

Preconditioning elements of cardiac complications among patients with diabetes and acute myocardial infarction

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ABSTRACT

Objective: To identify the risk factors based on demographic, clinical, echocardiographic and therapeutic parameters which predict the development of cardiac complications among patients with diabetes and acute myocardial infarction (AMI).

Materials and methods: An observational, analytical, case-control study was conducted at Centro de Cardiología y Cirugía Cardiovascular de Santiago de Cuba, attached to Hospital Provincial Saturnino Lora, from 2019 to 2021. The sample consisted of 266 patients, chosen by simple random sampling 1:2. The study included demographic, clinical, echocardiographic and therapeutic variables. A multivariate analysis was performed with all the variables considered as risk factors; one-way analysis of variance and binary logistic regression were used.

Results: The most frequent cardiac complications were atrial fibrillation and heart failure (approximately 12 %). A metabolic control analysis on admission yielded altered results ($OR = 6.92$; $LL: 2.61$; $UL: 18.32$; $p = 0.001$). The univariate analysis showed that ten factors increased the risk of complications, including the diagnosis of diabetes mellitus ≥ 10 years ($OR = 2.50$; $LL: 1.14$; $UL: 5.45$; $p = 0.020$). On the other hand, the multivariate analysis revealed six factors that predict the development of cardiac complications: age ≥ 60 years ($OR = 5.624$; $CI = 1.607-19.686$; $p = 0.007$), altered metabolic control on admission ($OR = 5.245$; $CI = 1.491-18.447$; $p = 0.010$), non-administration of thrombolytic therapy ($OR = 5.74$; $CI = 1.46-22.586$; $p = 0.012$), left ventricular ejection fraction (LVEF) ≤ 40 % ($OR = 5.245$; $CI = 1.17-23.433$; $p = 0.030$), left atrial pressure ≥ 15 mmHg ($OR = 12.335$; $CI = 3.45-44.08$; $p = 0.001$) and wall motion score index ≥ 1.5 points ($OR = 4.702$; $CI = 1.258-17.575$; $p = 0.021$).

Conclusions: The study demonstrated the value of six risk factors of cardiac complications among patients with diabetes and AMI, where glycemic control on admission, decreased LVEF, increased left atrial pressure and no reperfusion therapy stand out.

Keywords: Diabetes Mellitus, Type 2; Diabetic Angiopathies; Myocardial Infarction (Source: MeSH NLM).

INTRODUCTION

Diabetes mellitus (DM) is a growing global health problem. According to World Health Organization (WHO) statistics, the number of patients with DM worldwide ranges from 340 to 536 million ⁽¹⁾. It is estimated that, by 2040, this number will increase from 521 to 821 million, with a prevalence of 10.4 % expected by that year ⁽²⁾.

Sánchez-Delgado and Sánchez Lara ⁽³⁾ note that countries with developed, emerging and underdeveloped economies—including China, India, the United States, Brazil and Russia—exhibit high percentages of DM in adults.

A 2021 health survey conducted in Mexico ⁽⁴⁾ reported a DM prevalence of 15.8 % among adults, with a mortality rate ranging from 8.24 % to 11.95 % between 2019 and 2020.

This places DM as the third leading cause of death in the country ⁽⁵⁾.

Cuba is not exempt from this problem. By the end of 2020, the prevalence of DM in Cuba was 66.9 per 1,000 inhabitants, with 2,381 deaths attributed to the disease, resulting in a mortality rate of 21.2 per 100,000 inhabitants. According to the reviewed literature, DM was the seventh leading cause of death in the country ⁽⁶⁾.

Patients diagnosed with DM face significantly higher morbidity and mortality from coronary heart disease, at a rate two to four times higher than in the general population. In addition, the extent of vascular involvement is greater compared to people without diabetes ^(7,8).

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In the United States, 600,000 new cases of acute myocardial infarction (AMI) occur annually, with a 25 % mortality rate ⁽⁹⁾. Rosabal et al. ⁽¹⁰⁾ highlight that, in Latin America, cases of cardiovascular diseases are on the rise due to lifestyle factors. This region also has one of the highest burden of cardiovascular risk factors such as overweight, dyslipidemia, DM and hypertension (HTN).

