in the population and include different clinical conditions that have precordial pain in common.

From my point of view, the greatest difficulty is not the diagnosis, but the categorization of each patient's individual risk, since it is a clinical entity of erratic course and difficult to evaluate, because of a complex pathophysiological substrate. The ReSCAR registry provides detailed information on the entire broad spectrum of ACS, as opposed to previous registries that only focused on a single clinical presentation (unstable angina [UA], non-ST-elevation myocardial infarction [NSTEMI] or ST-elevation myocardial infarction [STEMI]).

Ischemic heart disease is the leading cause of death in our country, and the factors that lead to it remain unchanged. In more than 20 years since the STRATEG-SIA registry, from 2001 to the present, the strong relationship between the lack of control of coronary risk factors and ACS (hypertension [HT] in more than 60% of patients, diabetes [DM] in more than 25%, dyslipidemia in more than 50%, current or past smoking in more than 40%) has been worryingly repeated. (2)

This evidence should prompt the State to implement healthcare programs aimed at modifying the concept of "lifestyle," which seems to represent an individual choice, on the basis of the concept of "way of life", a sociological category that systematically considers the economic, socio-political, and cultural conditions as the characteristic, stable and repeated forms of the daily life of individuals and communities. (3)

Plaque disruption on atherosclerotic lesions in the epicardial coronary arteries is the most frequent cause of acute coronary syndromes. However, there is a subgroup of individuals with clinical evidence of acute myocardial damage and coronary arteries without lesions greater than 50% on conventional coronary angiography.

A noteworthy finding in the registry is that 8.6% of patients were diagnosed with myocardial infarction with non-obstructive coronary arteries (MINOCA), which is closer to the literature data. In the CRUSADE study, 9% of patients with non-ST- elevation acute coronary syndrome showed no significant lesions in the angiography. (4)

A subsequent meta-analysis including 176 000 consecutive patients from 27 clinical trials, who presented with myocardial infarction according to the angiography, described a prevalence of MINOCA of 1-14%, an average of 6%. (5)

In national registries, the incidence of MINOCA was found to be between 1 and 2.8%; these differences can be attributed to the cut-off point considered for the percentage of coronary stenosis. (6, 7) The range is 1-4% when the definition is restricted to completely normal coronary arteries (0% stenosis), but it reaches 5-14% when a stenosis threshold of <50% is considered. (8)

For many years, and still today, there have been misconceptions about coronary artery disease.

The problem is often falsely believed to be restrict-

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[1] Sanatorio de la Trinidad Mitre

ed to the obstructive disease of the epicardial coronary vessels, but the coronary arterial system is much more complex than the anatomy visualized on the coronary angiography. The incorporation of the concept of the microvascular disease is essential to understand other mechanisms involved in the ischemia/necrosis process.

The paradigm should be based on ischemia rather than atherosclerotic plaque, as it allows for a more pathophysiological and dynamic thinking of the coronary insufficiency.

Regarding STEMI, we observed a common feature in all registries (CONAREC XVII, ARGEN-IAM and ReSCAR): the long time between the onset of symptoms and admission to the medical center, more than 300 minutes. (9,10)

With the aim of modifying this reality, in 2008 a document was published by all the Scientific Societies related to the infarction, and, at that time, it was recommended to implement permanent educational campaigns in the public media and at different educational levels on the recognition of chest pain and the importance of early consultation. (11)

Unfortunately, it has not had the expected impact to change this reality.

In-hospital mortality due to STEMI remains high, closer to that reported by the ARGEN-IAM registry of 8.7% than that observed by the ReSCAR registry of 7.6%. This is probably a result of the lower number of patients in the latter (2464 vs. 237), so the 95% CI of the estimate is higher.

Based on information from the ACS registries in our country, it is estimated that the number of non-ST-elevation ACS is approximately 60%, significantly higher than that of STEMI.

In STEMI, the advantage of systematic and early intervention has modified the natural history, whereas in non-ST-elevation acute coronary syndromes, the results are more controversial.

The ReSCAR registry shows a predominance of the invasive treatment (84%) and early treatment (61% of patients underwent coronary angiography within 24 hours of admission), similar to that observed in several national STEMI registries.

These findings emphasize the discrepancy between multiple guidelines from national and international scientific societies and current practice in centers with Cath lab. (12)

There is a subgroup of extremely severe patients (evolving ischemia with non-ST elevation, hemodynamic or electrical instability) who require catheterization as soon as possible and eventual urgent revascularization.

However, a vast majority of cases admitted to coronary units do not present such characteristics, which provides more time to select the strategy to be implemented. The longer the time between admission and catheterization, the greater the importance of antiplatelet pretreatment.

Whether and when an invasive strategy is indicated depends on a proper and thorough early risk stratification in a heterogeneous population.

In the registry of Dr. Rivero et al., the population studied is at the most intermediate risk (median GRACE score 127, mean left ventricular ejection fraction 56%, Killip and Kimball A 88%, with low risk of bleeding) and an important fact is that there are no patients older than 75 years, a population with a more torpid evolution. (13)

In these centers, the choice of the initial management strategy was obviously not made according to the risk categorization of the individual patient. The choice of the therapeutic strategy can be independently influenced by socioeconomic factors, demographics, and the characteristics of the medical center. (2,14)

The medical decision may also be driven by the intention to solve the problem quickly, the fear of malpractice, or the belief that it is the best treatment.

Regarding the Registry in-hospital evolution, ischemic complications are as expected for this population (reinfarction 2.84%, recurrent angina 2.43%, post-infarction angina 2% and intra-stent thrombosis 0.5%). A valuable data will be to consider the complications in the out-of-hospital follow-up.

However, these acute ischemic conditions do not end in the coronary unit; the possibility of events persists for several months, and inflammatory phenomena are involved in this period. The Buenos Aires 1 registry is a good example: in-hospital mortality was 2.7% and increased to 5.7% at 6-month follow-up, as did myocardial infarction (from 5.2% to 8.4% at follow-up). (15)

Finally, I would like to congratulate all the participants in the ReSCAR registry and thank them for their efforts to give us an insight into the reality of ACS.

During this complex time in medicine, I appreciate the voluntary and disinterested participation of physicians in providing us with this important document.

In Erich Fromm's words, "To know means to see reality naked and does not mean to possess the truth, but to penetrate beneath the surface and to strive critically and actively to get closer to the truth."

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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EDITORIAL

Mortality and Tobacco Consumption: the Population Attributable Fraction Method as a Tool to Estimate Damage

Mortalidad y consumo de tabaco: el método del riesgo atribuible poblacional como una herramienta de estimación del daño

MARIANO A. GIORGI[MTSAC, 1, 2, 3]

Do all risk factors influence the incidence of events in the same way? The answer is "no", and one of the main reasons mentioned by some cardiovascular medicine specialists is the INTERHEART study (1), which shows that the magnitude of the association among nine conditions or cardiovascular risk factors is heterogeneous with respect to the incidence of a first acute myocardial infarction (AMI). For example, the odds ratios (ORs) observed were 1) 1.91 for history of arterial hypertension; 2) 2.37 for diabetes; 3) 2.87 for smoking (smokers vs. non-smokers); 4) 3.25 for an elevated ApoB/ApoA1 ratio, among others. This information has had healthcare consequences: it provided us with evidence to establish a hierarchy or prioritization of health problems in order to avoid overwhelming patients and support their long-term efforts. However, the INTERHEART study also provided population health information by widely spreading the concept of risk or *population attributable fraction* (PAF) –a "measure to estimate the proportion of cases that are attributed to a given exposure"– among healthcare professionals. (2) Thus, considering the contribution of each of these risk factors to the incidence of a first AMI event, the hierarchy defined by the ORs was modified since the PAF was 1) 49.2% for an elevated ApoB/ApoA1 ratio; 2) 35.7% for smoking; 3) 17.9% for history of arterial hypertension; and 4) 3.9% for diabetes. Same data, but different information: on the one hand, a more "clinical-related" perspective and, on the other hand, an epidemiological-related perspective. The epidemiological perspective is used to understand population health problems, evaluate the results of the actions (or lack of actions) and propose improvements.

The epidemiological approach has had some relevant milestones in our country and in the region, such as the publications of the CARMELA Study (3,4) and the National Survey of Risk Factors conducted as from 2005 by the National Ministry of Health, with the last edition in 2019. (5) Based on them, all healthcare stakeholders have been able to understand the relevance of the different health problems in our country.

From the healthcare approach, smoking is one of the conditions primarily evaluated by physicians when stratifying risk, according to the guidelines. (6) Likewise, we are challenged by this issue due to the levels of smoking which are likely high among physicians, as shown in the TAMARA I and II studies (7, 8) conducted by the Council on Epidemiology and Cardiovascular Prevention and the Research Area of the Argentine Society of Cardiology.

In this regard, the Bolzán et al.'s study (9) published in this issue of the Argentine Journal of Cardiology is an example of the relevance of the epidemiological information. Based on local data, this study provides evidence on the magnitude of smoking as a contributing factor to mortality in related chronic noncommunicable diseases, such as cancer, cardiovascular and respiratory diseases. By applying an approach based on smoking prevalence, the authors used the publicly available databases of the National Survey of Risk Factors (conducted between 2005 and 2018) in the Province of Buenos Aires (one of the most populated districts of the Argentine Republic) and applied the concept of the population attributable fraction, that is, *the proportion of fatal cases in 19 smoking-related diseases (cancer, cardiovascular and respiratory diseases) that could be avoided if smoking was eliminated*. A decrease in smoking prevalence was observed (an absolute reduction of 6.4% and a percentage reduction of 21.7%). However, smoking remains responsible for 23.1% of all deaths caused by related diseases. The study explores the differences between genders and age groups. For example, in the specific case of cardiovascular disease, mortality attributable

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to tobacco consumption decreased in both men and women aged between 35 and 64 years and increased in men and women aged 65 years and older. The authors appropriately emphasize that women aged 65 years or older were the group with the highest increase in smoking in the Province of Buenos Aires.

In conclusion, this study allows us to objectively state that there still remains work to be done. This involves all the healthcare system stakeholders. Considering that the efforts made at the healthcare centres (hospitals, clinics) are only a part of the healthcare continuum, we should emphasize the pending tasks regarding contributions from the health financing sector and the authorities in order to strengthen the necessary resources and implement policies to address this health problem. (10)

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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ORIGINAL ARTICLE

Use of the Pharmacoinvasive Strategy in Argentina. ARGEN-IAM ST Registry Analysis

Utilización de la estrategia farmacoinvasiva en Argentina. Análisis del registro ARGEN-IAM ST

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ABSTRACT

Background: Primary percutaneous coronary intervention (PPCI) is the treatment of choice for acute ST elevation myocardial infarction (STEMI). In Argentina, a country with a large area and suboptimal reperfusion times, the pharmacoinvasive (PI) strategy might be considered.
Methods: ARGEN-IAM-ST is a national prospective, multicenter, and observational registry that includes STEMI patients with less than 36 hours of progression. The PI strategy usage and its associated variables were defined.
Results: In this registry, 4788 patients were analyzed, of which 88.56% underwent PPCI, 8.46% received thrombolytics with positive reperfusion (TL+), and only 2.98% received PI strategy.
Median and interquartile range (IQR) of total ischemia time were lower in patients receiving TL+ (165 min, IQR 100-269) and PI (191 min, IQR 100-330) than in patients undergoing PPCI (280 min, IQR 179-520), p <0.001.
No differences in intra-hospital mortality were observed: 4.9% in the PI strategy group, 5.2% in the TL+ group and 7.8% in the PPCI group (p = 0.081). No differences in major bleeding events were observed.
It was observed that 57% of the TL+ patients met the criteria for high cardiovascular risk, but they did not receive PI strategy, as recommended.
Conclusions: Only 3 out of 100 reperfused STEMI patients received PI strategy. Its administration is not systematically associated to high cardiovascular risk.
Despite the under-usage, it remains an option to be considered due to its total ischemia time lower than in the PPCI, with no increase in clinically significant bleedings.

Key words: Myocardial infarction – ST-elevation myocardial infarction – Mortality – Reperfusion – Thrombolytics - Angioplasty

RESUMEN

Introducción: La angioplastia primaria (ATCp) es el tratamiento de elección para el infarto agudo de miocardio con elevación del segmento ST (IAMCEST). En nuestro país, de tanta extensión territorial y con tiempos a la reperfusión subóptimos, la estrategia farmacoinvasiva (Finv) podría considerarse.
Material y métodos: El ARGEN-IAM-ST es un registro prospectivo, multicéntrico, nacional y observacional. Se incluyen pacientes con IAMCEST dentro de las 36 horas de evolución. Se definió en el mismo la utilización de Finv y las variables asociadas.
Resultados: Se analizaron 4788 pacientes de los cuales en el 88,56 % se realizó ATCp, en el 8,46 % trombolíticos con reperfusión positiva (TL+), y solo en un 2,98% Finv.
La mediana y rango intercuartílico (RIC) del tiempo total de isquemia fueron menores en aquellos que recibieron TL+ (165 min, RIC 100-269) y los que fueron a Finv (191 min, RIC 100-330) que en aquellos que fueron a ATCp (280 min, RIC 179-520), p<0,001.
No existieron diferencias en mortalidad intrahospitalaria, en el grupo Finv 4,9%, 5,2% en el grupo TL + y en el grupo ATCp 7,8% (p= 0,081). No hubo diferencias en término de sangrados mayores.
Se observó que un 57% de los pacientes con TL+ reunían características de alto riesgo, y no recibieron Finv acorde a lo recomendado
Conclusiones: Solo 3 de cada 100 pacientes con IAMCEST que se reperfunden reciben Finv. Su implementación no está ligada en forma sistemática al alto riesgo de eventos.
Pese a esta subutilización, por presentar un menor tiempo total de isquemia que la ATCp, sin aumento en los sangrados clínicamente relevantes persiste como una opción a considerar en nuestra realidad.

Palabras clave: Infarto de miocardio - Infarto de miocardio con elevación del ST - Mortalidad - Reperfusión - Trombolíticos - Angioplastia

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INTRODUCTION

Cardiovascular diseases, particularly acute myocardial infarction (AMI), are the first mortality cause in our country and worldwide. Its acknowledgement and the standardization of treatment has a great effect on reducing associated morbimortality. (1-4)

In 2015, the Argentine Society of Cardiology (SAC) and the Argentine Federation of Cardiology (FAC) launched ARGEN-IAM-ST, the National Registry of ST elevation myocardial infarction (STEMI) to reveal the delays in the diagnosis and treatment of this disease, and the treatment modalities.

Published analysis show that 88.5% of STEMI patients received reperfusion therapy, but the administration time is far from ideal. (5) Only 35% of patients underwent primary percutaneous coronary intervention (PPCI) with a door-to-balloon time lower than 90 minutes. (6)

Some possible causes are the transfer to centers with hemodynamic services, the large distances to those centers, the lack of networks for diagnosis and treatment of STEMI and the lack of diffusion of warning guidance in population, all of which lead to consultation delays. At the same time, AMI diagnosis is a challenge in centers without on-call cardiologists.

In this context, the pharmacoinvasive (PI) strategy, defined as that in which a PCI is performed within the first 24 hours in patients who received fibrinolytic treatment and progressed with positive reperfusion criteria, has shown benefits in the STREAM (7) study on the prevention of reinfarction and recurrent ischemia, and reduction of infarction size, but no decrease in mortality in relation to PPCI at 30 days and 1 year. (8,9) In recent European registries with a longer follow-up period (3-5 years), a difference in mortality in favor of the PI strategy has been established compared to patients who waited more than 120 minutes to access to a PPCI. The longer the door-to-balloon time for these patients, the better the observed benefit on mortality in favor of the PI strategy. (10,11)

Therefore, the PI strategy may be considered valid in the context of large distances and multiple centers without hemodynamic resources to decrease reperfusion times using coordinated care networks.

The difference between door-to-needle and door-to-balloon times is a key factor to determine the success of the PI strategy, (12,13) as observed in said European registries.

However, the usage rate of this strategy in our country is low, (5) despite the fact that it is indicated by the Argentine Consensus Statement for ST-elevation acute coronary syndrome in a subgroup of patients defined as "high-risk" if they meet at least 1 of the following criteria: (14)

- Heart rate >100 bpm
- Systolic blood pressure <100 mm Hg
- Extensive AMI
- Inferior AMI with right ventricle involvement
- Previous AMI
- Left ventricular ejection fraction <35%
- Killip and Kimball ≥ II
- Complete left bundle-branch block

Therefore, the purpose of this study was to examine the distinctive characteristics of the PI strategy in our country and its correlation with the patient's risk (selective pharmacoinvasive strategy).

METHODS

ARGEN-IAM-ST is a national prospective, multicenter, observational, and transversal registry. (15)

It includes STEMI patients with less than 36 hours of progression, and, to date, 6775 patients have been enrolled. This analysis included 5989 patients enrolled up to May 2022.

We performed a descriptive analysis of the characteristics of the population treated with the PI strategy, the reported times to treatment, its indication and the results obtained, and compared it to PPCI and thrombolysis with positive reperfusion criteria (TL+). We also analyzed its indication in relation to patient's risk according to the SAC Consensus criteria on STE-ACS. Patients who were not reperfused and those treated with rescue PPCI, or other late reperfusion types were excluded.

Statistical analysis

Qualitative variables are shown as frequencies and percentages with their corresponding confidence intervals (CI 95%). For quantitative variables, means ± standard deviation (SD) or median and interquartile range (IQR) were used according to its distribution. The analysis of qualitative variables was performed with the chi-square test or the Fisher test, as applicable; the analysis of continuous variables was performed with the t-test or Kruskall-Wallis test for non-matched data or through the analysis of variance (ANOVA), as applicable. For the analysis, Stata 13.0® was used and a p-value <0.05 was considered significant.

Ethical considerations

The protocol was approved by the SAC Ethics Committee and registered at clinicaltrials.gov under the number NCT2458885.

RESULTS

As of May 2022, a total of 5989 patients were enrolled, of which 4788 were analyzed after excluding patients who were not reperfused and those who underwent rescue angioplasty or other types of late revascularization.

Within this group, only 143 patients underwent PI strategy as reperfusion therapy (2.98%), whereas most patients were treated with PPCI (n = 4240, 88.56%), and the remaining 405 patients (8.46%) with TL+.

Characteristics are described in Table 1.

Patients who underwent PI strategy were significantly younger, more frequently smokers, and less hypertensive than those who underwent PPCI. Median (IQR) time from onset of pain to consultation was 90 min (48-180), higher than the group that only received fibrinolytics (60 min) and lower than the PPCI group (115 min) (p <0.001) (Table 2).

Median door-to-needle time in the PI strategy

group was 45 min (IQR 30-90), while door-to-balloon time in the PPCI group was 98 min (IQR 53-180) (p <0.01).

A lower total ischemic time (TIT) was observed in patients who received thrombolytics, with a median (IQR) of 165 min (100-269), and in those who underwent PI strategy (191 min, IQR 100-330) compared to PPCI patients (280 min, IQR 179-520), p <0.001.

Based on the above data, there are 89 minutes of difference in total ischemic time (TIT) in favor of patients who received PI strategy compared to those treated with PPCI.

It is worth noting that analysis of PPCI door-to-balloon time includes 38% of patients who required referral to PPCI, and a remaining 62% who had a consultation in centers with hemodynamics services (Table 1). If we analyzed the TIT of the 38% of the patients who were transferred, the median TIT was 435 minutes (260-778), therefore the difference in time to PI strategy would be 244 minutes in this group.

In our analysis, no significant differences were observed in mortality as regards the adopted reperfusion strategy. When considering the subgroup of patients who underwent PPCI with more than 120 minutes of door-to-balloon time, while no significant differences were observed in intra-hospital mortality, development of cardiogenic shock and heart failure, there was a trend favoring the PI strategy.

Bleeding rate in the PI strategy group was 7.6%, with a significant difference compared to PPCI, 2.5%. However, this difference was due to minimal bleedings rather than major ones (Table 3).

No significant differences were observed when choosing the reperfusion strategy according to patient's clinical risk. Out of the enrolled patients, 58% met the criteria for high clinical risk and 49% of them were transferred for reperfusion treatment, mainly PPCI (73%), while only 3% received PI strategy.

At the same time, within the group of TL+ patients, more than a half was transferred to other fa-

Table 1. Patients' characteristics

	PI (n = 143)		TL+ (n = 405)		PPCI (n = 4,240)		p
	n	%	n	%	n	%	
Male	104	73	222	55	2756	65	<0.001
Age (mean ± SD)	58 ± 11		58 ± 10		61 ± 12		0.001
HTN	74	52	230	57	2459	58	0.007
DM	28	20	68	17	975	23	0.002
Smoking status	94	66	238	59	1780	42	<0.001
DLP	47	33	3	33	1865	44	<0.001
Previous AMI	14	10	48	12	466	11	0.779
Previous PCI	47	33	77	19	1229	29	0.017
Previous CABG	-		6	1,7	50	1.2	0.241
Previous stroke	-		-		8	0.2	0.810
Peripheral vascular disease	-		-		8	0.2	0.782
CKD	-		-		1	0.01	0.901
High-risk patients	93	65	231	57	2586	61	0.126
Patient referred from another center	109	76	227	56	1611	38	0.001

AMI: acute myocardial infarction; CABG: coronary artery bypass grafting; CKD: chronic kidney disease; DM: diabetes; DLP: dyslipidemia; HTN: hypertension; PI: pharmacoinvasive strategy; PPCI: primary percutaneous coronary intervention; SD: standard deviation; TL+: thrombolyzed with positive reperfusion criteria.

Table 2. Analysis of times as per the strategy used

	PI (n=143)	TL+ (n= 405)	PPCI (n=4240)	p
Time from pain to consultation	90 (48-180)	60 (30-150)	115 (50-240)	<0.001
Time to reperfusion (needle-balloon)*	45 (30-90)	65 (35-127)	98 (53-180)	<0.001
Total ischemia time	191 (100-330)	165 (100-269)	280 (179-520)	<0.001
Patients with pain-consultation time >120 min, n (%)	68 (48%)	251 (62%)	2586 (61%)	0.2

*: For the PI strategy group and the TL group, this time corresponds to door-to-needle time. For the PPCI group, this time corresponds to door-to-balloon time.
Times are expressed in minutes with median and interquartile range (IQR).
PI: pharmacoinvasive strategy; PPCI: primary percutaneous coronary intervention; TL+: thrombolyzed with positive reperfusion criteria.

cilities, and a similar proportion (57%) of patients met the criteria for high risk. None of these two variables affected the PI strategy selection.

DISCUSSION

PI has a class I-A indication in the European guidelines for myocardial infarction (16) and the American guidelines recommend it with a class II indication and level of evidence B, although the concept of transferring all thrombolyzed patients to a center with hemodynamics is not prioritized. (17) Our national guidelines indicate it with a class I-B recommendation, especially in patients at high clinical risk, based on the risk criteria presented in the CARESS-IN-AMI study. (18) However, usage rate of this strategy is very low (below 3%) and has not changed since the beginning of this registry. If we only consider reperfused patients, there is also no difference in the usage rate of the PI strategy in relation to the total sample (only 3% high-risk patients received pharmacoinvasive strategy). Delays associated with the intrahospital care system due to multiple barriers are predictors of poor prognosis in patients with coronary syndrome. (19)

As regards the times, previous data obtained in our registry show that the TIT of a patient transferred to another center for a primary angioplasty is 350 minutes, more than double compared to patients that might initiate a therapy with thrombolytics in their center of origin (50 minutes door-to-needle and 170 minutes TIT)). (20)

In our analysis, door-to-needle time for the PI strategy group was 45 minutes, with 191 minutes of TIT, a difference of 244 minutes compared to the TIT of a patient who required a transfer for PPCI.

Considering this data and what has been observed in international registries, PI therapy might have an important role in our population.

When analyzing possible reasons for this underusage, we observed there is a high percentage (56%) of thrombolyzed patients with positive criteria who are transferred to tertiary healthcare centers; however, they do not receive pharmacoinvasive therapy. This evidences that access to a potential transfer would not be a barrier hindering access to PI strategy.

In addition, acknowledgement of high-risk patients does not affect decision-making. Just over a half of the patients met high-risk criteria, and 49% of them required transfer to be reperfused, especially with PPCI. These patients might benefit from a PI strategy.

The high-risk patients present heterogeneous definitions and prognoses in the different studies that evaluated them (18,21,22). In our registry, the mortality of this subgroup of patients is higher than those who do not belong to the high-risk profile. This finding is supported by significant differences among patients undergoing PPCI and thrombolytics. However, in the PI strategy group, mortality of high-risk patients is not significantly higher than that in the rest of patients, probably due to the number of enrolled patients.

Based on the foregoing, usage or non-usage of PI strategy seems to be explained by a random criterion of certain centers that may have established this strategy as routine compared to centers in which this strategy has not been adopted.

There is a lack of benefit observed in patients with pain-consultation time >120 min and the absence of significant differences in HF and shock incidence during hospitalization, but still a trend favoring this group, indicating the strategy is safe and beneficial. However, the issues mentioned above may be explained by an insufficient sample of patients receiving PI strategy.

As a result, no clear barriers appear to be identified to increase the usage of this strategy beyond its diffusion. Our analysis may be relevant in this context where a selection bias seems to be inexistent.

Regarding the increase in bleeding, whereas a difference against the PI strategy is observed, the bigger

Table 3. Intra-hospital events

	PI (n=143)	TL + (n = 405)	PPCI (n = 4,240)	p
HF, n (%)	41 (29)	109 (27)	1,314 (31)	0.6
Cardiogenic shock, n (%)	24 (17)	81 (20)	932 (22)	0.5
Mortality, n (%)	7 (5)	21 (5.2)	334 (7.9)	0.081
Mortality of pain-consultation time >120 min, n (%)	4 (3)	27 (6.7)	349 (8.24)	0.2
Mortality in high-risk patients	8 (6)	33 (8.26)	483 (11.4)	0.126
Major bleeding	1 (0.7)	6 (1.5)	38 (0.9)	0.45
Bleeding, %				
Total	7.6%	3.6%	2.5%	0.002
Minimal	80%	57%	12.5%	

HF: heart failure; PI: pharmacoinvasive strategy; PPCI: primary percutaneous coronary intervention; TL+: thrombolyzed with positive reperfusion criteria.

risk is due to bleedings defined as minimal.

For this reason and as a first experience analyzing the PI strategy usage in our country, we believe the data obtained may be useful for planning new studies in order to further analyze this issue and promote the actual usage of this strategy in our context.

There are some limitations: ARGEN-IAM-ST registry is a study with voluntary participation; thus, it does not represent the overall situation in the country. It includes participating sites that are mostly affiliated to scientific associations. From another point of view, those non-participating low-complexity low-income sites might have even more difficulties to reach the adequate reperfusion times, and this might result in larger clinical advantages by using the PI strategy. In addition, the number of patients who received PI strategy is low and this may affect the external validity of the results. However, the trend towards fewer ischemic complications than in the PPCI group and the higher risk of bleeding, but minor bleeding, should be highlighted. Moreover, the thrombolytic agent used in the vast majority of referenced registries and papers is tenecteplase (TNK), not available in Argentina.

CONCLUSION

Only 3 out of 100 reperfused patients received PI strategy. Despite the high risk criteria to benefit from this strategy are established and recommended in our national guidelines, it is underused.

Its implementation is not systematically related to high-risk patients, as more than a half of patients who received thrombolytics have not underwent PI strategy, despite having been transferred to other facilities and belonging to a high-risk population.

Despite the under-usage, as the TIT in the PI strategy group is lower than in the TPCA group, the PI strategy remains an option to be considered in our context. It has shown to be a safe strategy with no increase in the number of clinically significant bleeding, and promising for its clinical benefits for patients who cannot reach adequate times for a primary angioplasty.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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ORIGINAL ARTICLE

Cardiovascular Risk Profile in Women from Three Different Areas of the Province of Tucumán, Argentina

Perfil de riesgo cardiovascular en mujeres de tres entornos de la Provincia de Tucumán - Argentina

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ABSTRACT

Background: The role of the environment on female population health in Tucumán has been little studied. This study aimed to evaluate the cardiovascular risk profile in women from rural, peri-urban and urban areas in the province of Tucumán (Argentina) and to analyse their differences.
Methods: An analytical cross-sectional study was conducted in 3 groups of women from Tucumán: rural (n = 125), peri-urban (n = 50) and urban (n = 112).
Results: Blood pressure (BP) was lower in the rural group; the urban group showed higher heart rate and smaller neck circumference. Of the studied women, 29.7% were overweight and 42.4% obese, and no significant differences were found in the 3 groups. Increased neck circumference was observed in 62% of women in the rural group, 79% in the peri-urban group and 41% in the urban group (p <0.001). Smoking was more frequent in the urban group. In the urban and peri-urban groups, the proportion of women with higher education level was greater (p <0.001). Education level was positively correlated with heart rate.
Conclusion: Regardless of the environment, women from Tucumán are overweight or obese and have other risk factors for cardiovascular disease. This should be considered when planning policies and making decisions in order to improve their prognosis.

Keywords: Cardiovascular Disease - Women - Environment

RESUMEN

Introducción: El rol del entorno sobre la salud en la población femenina de Tucumán está poco estudiado. El objetivo del presente trabajo fue evaluar el perfil de riesgo cardiovascular de mujeres de los entornos rural, periurbano y urbano de la provincia de Tucumán (Argentina).
Material y métodos: Se efectuó un estudio analítico transversal en 3 grupos de mujeres de Tucumán: rural (n=125), periurbano (n= 50) y urbano (n=112).
Resultados: La presión arterial (PA) fue menor en el grupo rural; el grupo urbano presentó mayor frecuencia cardíaca y menor circunferencia de cuello. El 29,7% de las mujeres presentaron sobrepeso y el 42,4% obesidad, sin diferencia significativa entre los 3 grupos. La circunferencia de cuello estuvo aumentada en el 62% de las mujeres del grupo rural, 79% del periurbano y 41% del urbano (p<0,001). El grupo urbano presentó más frecuentemente tabaquismo. En los grupos urbano y periurbano fue mayor la proporción de mujeres con estudios superiores (p <0,001). El nivel educativo se correlacionó positivamente con la frecuencia cardíaca.
Conclusiones: Independientemente del entorno las mujeres de Tucumán presentan sobrepeso u obesidad asociados a otros factores de riesgo para enfermedad cardiovascular. Ello debe ser tenido en cuenta para la elaboración de políticas y la toma de conductas a fin de mejorar su pronóstico.

Palabras claves: Enfermedades Cardiovasculares - Mujeres - Entorno

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide (1) and in Argentina. (2) The so-called "social gradient" (decrease in mortality and morbidity rates as social status increases) (3) has already been shown to occur in a wide range of conditions, including CVD. (4)

In urban areas, population has easier access to health services, but environmental factors, such as pollution, noise, and daily stress, affect the cardiovascular health. (5) The peri-urban areas have the disadvantage of being a transitional and unstable territory in terms of social networks, which is associated with increased cardiovascular risk. (6,7) In addition, it has been conventionally described that the prevalence of CVD is lower in rural areas. (8) However, this concept is changing, (9) since a high prevalence of overweight was observed in different indigenous communities. (10,11) In Argentina, a 38% prevalence of metabolic syndrome has been found in the Toba community (indigenous people living in central Chaco). (12) More recently, we have found that the Quilmes community (rural indigenous people living in the middle and high mountains who still preserves pre-Inca traditions) in Tucumán has a prevalence of risk factors for CVD similar to that in urban areas. (13)

The province of Tucumán, located in northwestern Argentina, with an area of 22 525 km^2, has rural areas with difficult access, densely populated urban areas (the capital city has 605 000 inhabitants in 91 km^2) and strings of peri-urban areas surrounding the cities. In the urban and peri-urban areas of Tucumán, according to data from the National Institute of Statistics and Censuses (Instituto Nacional de Estadísticas y Censos, INDEC), the poverty rate was 42.7% in the second quarter of 2022. (14) However, the impact of the environment on CVD risk factors in women is still being studied. This view is consistent with the worldwide literature which indicates that there is a dichotomy between real and perceived CVD risk in women. (15,16)

This study aimed to evaluate the cardiovascular risk profile in adult women from rural, peri-urban and urban areas of the province of Tucumán (Argentina) and to analyse their differences.

METHODS

An analytical cross-sectional study conducted in 3 population groups of women from different areas of Tucumán.

- Rural group: Women from Quilmes, a middle and high mountain area where pre-Inca traditions are still preserved, who participated in the Sonqo Calchaquí 2018 study (13) (n = 125).

- Peri-urban group: Women from Villa Muñecas, a peripheral neighbourhood located 3 km away from the city, who participated in a cardiovascular health activity organized by the Argentine Society of Cardiology (Sociedad Argentina de Cardiología, SAC), Tucuman District, on Women's Day in March 2021 (n = 50).

- Urban group: Women living in the city of San Miguel de Tucumán and performing desk jobs at the Municipality, who underwent a cardiovascular health registry in September 2019 (n = 112).

In this study, the following variables were assessed:

- Age: Expressed in years.

- Education level: Expressed as completed level (illiterate, primary school, secondary school or higher education).

- Presence of the following CVD risk factors: Smoking, dyslipidemia, hypertension (HT) or diabetes. Women were asked about the presence of said risk factors. A semiquantitative score was made according to the number of risk factors mentioned (0 to 4).

- Salt added to cooked food.

- Weight (kg): It was measured with a digital scale.

- Height (cm): It was measured with a portable height rod.

- Neck circumference (cm): It was measured with a non-expandable measuring tape. It was considered increased when it was greater than 34 cm. (17)

- Waist circumference (cm): It was measured with a non-expandable measuring tape. It was considered increased when it was greater than 88 cm. (17)

- Body mass index (BMI): It was calculated as weight in kg/(height in m^2. Women were classified according to their nutritional status as follows: underweight (BMI <18.5); normal weight (BMI ≥18.5 and <25); overweight (BMI ≥25 and <30); obesity (BMI ≥30 and <35); severe obesity (BMI ≥35 and <40); and morbid obesity (BMI ≥40).

- Systolic blood pressure (SBP) and diastolic blood pressure (DBP) values were expressed in mmHg: It was measured with an Omron 7120® automatic digital sphygmomanometer according to the applicable guidelines. (18) Pulse pressure (PP) was calculated as SBP - DBP and mean blood pressure (MBP) as DBP + (PP/3).

- Heart rate and O2 saturation were measured with an An Mat® pulse oximeter.

Statistical Analysis

The results were compiled in a Microsoft Excel 2010 spreadsheet and expressed as percentage (%) or mean ± standard error, as required. The statistical analysis was performed with GraphPad Prism 5.02 software. Student's t-test, ANOVA with Newman-Keuls' post-test, Pearson's correlation (r) or chi-square test (2) were used, as required. Results were considered significant with a <5% probability (p <0.05).

Ethical Considerations

All participants granted the appropriate oral and written informed consent to participate in this study.

RESULTS

The average age of the studied women was 48.9 ± 0.9 years, with no differences among the 3 groups: (rural: 50.2 ± 1.8 years, peri-urban: 47.7 ± 1.9 years, urban: 48.1 ± 1.0 years, p = NS).

Education level of the studied women is shown in Figure 1. Illiterate women were reported only in the rural group. The percentage of women with higher education level was greater in the urban and peri-urban groups than in the rural group (p <0.001).

Anthropometric and hemodynamic values are shown in Table 1. Weight and height values were lower in the rural group than in the other two groups, but the average BMI was elevated in all the studied population, with no differences among the 3 groups.

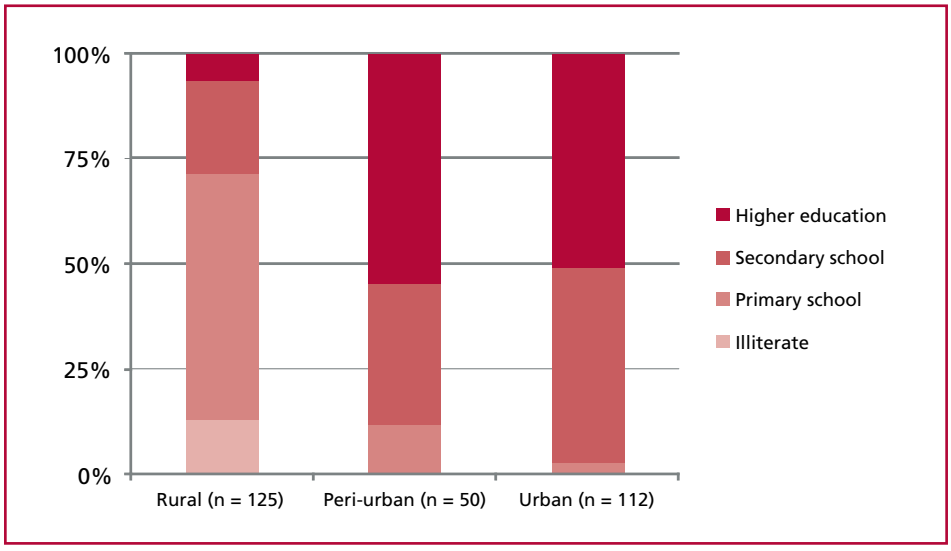


Fig. 1. Education level in the studied population.

Table 1. Anthropometric values in the studied population

	Rural (n = 125)	Peri-urban (n = 50)	Urban (n = 112)	Total (n = 287)
Weight (kg)	68 ± 1	73 ± 2+	78 ± 2***	72.6 ± 1.0
Height (cm)	154 ± 1	160 ± 1***	160 ± 1***	1.6 ± 0.1
BMI	28.5 ± 0.5	28.5 ± 0.8	30.3 ± 0.6	29.3 ± 0.4
Neck circumference (cm)	36.9 ± 0.8	36.1 ± 0.4	34.3 ± 0.4**	35.7 ± 0.4
Waist circumference (cm)	95.6 ± 1.3	97.9 ± 2.0	95.0 ± 1.8	95.8 ± 1.0
BP (mmHg) SBP	123.7 ± 1.9	131.5 ± 2.4**	131.2 ± 1.8***	128.0 ± 1.2
DBP	75.6 ± 0.9	82.8 ± 1.9**	80.7 ± 1.0**	79.1 ± 0.7
PP	44.9 ± 1.4	48.7 ± 2.0	50.5 ± 1.2**	49.0 ± 0.8
MBP	90.5 ± 1.2	99.0 ± 1.9***	97.6 ± 1.2***	94.7 ± 0.8
Heart rate (bpm)	76.4 ± 1.2	78.4 ± 1.1	79.0 ± 1.1*	77.6 ± 0.7
O2 saturation (%)	94.9 ± 0.3	97.0 ± 0.2***	97.3 ± 0.2***	96.7 ± 0.2

BMI: body mass index; DBP: diastolic blood pressure;
MBP: mean blood pressure; PP: pulse pressure; SBP: systolic blood pressure.
Values are expressed as mean ± standard error.
*: p <0.05 vs. rural; **: p <0.01 vs. rural; ***: p <0.001 vs. rural; +: p <0.05 vs. urban.

Neck circumference was smaller in the urban group, but waist circumference was similar in the 3 groups. Although SBP and DBP values, on average, remained within the normal rank, they were higher in the peri-urban and urban groups than in the rural group, and PP values were higher in the urban group than in the peri-urban group. Heart rate values were also higher in the urban group, and O2 saturation was lower in the rural group.

When nutritional status was evaluated, 27.9% of women showed normal weight; 29.7% was overweight and the remaining 42.4% had some level of obesity (26.5% obesity; 10.6% severe obesity and 5.3% morbid obesity). No underweight women were found. The nutritional status distribution was similar in the 3 groups (p = NS).

Increased neck circumference was observed in 62% of the women in the rural group, in 79% in the peri-urban group and in 41% in the urban group (p <0.001) and increased waist circumference was observed in 69% of the studied women, with no significant differences among the 3 groups.

The number of risk factors for CVD, according to the semiquantitative score, was higher in the urban group (Figure 2A). The proportion of women with no risk factor was higher in the rural group (53%) than in the peri-urban (44%) and urban (33%) groups (p <0.001). When each risk factor was analysed separately, HT was the most prevalent (30%), followed by dyslipidemia (25%), smoking (23%) and diabetes (6%). The urban group reported a higher percentage of smoker women (p <0.001). Similar percentages for

the other risk factors were found in the 3 groups (Figure 2B).

Addition of salt to cooked meals was observed in 47% of women. There were no significant differences regarding this in the 3 groups.

A positive correlation was found between neck and waist circumferences (r 0.65; 95% CI: 0.57-0.71; p <0.001). At the same time, neck and waist circumferences were positively correlated with BMI, the number of CVD risk factors and blood pressure (BP) (Table 2).

Education level was positively correlated with heart rate (r 0.21; 95% CI 0.09-0.31; p <0.001) and O2 saturation (r 0.38; 95% CI 0.27-0.47; p <0.001) and negatively correlated with neck circumference (Figure 3) and PP (r -0.1470; 95% CI: -0.26 to -0.03; p <0.05). Age was positively but poorly correlated with neck circumference, waist circumference, the number of risk factors, SBP and DBP, but was not correlated with BMI (r: 0.06; 95% CI: -0.05-0.18; p = NS).

DISCUSSION

The main result of this study is that, regardless of the area where the studied women live (rural, peri-urban or urban), they had increased BMI, large waist circumference and high percentage of obesity. When observing the anthropometric values in the 3 populations, women in the rural group showed lower weight;

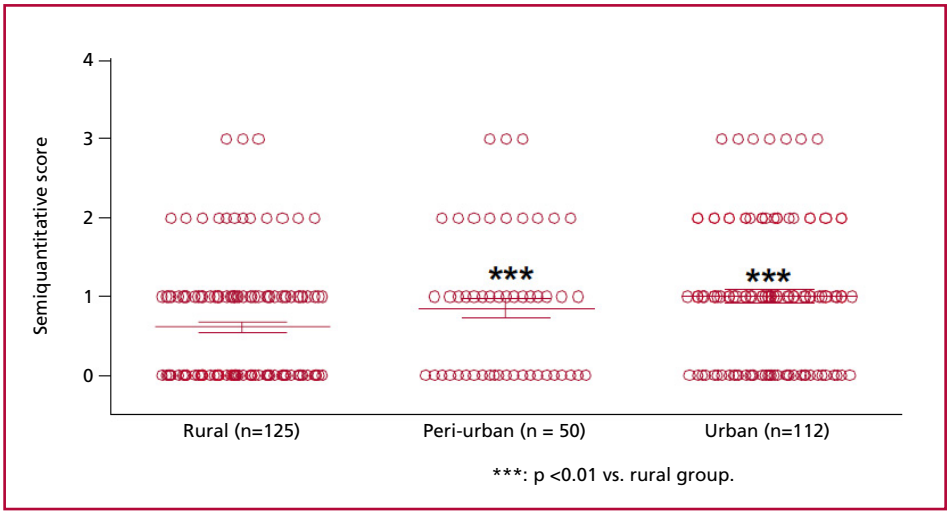


Fig. 2A. Number of risk factors for CVD in the studied groups.

Red dots represent each patient. Blue lines represent the mean ± standard error of each group.

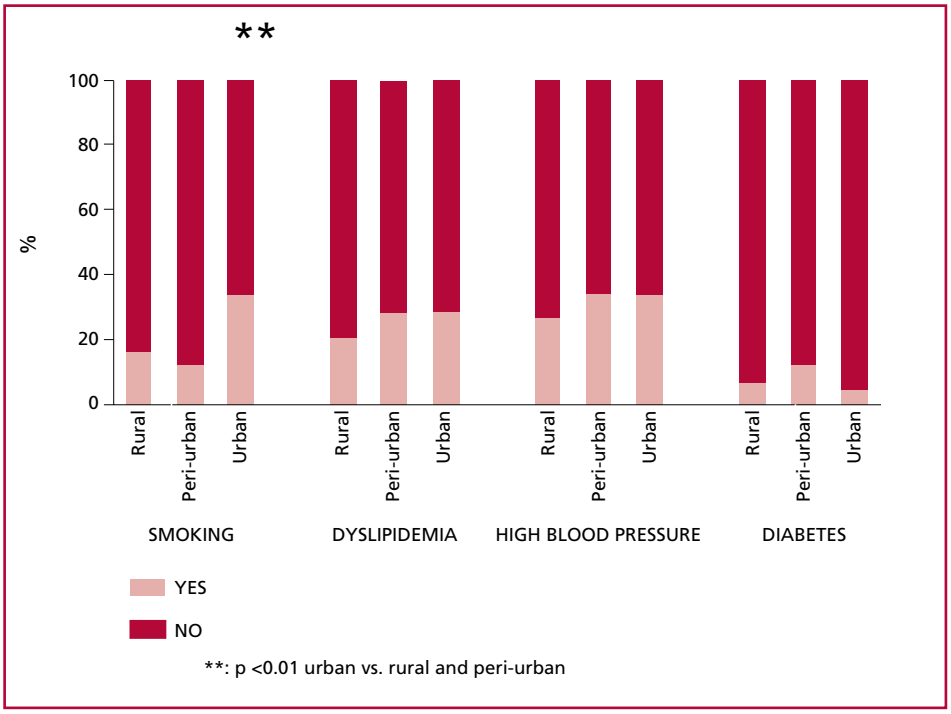


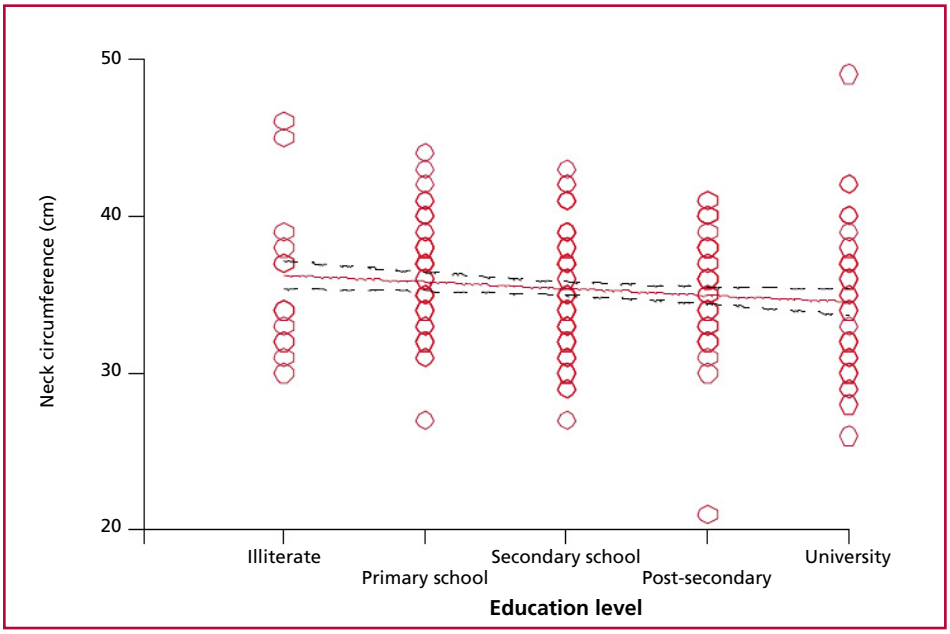
Fig. 2B. Presence of the studied risk factors in each group.

Table 2. Predictors of major cardiovascular events (cardiac surgery/death/acute aortic syndrome)

	Neck circumference	Waist circumference
BMI	r: 0.62 95% CI: 0.54-0.69	r: 0.76 95% CI: 0.71-0.81
Number of risk factors	r: 0.21 95% CI: 0.09-0.32	r: 0.22 95% CI: 0.11-0.33
SBP	r: 0.31 95% CI: 0.19-0.41	r: 0.34 95% CI: 0.23-0.44
DBP	r: 0.31 95% CI: 0.20-0.41	r: 0.34 95% CI: 0.23-0.44
PP	r: 0.19 95% CI: 0.07-0.30	r: 0.21 95% CI: 0.09-0.32
MBP	r: 0.33 95% CI: 0.22-0.43	r: 0.36 95% CI: 0.26-0.46

BMI: body mass index; DBP: diastolic blood pressure; MBP: mean blood pressure; PP: pulse pressure; SBP: systolic blood pressure.
r: Pearson's r coefficient; 95% CI: 95% confidence interval.
In all cases, p <0.001.

Fig. 3. Correlation between the patients' education level and the neck circumference.



Education level: fully completed education level. Pearson's r: -0.13; 95% CI: -0.25 to -0,01; p <0.05.

however, as they also were smaller in height, they had a BMI similar to that of the other two groups, suggesting that these differences could be racial rather than nutritional.

It should be noted that 42.4% of the studied women had some level of obesity. According to the 4th National Risk Factor Survey (Encuesta Nacional de Factores de Riesgo, ENFR), (2) the prevalence of obesity in Argentina was 33.4%, and 26.9% in Tucumán, without discriminating by sex. The level of obesity observed in this study, which is higher than that reported by the ENFR, (2) could be due to the fact that in the rural and peri-urban groups, we studied women who attended health services (which could be biased, since women with a lower BMI may not have attended health services), and in the urban group, we studied women who worked in offices –and therefore had a higher degree of sedentary lifestyle. The high prevalence of obesity is worsened by the fact that 5.3% of women are morbid obese. In addition, the increased waist circumference values indicate central (abdominal) fat distribution. Central obesity is associated with a poor quality diet and lack of physical activity. (19) Furthermore, there is a direct relation between central fat distribution and CVD onset. (20) The presence of central obesity indicates risk for CVD in the studied women, regardless of the area where they live. This view is supported by the fact that neck circumference –although, on average, had not increased– had changed in more than half of the women, and its value

was positively correlated with BMI, waist circumference, BP and a number of CVD risk factors. In this regard, it has been indicated that an increased neck circumference is associated with metabolic alterations (21) and higher mortality, even with normal BMI. (22) Based on the negative correlation between education level and neck circumference, we could assume that higher education level is associated with better diet choice or access to a healthier diet. In this regard, no differences were observed in the addition of salt to food, so the diet of the 3 groups should be investigated in future studies.

Women in urban areas have higher prevalence of smoking, a fact that could dilute the protection suggested by lower values of the neck circumference. In contrast to our findings, in a study conducted in the USA it was found that in urban areas, where the education level is higher, the prevalence of smoking is lower than in rural areas, (23) and in a study conducted in China it was observed that education level was inversely related to smoking. (24) The positive association between heart rate and education level suggests greater stress in women with a higher level of education, a fact that may be associated with increased smoking in this population. In a population of recycling workers, it was shown that elevated heart rate is associated with a higher degree of stress, (25) and under laboratory conditions it was shown that stress increases cigarette consumption in both men and women. (26)

Historically, regarding CVD risk factors, the prevalence of CVD and diabetes has been higher in urban than in rural populations. (8) Nowadays, this difference is controversial. Decreased survival and increased CVD have been reported in indigenous communities in several areas, including Australia, New Zealand, and the United States. (9) More recently, our working group found that in the Quilmes community, both men and women have a prevalence of CVD risk factors similar to that in urban areas. (13) Interestingly, this trend is replicated in the studied women of this population, which supports the hypothesis raised in the previous paragraphs: regardless of the environment, the levels of obesity and the cardiovascular risk profiles in women are similar.

It should be highlighted, among other points, that the BMI is within the overweight rank in the rural and peri-urban groups and within the obesity rank in the urban group;

neck circumference is higher in the rural and peri-urban groups; the percentage of women without risk factors is higher in the rural group; and smoking is higher in the urban group. However, the fact that the distribution of body fat is similar (central type) in the 3 groups would indicate a high risk for CVD in the entire studied population and a different impact of the risk factors in the 3 groups, which suggests that the preventive approach should also be differentiated.

Furthermore, although BMI did not change with increasing age, we observed a correlation between age and waist and neck circumferences, SBP, DBP, and the number of risk factors. It has been shown that fat body mass increases and lean body mass decreases with aging, (27) which could explain why BMI is maintained over time.

CONCLUSIONS

Regardless of the environment (urban, peri-urban or rural), women in Tucumán are overweight or obese and have other risk factors for CVD, which could significantly affect their cardiovascular health in the future. Although in all cases women should be made aware of the benefits of a healthy diet and preventive lifestyle including weight control, physical activity and stress reduction, in rural and peri-urban areas more emphasis should be given to improve the level of education and access to healthcare systems, while in urban areas the priority is to work on other aspects, such as smoking cessation.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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ORIGINAL ARTICLE

Mortality Attributable to Tobacco Consumption in the Province of Buenos Aires. Estimation from the National Surveys of Risk Factors

Mortalidad atribuible al consumo de tabaco en la Provincia de Buenos Aires. Estimación a partir de las Encuestas Nacionales de Factores de Riesgo

ANDRÉS G. BOLZÁN[1], HANNA FRITZ HECK[1], SILVIA REY[2]

ABSTRACT

Background: Tobacco consumption is the leading cause of death from non-communicable diseases, such as heart disease, lung disease and cancer. Estimating prevalence-based mortality attributed to tobacco consumption is based on prior knowledge of the number of smokers, ex-smokers, and non-smokers in the population. These data derive from the four National Surveys of Risk Factors (Encuestas Nacionales de Factores de Riesgo, ENFR).
Objectives: This study aims to show the burden of mortality due to tobacco consumption in the Province of Buenos Aires in the assessed periods of the four ENFRs (2005, 2009, 2013, 2018).
Methods: Mortality attributable to tobacco consumption was estimated by using a prevalence-based method and assuming the risks associated with smoking in the 19 causes classified as associated with smoking, in accordance with the Cancer Prevention Study II (CPSII). The deaths were grouped into periods equivalent to those relevant to each ENFR. The CSPII attributable fractions were then applied by estimating the absolute deaths and attributable fractions of mortality by cause and groupings: tumours, circulatory diseases and respiratory diseases.
Results: Overall, in persons aged 18 years or older, there was a decrease in smoking prevalence from 29.5% in 2005 to 23.1% in 2018 (an absolute reduction of 6.4% and a percentage reduction of 21.7%). A total of 6293 out of 18 255 deaths from cardiovascular diseases in the four surveys were attributed to smoking, that is, 34.4%, compared to 68% of deaths from tumours and 40.0% of deaths from respiratory diseases.
Conclusion: It is necessary to further strengthen measures to reduce exposure to tobacco.