By the end of 2020, a total of 7,804 patients in Cuba had died from AMI, accounting for 6.94 % of the country's total deaths. The province of Santiago de Cuba is no exception to this epidemic trend of cardiovascular diseases, and an analysis of its health situation reveals the magnitude of the challenge. According to the reviewed literature, there were 2,700 cardiovascular-related deaths in Santiago de Cuba in 2020, representing a mortality rate of 258 per 100,000 inhabitants ⁽⁶⁾.

Cuban research ⁽¹¹⁾ reveals limited evidence on predictive factors of cardiac complications among patients with DM in Cuba. Moreover, no studies have focused on clinical, echocardiographic and therapeutic parameters among patients with DM experiencing myocardial ischemia, tailored to Cuba's clinical and epidemiological context.

These considerations underscore the importance of conducting research to accurately identify predictive factors of AMI complications in people with DM, with a focus on specific diabetes-related factors tailored to the Cuban population. This research aims to identify the risk factors based on demographic, clinical, echocardiographic and therapeutic parameters which predict the development of cardiac complications among patients with DM and AMI.

MATERIALS AND METHODS

Study design and population

An observational, analytical, case-control study was conducted at Centro de Cardiología y Cirugía Cardiovascular de Santiago de Cuba (Cardiocentro), attached to Hospital Provincial Saturnino Lora, from 2019 to 2021.

The study population consisted of 1,303 patients diagnosed with AMI during the aforementioned period. From this group, 266 patients with a previous diagnosis of DM were selected as the study sample. The sample was differentiated solely by the presence or absence of cardiac complications during hospitalization, with all patients admitted to the referenced health center. The center provides specialized care—clinical, interventional and surgical treatments—to patients with cardiovascular conditions from the province of Santiago de Cuba and the Eastern Region. The minimum sample size for the study was determined using the formula outlined by Soto et al ⁽¹²⁾.

$$n_c = \frac{(p_1 x q_1 + p_2 x q_2) x (Z_a + Z_b)^2}{(p_1 - p_2)^2}$$

Where:

n_c = unadjusted number of cases and controls

p_1 = expected factor ratio in cases (0.25)

$q_1 = 1 - p_1$

p_2 = expected factor ratio in controls (0.5)

$q_2 = 1 - p_2$

$Z_a = 1.96$ and $Z_b = 0.84$

The number of cases and controls was derived from the standard normal distribution, based on a 95 % confidence interval and 80 % statistical power. Additionally, sample size adjustment was made considering an odds ratio of 2.5 and an unequal ratio between cases and controls, i.e., different from 1.

The adjusted number of controls was calculated using:

$$n_a = \frac{n_c \cdot (1 + c)}{2c}$$

Where:

n_a = adjusted number of controls

n_c = unadjusted number of controls

c = ratio of controls to cases

Thus, the case group (cardiac complications) consisted of 40 patients and the control group of 80. The sample size was calculated using the EPIDAT statistical package, version 4.2, and chosen by simple random sampling 1:2.

a) Case group: Patients diagnosed with AMI, whose medical records included all the study variables and the following complications: third-degree atrioventricular (AV) block, paroxysmal atrial fibrillation (AF), ventricular tachycardia/ventricular fibrillation (VT/VF), acute heart failure (AHF), cardiopulmonary arrest (CPA), cardiogenic shock, mechanical complications and stent thrombosis.

b) Control group: Patients with DM diagnosed with AMI but without complications, whose medical records included all study variables.

A data collection form was prepared to capture the study variables, which were identified after a review of relevant literature on the subject:

Dependent variable: Presence of complications based on clinical or paraclinical diagnosis.

Independent (explanatory) variables: Divided into demographic, clinical, echocardiographic and therapeutic variables.

Variables and measurements

Demographic and clinical variables: Age (> 60 years and ≤ 60 years), sex (male or female), history of HTN (yes or no), history of ischemic heart disease (yes or no) and infarct location (based on electrocardiographic changes: inferior AMI or anterior AMI). In addition, the diagnosis of DM (< 10 years or ≥ 10 years) was considered. Metabolic control on admission was assessed according to the American Diabetes Association (ADA) guidelines⁽¹³⁾ for lipids, which include LDL cholesterol < 100 mg/dL, HDL cholesterol > 40 mg/dL in men and > 50 mg/dL in women, triglycerides < 150 mg/dL and blood pressure $< 140/90$ mmHg after initial diagnosis of type 2 DM. Based on these parameters, metabolic control was categorized as either adequate or altered.

Therapeutic variables: Administration or non-administration of reperfusion therapy and type of coronary reperfusion therapy (simple therapy, through percutaneous coronary intervention [PCI] with intracoronary stenting; thrombolytic therapy with recombinant streptokinase; or a combination of both reperfusion procedures).

Echocardiographic variables: The specific type of disease or disorder was determined by imaging findings. The cut-off point for the echocardiographic variables was taken as referenced⁽¹⁴⁾.

- Left ventricular ejection fraction (LVEF): > 40 % (normal value) and ≤ 40 % (abnormal value).
- Left atrial pressure (LAP): < 15 mmHg (normal value) and ≥ 15 mmHg (abnormal value).
- Mean pulmonary artery pressure (MPAP): < 25 mmHg (normal value) and ≥ 25 mmHg (abnormal value).
- Right ventricular ejection fraction (RVEF), determined by the peak S' velocity of the right ventricular pulsed wave tissue Doppler imaging (RV TDI): > 9.5 cm/s (normal value) and ≤ 9.5 cm/s (abnormal value).
- Left atrial volume (LAV): ≥ 34 ml/m² (normal value) and < 34 ml/m² (abnormal value).
- Wall motion score index (WMSi): ≤ 1.5 points (normal value) and > 1.5 points (abnormal value).

Data were collected through a spreadsheet that compiled information from individual medical records and echocardiographic reports. Inpatient follow-up was conducted for all patients with DM and AMI.

The cut-off points used to convert quantitative into dichotomous variables for bivariate and multivariate analyses were determined using the optimal cut-point value or minimum p value. Thus, the following values were

established: age ≥ 60 years, diagnosis of DM ≥ 10 years, LVEF ≤ 40 %, LAP ≥ 15 mmHg, WMSi ≥ 1.5 points, RV TDI ≤ 9.5 cm/s, MPAP ≥ 25 mmHg and LAV ≥ 34 ml/m².

Statistical analysis

Data analysis was conducted using IBM Statistical Package for Social Sciences (SPSS) Statistics V22.0. Absolute and relative frequencies were determined for qualitative variables, while means and standard deviations were calculated for quantitative variables. A one-way analysis of variance (ANOVA) was applied where possible, with the following null and alternative hypotheses:

- H_0 (null hypothesis): $\mu_1 = \mu_2 = \mu_3 = \dots = \mu_k$ (all population means are equal).
- H_a (alternative hypothesis): at least one population mean differs from the others.

To assess the strength of associations, odds ratios (ORs) with 95 % confidence intervals were calculated. A variable was considered a predictive factor of complications if $OR > 1$ and $p < 0.05$, and a protective factor if $OR < 1$ and $p < 0.05$. In cases where $OR > 1$ but $p < 0.25$, the variable was deemed to have a weak association with the dependent variable.

A multivariate analysis was performed on all variables identified as risk factors in the bivariate analysis and the Wald test was used for logistic regression. This enabled the evaluation of each variable's independent influence on the probability of developing complications, while controlling for all other variables. The Hosmer-Lemeshow test was also administered to assess the chi-square goodness of fit. A probability value greater than 0.05 was considered indicative of a good fit. Additionally, Nagelkerke's R^2 was calculated. All data analyses were conducted using IBM SPSS Statistics V22.0.

Ethical considerations

The authors affirm their commitment to maintaining confidentiality and safeguarding the information collected throughout the research. Authorization was also requested from the center's management, along with approval of the scientific council, to conduct the study.

RESULTS

In the analysis of the distribution of patients in the case group (cardiac complications), a higher percentage was observed for conditions such as AHF (13 %), paroxysmal AF and ventricular arrhythmias (12 % each) and AV block (9.17 %) (Table 1).

Table 1. Percentage distribution by presence of complications**

Complications N = 40		
	n	%*
Ventricular arrhythmias	14	11.67
AV block	11	9.17
Mechanical complications	5	4.17
Paroxysmal AF	14	11.67
AHF	15	12.50
CPA	4	3.33
Cardiogenic shock	5	4.17
Stent thrombosis	3	2.50

Source: Data extraction form.