Keywords: Tobacco - Mortality - Attributable Risk

RESUMEN

Introducción: El consumo de tabaco es la principal causa de defunción por enfermedades no transmisibles como las cardiopatías, las neumopatías y el cáncer. Estimar la mortalidad atribuida al consumo de tabaco dependiente de su prevalencia se basa en el conocimiento previo del número de fumadores, exfumadores y no fumadores en la población. Estos datos provienen de las cuatro Encuestas Nacionales de Factores de Riesgo (ENFR).
Objetivos: El presente trabajo pretende mostrar la carga de mortalidad por consumo de tabaco en la Provincia de Buenos Aires en los períodos de relevamiento de las cuatro ENFR (2005-2009-2013-2018).
Material y métodos: La mortalidad atribuible fue calculada utilizando un método dependiente de la prevalencia, y asumiendo los riesgos asociados al consumo en las 19 causas clasificadas como asociadas al tabaquismo según el estudio Cancer Prevention Study II (CPSII). Las defunciones fueron agrupadas en períodos equivalentes a los relevamientos de cada ENFR. Las fracciones atribuibles del CSPII se aplicaron entonces calculando las defunciones absolutas y atribuibles de mortalidad por causa y sus agrupamientos: tumores, circulatorias y respiratorias.
Resultados: Globalmente, para todas las edades de 18 años y más, se pasó de una prevalencia de tabaquismo del 29,5% en 2005 al 23,1% en 2018 (reducción absoluta de 6,4% y porcentual del 21,7%). De las 18 255 muertes producidas por enfermedades cardiovasculares coincidentes con los cuatro relevamientos, 6293 fueron atribuibles al tabaquismo (34,4%), frente al 68% de las muertes por tumores y el 40% de las muertes de causa respiratoria.
Conclusión: Se hace necesario fortalecer aún medidas para reducir la exposición al tabaco.

Palabras clave: Tabaco - Mortalidad - Riesgo atribuible

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INTRODUCTION

Smoking is one of the leading causes of morbidity and mortality. According to the World Health Organization (WHO), tobacco consumption is the leading cause of death from non-communicable diseases, such as heart disease, lung disease and cancer. (1) Global figures show that tobacco consumption causes more than 7 million deaths each year, of which more than 6 million are smokers and about 890 000 are non-smokers exposed to second-hand smoke. Almost 80% of more than 1 billion smokers in the world live in low- or middle-income countries. (2) In Argentina, more than 44 500 people die annually from smoking-related diseases and these deaths represent 13.2% of all deaths occurring in people older than 35 years, mainly due to cardiovascular diseases, chronic obstructive pulmonary disease (COPD) and lung cancer. (3) Based on the evidence from a large number of studies on the effects of tobacco consumption, several methods have been proposed to measure it and estimate the burden of disease. In our country, four National Surveys on Risk Factors (Encuestas Nacionales sobre Factores de Riesgo, ENFR) have been performed in 2005, 2009, 2013 and 2018, in which, among other aspects, tobacco consumption has been measured based on the population's statements about their status as smokers, non-smokers or ex-smokers. (4-7) Since 1980, the impact estimate of different risk factors on population mortality by applying epidemiological methods has become frequent in Anglo-Saxon countries, mainly in the United States. To estimate mortality attributable to different risk factors, several methods are available, which vary in terms of both data required and acceptance of assumptions. These methods are mainly based on the concept of the population attributable fraction, that is, the percentage of cases that could be prevented if exposure to the risk factor under study was removed. To estimate mortality attributed to tobacco consumption, different calculation processes are identified, (8) which may be classified according to whether they are dependent or independent of smoking prevalence, that is, whether or not smoking prevalence is used to estimate the mortality burden. The application of a prevalence-based method to estimate attributed mortality is based on prior knowledge of the number of smokers, ex-smokers and non-smokers in the population. These data derive from the four ENFRs. The present work aims to show the burden of mortality due to tobacco consumption in the Province of Buenos Aires in the survey periods of the four ENFRs.

METHODS

Mortality attributable to tobacco consumption was calculated by using a prevalence-based method and assuming the risks associated with tobacco consumption according to the Cancer Prevention Study II (CPSII). (9) Two data sources were available for its implementation:

1. Calculation of the prevalence of tobacco consumption: smokers, ex-smokers and non-smokers for men and women by risk age groups: 35-64 years old and 65 years or older. The data sources were the ENFR microdata bases: 2005/2009/2013/2018 from the Instituto Nacional de Estadística y Censos (INDEC; the National Institute of Statistics and Censuses in Argentina). (7)
2. Table of observed mortality by age group and sex according to the cause of death. The database was that containing overall mortality data from 2005 to 2018 reported by the Dirección Provincial de Estadísticas de la Salud (DIS; Provincial Department of Health Statistics) of the Province of Buenos Aires.

Statistical analysis

1. Prevalence of tobacco consumption: the microdata bases of the ENFRs were exported to SPSS (Statistical Package for the Social Sciences) and the prevalences were calculated by the survey year and by risk groups (age and sex). The results published by the INDEC for each ENFR served as control, so that, the overall estimates should be consistent with those published. Point values and confidence intervals were calculated for complex samples by using the weighting factors provided by the database.
2. Observed mortality: DIS's databases were exported to SPSS and deaths by smoking-related cause were calculated according to the risk group (age and sex). The calculation was performed using the following formula:

$$AM = OM*FAP, \text{ where } PAF = [p0 + p1RR1 + p2RR2]-1 / [p0 + p1RR1 + p2RR2]$$

AM means attributable mortality; OM, observed mortality (number of deaths by cause, age and sex); PAF, population attributable fraction; p0, p1, and p2 represent the prevalence of non-smokers, smokers and ex-smokers, respectively; RR1 and RR2 represent the relative risk in smokers and ex-smokers, respectively. Each p value was calculated for each ENFR adjusted for age group and sex.

Variables: 1–Risk groups: Age of 35-64 years and 65 years or older. These categories are established in the CPSII. 2–Tobacco consumption: The document used was that published by the INDEC for the management of the ENFR databases. It classifies tobacco consumption variable into three categories: smoker, ex-smoker, and non-smoker. 3–Cause of death: It was classified according to the International Classification of Diseases (ICD)-10th Revision. Individual data on age, sex and cause of death were assigned for each of the diseases in the CPSII model. Deaths and tobacco consumption prevalences were grouped into four periods equivalent to each ENFR. The CPSII attributable fractions were applied considering those cut-off points. Similarly, specific mortality rates were calculated by risk age group and sex for the total of each set of diseases associated with tobacco consumption: tumours, cardiovascular and respiratory diseases, from the list of tobacco-attributable causes according to the model. The population used as denominator to estimate the overall death rates was based on the demographic projections for the Province of Buenos Aires published by the DIS. This led to observe the evolution of the raw death rates by age group and sex for each annual period evaluated. The statistical softwares Epi Dat 4.2 and SPSS 20 were used.

Ethical considerations

This study considers grouped data. Patients were not individualized

RESULTS

In Table 1, the prevalences of tobacco consumption by sex and age according to each one of the four ENFR estimates are shown. In Tables 2 to 5, absolute deaths and attributable mortality fractions by cause and groupings in persons aged 35 years or older are shown. Overall, there was a decrease in smoking prevalence from 29.5% in 2005 to 23.1% in 2018 (absolute reduction of 6.4%, and percentage reduction of 21.7%). The prevalence of ex-smokers increased from 17.2% in 2005 to 17.7% in 2018; expressed in inhabitants, from 1 673 861 to 1 925 674 (251 813 more). There were 223 925 deaths recorded within the 19 smoking-related causes, 51 890 (23.1%) of which were attributed to smoking. Of these, 36 690 (70%) were men and 15 200 (30%) were women.

The leading cause of death from smoking-related tumours included trachea, lung and bronchi cancer. Among men aged 35-64 years, 90% of tumours were attributed to tobacco; 3688 out of 4090 deaths in the four years analysed were attributed to smoking. As regards laryngeal cancer, 431 out of 507 deaths in the four years analysed were attributed to smoking. In men aged 35-64 years, overall cardiovascular diseases represented 18 255 deaths, 6293 of which were attributed to tobacco consumption (34%). In the case of respiratory diseases in men aged 35-64 years, 1462 out of the 3653 deaths were attributed to tobacco consumption (40%), and in the case of smoking-attributable pneumonia, 673 out of 2696 deaths were attributed to tobacco consumption (24.9%). In this age group and sex, COPD has not modified its incidence or death rates or its attributable fraction. Out of 878 cumulative deaths, 718 (81.7%) were attributed to tobacco consumption. In men older than 64 years, there is a trend towards a reduction in mortality attributable to all smoking-related tumours. Lung, trachea and bronchi cancer produced 6319 deaths in the four cumulative years, 5417 of which were attributed to smoking (85%). Regarding laryngeal cancer, the second tumour with the second highest attributable fraction, 572 out of 717 cumulative deaths were attributed to smoking (79.5%). In the group of cardiovascular diseases in men older than 64 years, 8166 out of 55 114 cumulative deaths were attributed to smoking (14.8%). The largest fraction attributable to smoking was that of aortic aneurysm: 680 out of 1132 deaths (60%). In absolute terms, the highest mortality was observed in the group of other cardiac diseases with accounting for 31230 deaths, 4951 of which were attributed to smoking (15.9%). In the case of respiratory diseases, 5806 out of 17 446 deaths in men older than 64 years were caused by tobacco consumption (33.2%).

In women aged 35-64 years, there was a cumulative total of 4817 deaths from smoking-related tumours in the four years analysed, 2148 of which were directly attributed to smoking (45%). Laryngeal cancer presented the highest PAF: 57 out of 72 deaths in the four years analysed could have been prevented with smoking control. Trachea, lung and bronchi cancer represented 1748 deaths, 1379 of which were attributed to tobacco consumption. Oesophagus tumours and lip and oral cavity cancer presented PAFs near 60%. Smoking-attributable mortality due to heart disease showed a decrease from 2005 (29.1 per 100 000) to 2018 (18.7 per 100 000), a 35.5% reduction. In total, there were 8008 deaths from cardiovascular causes in women aged 35-64 years during the four cumulative years, 2310 of which were attributed to smoking (28%). Cerebrovascular disease shows the highest attributable fraction: 47% (1042 out of 2212 cumulative deaths were attributed to smoking). This was followed by ischemic heart disease (1704 deaths in the four years, 38.2% attributed to smoking). Although the group of other cardiac diseases produced a greater number of deaths, only 13.7% out of 3946 cumulative deaths in the four years analysed were attributed to smoking. As regards smoking-related respiratory diseases in women aged 35-64 years, 37.4% out of 2167 deaths were attributed to smoking. Women aged 65 years or older were the group with the highest increase in tobacco consumption in the Province of Buenos Aires. Among them, death rate resulting from smoking-related tumours has in-

Table 1. Prevalence of tobacco consumption (%) as per the ENFRs performed in the Province of Buenos Aires

	Smoker				Ex-smoker				Non-smoker			
	2005	2009	2013	2018	2005	2009	2013	2018	2005	2009	2013	2018
Both sexes (≥18 years old)	29.5	28	25.8	23.1	17.2	18.5	17.7	20.8	53.3	53.5	56.6	56.1
Males 35-64 years old	35.9	35.9	32.2	29	25.5	26.5	22.9	24.9	38.6	37.6	45	46.1
Males ≥ 65 years old	11.6	15.3	12.3	10.1	50.1	45.9	46.3	51.9	38.3	38.8	41.4	36.4
Overall males	30.6	31.2	27.9	24.3	30.8	30.9	27.9	32	38.5	37.9	44.2	43.8
Females aged 35-64 years	28.4	26.7	24	23.6	14.7	16.4	16.9	17.7	56.9	56.9	59.1	58.7
Females ≥ 65 years old	4.8	7.3	11.2	9.6	8.8	16.6	16.8	19.6	86.4	76.1	72	70.8
Overall females	22.4	21.5	20.5	20	13.2	16.5	16.9	18.2	64.5	62	62.6	61.8

ENFR: Encuesta Nacional de Factores de Riesgo (National Survey on Risk Factors)

Table 2. Mortality attributable to tobacco consumption in males aged 35-64 years. Province of Buenos Aires. ENFR series: 2005, 2009, 2013, 2018

	2005			2009			2013			2018		
	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM
Lips, oral cavity, pharynx cancer	135	0.78	106	128	0.81	103	129	0.79	102	107	0.79	84
Oesophagus cancer	163	0.72	117	141	0.75	106	170	0.73	123	145	0.73	105
Pancreas cancer	214	0.31	65	244	0.34	82	234	0.31	73	255	0.3	78
Larynx cancer	171	0.84	144	120	0.86	104	109	0.85	92	107	0.85	91
Trachea, lung, bronchi cancer	1122	0.9	1005	1044	0.91	949	1070	0.9	962	854	0.9	772
Urinary bladder cancer	76	0.49	37	87	0.52	46	94	0.49	47	84	0.49	41
Kidney and renal pelvis cancer	167	0.41	68	175	0.45	78	198	0.42	83	217	0.42	90
Stomach cancer	236	0.29	68	204	0.32	65	220	0.29	65	224	0.29	66
Acute myeloid leukaemia	57	0.25	14	54	0.28	15	38	0.26	10	50	0.26	13
Tumours subtotal	**2341**		**1624**	**2197**		**1548**	**2262**		**1557**	**2043**		**1340**
Ischemic heart disease	1532	0.41	630	1457	0.45	655	1538	0.42	647	1549	0.42	643
Other cardiac diseases	2033	0.23	458	2121	0.25	536	2036	0.23	471	1910	0.23	438
Cerebrovascular disease	1000	0.42	417	841	0.45	380	894	0.43	380	787	0.41	323
Atherosclerosis	4	0.34	1	4	0.38	2	3	0.35	1	83	0.34	29
Aortic aneurysm	102	0.67	69	105	0.71	74	91	0.68	62	83	0.68	56
Other arterial diseases	18	0.25	5	15	0.28	4	17	0.26	4	32	0.25	8
Cardiovascular diseases subtotal	**4689**		**1580**	**4543**		**1651**	**4579**		**1565**	**4444**		**1497**
Pneumonia	419	0.24	100	718	0.27	192	603	0.24	147	956	0.25	234
Bronchitis, emphysema	17	0.89	15	21	0.91	19	13	0.89	12	28	0.9	25
COPD	229	0.81	185	185	0.83	154	234	0.82	191	230	0.82	188
Respiratory diseases subtotal	**665**		**300**	**924**		**365**	**850**		**350**	**1214**		**447**
Total	**7695**		**3504**	**7664**		**3564**	**7691**		**3472**	**7701**		**3284**

AM: attributable mortality; COPD: chronic obstructive pulmonary disease; ENFR: Encuesta Nacional de Factores de Riesgo (National Survey on Risk Factors); OM: observed mortality; PAF: population attributable fraction

creased concomitantly. If we consider the rates of all smoking-related tumours and we focus exclusively on smoking-attributable death rates, the increased from 49.9 per 100 000 in 2005 to 75.9 per 100 000 in 2018. Out of 8487 deaths from cancer in women aged 65 years or older accumulated in the four years analysed, 2644 were attributed to smoking (31%). Lung, trachea and bronchi cancer resulted in 2560 deaths in women aged 65 years or older in the four years analysed, 1582 attributed to smoking (62%). Death rate resulting from these tumours increased from 51.4 per 100 000 in 2005 to 69.9 per 100 000 in 2018. In the case of lip and oral cavity cancer, there were 261 deaths, 36.3% attributable to smoking. Cardiovascular diseases in women aged 65 years or older represented 64 310 deaths, 4195 attributable to smoking (3.7%).

DISCUSSION

The presumption that tobacco consumption was a risk factor for health emerged in 1920. It was only until 1980 that the grounds for estimating the smoking impact on mortality were made explicit by means of epidemiological methods. (8,10) CPSII is a cohort study conducted by the American Cancer Society which began in September of 1982. (9) CPSII limits the causes of death attributable to smoking to 19 and identifies them under the heading "established causal relationship". Estimation of attributed mortality using a prevalence-based method is the simplest calculation procedure in terms of data availability. This method, the most widely used in the scientific literature to estimate tobacco-attributable mortality, which has been implemented in the CDC's SAMMEC (Smoking Attributable Mortality Morbidity and Eco-

Table 3. Mortality attributable to tobacco consumption in females aged 35-64 years. Province of Buenos Aires. ENFR series: 2005, 2009, 2013, 2018

	2005			2009			2013			2018		
	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM
Lips, oral cavity, pharynx cancer	22	0.62	14	21	0.57	12	24	0.54	13	33	0.55	18
Oesophagus cancer	47	0.73	34	52	0.68	35	61	0.66	40	58	0.67	39
Pancreas cancer	161	0.34	55	206	0.3	61	192	0.28	54	216	0.29	63
Larynx cancer	18	0.83	15	19	0.8	15	17	0.78	13	18	0.79	14
Trachea, lung, bronchi cancer	376	0.82	309	401	0.79	316	509	0.77	393	462	0.78	361
	194	0.19	36	200	0.15	31	209	0.14	30	279	0.15	42
Urinary bladder cancer	20	0.36	7	33	0.32	11	26	0.31	8	29	0.32	9
Kidney and renal pelvis cancer	62	0.1	6	68	0.08	5	86	0.07	6	96	0.08	8
Stomach cancer	121	0.15	18	107	0.13	14	120	0.12	15	111	0.13	15
Acute myeloid leukaemia	41	0.09	4	43	0.09	4	17	0.09	1	42	0.1	4
Tumours subtotal	**1062**		**498**	**1150**		**504**	**1261**		**573**	**1344**		**573**
Ischemic heart disease	391	0.44	172	387	0.38	146	453	0.36	161	473	0.36	172
Other cardiac diseases	979	0.16	158	1067	0.13	142	954	0.12	118	946	0.13	126
Cerebrovascular disease	682	0.53	359	554	0.46	255	479	0.44	208	497	0.44	220
Atherosclerosis	1	0.23	0	2	0.18	0	5	0.17	1	1	0.17	0
Aortic aneurysm	21	0.7	15	27	0.64	17	13	0.62	8	33	0.63	21
Other arterial diseases	8	0.3	2	5	0.25	1	11	0.23	3	19	0.24	5
Cardiovascular diseases subtotal	**2082**		**706**	**2042**		**561**	**1915**		**499**	**1969**		**544**
Pneumonia	234	0.3	70	428	0.25	106	401	0.23	92	613	0.24	145
Bronchitis, emphysema	9	0.84	8	15	0.82	12	10	0.82	8	19	0.83	16
COPD	81	0.84	68	80	0.81	65	117	0.79	93	160	0.8	129
Respiratory diseases subtotal	**324**		**146**	**523**		**183**	**528**		**193**	**792**		**290**
Total	**3468**		**1350**	**3715**		**1248**	**3704**		**1265**	**4105**		**1407**

AM: attributable mortality; COPD: chronic obstructive pulmonary disease; ENFR: Encuesta Nacional de Factores de Riesgo (National Survey on Risk Factors); OM: observed mortality; PAF: population attributable fraction

nomic Cost) software, is commonly used for the serial estimation of tobacco-attributable mortality in the United States, and its use is widely spread. (11,12) To properly estimate and use modelling, it is necessary to know the excess risk of death of those exposed (smokers and/or ex-smokers), data that may be collected from a cohort study. (13) In 2008, the WHO adopted a set of practical and cost-effective measures to strengthen the implementation of the main provisions on demand reduction under the WHO Framework Convention on Tobacco Control (WHO FCTC): the MPOWER measures. Each measure corresponds to at least one provision of the WHO FCTC. (1,2) The six MPOWER measures are the following: •To monitor the consumption of tobacco and the prevention measures. •To protect population from tobacco smoke. •To offer help to people to quit smoking. •To warn of dangers associated with smoking. •To enforce prohibitions on advertising, promotion and sponsorship. •To increase tobacco taxes. It is necessary to strengthen these and other promotion and prevention measures in order to reduce exposure to tobacco. If tobacco consumption could be reduced to zero (obviously an unrealistic but ideal scenario), 19 756 deaths due to tobacco-related tumours, 20 966 deaths related to cardiovascular causes and 11 168 deaths related to pneumonia, bronchitis and COPD would have been avoided in the province of Buenos Aires; in other words, 51 890 deaths occurred in the four years analysed. This represents 23.1% of the total 223 925 deaths derived from the 19 causes attributable to tobacco consumption. In contrast to the analysis focused exclusively on adjusted death rates, smoking-attributable mortality indicates the

Table 4. Mortality attributable to tobacco consumption in males aged >64 years. Province of Buenos Aires. ENFR series: 2005, 2009, 2013, 2018

	2005			2009			2013			2018		
	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM
Lips, oral cavity, pharynx cancer	105	0.63	66	99	0.72	72	135	0.7	94	118	0.7	83
Oesophagus cancer	322	0.63	202	280	0.71	199	280	0.7	195	294	0.71	209
Pancreas cancer	407	0.14	58	472	0.21	100	510	0.19	96	565	0.17	98
Larynx cancer	175	0.75	132	180	0.82	147	186	0.81	150	176	0.82	143
Trachea, lung, bronchi cancer	1541	0.82	1266	1570	0.87	1372	1550	0.86	1338	1658	0.87	1445
Urinary bladder cancer	380	0.36	138	321	0.46	147	318	0.44	140	355	0.45	159
Kidney and renal pelvis cancer	213	0.29	61	250	0.37	94	289	0.35	102	340	0.36	122
Stomach cancer	502	0.2	99	407	0.27	108	384	0.25	97	420	0.26	107
Acute myeloid leukaemia	71	0.16	11	50	0.22	11	76	0.21	16	84	0.2	17
Tumours subtotal	**3716**		**2033**	**3629**		**2250**	**3728**		**2228**	**4010**		**2383**
Ischemic heart disease	3199	0.1	335	2584	0.15	384	2987	0.14	412	3538	0.14	482
Other cardiac diseases	7538	0.13	950	8097	0.18	1462	8233	0.17	1360	7362	0.16	1179
Cerebrovascular disease	2639	0.07	172	2246	0.1	231	2510	0.09	220	2295	0.07	170
Atherosclerosis	166	0.19	32	90	0.27	24	59	0.25	15	68	0.24	16
Aortic aneurysm	318	0.54	171	280	0.64	178	282	0.62	174	252	0.62	157
Other arterial diseases	85	0.09	8	82	0.14	12	80	0.12	10	124	0.1	12
Cardiovascular diseases subtotal	**13945**		**1668**	**13379**		**2291**	**14151**		**2191**	**13639**		**2016**
Pneumonia	2280	0.16	363	2490	0.22	545	3214	0.21	661	5505	0.21	1143
Bronchitis, emphysema	83	0.89	15	70	0.9	63	70	0.9	63	124	0.91	113
COPD	919	0.74	679	638	0.8	514	924	0.79	734	1129	0.81	913
Respiratory diseases subtotal	**3282**		**1057**	**3198**		**1122**	**4208**		**1458**	**6758**		**2169**
Total	**20943**		**4758**	**20206**		**5663**	**22087**		**5877**	**24407**		**6568**

AM: attributable mortality; COPD: chronic obstructive pulmonary disease; ENFR: Encuesta Nacional de Factores de Riesgo (National Survey on Risk Factors); OM: observed mortality; PAF: population attributable fraction

magnitude of the risk factor burden on mortality. (14,15) The PAF magnitude of death due to tobacco consumption continues being a challenge for public health, mainly because of the burden of disease and the demand on health services. (16) Particularly, in America, the estimates of healthcare costs have yielded 33 billion dollars directly, which is equivalent to 0.7% of the Gross Domestic Product of the region. (17) Similarly, tax burden on tobacco industry does not directly cover healthcare costs, which in Argentina have been calculated at 37%. Although the studies are not numerous, they have estimated the burden of attributable mortality in the country (as in the Province of Tucumán) (18) showing that 4.1% of deaths could be attributed to smoking, which is lower than the data recently reported for Argentina (14%). (3) It is necessary to measure the magnitude of the situation by considering the percentage of reduction that could be expected not only for the total number of deaths, but specifically for the causes associated with tobacco consumption, because there, the burden of smoking is clearly more significant. (19,20)

CONCLUSIONS

Prevalence studies like this have important limitations: they assume the risks linearly as weighting factors of a population group, whereas covariables are completely unknown. Similarly, other epidemiological weighting factors are left outside the estimates. The ENFRs have weaknesses since the measurement of habits are self-reported. Nevertheless, in many cases, they are the only potential large models to estimate the burden of disease from recognized risk factors. Mortality attributable to smoking remains high and is unacceptable because there are concrete possibilities

Table 5. Mortality attributable to tobacco consumption in females aged >64 years. Province of Buenos Aires. ENFR series: 2005, 2009, 2013, 2018

	2005			2009			2013			2018		
	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM	OM	PAF	AM
Lips, oral cavity, pharynx cancer	58	0.29	17	57	0.34	19	64	0.4	26	82	0.4	33
Oesophagus cancer	150	0.39	58	135	0.44	60	132	0.51	68	155	0.51	79
Pancreas cancer	527	0.13	68	567	0.15	88	611	0.19	115	673	0.2	132
Larynx cancer	28	0.56	16	18	0.61	11	26	0.67	17	37	0.67	25
Trachea, lung, bronchi cancer	476	0.54	256	605	0.59	357	689	0.66	452	790	0.65	517
Uterine cervix cancer	84	0.05	4	78	0.06	5	71	0.08	6	105	0.09	9
Urinary bladder cancer	121	0.16	20	92	0.19	18	110	0.22	24	100	0.24	24
Kidney and renal pelvis cancer	122	0.02	3	104	0.03	3	150	0.04	6	185	0.05	9
Stomach cancer	273	0.06	17	256	0.07	19	282	0.09	24	254	0.1	25
Acute myeloid leukaemia	61	0.06	3	46	0.07	3	61	0.07	4	52	0.09	5
Tumours subtotal	**1900**		**462**	**1958**		**583**	**2196**		**742**	**2433**		**858**
Ischemic heart disease	2546	0.06	150	2288	0.07	164	2502	0.09	229	3080	0.1	303
Other cardiac diseases	9562	0.05	436	10427	0.06	581	10938	0.07	795	9371	0.08	744
Cerebrovascular disease	3355	0.03	106	2925	0.04	115	2979	0.06	168	2752	0.06	166
Atherosclerosis	356	0.05	16	245	0.06	14	126	0.09	11	117	0.08	10
Aortic aneurysm	89	0.33	30	84	0.38	32	81	0.46	37	102	0.45	46
Other arterial diseases	85	0.08	7	62	0.1	6	85	0.13	11	153	0.13	20
Cardiovascular diseases subtotal	**15993**		**745**	**16031**	**0.09**	**912**	**16711**		**1251**	**15575**		**1289**
Pneumonia	2612	0.08	197	2796	0.72	259	3838	0.13	494	6579	0.13	833
Bronchitis, emphysema	30	0.68	20	24	0.65	17	39	0.75	29	94	0.77	72
COPD	322	0.6	193	283		183	487	0.7	340	638	0.71	451
Respiratory diseases subtotal	**2964**		**410**	**3103**		**459**	**4364**		**863**	**7311**		**1356**
Total	**20857**		**1617**	**21092**		**1954**	**23271**		**2856**	**25319**		**3503**

AM: attributable mortality; COPD: chronic obstructive pulmonary disease; ENFR: Encuesta Nacional de Factores de Riesgo (National Survey on Risk Factors); OM: observed mortality; PAF: population attributable fraction

for its reduction. It is necessary to further strengthen measures to reduce exposure to tobacco.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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ORIGINAL ARTICLE

Acute Coronary Syndromes in High Complexity Centers of Argentina. The ReSCAR Registry

Registro de síndromes coronarios agudos en centros de alta complejidad de Argentina. ReSCAR 2022

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ABSTRACT

Background: We conducted a multicenter registry to analyze the diagnostic and therapeutic approach to all types of acute coronary syndromes; this registry is the first to provide detailed information on conditions without significant epicardial coronary artery disease. Knowing the reality of current medical practice is important to find opportunities for improvement.
Methods: Patients hospitalized for acute coronary syndrome between January and August 2022 in 15 centers of Argentina, with high-sensitivity cardiac troponin, coronary care unit, and catheterization laboratory available 24 hours, were prospectively recorded.
Results: A total of 984 consecutive patients were included, 22.2% with unstable angina, 39.1% with non-ST-segment elevation myocardial infarction (NSTEMI) and 24.1% with ST-segment elevation myocardial infarction (STEMI). Additionally, 4.1% presented as type 2 AMI, 1.2% as myocarditis, 0.7% as Takotsubo syndrome and 8.6% as myocardial infarction with non-obstructive coronary arteries (MINOCA). Median age was 66 years [interquartile range (IQR) 56.5-74] and 75.3% were men. An early invasive management was used in 84% of patients without ST segment elevation, and 76.5% of them had significant coronary artery disease. During hospitalization, 2.84% of the patients presented reinfarction, 2.43% recurrent angina, 2% postinfarction angina and 0.5% stent thrombosis. Bleeding events occurred in 4.4% of the patients, and overall in-hospital mortality was 3.76%.
Conclusions: The registry has a good representation of the spectrum of patients with initial suspicion of "acute coronary syndrome", managed in centers with an invasive initial strategy and with low rate of in-hospital complications and acceptable overall mortality.

Key words: Acute Coronary Syndrome - Myocardial Infarction - Myocardial revascularization - MINOCA

RESUMEN

Introducción: Realizamos un registro multicéntrico para analizar el abordaje diagnóstico y terapéutico de todos los tipos de síndromes coronarios agudos; este registro es el primero en abordar en detalle aquellos cuadros que cursan sin enfermedad coronaria epicárdica significativa. Es importante conocer la realidad del actual accionar médico con el objeto de hallar oportunidades de mejora.
Material y métodos: Se registraron en forma prospectiva pacientes hospitalizados por síndrome coronario agudo en 15 centros de Argentina, con diagnóstico con troponina ultrasensible, servicio de unidad coronaria y hemodinamia disponible las 24 horas, entre enero y agosto de 2022.
Resultados: Se incluyeron 984 pacientes consecutivos, un 22,2% con angina inestable, 39,1% con infarto agudo de miocardio sin elevación del segmento ST (IAMSEST) y 24,1% con infarto agudo de miocardio con elevación del segmento ST (IAMCEST). Por otro lado, el 4,1% se presentó como infarto de tipo 2, 1,2% como miocarditis, 0,7% como síndrome de Takotsubo y 8,6% como infarto de miocardio con enfermedad coronaria no obstructiva (MINOCA). La mediana (rango intercuartílico, RIC) de edad fue de 66 años (56,5-74), con un 75,3 % de pacientes de sexo masculino. El manejo inicial de los pacientes sin elevación del segmento ST fue invasivo en el 84%, con una tasa de enfermedad coronaria significativa del 76,5%. En cuanto a la evolución intrahospitalaria, las complicaciones isquémicas más relevantes fueron el reinfarto (2,84%), angina recurrente (2,4%), angina post infarto (2%) y trombosis intra stent (0,5%). El porcentaje de eventos hemorrágicos totales fue de 4,4% y la mortalidad intrahospitalaria total fue de 3,76%.
Conclusiones: El registro tiene una buena representación del espectro de pacientes con sospecha inicial de síndrome coronario agudo, manejados en centros con una estrategia inicial principalmente invasiva, con una baja tasa de complicaciones hostalarias y una mortalidad global aceptable.

Palabras claves: Síndrome coronario agudo - Infarto de miocardio - Revascularización coronaria - MINOCA

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INTRODUCTION

Acute coronary syndromes (ACS) are mainly made up of the spectrum of patients with epicardial coronary artery disease in whom the index event is secondary to plaque rupture, and are classified as unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). (1) Patients without significant epicardial coronary artery disease may also fall into the ACS spectrum and are divided into different categories; although their etiology and pathophysiology may differ widely, the final event is myocardial injury in all the categories. (2-4)

Over the past few years, several randomized and observational studies have provided new treatments and interventional strategies to address the different types of ACS. However, due to the situation in our region, it is difficult to determine which modalities are implemented in our daily practice and to what extent they are used, especially considering the wide spectrum of diseases due to acute myocardial injury.

In our country, the most updated information available comes from the BUENOS AIRES 1 registry published in July 2020, which gathered 1100 patients with a diagnosis of NSTEACS in multiple centers in the Autonomous City of Buenos Aires and the Province of Buenos Aires. (5) Previous information was provided by registries developed by the Argentine Society of Cardiology (SCAR registry) in 2011 and the Argentine Council of Residents in Cardiology (CONAREC XVII registry), which collected information from patients treated during 2010. (6,7) Furthermore, the ARGEN-IAM-ST registry is continuously evaluating the in-hospital outcome of patients with ST-segment elevation myocardial infarction and has even published an analysis of patients without significant epicardial lesions. (8-11) These registries have provided extremely valuable information for understanding the current regional situation; however, in our case, and unlike previous registries, our intention is to expand this information by adding to our registry data on the prevalence, diagnosis and treatment of the entire spectrum of acute coronary syndromes, including, for the first time, those without significant epicardial coronary artery disease.

METHODS

ReSCAR was a prospective multicenter observational registry carried out in medical centers of Argentina and included patients between January and August 2022. The registry was designed and conducted by the Council on Cardiovascular Emergency Care of the Argentine Society of Cardiology (SAC).

Participating centers

The participating centers were affiliated to the Argentine Society of Cardiology and fulfilled the following requirements: they had coronary care unit, 24-hour catheterization lab availability and cardiovascular surgery capabilities. All the centers in Argentina were invited to participate.

Follow-up

The pre-established follow-up of patients at 12 months is ongoing; therefore, we do not have final data at the time of publication of the initial analysis. We used the information obtained by telephone contact and complemented with data retrieved from the medical records.

Objectives

- To describe the characteristics of patients hospitalized for a coronary event, the diagnostic modalities, and their treatment.
- To analyze the in-hospital outcome of patients with ACS, according to the different etiologies and treatment strategies implemented.

Inclusion criteria

- Patients older than 18 years, with ACS (with or without significant epicardial coronary artery disease) who signed the informed consent were included.

Exclusion criteria

- Impossibility of follow-up.

Sample

We planned to include 1000 patients, which should allow us to have enough number of the different ACS categories. Patients' data were uploaded using the RedCap platform, with one user per center.

Collected data

Past medical history: cardiovascular risk factors and relevant medical history and comorbidities were obtained during history taken at the time of hospital admission. The following variables were recorded: history of hypertension, diabetes mellitus, dyslipidemia, smoking habits (current or former smoker), (12) family history of early cardiovascular disease, sedentary lifestyle, self-reported emotional stress, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), history of COVID-19 and other relevant medical history and comorbidities. In addition, we asked about history of cardiovascular diseases, acute myocardial infarction (AMI), percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), chronic stable angina (CSA), stroke, transient ischemic attack (TIA), atrial fibrillation (AF), peripheral vascular disease (PVD), and previous bleeding events.

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

a) Type of ACS: UA, NSTEMI, STEMI, type 2 AMI, myocardial infarction with non-obstructive coronary arteries (MINOCA), myocarditis or Takotsubo syndrome. (1,2)
b) Killip and Kimball (KK) class at admission and during hospitalization.
c) Electrocardiographic (ECG) changes: temporary ST-segment elevation; ST-segment depression, T-wave changes, Q waves associated with ST-segment deviations or T-wave changes, left bundle branch block (LBBB), pacemaker rhythm or absence of acute ischemic changes.
d) Initial strategy used (invasive or conservative) and time to coronary angiography (CA).
e) Treatment implemented: aspirin (ASA), P2Y12 receptor inhibitor (P2Y12i) used and time of prescription, and anticoagulant therapy and drug used.

f) Result of CA, type of lesions, number of vessels and type of stent used.
g) Ischemic complications:
   1. Recurrent angina, refractory angina, post-infarction angina
   2. Reinfarction
   3. Stent thrombosis
   4. Need for CABG
   7. Stroke/TIA
h) Electric complications: atrial fibrillation, ventricular tachycardia or ventricular fibrillation and high-degree atrioventricular block.
i) Mechanical complications: ventricular septal defect, acute mitral regurgitation, free wall rupture.
j) Need for mechanical ventilation or ventricular assist device.
k) Other complications: contrast-induced nephropathy, acute kidney injury (AKI) and heart failure.
l) Bleeding during hospitalization according to BARC types 1-5 (13)
m) In-hospital mortality.
n) Treatment on hospital discharge: antiplatelet therapy (aspirin, clopidogrel, prasugrel or ticagrelor), oral anticoagulation, beta-blockers (BB), angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), statins, ezetimibe, aldosterone antagonists, trimetazidine and calcium channel blockers.
o) 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 median and interquartile range (IQR) according to the characteristics of their distribution. Categorical variables are expressed as frequencies and percentages. Normality of variables distribution was assessed using the Kolmogorov-Smirnov test or the Shapiro-Wilk test, as applicable. The chi square test or Fisher's exact test were used to compare the categorical variables, and continuous variables were analyzed using the Student's t test or the Mann-Withney test according to their distribution. A type I error < 5% (two-tailed p value < 0.05) was considered statistically significant.

Ethical considerations

All the 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 of the information included in the informed consent and answered all the participant's questions regarding the study. The consent was submitted for approval by the local institutional review board, 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 will remain anonymous, and only the researchers and the members of the learning, teaching and research ethics committee would have access to these 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 984 patients were included; median age was 66 years (IQR 56.5-74), and 75.3% were men. The prevalence of hypertension was 68.1%; 25.9% of the patients had diabetes mellitus, 46.1% had dyslipidemia, 56.9% were current or former smokers and 7.8% presented family history (Table 1). A history of UA or NSTEMI, remote PCI, recent PCI, and previous CABG was reported by 25.4%, 19,5%, 7.1% and 7.1% of the patients, respectively.

On admission, median GRACE score and median CRUSADE score were 127 (IQR 104-154) and 22 (IQR 13-34), respectively. The hemodynamic status was classified as Killip and Kimball (KK) class A in 88.1% of patients, B in 8.2%, C in 1.3% and D in 2.4%.

Most ACS corresponded to epicardial coronary artery disease: UA 22.2%, NSTEMI 39.1% and STEMI 24.1%. Additionally, 4.1% presented as type 2 AMI, 1.2% as myocarditis, 0.7% as Takotsubo syndrome and 8.6% as MINOCA.

An initial invasive strategy was used in 84% of the patients without ST segment elevation; 76.5% of them had significant stenosis > 50% with multivessel disease in 33.7% and left main coronary artery disease in

Table 1. Baseline characteristics of the population. N = 984

Variables	Values
Age – years, median (IQR)	66 (56.5-74)
BMI – kg/m2, median (IQR)	27.8 (25.5-31.2)
HR – bpm, median (IQR)	77 (70-88)
SBP – mm Hg, median (IQR)	130 (120-150)
LEVF - %, median (IQR)	56 (45-60)
Female sex – n (%)	243 (24.7)
Hypertension – n (%)	671 (68.1)
Diabetes mellitus – n (%)	255 (25.9)
Dyslipidemia - n (%)	560 (56.9)
Smoking habits - n (%)	377 (37.7)
Family history - n (%)	77 (7.8)
CKD - (%)	69 (7)
COPD - n (%)	59 (6)
Sedentary life - (%)	460 (46.7)
Stress - n (%)	69 (7)
Gestational diabetes - (%)	2 (0.2)
Gestational hypertension - (%)	5 (0.5)
Menopause - (%)	176 (77.5)

BMI: body mass index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; HR: heart rate; IQR: interquartile range; LVEF: left ventricular ejection fraction; SBP: systolic blood pressure.

13.8%. Percutaneous revascularization was performed in 61.2% and surgical revascularization in 8.5%. Delay to CA was measured in intervals of ≤ 2 h (4.3%), 2-23 h (57.2%), 24-48 h (20.6%) and > 48 h (11.4%). Among patients in whom CA was carried out, pretreatment with a P2Y12 inhibitor was used in 26.4% and clopidogrel was the agent most used, in more than 80% of the cases. Among those patients treated with a P2Y12 inhibitor in the catheterization lab (32%), prasugrel was the one more commonly used. (Table 2).

Primary PCI was the most frequent strategy in STEMI patients (87.2%), followed by rescue PCI (4.2%), thrombolytic therapy (2.5%) and pharmacoinvasive strategy (2.1%). In patients undergoing primary PCI, median (IQR) times were as follows: pain-to-balloon time, 335 min (90-687); first medical contact-to-balloon time, 108.5 min (62-240); and door-to-balloon time, 72 min (41-120). In patients treated with thrombolysis, median door-to-needle time was 30 minutes (22.5-24) (Table 3).

Median length of hospital stay was 3 days. During hospitalization, 2.84% of the patients presented reinfarction, 2.43% recurrent angina, 2% postinfarction angina and 0.5% stent thrombosis. Bleeding events occurred in 4.4% of the patients and were almost equally distributed (34% BARC type 1, 34% BARC type 2, and 32% BARC type 3).

Total in-hospital mortality was 3.76% (37 events). The highest mortality rate occurred in those patients with STEMI (7.6%) followed by NSTEMI (3.6%) and UA (2.3%); none of the patients with the other types of ACS died.

Finally, we analyzed the discharge medication. Among the antithrombotic regimen, 86.9% of patients were discharged with aspirin, 76% with a P2Y12i (clopidogrel in 56.6%) and 10.7% with oral anticoagulants, mostly (52.4%) direct anticoagulants (DOACs) and vitamin K antagonists in the rest of the cases. Statins were indicated in 90.9% of the patients and beta blockers in 78%.

Table 2. Management of patients without ST segment elevation. N = 737

Variable	Values
Initial strategy	
Invasive – n (%)	619 (84)
Conservative – n (%)	118 (16)
Time-to-CA	
< 2 h - n (%)	32 (4.3)
1-23 h - n (%)	422 (57.2)
24-48 h - n (%)	152 (20.6)
> 48 h - n (%)	84 (11.4)
Pretreatment (n=690)	
Clopidogrel - n (%)	150 (21.7)
Ticagrelor - n (%)	26 (3.7)
Prasugrel - n (%)	7 (1)
Treatment in Cath lab (n=690)	
Clopidogrel - n (%)	90 (13)
Prasugrel - n (%)	113 (16.4)
Ticagrelor – n (%)	18 (2.6)

CA: Coronary angiography

Table 3. Management of STEACS. N = 237

Variable	Values
Reperfusion strategy	
Primary PCI - n (%)	206 (87.2)
Rescue PCI - n (%)	10 (4.2)
Thrombolysis - n (%)	6 (2.5)
Pharmacoinvasive - n (%)	5 (2.1)
Times - minutes	
Symptom onset-to-balloon time, min - median (IQR)	335 (190-687)
FMC-to-balloon time, min - median (IQR)	108 (62-240)
FMC-to-balloon time, min - median (IQR)	71 (45-120)
Door-to-needle time, min - median (IQR)	30 (22.5-240)

FMC: first medical contact; IQR: interquartile range; PCI: percutaneous coronary intervention; STEACS: ST-segment elevation acute coronary syndromes

DISCUSSION

The ReSCAR registry emerges from a multicenter database that provides the possibility of analyzing updated information about the diagnostic approach, treatment strategies implemented, outcome, complications, and prognosis of all the ACS, and of each ACS category. We would like to highlight five aspects of the data collected.

First, the registry has adequate representation of the spectrum of patients with "acute coronary syndrome" with a similar percentage of UA, NSTEMI, and STEMI. In addition, there is a place for describing the prevalence of MINOCA, myocarditis and Takotsubo syndrome, which represent part of the differential diagnoses of patients admitted with suspected ACS.

Second, in patients without ST segment elevation at presentation, as in the BUENOS AIRES 1 registry, invasive treatment predominated (84% vs. 86%); this implies a more aggressive approach despite most cases were NSTEMI (39.1%), the median GRACE score was 127, which represents an intermediate risk, and most of the sample presented with KK class A (88.1%). (5) We may consider that the predominance of invasive treatment was due to the preference of the treating medical team rather than to the ischemic risk, which was favored by the context of high complexity centers with high access to PCI. However, this was not so common in international registries, as the Swedish SCAAR registry (NSTEACS n = 15 442), where the rate of coronary angiography as initial management for patients with NSTEACS is 62.9%. (14-16)

Third, this last registry showed a decrease in the

pretreatment strategy (26.4%) compared with the BUENOS AIRES 1 registry, with a pretreatment rate of 65%. This could be explained by the latest recommendations of the ESC guidelines on NSTEMI which, based on the recent ACCOAST and ISAR REACT 5 studies, do not recommend the pretreatment strategy if an early CA strategy (<48hs) is decided. (5,17,18) Since most of the participating centers in our study have catheterization lab availability, this strategy was implemented in more than 60% of patients within 24 h and in 88% within 48 h. Clopidogrel was still the antiplatelet agent most used for pretreatment as in the BUENOS AIRES 1 registry, probably because of its lower cost and greater accessibility compared with ticagrelor, while in those treated in the catheterization laboratory, prasugrel was the antiplatelet agent most used (more than half of the cases) in line with the recent evidence available from the ISAR REACT 5 study. (5,17-23)

Fourth, the analysis of STEMI shows a high reperfusion rate with primary PCI with long out-of-hospital times and, in contrast, in-hospital times in line with the recommendations of the clinical practice guidelines and similar to those found in other international registries. (15,16) Mortality is higher than that reported by high complexity centers in the United States or Europe, close to 4.5%, but lower than the one shown in the analysis of the ARGEN-IAM registry. (11)

Fifth, in-hospital mortality rate was 3.76%, higher than that of the BUENOS AIRES 1 registry (2.7%), which could be explained because high-risk patients were included, considering a GRACE score of 104 in the BUENOS AIRES I registry and the fact that patients with STEMI were included in the ReSCAR registry. These patients had the highest mortality rate, 7.6% versus 3.6% in NSTEMI patients and 2.3% in those with UA. (7,11)

Finally, the rate of bleeding events was low (4.4%), less than expected, and significantly lower than the one recorded in previous similar studies, such as BUENOS AIRES 1 (20.9%). (5) It should be noted that all the patients in BUENOS AIRES I had epicardial coronary artery disease, with a revascularization rate of 76.5% of the sample by both revascularization methods. Despite the ReSCAR study included patients without heart disease, the revascularization rate was 69.5% (8.5% by CABG), which should result in similar bleeding risks associated with revascularization, especially considering the group of patients with diagnosis of STEMI. Therefore, we conclude that part of the bleeding events, especially those categorized as BARC type 2 or type 1, were probably under-recorded.

CONCLUSION

The multicenter ReSCAR registry represents a first approach to the wide spectrum of patients with myocardial injury as the final event, independently of the etiology. The registry has a good representation of the spectrum of patients with initial suspicion of "acute coronary syndrome", managed in centers with an invasive initial strategy, low rate of in-hospital complications and acceptable overall mortality. The subgroup analysis will provide further conclusions..

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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Appendix. Participating centers in alphabetical order.

Centro de Educación Médica e Investigación Médica Norberto Quirno, CEMIC: Mirza Rivero, Mayra Meza, Sol Kersten, Carlos Boissonnet.
Clínica CEMEP: Gerardo Filippa.
Clínica Olivos: Fernando Guardiani, Sebastián Nani.
Fundación Favaloro: Ernesto Duronto, Gastón Procopio, Camila Marian Abud, Santiago Andres Ahuad Calvelo.
Hospital Austral: Jorge Bilbao, Nicolás Torres.
Hospital Británico: Mauro Gingins, Gisela Gómez, Federico Deveter.
Hospital de Clínicas: Sandra Swieszkowski, Martín Aladio, Maia Matsudo.
Hospital Durand: Valentín Roel.
Hospital Naval: Guillermo Pérez.
Instituto Cardiovascular de Buenos Aires, ICBA: Juan P Costabel, Julián Feder, Alan Sigal.
Instituto Médico de la Ribera: Valerio Pessano, Juan Pablo Larralde
Sanatorio Anchorena San Martín: Leandro Rodríguez. Juan Manuel Souto.
Sanatorio Finochietto: Diego Crippa.
Sanatorio Güemes: Ricardo Villareal, Joaquín Perea, Agustina Saucedo, Elena Vargas.
Sanatorio Trinidad de Palermo: Federico Cardone.

ORIGINAL ARTICLE

Survey on Women's Perception and Awareness of Cardiovascular Risk Factors and How They Are Managed

Encuesta sobre factores de riesgo de enfermedad cardiovascular en la mujer, su percepción, conocimiento y conducta de prevención

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ABSTRACT

Background: Cardiovascular disease (CVD) is the leading cause of death in women. Nevertheless, women are less likely than men to receive guidance or preventive treatment to reduce it.
Objective: The aim of this study was to detect the prevalence of cardiovascular risk factors (CRF) and detect the level of women's perception and awareness of CRF and CVD.
Methods: We conducted an observational, cross-sectional study in July 2021 using a voluntary, anonymous, and online survey. The information collected included age range, CRF, CVD, risk perception and implementation of healthy habits and behaviors.
Results: A total of 3888 women participated (age between 46 and 65 years in 50.1%); 34.1% had excess weight and 43.6% had a waist circumference > 80 cm. Hypertension (HTN) was reported by 24.2%; total cholesterol was > 200 mg/dL in 19.6%; 5,4% were diabetics (DM); 44.3% had sedentary lifestyle; 11.3% were current smokers and 34.5% were former smokers; 82.1% had been pregnant at least once and 26.9% reported a complication during pregnancy. A bad obstetric history was more commonly associated with HTN (34% vs. 24%, $p < 0.01$), DM (7% vs. 5%, $p = 0.04$) and CVD (14% vs. 11%, $p < 0.01$). Among the 10.9% who reported a history of CVD, myocardial infarction was the most common condition (51.1%). Sixty-two percent of survey respondents considered that cancer, and particularly breast cancer (53.4%), is the main cause of death in women.
Conclusions: We found a high prevalence of modifiable CRF with low perception of cardiovascular risk. A bad obstetric history was associated with higher prevalence of CRF.

Keywords: Woman - Perception - Risk - Habits - Pregnancy.

RESUMEN

Introducción: La enfermedad cardiovascular (ECV) es la principal causa de muerte en la mujer. A pesar de esto, las mujeres reciben menos frecuentemente que los hombres asesoramiento y/o tratamiento preventivo con el objetivo de disminuir la ECV.
Objetivo: Detectar la prevalencia de factores de riesgo cardiovascular (FRC) y pesquisar el nivel de percepción y conocimiento de la mujer sobre FRC y ECV.
Material y métodos: Estudio observacional, de corte transversal realizado en julio 2021, mediante una encuesta en formato digital de participación anónima y voluntaria. Se recabó información sobre edad, FRC, ECV, percepción de riesgo, implementación de hábitos y conductas saludables.
Resultados: Participaron 3338 mujeres. El 50,1% tenía entre 46 y 65 años. El 34,1% tenía sobrepeso, el 43,6% perímetro de cintura mayor que 80 cm, el 24,2% hipertensión (HTA), el 19,6% colesterol mayor que 200 mg/dL, el 5,4% diabetes (DBT); 44,3% eran sedentarias, 11,3% fumaban y 34,5% eran exfumadoras. El 82,1% tuvo al menos un embarazo y el 26,9% refirió alguna complicación. Entre las pacientes con antecedentes de complicaciones del embarazo fueron significativamente más frecuentes la HTA (34% vs 24%, $p < 0,01$), la DBT (7% vs 5%, $p = 0,04$) y la ECV (14% vs 11%, $p < 0,01$). Del total de encuestadas 10,9% refirió ECV, el antecedente de infarto de miocardio fue el más frecuente (51,1%). El 62% de las encuestadas consideró que la principal causa de muerte en la mujer es el cáncer, particularmente de mama (53,4%).
Conclusiones: Se encontró una alta prevalencia de FRC modificables con baja percepción del riesgo cardiovascular. El antecedente de complicaciones del embarazo se asoció con mayor prevalencia de FRC.

Palabras clave: Mujer - Percepción - Riesgo - Hábitos - Embarazo

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INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in women and its prevalence has increased over the past decades. Despite this fact, women are less likely to receive guidance or preventive treatment to reduce it. (1)

The effect of cardiovascular risk factors (CRF) as hypertension (HT), diabetes (DBT), hypercholesterolemia (HC), smoking, excess weight and sedentary lifestyle on cardiovascular health is well known, but the evidence shows that the magnitude of their impact exhibits sex-related variations. (2) In addition, women are exposed to unique sex- and gender-specific CRF as low socioeconomic status, certain psychosocial factors, gender-based violence, low education level, and environmental pollution. (3-6)

Nowadays, most of the information on CRF and CVD in women comes from international studies, and although the national survey of risk factors (NSRF) (7) and the study published by the Heart and Women Area of the SAC in 2006 (8) collected local information, there are no current data on women's perception of their own risk.

Through this survey on women's perception, awareness and management, the Heart and Women Area of the Argentine Society of Cardiology (SAC) sought to establish a diagnosis of the situation of self-perception of CRF and CVD, detect their prevalence and investigate the level of perception and awareness of women on CRF and CVD to define the most vulnerable groups to guide specific actions.