*Percentage of the total study population.

**There were cases with more than one complication.

Table 2 shows a predominance of variables such as age ≥ 60 years ($OR = 3.11$; $LL: 1.27$; $UL: 7.58$; $p = 0.011$), diagnosis of DM ≥ 10 years ($OR = 2.50$; $LL: 1.14$; $UL: 5.45$; $p = 0.020$) and altered metabolic control on admission ($OR = 6.92$; $LL: 2.61$;

$UL: 18.32$; $p = 0.001$). These variables demonstrated a significant association with the dependent variable and were identified as risk factors in the study sample.

Table 2. Univariate analysis of risk factors

Variables	Study group				Total	p	OR	95 % CI		
	Case		Control					N	LL	UL
	n	%	n	%						
Age ≥ 60 years	32	80.00	45	56.25	77	64.17	0.011	3.11	1.27	7.58
Male sex	28	70.00	55	68.75	83	69.17	0.88	1.06	0.46	2.42
History of HTN	36	90.00	59	73.75	95	79.17	0.039	3.20	1.01	10.04
History of ischemic heart disease	24	60.00	33	41.25	57	47.50	0.053	2.13	0.98	4.63
Diagnosis of DM ≥ 10 years	25	62.50	32	40.00	57	47.50	0.020	2.50	1.14	5.45
Altered metabolic control on admission	34	85.00	36	45.00	70	58.33	0.001	6.92	2.61	18.32

Source: Data extraction form.

Chi-square = $X^2 \leq 0.05$. OR: odds ratio. LL: lower limit; UL: upper limit; 95 % CI: 95 % confidence interval.

Table 3 highlights that reperfusion therapy was not administered in 24.2 % (29) of the patients, which showed a statistically significant association with the study variable ($p \leq 0.05$). Thrombolytic therapy with recombinant streptokinase was the most commonly used reperfusion therapy, accounting for 39.6 % (36) of the patients. A one-way ANOVA was performed to assess the differences between the three types of coronary reperfusion therapy, revealing a statistically significant difference between at least two groups ($F = 4.67$, $p = 0.012$). Thus, this indicated that at least one of the group means differed from the others.

Tukey's multiple comparison test revealed that the mean scores of the reperfusion therapy were significantly different between patients administered the thrombolytic therapy with recombinant streptokinase and those administered the combination of both reperfusion procedures ($p = 0.008$, 95 % CI = 0.07-0.60).

No statistically significant differences were found between PCI and the combination of both reperfusion procedures ($p = 0.208$) or between PCI and the thrombolytic therapy with recombinant streptokinase ($p = 0.395$).

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Table 3. Analysis of reperfusion therapy by study group

Variables		Study group						p
		Case		Control		Total		
		n	%	n	%	N	%	
Reperfusion therapy	Administration	15	37.50	14	17.50	29	24.20	0.016
	Non-administration	25	62.50	66	82.50	91	75.80	
Type of coronary reperfusion therapy**	Thrombolytic therapy with recombinant streptokinase	15	60.00	21	31.82	36	39.66	0.01
	PCI	8	32.00	21	31.82	29	31.97	
	Combination of both reperfusion procedures	2	8.00	24	36.46	26	28.67	

Source: Data extraction form.

Chi-square = X^2 . Percentage of total columns.

**ANOVA: ($F = 4.67$; $p = 0.012$).

Significant associations were found with echocardiographic parameters such as $LAP \geq 15$ mmHg ($OR = 7.49$; $LL: 3.20$; $UL: 17.52$; $p = 0.001$), $LVEF \leq 45$ % ($OR = 5.68$; $LL: 1.81$; $UL: 17.80$; $p = 0.001$) and RV TDI ($OR = 2.80$; $LL: 1.26$;

$UL: 6.22$; $p = 0.010$). These parameters demonstrated statistical significance with the dependent variable and were identified as risk factors for complications in the study population (Table 4).