METHODS

We conducted an observational, cross-sectional study in July 2021, using a voluntary, anonymous, and self-administered online survey. A form was created on the RedCap platform and was accessed via a link distributed through social media and WhatsApp by members of the Heart and Women Area, with broad participation of the regional SAC districts. The information collected included age range, CRF, CVD, and risk perception (Appendix 1). In this self-administered survey, women reported if they perceived they had HTN, DM, dyslipidemia, or a history of CVD (myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery or a positive stress test). Hypercholesterolemia was considered independently of the last time cholesterol levels were tested. Similarly, we inquired about pregnancies and bad obstetric history (miscarriage, fetal death, gestational hypertension, gestational DM, and preterm birth before 37 weeks). Sedentary lifestyle was considered when the exercise time reported was less than 150 min per week. Former smoker was considered after 1 year of having quit smoking. Predefined categories of weight and waist circumference data were provided.

Women >18 years and older from different geographic locations in Argentina were included, and female doctors were excluded.

Statistical analysis

The population was divided into two groups according to age, ≤ 45 years, and > 45 years, to explore differences in the main variables in two different generations.

Qualitative variables are presented as frequencies and percentages. Discrete variables were analyzed using the chi square test or Fisher's exact test. For continuous variables, the t test or the Mann-Withney test were used. ANOVA and the Kruskal-Wallis test were used for comparisons among 3 groups or greater. A p value < 0.05 was considered statistically significant.

Ethical considerations

The survey was approved by the Committee on Ethics of the Argentine Society of Cardiology; informed consent was not required due to the characteristics of the survey.

RESULTS

Conventional risk factors

A total 3338 women participated in the survey. Table 1 shows the baseline characteristics of the women surveyed; 34.8% were < 45 years and half of them (50.1%) belonged to the age range between 46-65 years.

In response to body measurements, 34.1% reported a weight > 70 kg and this answer was more common in women > 45 years than in younger women (38% vs. 29%, $p < 0.01$). A waist circumference > 80 cm was reported by 43.6% of respondents and was more common in women > 45 years (48% vs 35%, $p < 0.01$) (Figure 1).

Among conventional CRF, 12.1% did not know their blood pressure (BP) values and 24.2% considered that they had hypertension (HTN). When they were asked about their BP values, 6.1% responded their systolic BP was > 140 mm Hg (1.4% corresponded to the group that did not perceive they had HTN). Considering both criteria (reported HTN and elevated BP values), 25.6% of all the survey respondents had HTN, more frequent in the age group > 65 years (37.6%) (Figure 1).

Elevated total cholesterol (ETC) levels, > 200 mg/dL were reported by 19.6% of the survey respondents while 29.2% did not know their values. Of the patients with ETC levels, 16.7% were taking lipid-lowering agents and 10.1% followed diet and exercise. Among women who were following an indication to manage ETC levels (diet, exercise or medication), 37% had values > 200 mg/dL despite these measures. On the other hand, 23% of women with TC levels > 200 mg/dL did not follow any recommendation. Elevated TC levels were more common in > 45 years (31%) compared with those ≤ 45 years old (18%), $p < 0.01$.

Diabetes was reported by 5.4% and most survey respondents knew their blood glucose values (only 2.6% were not aware of them).

A waist circumference > 80 cm was more common in women with HTN (33.3% vs 16.7%), ETC levels (22.2% vs. 17.6%) and DBT (8.6% vs. 3.0%). Excess weight was associated with HTN (35.6% vs. 18%) and DM (10.6% vs. 2.8%).

Women with systolic blood pressure >140 mm Hg were more likely to have DM (16.5% vs. 5.2%), waist circumference > 80 cm (68.3% vs. 43.2%), and weight > 70 kg (60% vs. 33.5%).

Table 1. Baseline characteristics of the population surveyed (n = 3338)

Characteristics	n (%)
AGE	
≤ 45 years	1160 (34.8)
46 to 55 years	983 (29.5)
56 to 65 years	690 (20.6)
> 65 years	505 (15.1)
CONVENTIONAL CRF	
HTN (n = 3301)	799 (24.2)
Diabetes (n = 3314)	179 (5.4)
Smoking habits (n = 3333)	370 (11.1)
Former smoker (n = 3333)	1023 (30.7)
Elevated cholesterol levels (n = 3280)	643 (19.6)
Family history of CVD (n = 3303)	1827 (55.3)
WEIGHT (n = 3296)	
≤ 60 kg	1009 (30.6)
61 to 70 kg	1162 (35.3)
71 to 80 kg	640 (19.4)
> 80 kg	485 (14.7)
WAIST CIRCUMFERENCE (n = 3265)	
≤ 70 cm	593 (18.2)
71 to 80 cm	1248 (38.2)
81 to 90 cm	784 (24)
> 90 cm	640 (19.6)
HEIGHT (n = 3322)	
≤ 150 cm	124 (3.7)
151 to 160 cm	1384 (41.7)
161 to 170 cm	1542 (46.4)
> 170 cm	272 (8.2)
Sedentary lifestyle (n = 3300)	1462 (44.3)
CV ASSESSMENT AND HISTORY OF CVD	
Underwent cardiovascular assessment (n = 3316)	2885 (87)
History of CAD (n = 2902)	359 (10.9)
History of stroke, (n=3306)	324 (9.8)
NON-CONVENTIONAL CRF	
Alcohol > 4 days/week (n = 3291)	260 (7.9)
Pregnancy (n = 3309)	2717 (82.1)
Complications of pregnancy	731 (26.9)
Early menopause (n = 3305)	443 (13.4)
Contraception/HT (n = 3289)	500 (15.2)
Thyroid disease (n = 3307)	1032 (31.2)
History of cancer (n = 3316)	262 (7.9)
Healthy diet > 4 days/week (n=3315)	1903 (57.4)
Sleep disorders > 4 days/week (n=3314)	464 (14)
Irritability > 4 days/week (n=3288)	365 (11.1)

CAD: coronary artery disease; CRF: cardiovascular risk factors; CVD: cardiovascular disease; HT: hormone therapy; HTN: hypertension; For each variable, the total number of respondents is indicated.

In addition, women with diabetes had more prevalence of HTN (57% vs. 22.7%), waist circumference > 80 cm (68% vs. 41.8%) and weight > 70 kg (65% vs 32%). These differences were statistically significant in all the cases ($p < 0.01$).

Sex-specific risk factors

The obstetric history was also explored. Among survey respondents, 82.1% had been pregnant at least once, and 26.9% of them reported at least one of the following complications: HTN (8.2%), preterm birth (7.9%), miscarriage (7.4%) and gestational diabetes (4.9%). Only 37% underwent cardiology monitoring one year after the index delivery (vs. no monitoring $p < 0.01$). A bad obstetric history was more commonly associated with HTN (34% vs. 24%, $p < 0.01$), DM (7% vs. 5%, $p = 0.04$) and current CVD (14% vs. 11%, $p < 0.01$).

Oral contraceptives or hormone therapy was used by 15.2%, and most of these women (65%) belonged to the younger age group. Hormone therapy was less common in women with HTN (11.8% vs. 26.2%), ETC levels (13.5% vs 21%), waist circumference > 80 cm (35% vs 45%), and weight > 70 kg (26% vs 35%). All these differences were statistically significant ($p < 0.01$).

Cancer was reported by 7.9% and 91.4% had not been evaluated by a cardiologist during or after cancer therapy. A history of cancer was found in 11% of women > 45 years vs. 2% in younger women ($p < 0.01$). Hypertension was more common in women with a history of cancer (35% vs. 23%).

Habits, behavioral factors, and emotional sphere

Among survey respondents, 45.8% had a history of smoking and 11.3% were current smokers. Smoking was significantly associated with a waist circumference > 80 cm, sedentary lifestyle, and alcohol intake (13% vs. 7%).

We also explored habits as exercise, diet, and medical check-ups. A sedentary lifestyle was reported by 44.3%, and 57.4% admitted lack of adherence to a healthy and balanced diet. Sedentary lifestyle was more common in women aged 45 or less (42% vs 50%, $p < 0.01$). Women who exercised had significantly lower prevalence of HTN (21.7% vs. 26.8%), DM (4.4% vs. 7%), smoking habits (9% vs. 13.3%), waist circumference > 80 cm (38% vs. 50.1%) and weight >70 kg (27% vs 42.5%).

Most women had undergone cardiovascular assessment (87%), but this was less common in younger women.

Data on irritability, alcohol intake and sleep were collected to explore the emotional and behavioral spheres; 62.6% became easily irritable, mostly women up to 55 years of age (74%), and nearly half of them reported regular alcohol intake (48.6%). Sleeping difficulty was more common among women who reported regular alcohol intake (19% vs. 13.5% $p < 0.01$). Sleep

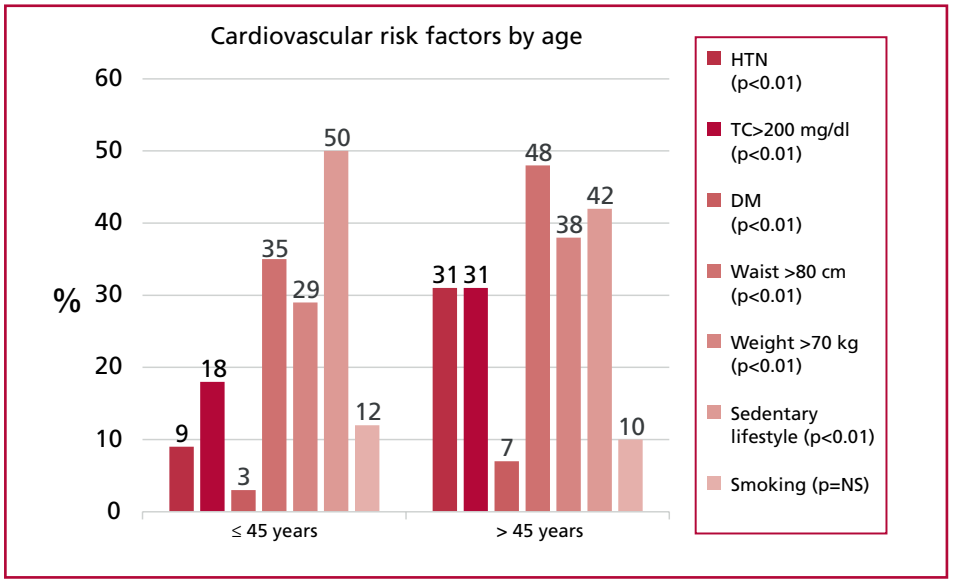


Fig. 1. Comparison of cardiovascular risk factors by age

DM: diabetes; HTN: hypertension; TC: total cholesterol

disorders were reported by 49.5% and there was a significant association between ETC levels and weight > 70 kg. Sleep disorders were more common in women > 45 years.

Awareness and perception of cardiovascular disease

Among survey respondents, 10.9% had CVD, which was more common in those > 55 years. A history of myocardial infarction was the most common disease reported (51.1%), followed by revascularization procedures (30.4%) and indication of medical treatment after an exercise stress test (28.6%). Stroke was reported by 9.8% of the respondents.

When awareness of cardiovascular risk was explored, more than 50% responded that cancer was the main cause of death in women (62%) and gynecologic tumors were the most common causes reported (breast cancer in 53.9% and ovarian cancer in 7.5%). Only 34.9% considered CVD as the main cause of death in women. There were no differences by age on this question.

DISCUSSION

The present survey shows an increase in self-reported CRF compared to the data obtained in the previous survey conducted by the Heart and Women Area in 2006. (8) These findings are in line with the results of the fourth NSRF. (7) A matter of concern is the increased prevalence of CRF in the female population at the expense of excess weight, HTN, DM, and ETC levels over the 15-year period. We observed several CRF in women > 45 years, in those with known CVD, and a combination of CRF in those who did not know they had CVD, thus increasing the cardiovascular risk (Figure 1). When HTN was analyzed, some women did not know their BP levels (12%) and another group of women (4.7%) who did not consider themselves to be hypertensive had elevated values (> 140 mm Hg), which demonstrates the lack of awareness of this important CRF. Something similar occurred with cholesterol levels: 29.2% were unaware of their values, and among those who recognized that they had ETC, 37% had not reached the therapeutic targets (<200 mg/dL) despite drug treatment or hygiene and dietary measures.

In the participating population the prevalence of a history of pregnancy was high (81.2%) and 26.9% reported complications. In line with previous series, a bad obstetric history was more commonly associated with HTN, DBT and future CVD (Figure 2). (3,5,9-11) The guidelines on cardiovascular prevention in women highlight the need for periodic cardiovascular monitoring in women with bad obstetric history due to the association with atherosclerotic CVD and CVD-related mortality. Reassessment of the cardiometabolic profile is recommended one year after the index pregnancy (12-15) to screen for HTN, DM and ETC and to encourage women to return to their pre-pregnancy weight. In the population surveyed, only 37% of the women with complications of pregnancy underwent cardiovascular monitoring one year later, which highlights that women and probably their health care professionals were not aware of this risk. Something similar occurred in patients with a history of cancer, as most of them (91.4%) had not been evaluated by a cardiologist during or after cancer treatment.

The use of oral contraceptives was more common in young women (65% < 45 years) and the prevalence of HTN, ETC levels and excess weight was lower in those using oral contraceptives. As this treatment is prescribed by obstetricians and gynecologists, these results could be due to a selection of the method of contraception indicated, based on the woman's cardiometabolic risk profile.

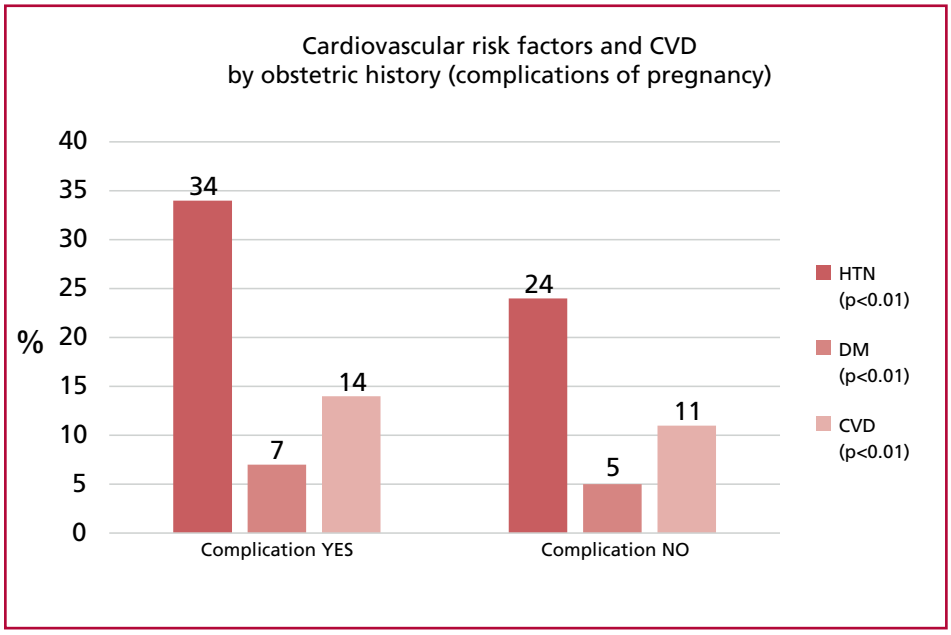


Fig. 2. Cardiovascular risk factors and cardiovascular disease (CVD) during follow-up according to obstetric history

DM: diabetes; HTN: hypertension; TC: total cholesterol

Regarding smoking habits, the implementation of the anti-smoking law 26 687 in 2011 has had a favorable impact on smoking reduction. (16) In the current survey, 11.3% of the respondents smoked versus 29.3% in the previous survey in 2006, and these data agree with the fourth NRFS which showed a reduction in tobacco use. (7)

Women tend to be less active, and, probably because of cultural issues, girls are less encouraged to engage in sports; in the population surveyed, there was a high proportion of sedentary women, particularly among those ≤45 years. This could be due to the fact that younger women play many roles and activities related to parenting, household chores and work activities, and have less time available to adhere to healthy guidelines. Women who exercised regularly had less excess weight, HTN, DBT and irritability, and better quality of sleep. Irritability (62.6%) and regular alcohol intake (56.5%) were also more common in young women.

The importance of sleep in the prevention of CVD has recently been recognized. (17-19) Fragmented sleep or sleeping less than 7 hours has been associated with subclinical atheromatosis in multiple territories and with increased cardiovascular morbidity and mortality. (20) In the population surveyed, 49.5% reported sleep disorders that were more common in those who drank alcohol, and in those with ETC levels and excess weight.

Cardiovascular disease was reported by 10.9% of the survey respondents and was more common in women > 55 years; myocardial infarction was the most common CVD. Women with CVD also had more associated comorbidities (HTN, DM) and excess weight.

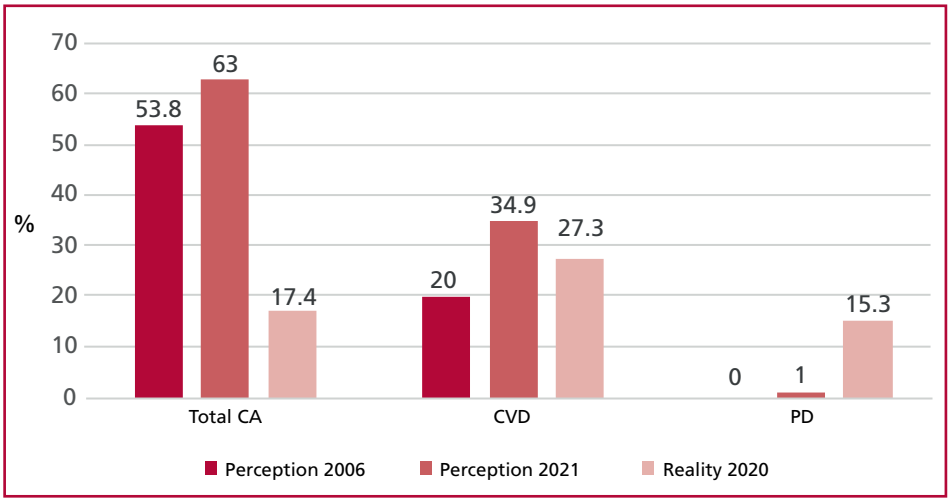
As for the cause of death, women still have the erroneous perception that cancer is the main etiology. In the previous survey conducted in 2006, 53.8% of women considered tumors as the main cause of death and only 20% considered CVD. Fifteen years later, the discrepancy between perception and reality persists, since 62% considered cancer and 34.9% considered CVD as the main cause of death, while according to the vital statistics published by the Ministry of Health in 2020, (21) 17.4% of deaths were due to cancer and 27.3% to CVD (Figure 3). This discrepancy between perception and reality could be associated with the gynecologic cancer prevention campaigns carried out by the societies of gynecology of our country and, in some way, exposes the lack of effective communication by the cardiology community about CRF that have an impact on cardiovascular health and CVD.

CONCLUSION

Women's own perception of their risk is clearly low, and the data collected from the population surveyed suggests poor CRF control. Younger women show the greatest difficulty in the adherence to healthy behaviors, receive less counseling about their risk, and therefore constitute the most vulnerable population. Actions should be taken to spread the information and thus reduce the gap between perception and reality of CVD in women.

Study limitations

The non-probabilistic sampling design (social media/WhatsApp/contacts) generates a response bias, with lower probability of participation of those women with less access to these resources and without contact with physicians in the SAC area. Although the survey was distributed nationwide by representatives of SAC



Ca: Cancer; CVD: cardiovascular disease; PD: pulmonary disease.

Fig. 3. Comparison of perceived cause of death in 2006 and 2021 versus reality in 2020

regional districts, the lack of residency data does not allow us to know the representation of all the regions of Argentina. The distribution by social media did not allow us to corroborate participants' sex and age. As body measurements were collected by ranges, it was not possible to calculate excess weight by body mass index.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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Survey on perception, awareness and measures to prevent cardiovascular diseases in women
All data (All registries and files)

How old are you?
o ≤ 45 years
o Between 46 and 55 years
o Between 56 and 65 years
o > 65 years

Weight:
o ≤ 60 kg
o Between 61 and 70 kg
o Between 71 to 80 kg
o > 80 kg

Height:
o ≤ 150 cm
o Between 151 and 160 cm
o Between 161 and 170 cm
o > 170 cm

Waist:
o ≤ 70 cm
o Between 71 and 80 cm
o Between 81 and 90 cm
o > 90 cm

Do you suffer from hypertension or are you taking any medication to control your blood pressure?
o Yes
o No

Which is your maximum blood pressure value?
o ≤ 120 mm Hg
o Between 121 and 140 mm Hg
o Between 141 and 160 mm Hg
o > 160 mm Hg
o Don't know

Do you know your blood cholesterol value?
o No
o ≤ 160 mg/dL
o Between 161 and 200 mg/dL
o Between 201 and 240 mg/dL
o > 240 mg/dL

Are you taking any medication to control your blood cholesterol?
o No
o Yes
o I exercise and follow a diet

Are you diabetic?
o Yes
o No
o Don't know

Do you smoke?
o Yes
o No, never
o Not now, but I used to smoke

Do you exercise at least 150 minutes per week?
o Yes
o No

Have you ever undergone cardiovascular check-up?
o Yes
o No

Do you have history of cardiovascular disease?
o Yes
o No

Which one?
o Infarction
o Angioplasty
o Coronary artery bypass graft surgery
o I started medication after an exercise stress test

Do you consider you have had or have cardiovascular disease?
o Yes
o No
o Don't know

continue

Do you have a history of stroke?
o Yes
o No

Do you drink alcohol?
o Never
o 4 days or fewer
o > 4 days
o Every day

Have you ever been pregnant?
o Yes
o No

Did you have complications during any of your pregnancies?
o No
o No, but I need fertility treatment
o I lost one/all pregnancies
o Hypertension
o Gestational diabetes
o Delivery before 37 weeks of gestation

Did you experience early menopause? (before the age of 45)
o Yes
o No

Did you undergo cardiovascular check-up one year after delivery?
o Yes
o No

Are you taking oral contraceptives or hormone therapy?
o Yes
o No

Do you have any thyroid disorder?
o Yes
o No

Is there a family history of cardiovascular disease?
o No
o Yes, before 40 years old
o Yes between 40 and 49 years old
o Yes, between 50 and 70 years old
o Yes, > 70 years old

Which of the following diseases do you consider is the most common cause of death in women?
o Breast cancer
o Ovarian cancer
o Lung cancer
o Cardiovascular disease
o COPD
o Alzheimer disease

Do you consider your diet is balanced and healthy?
o Never
o 4 days or fewer
o > 4 days
o Every day

Do you have any difficulties to fall asleep or remain asleep?
o Never
o 4 days or fewer
o > 4 days
o Every day

Do you easily become upset of irritable?
o Never
o 4 days or fewer
o > 4 days
o Every day

Do you have or did you have cancer requiring treatment?
o No
o Yes, chemotherapy
o Yes, radiation therapy
o Yes, surgery
o Yes, immunotherapy: monoclonal antibodies e.g., trastuzumab (Herceptin), others
o Yes, chemotherapy and radiotherapy

Have you been examined by a cardiologist during or after cancer therapy to evaluate if your heart suffered any damage due to treatment?
o No
o Yes, with an electrocardiogram
o Yes, with echocardiography (heart ultrasound)
o Yes, with both

BRIEF ARTICLE

Minimally Invasive Surgery with the Bentall-De Bono Technique. Initial Experience at Hospital Italiano de Buenos Aires

Cirugía de Bentall de Bono por abordaje miniinvasivo. Experiencia inicial del Hospital Italiano de Buenos Aires

CARLOS ÁLVAREZ TAMARA[1], GERMÁN A. FORTUNATO[1], GUILLERMO STÖGER, EMILIANO ROSSI[2], RICARDO POSATINI[1], VADIM KOTOWICZ[1]

ABSTRACT

Background: Cardiac surgery avoiding full sternotomy began to emerge in the 1990s with the first hemi-sternotomies and mini-thoracotomies. Aortic valve and root surgery is one of the most common procedures in our field. In this paper, we analyze our experience in minimally invasive cardiac surgery (MICS) for the aortic root with the Bentall-De Bono technique (MICS-Bentall).
Objective: To analyze the surgical results in the first 10 patients underwent a MICS-Bentall procedure at our site.
Methods: A retrospective observational study was carried out including patients with valve disease and aortic root dilation who underwent a surgery with the MICS-Bentall procedure in a tertiary care hospital from December 2019 to December 2020. Continuous variables were expressed as mean and standard deviation or median and interquartile range according to the observed distribution. Categorical variables were expressed as absolute and relative frequency.
Results: Out of 165 patients undergoing aortic root surgery, 10 patients were included. Mean age was 56 ± 17.03 years, 70% male; all cases were elective. Median (interquartile range, IQR) STS PROM % was 1.48 (1- 2.02). Eighty percent had bicuspid valve. Fifty percent of patients were extubated within 6 hours. In the 30-day follow-up, no death was recorded, and two complications were registered: one patient experienced atrial fibrillation without hemodynamic decompensation and another a wound infection. The mean hospital length of stay was 5 days.
Conclusion: In our experience, MICS using the Bentall technique showed satisfactory results in terms of low perioperative mortality, early extubation, and short hospital stay.

Keywords: Cardiac Surgical Procedures - Minimally Invasive Surgical Procedures - Aortic Valve Disease - Bicuspid Aortic Valve Disease - Aorta

RESUMEN

Introducción: La cirugía cardíaca libre de esternotomía completa surge en los años 90 con las primeras esternotomías y toracotomías mínimas. La cirugía de la válvula y la raíz aórtica constituyen uno de los procedimientos más frecuentes en nuestro campo. En este trabajo analizamos nuestra experiencia en Cirugía Cardíaca Miniinvasiva (MICS) de la raíz aórtica con la técnica Bentall de Bono (MICS-Bentall).
Objetivo: Analizar los resultados quirúrgicos en los primeros 10 pacientes intervenidos con MICS-Bentall en nuestra institución.
Material y métodos: Se realizó un estudio observacional retrospectivo en el que se incluyeron los casos de valvulopatía y dilatación de la raíz aórtica intervenidos quirúrgicamente mediante MICS-Bentall en un hospital de alta complejidad durante el periodo diciembre 2019 - diciembre 2020. Las variables continuas se expresan como media y desvío estándar o mediana y rango intercuartílico según la distribución observada. Las variables categóricas como frecuencia absoluta y relativa.
Resultados: Sobre 165 pacientes sometidos a cirugía de la raíz aórtica, se incluyeron 10 pacientes. La edad media fue de 56±17,6 años, 70% de sexo masculino, todos fueron electivos. La mediana (rango intercuartìlico, RIC) de STS PROM % fue de 1,48 (1-2,02). En el 80% la válvula aórtica era bicúspide. El 50% de los pacientes fue extubado dentro de las 6 horas. En seguimiento a 30 días no se registraron óbitos, y hubo 2 complicaciones: un paciente presentó fibrilación auricular sin descompensación hemodinámica, y otro infección de herida. La estadía hospitalaria fue en promedio de 5 días.
Conclusión: En nuestra experiencia con MICS con la técnica Bentall se obtuvieron resultados satisfactorios con baja mortalidad perioperatoria, extubación precoz y tiempos cortos de estancia hospitalaria.

Palabras Claves: Procedimientos quirúrgicos cardíacos - Procedimientos quirúrgicos mínimamente invasivos - Enfermedad de la válvula aórtica -Enfermedad de la válvula aórtica bicúspide - Aorta

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INTRODUCTION

Cardiac surgery avoiding full sternotomy began to emerge in the 1990s with the first hemi-sternotomies and mini-thoracotomies. (1-3) Over the years, these techniques became increasingly popular and are now routine procedures at tertiary care facilities. Minimally invasive procedure has also been developed in valve and aortic surgery. (4) Despite the experience confirmed by large facilities all over the world, we currently lack randomized controlled trials. The first experiences with minimally invasive aortic valve and root surgery have shown that at least we can achieve the same results as with conventional cardiac surgery. (5) In this paper, we analyze our experience in minimally invasive cardiac surgery (MICS) for the aortic root with the Bentall-De Bono technique (MICS-Bentall).

METHODS

A retrospective observational study was performed with 165 patients who underwent surgery using Bentall-De Bono procedure from December 2019 to December 2020 by searching our electronic medical records.

Out of 165 patients, 155 were excluded, since they had undergone combined procedures (double valve replacement and myocardial revascularization surgery), or they had endocarditis, "porcelain aorta" (calcification throughout the whole perimeter of the aorta), previous chest radiation, severe mitral ring calcification, or full sternotomy.

Ten patients who underwent minimally invasive surgery were evaluated.

The primary objective was to analyze 30-day mortality, and the secondary objective was to analyze technical and surgical outcomes with the following variables: postoperative bleeding and need for transfusion/coagulation factors, hospital length of stay, stroke, extracorporeal circulation (ECC)/aortic cross-clamping (ACC) times.

Surgical Technique

General anesthetic and intra-operative echocardiography were used in all patients. A 4-cm incision was performed from 2 to 3 cm under the angle of Louis. Preserving xiphoid, pre-sternal muscle flaps were created for ease of rib cage expansion when using the saw. The type of cannulation was decided on a case-by-case basis. However, aortic arch cannulation was chosen with reference to the arterial line (EOPA- Edwards™), and venous cannulation was peripherally performed using a guiding cord by means of the Seldinger technique towards the right atrium under long-cannula echocardiographic monitoring (Edwards™ or Medtronic™). Following aortic cross-clamping, antegrade and/or retrograde myocardial protection was performed via coronary sinus cannulation, and the type of cardioplegia was at the surgeon's discretion. Resection of the native aortic valve and root treatment were performed using conventional techniques. (6-8)

Statistical analysis

Consecutive sampling was used; therefore, all patients meeting eligibility criteria were enrolled. Continuous variables are expressed as mean and standard deviation, or median and interquartile (IQR) range according to the observed distribution. Categorical variables are expressed as absolute and relative frequency.

Ethical considerations

The study was conducted following recommendations for research in human beings and any applicable regulations. As medical records were reviewed and no holder identification data were reported, the patients did not provide their informed consents (except for missing data, collected via phone calls). The study members took actions to protect the privacy and confidentiality of data according to applicable regulations (Act 25 326 on Personal Data Protection).

RESULTS

Ten patients were included and underwent MICS.

Preoperative characteristics

Preoperative variables are described in Table 1. All patients had elective surgeries. Most were male (n = 7), and the mean age was 56 years. The most relevant comorbidities were hypertension and dyslipidemia; 2 patients were ex-smokers, and one had chronic renal failure.

Eight patients had bicuspid valve diagnosis, 9 had preserved ventricular function (left ventricular ejection fraction >55%), no patient had previous cardiac surgery, 5 patients had severe aortic valve stenosis, and 5 patients had moderate to severe aortic regurgitation. Nine patients had dilated ascending aorta >45 mm, and one patient had severe aortic stenosis, bicuspid valve, and 40 mm aneurysm. All sample patients had a mild average preoperative risk based on the STS score, except one with moderate risk (average STS 5).

Intraoperative characteristics (Table 2)

Half the patients received a biological and the other half received a mechanical valve prosthesis. The most commonly used valve size was 23 mm.

Mean extracorporeal circulation (ECC) and aortic cross-clamping (ACC) times were 168 minutes and 126 minutes, respectively. One patient required red blood cell transfusion, 5 patients required platelet transfusion, and 2 patients received fibrinogen. No patient underwent reoperation from bleeding, suffered from postoperative renal failure, had neurological events, or needed a permanent pacemaker.

Postoperative results (Table 3)

Only one patient required extubation beyond 24 hours and died 33 days after surgery due to urinary sepsis. One patient was reoperated 20 days after the procedure as a result of turbid secretion from the sternal wound; surgical toilet was performed.

On average, total length of stay was 5 days, except for one patient with prolonged hospitalization until day 10 due to heart failure.

No reoperation was performed, no cerebrovascular accident was observed, no permanent pacemaker was needed, and no perioperative death occurred.

DISCUSSION

The MICS technique is one of the less painful postoperative procedures, with the least amount of bleeding,

Table 1. Preoperative characteristics

Age, years, mean ± SD	56.09 ± 17.60
Male sex, n	7
HTN, n	5
COPD, n	0
Dyslipidemia, n	5
DM, n	0
CRF, n	1
Dialysis	0
Preoperative stroke, n	0
NYHA functional class, n	I: 5 II: 3 III: 2 IV: 0
Coronary surgery, n	0
AF, n	0
Obesity, n	2
Coagulation disorder, n	0
Peripheral artery disease, n	0
Ex-smoker, n	2
Bicuspid valve, n	8
Valve disease, n	Moderate to severe stenosis: 5 Moderate to severe regurgitation: 5
Aortic valve area (cm^2), mean ± SD	1.64 ± 1.23
Aortic ring diameter (cm), mean ± SD	2.41 ± 0.28
Aortic root diameter (cm), mean ± SD	4.11 ± 0.83
Ascending aorta diameter (cm), mean ± SD	4.66 ± 0.44
Pulmonary arterial pressure (mmHg), mean ± SD	25.6 ± 3.77
Hematocrit (%), mean ± SD	39.9 ± 2.60
STS average (%), median (IQR)	1.48 (1- 2.02)

AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; DM: diabetes mellitus; HTN: hypertension; IQR: interquartile range; NYHA: New York Heart Association heart failure scoring; SD: standard deviation; STS: Society of Thoracic Surgeons

Table 2. Intraoperative characteristics

ECC time, min., mean ± SD	168.5 ± 39.7
ACC time, min., mean ± SD	126.5 ± 15.3
Blood transfusion, n	1
Platelet transfusion, n	5
Fibrinogen transfusion, n	2
ECMO, n	0
IABP, n	0
Prosthesis, n	Biological: 5 Mechanical: 5
Cardioplegia	Blood: 7 Crystalloid: 3

ACC: aortic cross-clamping; ECC: extracorporeal circulation; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; SD: standard deviation

Table 3. Postoperative results

Extubation within less than 6 hours, n	5
Atrial fibrillation, n	1
Wound infection, n	1
Total length of stay, days (mean)	5

and the shortest hospitalization. (9)

MICS-Bentall is an increasingly popular procedure at cardiac surgery facilities worldwide. (10) Recently, Mikus et al. (8) published their experience in a retrospective study comparing patients who underwent aortic root surgery with full sternotomy versus minimal sternotomy, and they showed that the MICS group had lower mortality, shorter hospital length of stay, and early postoperative rehabilitation. However, minimally invasive approaches had longer ECC and ACC times.

In 2018, Abjigitova et al. published a retrospective study comparing 26 MICS-Bentall versus 91 Bentall under the full procedure, and they found no differences as regards ACC and ECC times or hospital length of stay. There was no death or reoperation from bleeding among the group of patients underwent MICS-Bentall. (11) In our group, despite the small sample size, there were no reoperations from bleeding, probably because of very careful hemostasis.

Our ECC and ACC times were similar to those in the literature. (8,11)

All our patients were electively operated under very careful planning. Cannulation over the aortic arch and peripheral vein has been essential for better exposure of the operative area after reducing elements within the surgical field.

In addition, there was no death after 30 days, and mean extubation and hospitalization was consistent with the condition.

As for hospital length of stay, 80% of our patients were discharged five days after surgery. As compared with other sites, the length of stay was similar. (12) This is because the minimally invasive procedure reduces trauma and pain in the rib cage, and, therefore, rehabilitation is rapid. (13)

Concerning the type of minimal ("J" or "T" shaped) sternotomy, in our experience, the T-shape approach provides better exposure when creating the ostium and enhanced dissection of the aortic root. The J incision is ideal for more simple procedures, such as aortic valve replacement or ascending aorta isolation. (12,14,15)

Some surgeons tend to open the right pleural chamber to avoid tamponade in case of bleeding, but we prefer not to do this, except if the pleura is inadvertently opened when using the sternal saw.

Following anastomosis of the ostium knob on the right coronary artery, we routinely insert Blake 24 French drainage over the xiphoid reflection, place the ventricular wires of epicardial pacemakers, and use 4 ml surgical sealant CoSeal® (BAXTER) over every

anastomosis and cannulation site. While CoSeal® (BAXTER) takes one minute, we prefer to wait three minutes for the gel to be properly formed over the anastomotic line.

A transesophageal echocardiogram is vital for this procedure, as it guides cannulation both centrally and peripherally, while providing postoperative monitoring. We performed intraoperative and post-ECC measurements using rotational thromboelastometry (ROTEM) throughout.

All patients had blockage close to sternotomy using a transverse chest plane on both sides at the T4-T5 level to manage postoperative pain. We believe this largely contributes to faster rehabilitation.

We also firmly believe that patients' and referring physicians' perceptions and expectations have changed, and surgeons should offer minimally invasive techniques as a valid therapeutic option. This requires not only surgical skills but also continuous training in the field. Our site has surgeons trained abroad at major sites and experienced in minimally invasive surgery.

Patients with a history of chest radiation, "porcelain aorta", reoperations, or severe mitral ring calcification are not good candidates for minimally invasive techniques, due to the complexity of small and hard to control incisions when complications occur.

Limitations

This is a retrospective single-center observational study with a small number of patients.

Conclusions

In our experience, minimally invasive surgery of the aortic root using minimal sternotomy has yielded promising results in terms of early mortality and morbidity. It is necessary to continue analyzing this procedure with a larger number of patients and a longer follow-up in the future.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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REVIEW ARTICLE

Management of Symptomatic Unruptured Abdominal Aortic Aneurysms: State of the Art

Manejo del aneurisma de aorta abdominal sintomático no roto: últimos adelantos

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ABSTRACT

Symptomatic unruptured abdominal aortic aneurysm (AAA) refers to a group of patients with intact AAA but who present abdominal and/or lumbar pain attributed to the aneurysm. This form of clinical presentation is potentially fatal, since its etiopathogenesis, involving acute changes in the aortic wall, including inflammation, increases the probability of impending rupture. It is clear that these patients should be referred to AAA repair. However, the timing of the intervention is controversial. Therefore, the aim of the present work was to review updated information on the diagnostic-therapeutic approach of symptomatic unruptured AAA.

Key words: Symptomatic unruptured abdominal aortic aneurysm - Inflammation - Open surgery - Endovascular aneurysm repair

RESUMEN

El aneurisma de aorta abdominal (AAA) sintomático no roto es una patología que involucra a aquellos pacientes con AAA intacto, pero que presentan dolor abdominal y/o lumbar atribuido al aneurisma. Esta forma de presentación clínica es potencialmente mortal, dado que su etiopatogenia comprende cambios agudos en la pared aórtica, incluyendo inflamación, lo que incrementa la probabilidad de ruptura inminente. Está claro que estos pacientes deben ser derivados a reparación del AAA. Sin embargo, el momento de la intervención es controvertido. Por lo tanto, el objetivo del presente trabajo fue revisar la información actualizada sobre el abordaje diagnóstico-terapéutico del AAA sintomático no roto.

Palabras clave: Aneurisma de aorta abdominal sintomático no roto - Inflamación - Cirugía abierta - Reparación endovascular del aneurisma

INTRODUCTION

The etymology of the word aneurysm can be traced in ancient Greek language. (1,2) It derives from the word *ἀνεύρυσμα* (aneurysma), which means "dilation". (2) Therefore, "aortic aneurysm" refers to an abnormal dilation of the aorta that compromises one or more wall segments. In this sense, an increase in diameter greater than 50% of the aortic diameter at the level of the diaphragm is accepted as abnormal. However, this definition is not always applicable, since often the limit between the healthy and pathological aorta is not precise. (3,4) Consequently, there is a general consensus in considering abdominal aortic aneurysm (AAA) to be a dilation of the aorta greater than or equal to 30 mm. (4-7) Multiple studies have been developed to evaluate the results of elective AAA repair, as well as those associated with emergency repair of ruptured aneurysms. (8-15) However, there is a third type of potentially fatal and scarcely studied clinical presentation of AAA: symptomatic unruptured AAA. (16) Therefore, the aim of the present work was to review updated information on the diagnostic-therapeutic approach of symptomatic unruptured AAA.

METHODS

Searches were carried out in PubMed/Medline, EMBASE, and Cochrane Clinical Trials electronic databases to identify clinical studies that evaluated the diagnostic-therapeutic approach of symptomatic unruptured AAA, using the terms "abdominal aortic aneurysm", "symptomatic aneurysm", "unruptured aneurysm", "open surgery", and "endovascular aneurysm repair".

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The selection of articles was made according to the following criteria: a) publications issued from 1990 to the present; b) observational studies, clinical trials, systematic reviews and recommendations of scientific societies; c) human studies; and d) articles referring to management of symptomatic unruptured AAA. Studies were excluded if the full text was not accessible.

Primary outcomes of this article were: a) to synthesize knowledge about epidemiology, prognosis and diagnostic-therapeutic approach of symptomatic unruptured AAA; and b) to develop an algorithm towards its diagnostic-therapeutic management.

Definition and epidemiology

Symptomatic unruptured AAA refers to a group of patients with intact AAA but who present abdominal and/or lumbar pain attributed to the aneurysm. Another symptom includes tenderness to palpation overlying the AAA in the abdomen, back, or flank. (17) The presence of pain is due to multiple causes, including acute changes in the aortic wall, as we will describe later. In large aneurysms, pain may be caused by compression of adjacent structures. Symptomatic unruptured AAA patients generally do not have arterial hypotension because the aortic wall is intact, with no evidence of retroperitoneal hemorrhage. (7) The reported incidence of this type of clinical presentation is between 3% and 15%. (18,19)

Pathophysiology

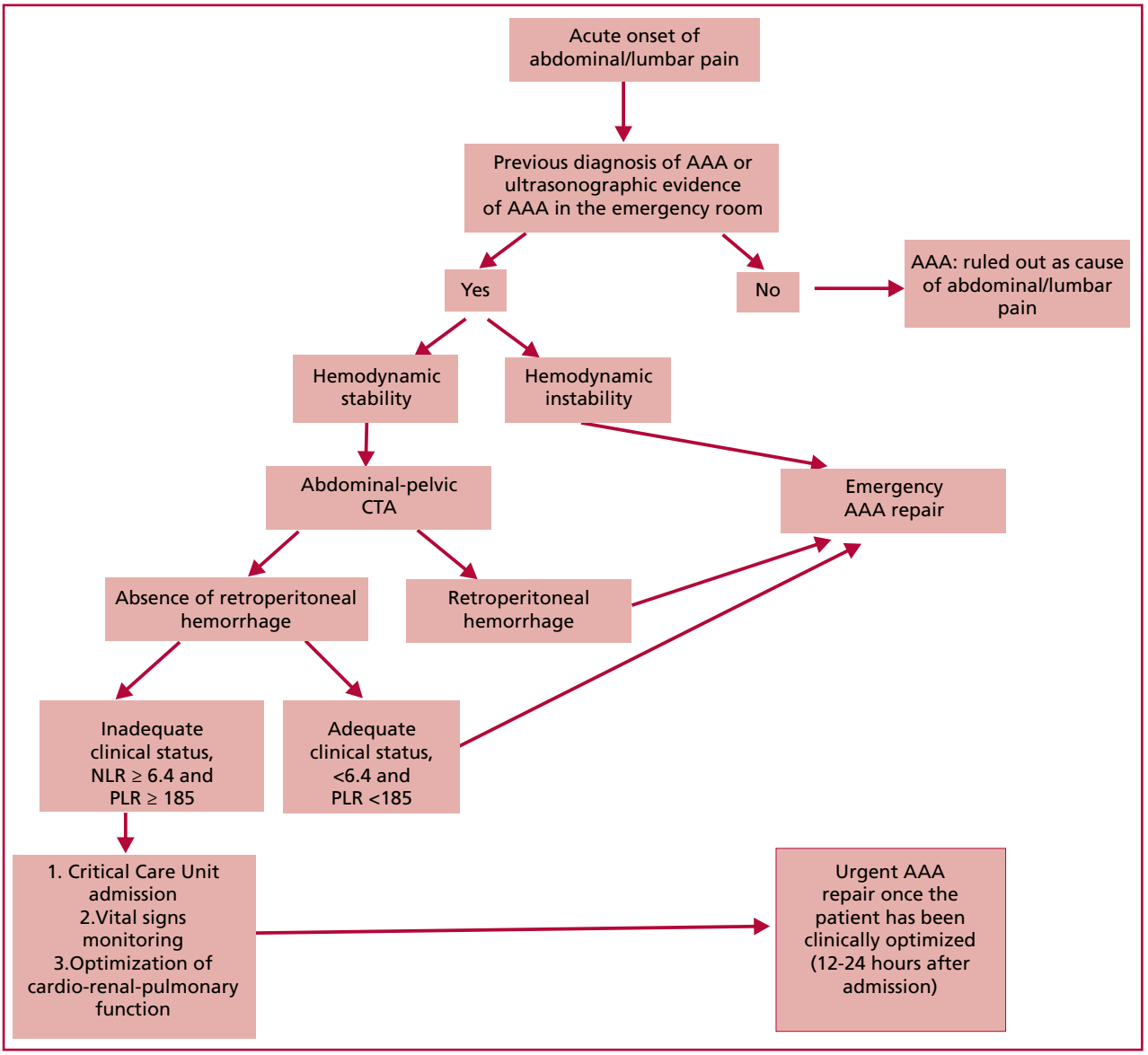
The pathophysiology of symptomatic unruptured AAA involves acute changes in the aneurysmal wall, including increased wall stress and intra-thrombus expansion or new bleeding, raising the probability of impending aneurysm rupture. (20) Evidence demonstrates the role of aneurysmal wall inflammation in the etiopathogenesis of this type of clinical presentation. In this sense, increased 18-fluorodesoxyglusose metabolism by positron emission computed tomography (PET/CT) in patients with symptomatic unruptured AAA compared with asymptomatic ones correlated with increased inflammatory infiltrate density in aneurysmal wall biopsies. (21)

Prognosis and repair outcomes

The current perioperative mortality rate in symptomatic unruptured AAA patients is below that previously reported in the literature. In this regard, De Martino et al. showed a global in-hospital mortality rate of 1.7% (2.2% in operated patients and 0% in patients undergoing endovascular repair). (22) Similarly, Chandra et al. published a contemporary (2005-2014) global perioperative mortality of 5.9%, involving 8% of surgical patients and 5% of those undergoing endovascular procedures. (17) Regarding postoperative complications and long-term survival, De Martino et al. reported that the rate of postoperative complications, including kidney failure, acute myocardial infarction, arrhythmias and respiratory insufficiency was 35% in patients with symptomatic unruptured AAA versus 20% and 63% in those with asymptomatic and ruptured AAA, respectively. In the case of 1 and 4-year survival, this was 83% and 68%, respectively, in patients with symptomatic unruptured AAA, while in asymptomatic ones it was 89% and 73%, and in those with ruptured AAA, 49% and 35%, respectively. (22) In conclusion, in-hospital mortality of symptomatic unruptured AAA repair is similar or discreetly superior to that observed for the elective intervention. However, the rates of postoperative complications and long-term survival are intermediate compared with asymptomatic and ruptured AAA repair. (23-27)

Diagnostic-therapeutic approach

When a symptomatic AAA is suspected, a large caliber venous access should be placed, invasive blood pressure monitoring should be performed, and diagnostic confirmation and immediate treatment should be accomplished at the center where the patient is located. If the conditions to carry out the diagnosis and treatment in the medical center are not met, immediate referral to a high complexity hospital should be activated. (7) Most patients will present with hemodynamic stability since, by definition, there is no rupture of the aortic wall. (17) A high degree of clinical suspicion is essential given the poor prognosis of ruptured and symptomatic unruptured AAA. In a meta-analysis that included studies published after 1990, ruptured AAA misdiagnosis was seen in 32% of cases. The most common erroneous differential diagnoses were ureteric colic and myocardial infarction. (28,29) Figure 1 postulates an algorithm for the diagnostic-therapeutic approach of symptomatic AAA. All individuals admitted to an emergency center with abdominal and/or lumbar pain with a known diagnosis of AAA and who are stable from a hemodynamic point of view, must quickly undergo an abdominal-pelvic computed tomography angiography (CTA). (5) Clinicians may use an abdominal ultrasound to help make the diagnosis whenever it is available. (30) While ultrasound can identify the presence of AAA and intraabdominal fluid, it is less effective at detecting signs of aortic rupture. (31) Ultrasound is therefore not considered a confirmatory test for rupture; however, it represents a useful tool in identifying AAA. Those patients with clinical suspicion and presence of AAA on ultrasound could be considered high-risk for symptomatic AAA, and this may allow for expedited referral CTA. On the other hand, in patients with low clinical risk of symptomatic AAA, the absence of AAA on ultrasound may be sufficient not to carry out further tests, especially if there is another more probable cause that explains the symptoms. (32) If symptomatic AAA is confirmed, a retroperitoneal hemorrhage or the absence of aortic rupture with persistent pain despite optimal medical treatment, including analgesia and control of vital signs, indicates mandatory emergency repair. If, on the contrary, no tomographic findings of aneurysmal rupture are observed, the timing of intervention is controversial and remains a challenge. (8) Numerous retrospective case series have published higher morbidity and mortality rates in emergency AAA repair compared with urgent intervention (18-26% vs. 4-5%). (33-35) In addition, no deaths associated with aneurysm rupture have been reported in patients with symptomatic unruptured AAA, in whom the intervention was postponed and performed semi-electively. (18) Concerning this aspect, different series which have evaluated the causes of death in this group of patients have shown that, in most cases, these are secondary to myocardial infarction, respiratory insufficiency, kidney failure, multiorgan failure and sepsis. (34,36) In our opinion, considering that the morbidity and mortality of patients with symptomatic unruptured AAA undergoing emergency surgery is related to cardio-reno-pulmonary dysfunction, it is reasonable to prioritize the optimization of these systems prior to AAA repair. In this sense, we consider that these objectives could be achieved in a short time span of 12-24 hours, provided the medical center has the necessary resources. It is essential that the patient be admitted to a critical care unit, with suitable vital sign monitoring. From a cardiovascular viewpoint, there is evidence on the usefulness of focused cardiac ultrasonogra-



Modified Sullivan's algorithm (34)
AAA: abdominal aortic aneurysm; CTA: computed tomography angiography; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio

Fig. 1. Algorithm for the diagnostic-therapeutic approach of symptomatic AAA

phy (FoCUS) for critical patient assessment, as well as for presurgical evaluation. (37) An echocardiogram performed in the emergency room will provide essential information for hemodynamic management, including left ventricular ejection fraction, presence of significant valve diseases and the degree of patient's preload, through the transmitral filling pattern, E/E' relationship, pulmonary systolic pressure, and inferior vena cava diameter, and inspiratory collapsibility. (37) Frequently, elderly patients present with reduced preload prior to surgery with a negative impact on cardiac output, and this can be optimized with an adequate volume load. Some cases may require more invasive monitoring with a Swan Ganz catheter, allowing therapeutic guidance as a function of the hemodynamic state of the patient. Moreover, achieving adequate preload will reduce the risk of postoperative kidney failure. From a respiratory standpoint, reversible obstructive pulmonary disease can improve through a short treatment with intravenous steroids and aerosol bronchodilators. (34)

Therefore, in this subgroup of patients with symptomatic unruptured AAA it is crucial to identify individuals at high preoperative risk who may benefit from a fast optimization of their clinical status (cardiological, pulmonary and/or renal) prior to an urgent intervention. (17,34) With the objective of answering this problem, different publications have evaluated the usefulness of scores and certain biochemical markers to predict in-hospital mortality in patients with symptomatic unruptured AAA. Antonello et al. reported that the Glasgow Aneurysm Score is a good predictor of perioperative morbidity and mortality after urgent open surgery of symptomatic unruptured AAA. The authors suggest that patients with score <90 can safely undergo an emergency open repair. However, patients with score ≥90 should undergo a thorough assessment and optimization of the preoperative clinical sta-

tus. (38) On the other hand, considering the role of inflammation in the etiopathogenesis of this disease, Garagoli et al. recently evaluated the usefulness of inflammatory biochemical markers for the prediction of in-hospital mortality in patients submitted to surgical and endovascular repair of symptomatic unruptured AAA. The authors concluded that patients with neutrophil-to-lymphocyte ratio ≥ 6.4 and/or platelet-to-lymphocyte ratio ≥ 185 are at high risk and could benefit from a surveyed waiting conduct prior to optimization of the presurgical clinical status or, even consider an endovascular repair. (36,39) These biomarkers are widely available, have low cost and, in addition, have the advantage of representing the inflammatory state of the patient at the time of hospital admission. This is different from the Glasgow Aneurysm Score that uses clinical variables referred to the patient's prior medical history and considers shock as the only variable of the clinical status at the time of presentation, which we regard as insufficient since, as previously mentioned, these individuals generally present with hemodynamic stability. (36,39)

However, during this preoperative evaluation, it is fundamental that the treating physician is alert to signs and symptoms leading to a mandatory emergency intervention. The development of hypotension, tachycardia, oliguria or metabolic acidosis requires an immediate repair. (7)

Decision on the type of symptomatic unruptured AAA repair: open surgery versus endovascular intervention

Evidence shows that endovascular intervention reduces morbidity and mortality after symptomatic unruptured AAA repair. In this sense, this type of repair offers some potential advantages compared with conventional surgical treatment in this clinical setting: less physiological aggression to the organism, less need for deep anesthesia, less blood loss, minimizes hypothermia and reduces intervention time. (7) The analysis of the ENGAGE Registry demonstrated lack of difference in the elective endovascular repair of asymptomatic AAA versus symptomatic unruptured AAA. (19) A systematic review identified 23 observational studies evaluating 7040 symptomatic unruptured and ruptured AAA repairs (with surgical and endovascular intervention) and showed that patients undergoing endovascular intervention presented a lower rate of in-hospital mortality compared with open surgery (odds ratio 0.624, 95% CI 0.518-0.752; p <0.0001), as well as reduced length of hospital stay, lower bleeding and decreased intervention time. (40)

However, to perform endovascular AAA repair it is essential to fulfill the required anatomical criteria in addition to an institutional program for the emergency endovascular intervention. In this context, the role of CTA is crucial to define those patients fit for endovascular repair. (5,8) Moreover, we consider that the transfer to a high-complexity vascular center is appropriate for hemodynamically stable patients and anatomically apt for endovascular repair, especially if the surgical risk is high.

CONCLUSIONS

Symptomatic unruptured AAA constitutes a clinical form of potentially life-threatening AAA, with an intermediate prognosis between asymptomatic patients and those with ruptured aneurysms. Although the timing of intervention is still controversial, we consider it is essential to stratify individual preoperative risk, with the object of identifying high-risk patients who would benefit from the optimization of their clinical status prior to the intervention. Endovascular repair is feasible in this clinical scenario, mainly in patients at high surgical risk, provided the required anatomical criteria are fulfilled and the institution has a program for emergency endovascular intervention.

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Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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OPINION ARTICLE

Is the Anatomy the New Paradigm in the Chronic Coronary Syndromes?

¿Es la anatomía el nuevo paradigma en síndromes coronarios crónicos?

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The condition widely known as chronic stable angina used to be considered as uncomplicated and generally easy to solve by percutaneous revascularization. However, this is no longer the case. Understanding of its true significance has evolved towards characterizing different pathophysiological forms currently and widely known as chronic coronary syndromes (CCS). This paper intends to briefly describe the most relevant data from the latest evidence and to reflect on the meaning of myocardial ischemia when making clinical decisions about revascularization in the year 2023.

We need to distinguish at least 4 subtypes of CCS: severe left main coronary artery (LMCA) lesion/severe proximal multivessel lesions; severe diffuse multivessel disease; severe focal lesion; and non-severe diffuse disease/without angiographically significant lesions, with microcirculation involvement. These are all synonyms of atherosclerosis and vascular dysfunction with considerable overlapping. The role of clinical cardiology is to be able to include the patient in the right part of the spectrum in order to maximize the treatment benefits. This analysis will not include microvascular disease with no significant epicardial lesions, as it demands a different approach. Concisely, evaluation ideally involves invasive tests of coronary physiology, including an acetylcholine test to rule out epicardial (and microcirculation) vasospasm, as well as the calculation of the coronary flow reserve and the microcirculatory resistance index. Furthermore, if a non-invasive evaluation is chosen, quantification of the absolute flow via a cardiac positron emission tomography (PET) is the most informative test. (1,2) Another possibility is the semiquantitative evaluation provided by the stress ECG through the anterior descending artery flow reserve. Please note that an abnormal flow reserve cannot be ruled out by absence of myocardial ischemia on a "conventional" single photon emission computed tomography (SPECT) or a stress echo. (3)

Further understanding of ischemic heart disease has increased, and the paradigm is changing again. From the anatomy to the ischemia, a little more than two decades have passed, ¿and now from the ischemia to the anatomy again? As reflected by the guidelines from nearly all scientific associations, a short time ago, (4,5) the presence of myocardial ischemia ≥10% was considered as high-risk for events and was an unquestioned cut-off point when deciding on an invasive revascularization strategy for chronic coronary disease. Ischemia was the focus of every decision. This outdated concept has been updated by the extensive observational study performed by Dr. Rory Hachamovitch et al. from Cedars-Sinai Medical Center and published in Circulation in 2003, which included more than 10 300 patients. (6) With all the evidence and data from the ISCHEMIA study, one question shocked the clinical scenario three years ago: has significant ischemia ceased to be a *sine qua non* sign of revascularization, even with symptoms present? The answer was yes. Why? Essentially because we have observed that "sustained long-term intensive" drug therapy has shown clinical efficacy and safety to the detriment of an invasive approach. Why? There is no simple answer to this question, but we could easily mention the following: stabilized (or even reduced) plaque with the resulting clinical and imaging slowdown in disease progression, myocardial protection, vascular function improvement, and symptom control. A healthy lifestyle (7) (exercise, a Mediterranean diet, avoidance of smoking, and stress control), a goal-directed therapy [angiotensin converting enzyme inhibitors/angiotensin receptor blockers, (7) β-blockers, (8) statins, (9) ezetimibe, (10) and PCSK9 inhibitors], and an eventually improved antithrombotic management, apart from aspirin in high-risk patients [P2Y12 receptor blockers (11) and antiXa-rivaroxaban (12,13)], have shown the strengths of selecting a conservative therapy. In addition, a deeper understanding of coronary circulation pathophysiology has introduced new concepts in clinical cardiology, such as coronary flow reserve (CFR), which has become a major prognostic

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marker providing additional information with no direct correlation both with the extent of coronary disease and the myocardial ischemia.

The ISCHEMIA study (2020) (14) and its long-term follow-up interim analysis with a mean of 5.7 years, and known as ISCHEMIA-EXTEND, (15) being recently published (November 2022), continue to follow the path first led by the revolutionary COURAGE study (2007), (16) and later by BARI 2D (2009) (17) and FAME-2 (2012), (18) among others: in patients with good ventricular function, myocardial ischemia *does not appear to be* a relevant prognostic marker, and revascularization regarding this has no significant impact on the disease course under the best available drug therapy (BADT). These studies were designed to compare a conservative drug strategy against revascularization in a scientific period when coronary angioplasty was essentially seen as the solution for stable angina. Many lessons have been learnt since then.

Some of the milestones worth considering are:

- The COURAGE and ISCHEMIA/ ISCHEMIA-EXTEND studies showed that revascularization fails to change prognosis in patients with obstructive epicardial disease and significant ischemia under the BADT.
- The FAME-2 study showed that revascularization guided by fractional flow reserve (FFR) reduced urgent revascularization and *marginally* reduced spontaneous infarction after 5 years.
- The ISCHEMIA study also showed that revascularization of a severe isolated proximal lesion of the descending anterior artery (≥ 50%) failed to reduce events, as typically thought in the past.
- The COURAGE and ISCHEMIA studies showed that angina is relieved by revascularization, although during the follow-up the differences with respect to the BADT are reduced or disappear.
- According to the ORBITA study, (19) angioplasty did not improve times of exercise or the frequency of precordial pain in patients with anatomical and functionally significant stenosis. This clever trial cleared up doubts about the potential "anti-angina placebo effect" of the percutaneous intervention itself when using a sham procedure as control.
- APPEAR (20) and CLARIFY (21) were large observational studies proving that most patients with chronic coronary artery disease had mild symptoms or remained asymptomatic.

It seems clear that patients with CCS and good ventricular function do not benefit from a systematic revascularization strategy as compared to the BADT in the case of focal anatomical lesions leading to ischemia. However, it is also evident that the multivessel anatomical and diffuse disease with a high atherosclerotic burden, as in patients with diabetes, is clearly favored by revascularization: this is confirmed by the BARI 2D, FREEDOM study, (22) the ISCHEMIA substudy, (23) COURAGE 10-year follow-up, (24) and the FAME 3 trial. (25) Support is also provided by another major and inescapable pathophysiological concept: thrombotic or plaque events are caused by various mechanisms in vulnerable lesions that, in many cases, are not anatomically obstructive. (26) In this subtype of patients, revascularization by coronary artery bypass grafting should protect the distal myocardium passing over a number of vulnerable (and non-vulnerable) lesions, in contrast to the angioplasty which revascularizes in a focal manner.

These ideas have resulted in a new model to assess the heart vasculature, together with the advances in multislice computed tomography (MSCT), which is currently available, and, in my opinion, this will be a game changer for CCS management. MSCT provides a precise non-invasive evaluation of obstruction sites, grades, and scope (particularly, in the main and proximal vessels), as well as plaque features (vulnerability). Something even more disruptive is the recent application of new softwares to estimate the coronary fractional flow reserve (FFR-CT) during the same study and with high precision. FFR derived from the MSCT or FFR-CT, when applying computational fluid dynamics, estimates FFR values in all epicardial coronary arteries with no need for any additional drugs, images, or protocol changes.

Two randomized studies of more than 14 000 patients [PROMISE (27) and SCOT-HEART (28)] and the DANISH registry, (29) with 86 700 patients, showed superiority in terms of CCS management using MSCT versus ischemia-evocative tests for death and myocardial infarction. Early and precise anatomical knowledge can be used to quickly dismiss high-risk patients (proximal multivessel or left main coronary artery), achieve better stratification, and work on treatment optimization/enhancement.

In addition, in 2021 Reynolds et al. published an important ISCHEMIA substudy in Circulation, (30) which showed that the severity of ischemia was not associated with death or infarction after 4 years, and that the scope of anatomical disease was independently associated with non-fatal infarction (HR 3.78, 95% CI 1.63–8.78) and all-cause death (HR 2.72, 95% CI 1.06–6.98) after 4 years. These data have been confirmed for the group of patients with severe proximal lesions in two or more vessels, including proximal left anterior descending artery.

Therefore, the paradigm is shifting towards assessment of new anatomical and functional aspects in CCS, which leads us to reinterpret a condition with a complex course, and evidence that avoids the dogmatic clinical routine of suspecting ischemia. In this setting, a MSCT is recommended by many authors as the main and initial element in the study/decision algorithm. "Systematic management" guided by a finding of ischemia through myocardial perfusion (SPECT) or stress echo is now left behind. Anatomy would serve to rule out proximal multivessel and LMCA prognostic disease, and eventually ischemia assessment studies would be used to readjust treatment in case of

symptoms, or their persistence, with a relative impact on intervention indication. Ischemia seems to be a complementary and substitute feature for the burden of atherosclerotic coronary disease, ¿except if higher than 15%? This question and new prognostic value emerges from an extensive retrospective analysis of more than 43 000 patients under cardiac rest-stress SPECT from 1998 to 2017 with a median follow-up of 11.4 years, recently published by Rozanski et al. (31) This needs to be confirmed by prospective studies.

The future goes beyond anatomy in this new CCS era: the characteristics and scope of atherosclerotic disease across the entire coronary tree and flow reserve in every artery, plus novel myocardial perfusion techniques within the same procedure. Impressively, all these elements will continue to evolve permanently towards a more precise diagnosis and clinical interpretation. (32,33)

To conclude, ischemia has been moved (though not removed) from central decision-making, and MSCT-aided anatomy has now become the most relevant prognostic marker in this respect. For practical reasons, the present revascularization indication should be guided by *symptoms incompatible with quality of life under the best available drug therapy, high-risk anatomy, and/or acute coronary syndrome.*

"There is no sin in finding out there is evidence that contradicts what we believe. The only sin is not using that evidence as objectively as possible to refine that belief going forward." @AnnieDuke.

Conflicts of interest

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

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Acute Myocardial Infarction Due to Coronary Embolism in a Young Woman with Mechanical Aortic Valve Prosthesis and Anomalous Origin of Two Coronary Vessels: A Case Report

Heart valve disease affects approximately 2.5% of adults in developed countries. Since 1960, valve replacement with mechanical prostheses is one of the therapeutic alternatives for the management of valve disease. Its main complication is the development of thrombosis or embolic phenomena, with an estimated annual incidence of 0.3-1.3% and 0.7-6%, respectively. (1) The risk is increased in the first months of implantation, depending on its anatomical position and its association with other thromboembolic risk factors (e.g., atrial fibrillation).

We present a case of ST-segment elevation acute myocardial infarction in a young woman with a prosthetic aortic valve who had voluntarily discontinued anticoagulation.

A 23-year-old woman, from the Colombian Pacific region, with a history of mitral regurgitation and mechanical valve prosthesis implantation at 8 years of age, was anticoagulated with warfarin until 2 years ago when she discontinued medical treatment. She consulted the emergency department due to 8 hours of high-intensity oppressive chest pain radiating to the right upper limb, with no other associated symptoms. On physical examination, she was afebrile, with blood pressure of 121/76 mmHg, heart rate 82 bpm, and respiratory rate 19 rpm. Auscultation revealed a grade III/VI holosystolic murmur in the mitral focus, and a grade III/VI diastolic murmur in the aortic focus, with no signs of acute heart failure and no other relevant findings. The electrocardiogram showed sinus rhythm with ST-segment elevation from V1 to V3 and inferior ST-segment depression, with the presence of pathological Q waves in leads I and aVL, and signs of left ventricular enlargement. Emergency coronary angiography was performed 12 hours after admission, which documented a total occlusion of chronic appearance in the mid-proximal segment of the left anterior descending artery (Figure 1) and a thrombotic lesion in the first obtuse marginal of the circumflex artery, with 90% stenosis (Figure 2), without other angiographically significant lesions. Loss of mobility of one of the hemidiscs of the double-disc mechanical valve prosthesis was evidenced, due to in situ thrombus.

An anomalous origin of the right coronary artery and a second marginal obtuse artery, independently from the left coronary sinus were demonstrated as incidental findings. Due to the high risk of prosthetic thrombosis, it was initially decided to anticoagulate the patient with low molecular weight heparin and warfarin until international normalized ratio (INR) goals were reached. Laboratory tests showed positive

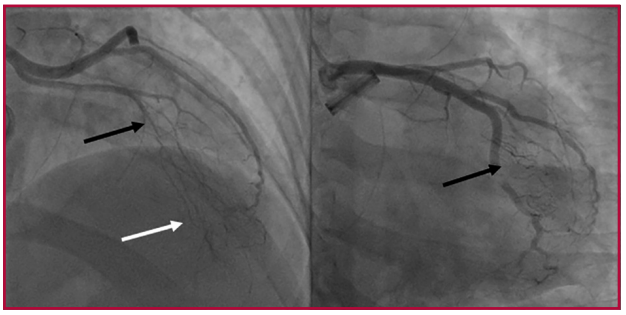

Fig. 1. **Left**: Chronic occlusion of the left anterior descending artery at the junction of the proximal to middle segment (black arrow) with heterocoronary and homocoronary collateral circulation (white arrow). **Right**: Obtuse marginal artery with filling defect compatible with thrombus generating subocclusion and TIMI 2 flow (black arrow).

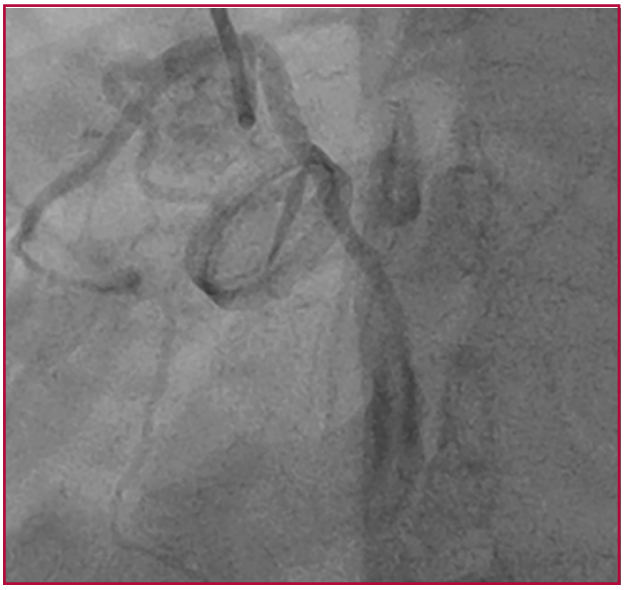

Fig. 2. Loss of mobility of one of the hemidiscs of a mechanical double disc prosthesis due to in situ thrombus

cardiac troponin I (6.53 ng/mL for a normal upper limit of 0.12 ng/mL). Transesophageal echocardiogram revealed akinesia without thinning of the anterolateral and inferolateral walls, with a left ventricular ejection fraction of 47% by Simpson's method. It also showed mechanical aortic prosthesis in adequate position with restriction of the posterior leaflet movement, and presence of pannus and marked turbulence in the antegrade flow, with maximum velocity of 3.2 m/s and a mean gradient of 22.5 mm Hg, as well as severe mitral regurgitation secondary to perforation of the anterior leaflet.

With these findings, she underwent aortic valve prosthesis replacement using a n° 23 Medtronic mechanical prosthesis. Enlargement of the aortic an-

nulus with a heterologous pericardial patch using Manougian´s technique, and repair of the mitral valve with closure of the anterior leaflet orifice were performed. Fresh thrombi in the aortic mechanical prosthesis at the hinge level of both discs and severe subvalvular pannus were found. It was not possible to perform revascularization of the anterior descending artery as its course could not be visualized due to the presence of epicardial-pericardial adhesions from the previous surgery, so coronary angioplasty was indicated. The second coronary angiography performed 25 days after admission revealed complete resolution of the thrombotic lesion in the obtuse marginal artery. The total occlusion of the left anterior descending artery persisted, but it was not possible to perform percutaneous revascularization as it was a vessel with a small caliber. It was decided to continue medical treatment, accompaniment by the Psychology and Education service, and she was discharged after 41 days of hospitalization, without complications, with an INR of 3.2 and indications for strict medical control.

Ischemic heart disease is the leading cause of death worldwide, mainly associated with atherosclerosis. Significant atherosclerotic lesions are not found in up to 7% of cases. Coronary embolism is a cause of non-atherosclerotic infarction, and it is estimated that it represents 3% of all myocardial infarctions. It generally affects the left coronary circulation, (1) as in the case of our patient.

The main associated causes are atrial fibrillation, cardiomyopathies, presence of prosthetic valves, endocarditis, tumors, and prothrombotic conditions. Coronary thrombosis associated with acute infection by SARS-CoV-2 during the pandemic has been reported for this entity. (2) Before the use of prosthetic valves, endocarditis was the main cause of death; now atrial fibrillation is mainly considered. (1) Currently, prosthetic valve replacement is the gold standard for the management of severe valve disease in patients with low or intermediate surgical risk. Mechanical valves have a longer life, but are prothrombotic, which requires indefinite anticoagulation to prevent valve thrombosis and embolic events.

There are three types of coronary embolism: direct, paradoxical, and iatrogenic. Direct coronary embolism occurs when an embolus enters the coronary circulation from the left ventricle, left atrial appendage, pulmonary veins, and the aortic or mitral valve. (3)

The clinical, electrocardiographic, and echocardiographic manifestations of myocardial infarction due to coronary embolism are indistinguishable from infarction of atherosclerotic origin, and it should be suspected in patients with prothrombotic risk factors who present with sudden chest pain. (4)

There are currently no guidelines for the management of coronary embolism. Intracoronary thrombus aspiration vs. angioplasty alone has been tested in patients with ST-segment-elevation myocardial infarction, without demonstrating an additional benefit in mortality. However, patients with a high thrombotic burden, such as patients with coronary embolism, could benefit more from this measure. (5) In cases of coronary embolism, systemic thrombolysis with tissue plasminogen activator (t-PA) has been reported to be successful in restoring coronary flow. Karakoyun et al (5) effectively and safely treated three patients with coronary embolism associated with prosthetic valves with low-dose intravenous t-PA. Similarly, intravenous infusion of bivalirudin for 48 hours in coronary embolism of the distal right coronary artery has been described, with complete resolution of the thrombus without major bleeding. (6) Other therapies include balloon angioplasty, which has been shown to be successful in restoring blood flow, both as isolated treatment and as adjunctive therapy to thrombotic aspiration. (5)

In conclusion, we describe the case of a young woman with mechanical aortic valve prosthesis who voluntarily discontinued anticoagulation and who presented an acute myocardial infarction due to coronary embolism. This condition is potentially fatal, so adherence to pharmacological treatment and education about the disease is essential in a patient at high risk of thrombosis. Permanent anticoagulation, strict clinical monitoring and education are the most important measures to prevent new events.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

Ethical considerations

Not applicable.

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Extracorporeal Ventricular Assistance in In-hospital Cardiac Arrest: A Feasible Reality in Our Setting?

Extracorporeal cardiopulmonary resuscitation (ECPR) is the use of extracorporeal membrane oxygenation (ECMO) in patients in whom standard cardiopulmonary resuscitation (SCPR) measures do not achieve a sustained return of spontaneous circulation after cardiac arrest (CA). (1) Patients undergoing ECMO implantation during or immediately after CA have a particularly unfavorable prognosis. (2)

Despite there are no current systematic recommendations on the indication of ECMO in CA, it could be considered an emerging therapy in selected cases when SCPR fails. (3) At present, no randomized controlled trials have been reported comparing the results of ECPR versus SCPR in in-hospital CA (IHCA). (1) Though numerous cohort studies have shown that this therapy is associated with a higher survival rate until discharge, and with favorable neurological results, (4) to our knowledge, limited information has been published in our setting.

The aim of this study was to analyze and report the characteristics and clinical results of a retrospective and consecutive cohort of adult patients treated with ECPR after IHCA in a high complexity center of Argentina.

Patients over 18 years of age treated with venoarterial (VA) ECMO for IHCA between 2014 and 2022 were analyzed. The study included patients with witnessed IHCA, possibly of cardiac origin (mainly ventricular tachycardia or ventricular fibrillation as initial rhythm, extending for more than 20 minutes), (1) even with adequate CPR since its onset. Patients with CA during cardiac surgery were excluded from the study. Table 1 summarizes the inclusion criteria for ECPR at our center.

An analysis of the ventricular assistance database, which is prospectively completed, including among its main variables, demographic characteristics, information on the type of ventricular assistance, complications, relevant clinical events and clinical evolution, biochemical and echocardiographic predictors was performed. Regarding relevant clinical events, two types of survival were evaluated:

- Survival in ECMO: It assesses survival in ECMO and up to 24 hours from ventricular assistance weaning. In this case, the reasons for weaning from ECMO are cardiac function recovery or heart transplantation.

Table 1. Inclusion criteria for ECPR

Age <70 years
In-hospital CA
Time of first CA onset <5 minutes
Initial cardiac rhythm: ventricular fibrillation, ventricular tachycardia, or pulseless electrical activity
Estimated time from CA to ECMO flow <60 minutes
Recovery from intermittent spontaneous circulation or from recurrent ventricular fibrillation
Absence of previously known life-limiting comorbidities

CA: cardiac arrest; ECMO: extracorporeal membrane oxygenation

- Survival at discharge. It evaluates survival at hospital discharge, either by release from hospital or referral to another healthcare center (e.g., third level of rehabilitation).

In addition, neurological complications, brain death (irreversible loss of consciousness and neurovegetative functions, including breathing capacity) and stroke (acute neurological focus and new ischemic or hemorrhagic changes in brain computed tomography) were analyzed.

The analysis included 8 patients, representing 11.9% of VA ECMO implanted during this period in the center. Median (interquartile range, IQR) age was 46 years (IQR 30-58) and 66% were women. Three patients had history of hypertension and dyslipidemia and one of diabetes. No patient presented with previous history of obstructive pulmonary disease, chronic kidney disease, stroke, peripheral vascular disease, atrial fibrillation, or anemia.

Three patients presented with acute coronary syndrome, two with electrical storm and the remaining causes were peripartum cardiomyopathy, myocarditis, and unidentified restrictive cardiomyopathy.

Cannulation was peripheral in 87.5% of cases (7 patients). The same number of patients required use of intra-aortic balloon pump, and 2 cases needed surgical left ventricular decompression, through pulmonary vein venting. In all the cases, ECMO was implanted as bridge to recovery.

Median circulatory assistance duration was 5 days (IQR 2-8). Successful VA ECMO weaning was achieved in 5 patients.

The rate of survival in VA ECMO was 62.5% (n=5) and at discharge 37.5% (n=3). The cause of death was non-cardiovascular in 4 of the 5 deaths.

Complications included major hemorrhage (66%), non-dialytic acute kidney failure (66%), infection (33%), seizures (11%) and thromboembolic complications (33%). No brain death was reported, and one patient suffered an ischemic stroke.

Median follow-up after discharge was 14 months (IQR 7-30). One of the 3 surviving patients is on the waiting list for elective heart transplantation, and 2 are followed-up with preserved biventricular function.

There is an increasing worldwide use of ECPR as a rescue technique in patients with refractory CA. Although controlled randomized trials are still missing demonstrating its efficacy in this setting, observational studies have reported 20% to 40% survival. (5) Currently, there is no sufficient data available to identify patients who could benefit from ECPR. It is internationally recommended to establish agreed inclusion criteria in each center to guide physicians on how to balance the intelligent use of resources among patients who are believed to have a better probability of survival after CA. (2) In our center, inclusion criteria were standardized since the creation of the multidisciplinary "ECMO team" (Table 1), considering that decision making for ECPR is often time critical and influenced by external factors such as hours and day of the week. It is therefore essential to present with adequate logistics, 24/7 trained staff for cannulation (as it is recommended that ECMO is functioning within 60 minutes after CA) and for the fast assembly and purge of the device in the emergency, and healthcare professionals who can detect within 10 minutes of CA the possible ECPR candidates.

Protocols and algorithms endeavor to quickly identify the cases with higher probability of survival with a favorable neurological outcome, as well as patients with witnessed CRA in whom high-quality CPR was quickly administered, and also cardiac arrests with a presumably reversible disorder, such as acute coronary obstructions. (2) Other factors which may influence ECPR indication are age, cause of CA, time, comorbidities and cardiac rhythm at CA onset. (3) Recently, the RESCUE-IHCA survival predictive score derived from 1075 patients was published, showing 28% survival at discharge, and identifying 6 variables associated with in-hospital mortality: age, time of day, initial rhythm, history of kidney failure, type of patient (cardiac vs. non-cardiac and clinical vs. surgical) and duration of cardiac arrest. (5) The greatest probability of success occurs in a young patient (in some working teams 50 years of age is considered the limit for ECPR), with few comorbidities, with a witnessed CA, preferably during daytime (when logistics is easier and there is more access to trained staff), with adequate CPR maneuvers performed immediately (preferably in intensive care units), and of cardiac origin, with a shockable initial rhythm.

Our results are comparable to those reported by the ELSO (Extracorporeal Life Support Organization) international multicenter registry, in which ECMO survival was 41%, and at hospital discharge 30% at an international level, (6) and to the results of the RESCUE-IHCA. (5)

In our center, VA ECMO as treatment for IHCA presented an acceptable survival at hospital discharge, and it can be considered an effective treatment in highly selected patients when conventional therapies fail, being useful and applicable in a country with low and medium income and limited access to circulatory assist devices. Probably these results cannot be extrapolated to other centers of the region, as our institution is a referral VA ECMO high complexity monovalent cardiovascular center, with a developed care program, more than 7-year experience and currently, with more than 15 implants per year. Although the number of patients included in this series was low, it is still a novelty, as it would be the first experience published analyzing the results of VA ECMO in refractory IHCA in our country.

Conflicts of interest

None declared.

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

Ethical considerations

The study was conducted according to research principles (Declaration of Helsinki) and was approved by the institutional Ethics Committee.

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Posterior Embolic Stroke Secondary to Subclavian Artery Thrombosis

Posterior stroke (PS) together with upper limb ischemia is an infrequently associated clinical presentation caused by embolism, aortic dissection, vascular trauma, thoracic outlet syndrome, coagulation disorders and, less commonly, subclavian artery thrombosis.

A 59-year-old male patient, former smoker (40 pack/year), hypertensive and dyslipidemic, presented with a 2-week gait disorder and referred a left upper limb hypotension record. Upon consultation with his occupational physician, expressive aphasia, right temporal hemianopsia and gait instability determined the decision to hospitalize him. The electrocardiogram confirmed sinus rhythm, and the echocardiogram evidenced preserved left ventricular systolic function, without shunt or intraluminal thrombi. Neck vessels Doppler ultrasound showed subintimal carotid plaques, without significant hemodynamic findings, and very low flow velocity in the left vertebral artery. Brain computed tomography (CT) revealed hypodense frontoparietal white matter areas in both hemispheres. Brain magnetic resonance angiography showed acute left temporo-occipital ischemic lesion in the left posterior cerebral artery territory, with absence of flow in the intracranial segment of the vertebral artery (Figure 1).

On the second day the patient referred left upper limb paresthesia, and lower temperature was detected with absence of humeral, radial, and ulnar pulses.

Left upper limb arterial echo-Doppler revealed very low velocity monophasic flow, and high resistance in the humeral, radial and ulnar arteries, with subclavian artery thrombosis. Neck vessels and aortic arch computed tomography angiography ruled out aortic dissection and thoracic outlet syndrome and showed complete left subclavian artery thrombosis from its origin, and part extending as intraaortic thrombus, and altered homolateral vertebral artery staining in the intraosseous and intracranial segments (Figure 2A). Thorax, abdomen, and pelvis CT scan revealed bilateral pulmonary emphysema. Laboratory results were: platelets 373 000 ml/mm3, normal D-dimer and IgG and IgM antiphospholipid antibodies, negative lupus inhibitor, normal homocysteine, negative anti-beta 2 antibodies and IgG and IgM glycoproteins, protein C 108% and free protein S 66%. Electrocardiographic 24-hour Holter monitoring indicated predominant sinus rhythm, without ventricular or

supraventricular extrasystoles. Control brain magnetic resonance imaging (MRI) performed on the 4th day did not evidence hemorrhagic temporo-occipital lesion transformation.

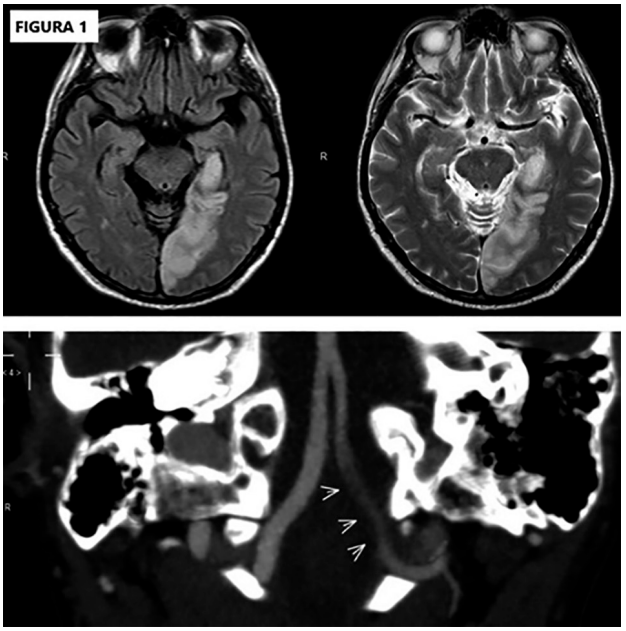

Fig. 1. Brain magnetic resonance angiography: acute left temporo-occipital ischemic lesion with absence of flow in the intracranial segment of the vertebral artery

Endovascular or surgical treatment for complete left subclavian artery thrombosis with intrathoracic extension associated with posterior ischemic stroke was discarded due to high risk of systemic embolic complications, and anticoagulation by continuous pump sodium-heparin infusion was decided, under strict neurological control and subsequent rotation to oral acenocoumarol. The patient was discharged on the 10th day with no neurological or upper limb ischemic complications. At 1-year oral anticoagulation was suspended due to recurrent episodes of hematuria and hematemesis, and the patient continued with oral clopidogrel and cilostazol. The last control computed tomography angiography at 3 years evidenced partial recanalization of the subclavian thrombosis, with complete disappearance of the intraaortic thrombus in the subclavian ostium. (Figure 2B)

The patient is currently asymptomatic, with humeral pulse recovery. Studies for thrombophilia were repeated with negative results.

Almost 20-25% of strokes occur in the posterior circulatory system (posterior cerebral, basilar and vertebral arteries) and can compromise the brainstem, cerebellum, thalamus and/or temporo-occipital region. Caplan et al. described embolism as the most frequent mechanism of posterior stroke (40-54%), mainly of cardiac origin (24% of cases), while arterio-arterial embolism was reported only in 14% of cases. (1) Other mechanisms are atherosclerotic lesions of the great arteries, small vessel occlusion, and rare causes such as coagulation disorders or carotid atheroembolism associated with the fetal origin of the posterior cerebral artery. Due to the wide cerebral area irrigated by

the vertebrobasilar arterial system, ischemic strokes in this territory exhibit with various signs and symptoms. The most frequent signs are gait ataxia, unilateral limb weakness, dysarthria, nystagmus, and visual field defects, while reported symptoms are usually vertigo, dizziness, nausea and vomiting, headache, and consciousness disorders.

Subclavian artery thrombosis occurs due to vascular wall intimal injury. Atherosclerosis is its most frequent etiology, and is more commonly located in the right carotid-subclavian and left subclavian-vertebral areas, so these regions are usually involved in occlusive thrombosis. Subclavian atherosclerosis risk factors are hypertension, smoking, diabetes, obesity, and dyslipidemia. (2) Subclavian artery thrombosis presents in less than 1% of the population and is generally asymptomatic, resulting in an underdiagnosed disease. Left subclavian thrombosis is four time more common that its right counterpart. (2)

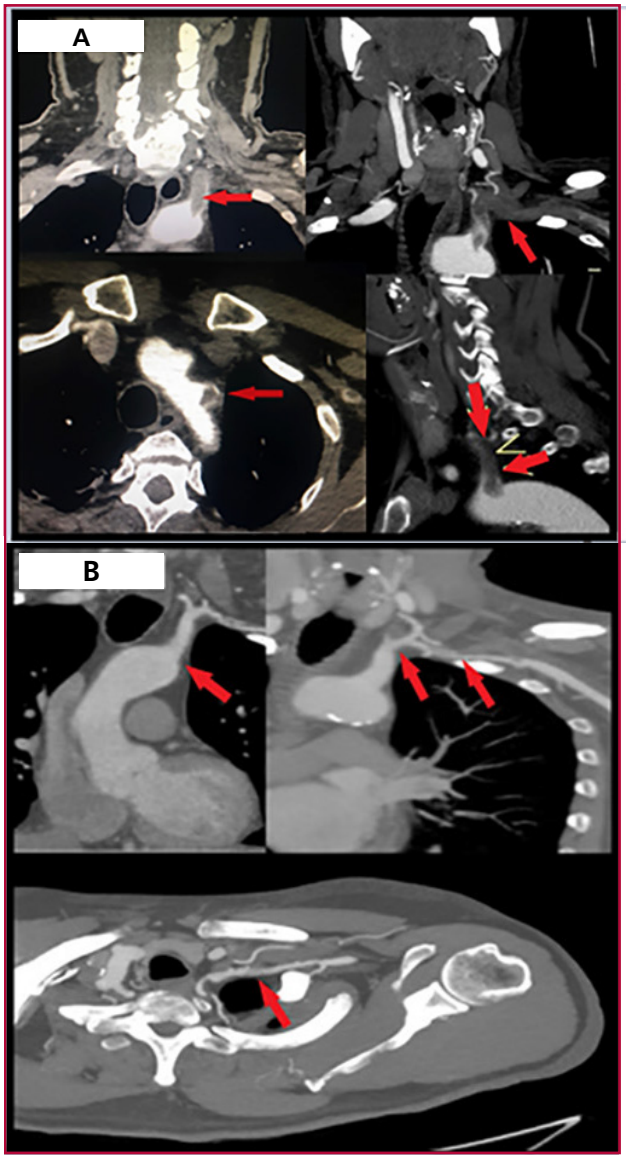

Fig. 2. A. Neck vessels and aortic arch computed tomography angiography: complete left subclavian artery thrombosis from its origin, with part of intraaortic thrombus. **B.** Control computed tomography angiography at 3 years: partial recanalization of subclavian thrombosis, with complete disappearance of the intraaortic thrombus in the subclavian ostium

The emergence of ischemic symptoms as a result of decreased arterial flow due to subclavian artery thrombosis is conditioned to the presence or not of collateral circulation, and the most usual clinical manifestations include upper limb intermittent claudication and paresthesia. Subclavian artery thrombosis complications are upper limb, mainly digital, ischemic gangrene, acute ischemia of the limb artery and rarely, posterior ischemic stroke. The pathogenesis of these infarctions in the vertebrobasilar territory is due to arterio-arterial embolism or the "retrograde" propagation to the vertebral artery from a homolateral subclavian artery thrombosis. (3,4)

Other causes of subclavian artery thrombosis associated with posterior stroke are hypercoagulability states (S-protein deficit, essential thrombocytopenia, etc.), aortic dissection, arterial trauma, cardiac embolism, and thoracic outlet syndrome with arterial involvement (arterial TOS). The latter is characterized by a subclavian artery disease due to compression by osseous anomalies as a cervical rib, with intimal lesion with or without post-stenotic dilation and thrombus formation prone to distal embolization, generating severe complications such as upper limb arterial ischemia and less frequently a posterior ischemic stroke. (3-6)

Castillo Costa et al. reported a case of posterior stroke with upper limb ischemia due to thrombosis of a structurally healthy aorta with systemic embolism. (7)

Computed tomography angiography of the aortic arch and the compromised upper limb allows confirming the diagnosis of subclavian artery thrombosis as possible embolic source in patients with posterior stroke, as well as identifying some of its causes (atherosclerosis, arterial TOS, dissection, trauma, etc.).

Treatment of subclavian artery thrombosis complicated with a posterior stroke will depend on the degree of upper limb ischemia and the vascular disease that originated it. In general, endovascular or surgical therapeutic interventions (embolectomy or decompression treatment with arterial TOS revascularization) are only indicated in patients presenting threatened upper limb, due to the risk of systemic embolization during the intervention. (3,4) Anticoagulant treatment through initial intravenous infusion of sodium heparin and subsequent oral anticoagulation is an effective therapy described for patients with subclavian artery thrombosis and posterior stroke coursing with compensated upper limb ischemia, to avoid arterial thrombosis and its progression. (2,5,6)

In conclusion, posterior ischemic stroke is an infrequent complication of subclavian artery thrombosis,

that should be suspected in patients with vertebrobasilar infarctions and absence of homolateral upper limb arterial pulse. Computed tomography angiography can confirm its diagnosis.

Conflicts of interest

None declared.

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

Ethical considerations

Not applicable.

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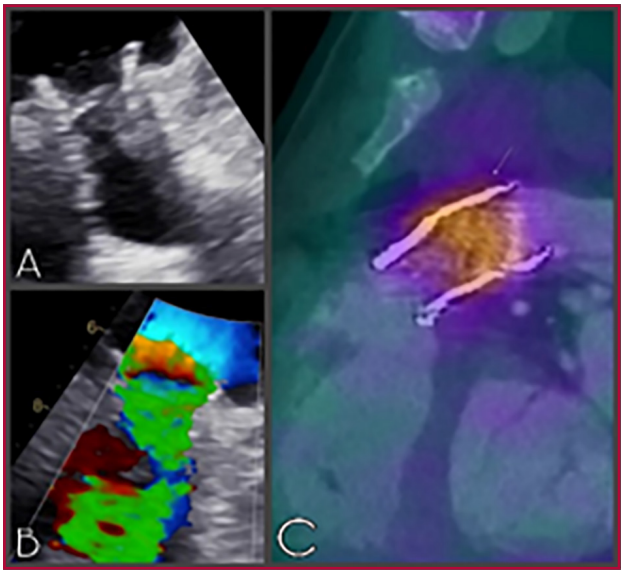

Fig. 1. Lreoperative studies. A, B: Pulmonary valve echocardiogram. C: PET/CT scan with prosthetic uptake.

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Pulmonary Valve Implant Infective Endocarditis. Surgical Resolution with Homograft

We present the case of a female 20-year-old patient who consults for a febrile syndrome of 7 days evolution, with asthenia and adynamia. As a relevant history, the patient presented pulmonary valve stenosis and aortic valve dysplasia at birth, as part of the clinical suspicion of Noonan syndrome. Throughout her growth, the patient had to undergo several surgeries: at one year of age, she was submitted to enlargement of the pulmonary artery outflow tract and plastic repair of the aortic valve; at 13 years, she required aortic valve replacement with a number 18 ATS type bi-disc mechanical prosthesis, with annulus enlargement and pulmonary valve replacement with a Nº 19 Freestyle type biological prosthesis; and then, at 17 years, given the marked increase in gradients through the lung graft, a number 20 Melody type valve was percutaneously implanted. It should be noted that despite the multiple interventions the patient had a normal physical, social, and intellectual development.

Given the relevant cardiological history, it was decided to hospitalize the patient to clarify and identify the focus that caused the fever. As positive data, the gram negative Cardiobacterium bacillus of the HACEK group was identified in serial blood cultures. The transesophageal color Doppler echo showed a marked increase in the Melody-type pulmonary valve gradients, with mobile structures compatible with vegetations (Figure 1. A and B) and the positron emission tomography (PET/CT) scan revealed a clear increase in the uptake of the pulmonary valve region (Figure 1. C).

Considering the clinical diagnosis and complementary studies, the febrile condition was interpreted as endocarditis of the pulmonary endoprosthesis, so a new surgery was performed to replace the clearly infected prosthesis and the pulmonary artery outflow tract with a number 21 homograft. The prosthetic aortic valve was undamaged, so its replacement was not required (Figure 2. A, B and C).

The postoperative evolution was satisfactory and the antibiotic therapy included ceftriaxone and gentamicin according the sensitivity of the Cardiobacterium. At one- year follow-up, the patient leads a normal, hemodynamically stable life, free of cardiac infection, with normal functioning of the pulmonary homograft.

The risk of infective endocarditis (IE) after percutaneous Melody pulmonary valve implantation (MPVI) is significant, at least during the first 3 years after implantation. However, the reported incidence varies considerably between different studies.

In a meta-analysis that included 851 patients, the cumulative incidence of IE on MPVI ranged from 3.2% to 25%, with an annualized incidence rate ranging from 1.3% to 9.1% patient-years. The median (interquartile range) time from MPVI to IE onset was 18 months (9-30.4), with a range between 1 and 72 months. The incidence of IE occurred in 32% of cases in the first year, 27% in the second year, 18% in the third year, and 23% beyond 3 years of MPVI. (1)

In a study conducted by McElhinney et al. in 309 patients with a follow-up of nearly 5 years, multivariate analysis found age under 12 years at the time of MPVI (OR 2.8; 95% CI 1.3–5.7; p=0.006) and a maximum gradient immediately after implantation greater than 15 mmHg (OR 2.6; 95% CI 1.3–5.2; p=0.008) as IE predictors. (2)

The diagnosis of this type of IE is challenging, especially in terms of documentation of the valve prosthesis infectious process. The modified classic Duke criteria, based on echocardiographic signs, confirm that the IE diagnosis after MPVI is not so simple. It is well known that echocardiography, especially transthoracic echocardiography (TTE), offers only modest sensitivity (30%) for the detection of pulmonary valve vegetations, probably due to the anterior position of the right ventricular outflow tract and prosthetic valve artifacts (stent, valve degeneration, calcification of the conduit, etc.). Moreover, transesophageal echocardiography (TEE), unlike the high sensitivity of IE detection in the aortic and mitral valves, does not always offer added value with respect to the TTE in pulmonary prosthetic valve IE. In the case reported, we believe that the PET/CT scan was able to identify the infectious process in the pulmonary prosthesis and ruled out aortic valve involvement, an extremely important data when planning a surgical strategy.

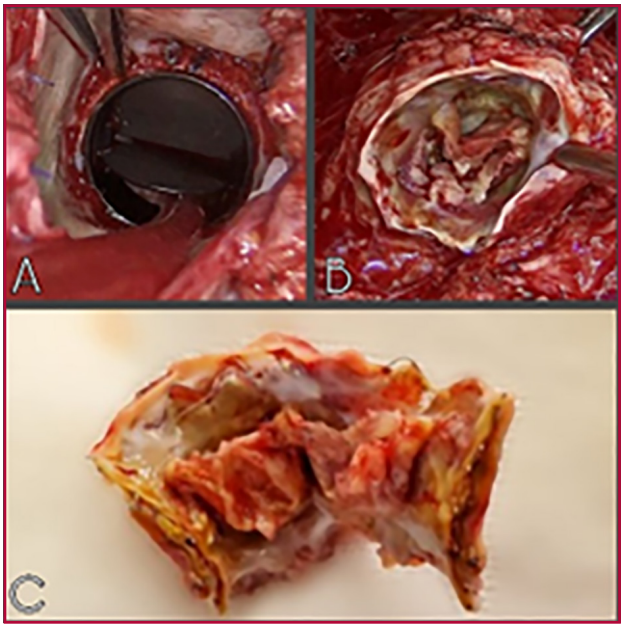

Fig. 1. Intraoperative images. **A**: Intact aortic valve. **B/C**: prosthesis in pulmonary position with clear signs of endocarditis

18F-FDG PET/CT combines a technique with high sensitivity to detect inflammatory-infectious activity and high anatomical resolution to assess structural lesions associated with endocarditis. With 91-97% diagnostic sensitivity, PET/CT has become a useful diagnostic tool in suspected IE of patients with prosthetic valves and/or devices, becoming a major criterion in the diagnostic algorithm for current guidelines. (3)

The most common clinical findings found in MPVI IE were positive blood cultures (93%), fever (89%), and progressive increase in the pulmonary transvalvular gradient (79%). Vegetations by TTE were detected only in 34% of cases. These data reported in the literature were also presented by our patient, with TTE being too weak to define the origin of the infective condition. In the cited meta-analysis, among 69 patients who developed IE after MPVI, 6 (8.7%) died and 35 (52%) underwent surgical and/or transcatheter reoperation. (1)

The most common germs that have been detected in the blood cultures of patients with IE post MPVI are: Staphylococcus 42%, Streptococcus 30.4%, Corynebacterium 5.8%, HACEK group 4.3% and Haemophilus 2.9%; and negative blood cultures have been detected in just over 7% of patients. (1, 4) Cardiobacterium hominis (germ responsible in our case) is a member of the HACEK group, which produces subacute IE; its natural habitat is the oropharynx .

The microbial entry route is related in most cases to oral processes. However, there are reports in patients with a history of gastroenteritis, cystitis, pneumonia, skin and nail processes, as well as skin tattoos. (5)

The incidence of IE after implantation of a percutaneous pulmonary valve is highly variable as reported in the studies, and it occurs mainly during the first 3 years after the procedure and mostly in the presence of increased transpulmonary gradients. The cardiac history should suggest IE in the presence of a febrile condition of unknown origin. Multi-imaging studies, including PET/CT scan, have been extremely useful in identifying the focus of infection secondary to Cardiobacterium IE in our patient. We believe that the satisfactory resolution of the case was due to the interaction of the members of the cardiology and sur-

gery service in adult congenital pathologies, given the complexity of decision-making and previous surgical interventions. The homograft has allowed us to resolve a complex surgical situation.

Conflicts of interest

None declared.

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

Ethical considerations

Not applicable.

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The Period after Vesalius. The Emergence of Physiology

La epoca posterior a Vesalio. Aparición de la fisiología

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As Andreas Vesalius appeared in the scientific firmament and his work developed (Chair of Padua and "*De Humanis Corporis Fábrica*"), Galenism began its collapse. Although the "*Fabrica*" was not free from errors, its research procedure based on human dissection left the necessary mark for a permanent revision, in the continuous search for the reality of nature, the Presocratics "*physis*". With Vesalius, in the field of Anatomy, an age clearly ends, the Middle Ages, and the Modern Age begins, but, after almost fourteen centuries of hegemony, Galen's concepts were not easily banished.

However, the seed had been sown. And as a result, a host of anatomists spread from the University of Padua, founded by Frederick II in 1222, to the rest of Europe, seeking precise knowledge from the dissection of the human body. The "*new corpse explorers*" in Padua were Realdo Matteo Colombo (1516-1559) (eye, ear), Gabriele Falloppio (1523-1562) (uterine tube, ear, eye), Fabrizio d'Acquapendente (1533-1619) (venous valves), Giulio Casserio (*circa* 1552-1616) (Harvey's teacher) and Adrian van den Spieghel (1578-1625) (liver lobe). In Bologna Costanzo Varolio (1543-1575) (annular pons) and Giulio Cesare Aranzio (1530-1589) ("*ductus arteriosus*", fourth ventricle). In Pisa Guido Guidi (died 1559) (brain, skull bones). In Rome Bartolomeo Eustacchio (1520-1574) (ear, kidney, teeth, the Eustachian tube. named after him) and Arcangelo Piccolomini (1525-1568) (fetal anatomy, abdominal muscles, brain). And in Naples Giambattista Carcano (1536-1606) ("*foramen ovale*", "*ductus arteriosus"*) and Giovanni Filippo Ingrassia (1510-1580) (sphenoidal process known as the Ingrassia process).

Bartolomeo Eustacchio, who practiced in Rome, deserves special mention. He was the author of the book "*De vena azygos*", where he refers to the thoracic duct and mentions the valve located at the mouth of the inferior vena cava that bears his name ("*valvula venae cavae inferioris*"). He had an advanced concept of the heart structure.

The most prominent Spanish doctors were: Pedro Jimeno (circa 1515-circa 1551) and Luis Collado (circa 1555) (both described the ear bone called stirrup, "*stapeda*"); Juan Calvo (circa 1580) (treatise writer), Juan Valverde (circa 1515-?) (wrote an excellent anatomical treatise); Alonso Rodríguez de Guevara (circa 1559); Francisco Díaz (circa 1588) (urology); and Bernardino Montaña de Monserrate (circa 1480) (first Spanish anatomical work).

Félix Platter (1536-1614) (excelled in dissection) and Gaspar Bauhín (1550-1624) (ileocecal valve) must be mentioned in Switzerland. Guillaume Rondelet (1507-1566) in Montpellier dissected the body of his eldest son, who died in infancy. In that place and date, this attitude motivated furious criticism, since people had a horror of anatomy. He also built the first anatomical theater in France, now extinct.

Leonard Fuchs (1501-1556) promoted anatomy in Germany, where Salomón Alberti (1540-1600) (venous valves) and Volcher Coitier (1534-1600) (osteogenesis) also excelled.

In Prague Johan Jessen (1566-1621) tried to describe the anatomy of phonetics. In England John Banister (1540-1610) (treatise writer) stood out, while in Leiden we must mention Pieter Paaw "*Pavius*" (1564-1617) (osteology, vomer bone).

But the change was even more important. Anatomy did not remain still, in its purely morphological status, but after the contribution of Jean Francois Fernel (1497-1558) with his "*Universa Medicina*" (1554), the human machinery was set in motion. The term physiology will no longer designate the concept of the Presocratics' "*physiologia*", but will be the study of the function and movement of living beings. Thus, this new development would have to include figures such as Fabrizio d'Acquapendente (circa 1533-1619) and Santorio Santorio (1561-1636). The latter, born in Capo d'Istria, Italy, was a professor in Padua. In addition to being the initiator of clinical thermometry, he is responsible for the construction of the "*pulsilogium*", a device to measure the pulse. In his work "*Commentaria in primam fen primi libri canonis Avicennae*" (Venice, 1625), he mentions seventy-three pulse varieties.

The foundations expressed above define that al-

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though Vesalius did not modify the concepts on circulatory physiology emanating from Galen, except for the previously mentioned fact of denying the existence of pores in the interventricular septum in his second edition of the "*Fabrica*" (1555), his study methodology allowed his followers to develop fundamental guidelines. Thus, the Spanish Juan Valverde de Amusco (born circa 1515), and the Italians Realdo Colombo (born circa 1516-1559), Andrea Cesalpino (1519-1603) and Fabrizio d'Acquapendente were in charge of carrying the torch of knowledge to the talent of William Harvey, the definitive discoverer of blood circulation.

Francisco de la Reyna also deserves to be named, more for the controversy than because of his real knowledge of circulation. Some authors tried to find in the text of this veterinarian born in Zamora (Spain), called "*Libro de Albeytería*", a description of the circulation in the paragraph "*by way that the blood goes in turnstile and wheel*", which he describes in the horse´s limbs. No copy of the first edition corresponding to 1546 has survived, but there has been a copy of the second published in Mondoñedo in 1552. There was also a third edition carried out later in Burgos in 1564. Galenist in his conceptions, Francisco de la Reyna places in the liver the origin of the vena cava venous system. Researchers of the stature of Lain Entralgo and Barón Fernández have concluded that no formal idea of blood circulation should be inferred from the Zamoran text.

Recap

Recapitulando

While writing these words, I am thinking that we are halfway through the current year, a time to reflect on the objectives we have set at the beginning of our management. I must say that, with great efforts, we are successfully meeting these objectives.

We have redefined the administrative section of the Argentine Society of Cardiology (Sociedad Argentina de Cardiología, SAC) to achieve a better performance, which will result in important improvements for our Society.

Regarding the projects that involve raising awareness by physicians and the entire community, we are enthusiastic about the bill submitted last May 4 by the Heart and Women Committee to the Argentine National Senate in order to designate a National Day of Women's Cardiovascular Disease Awareness. In Argentina, 1 out of 3 women die from cardiovascular disease; however, this is a fact that has not yet got the recognition it deserves, and there is an urgent need to achieve this to implement the appropriate prevention measures.

It is also worth mentioning that, in May, the 1st Argentine Symposium on Digital Health organized by the Digital Health Council was held in Rosario. This meeting brought national and international experts together where they discussed different issues related to the application of the information and communication technologies in the cardiology field.

The feedback generated between these disciplines and the cardiology field, on the one hand, helps digital experts to make fewer mistakes when developing their applications, and, on the other hand, helps us, the physicians, to make the most of their services to optimize the development of our professional practice.

During June, we attended the Inter-American Congress on Cardiology, in which several cardiologists representing our Society participated. We also attended the XXIX Dominican Congress on Cardiology and the II Congress on Cardiovascular Surgery 2023, being the only South American country invited.

The Congress of Imaging will soon be held, and it is always welcomed by the medical community, which is interested in the novelties on the diagnosis of cardiovascular diseases.

We continue working on position statements, such as the one on sodium-glucose linked transporter-2 inhibitors (SGLT2i), which was created in conjunction with other societies and is to be published soon.

We continue building projects and firmly believing that Cardiology is an exciting specialty. Although residencies in different public and private institutions are not able to fill the vacancies, we continue betting to enrich this scientific field as much as the evolution of the national management and our everlasting heart impulse allow us to do so.

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