Table 4. Univariate analysis of echocardiographic parameters by study group

Variables	Study group						p	OR	LL	UL
	Case		Control		Total					
	n	%	n	%	N	%				
$LAP \geq 15$ mmHg	28	70.00	19	23.75	47	39.17	0.001	7.49	3.20	17.52
$LAV \geq 34$ ml/m ²	15	37.50	39	48.75	54	45.00	0.243	0.63	0.29	1.37
RV TDI ≤ 9.5 cm/s	20	50.00	21	26.25	41	34.17	0.010	2.80	1.26	6.22
$WMSi \geq 1.5$ points	34	85.00	53	66.25	87	72.50	0.030	2.88	1.07	7.72
$MPAP \geq 25$ mmHg	30	75.00	43	53.75	73	60.83	0.025	2.58	1.11	5.97
$LVEF \leq 40$ %	11	27.50	5	6.30	16	13.33	0.001	5.68	1.81	17.80

Source: Data extraction form.

Chi-square = $X^2 \leq 0.05$. OR: odds ratio. LL: lower limit; UL: upper limit; 95 % CI: 95 % confidence interval.

Multivariate analysis identified six independent predictive factors for the development of complications among patients with DM and AMI: age ≥ 60 years ($OR = 5.624$; $CI = 1.607$ - 19.686 ; $p = 0.007$), altered metabolic control on admission ($OR = 5.245$; $CI = 1.491$ - 18.447 ; $p = 0.010$),

non-administration of thrombolytic therapy ($OR = 5.74$; $CI = 1.46$ - 22.586 ; $p = 0.012$), $LVEF \leq 40$ % ($OR = 5.245$; $CI = 1.17$ - 23.433 ; $p = 0.030$), $LAP \geq 15$ mmHg ($OR = 12.335$; $CI = 3.45$ - 44.08 ; $p = 0.001$) and $WMSi \geq 1.5$ points ($OR = 4.702$; $CI = 1.258$ - 17.575 ; $p = 0.021$) (Table 5).

Table 5. Multivariate analysis by study variables

Variables	B	Standard error	Sig.	Exp(B)	95 % CI for Exp(B)	
					LL	UL
Age ≥ 60 years	1.727	0.639	0.007	5.624	1.607	19.686
Altered metabolic control on admission	1.657	0.642	0.010	5.245	1.491	18.447
Non-administration of thrombolytic therapy	1.748	0.699	0.012	5.742	1.460	22.586
LVEF ≤ 40 %	-1.657	0.764	0.030	5.245	1.174	23.433
LAP ≥ 15 mmHg	-2.512	0.650	0.001	12.335	3.451	44.089
WMSi ≥ 1.5 points	1.548	0.673	0.021	4.702	1.258	17.575
Constant	-1.862	1.146	0.104	0.155		

Hosmer-Lemeshow test $p = 0.723$. Nagelkerke's $R^2 = 0.565$.

Source: IBM SPSS Statistics V22.0.

Chi-square = $X^2 \leq 0.05$. OR: odds ratio. LL: lower limit; UL: upper limit; 95 % CI: 95 % confidence interval.

DISCUSSION

When discussing cardiac complications in AMI, studies by Arredondo et al. ⁽¹⁵⁾ and Leandro et al. ⁽¹⁶⁾ reported that the most common complications were AHF and rhythm disorders—e.g., paroxysmal AF—which aligns with the findings of the present research. Regarding demographic parameters and major risk factors, Martínez García ⁽¹⁷⁾ and Arredondo Bruce et al. ⁽¹⁸⁾ have identified that factors such as age ≥ 60 years, male sex, history of HTN, non-administration of reperfusion therapy and altered glycemetic control on admission were associated with complications during AMI among patients both with and without diabetes. Furthermore, Valdez-Ramos and Álvarez Aliaga ⁽¹⁹⁾ and Santos et al. ⁽²⁰⁾ highlight that patients with DM are at increased risk of coronary events, with the diagnosis of DM ≥ 10 years and elevated glycemia on admission serving as predictive factors of complications. These findings complement those previously mentioned by the aforementioned authors ^(17,18). The reviewed literature ^(21,22) supports the association between adequate glycemetic control and the delay of cardiovascular complications, which helps to prevent atherosclerosis and endothelial dysfunction among patients with DM.

The present study confirms the critical role of glycemetic control and the years of diagnosis of DM in the development of cardiac complications during AMI among patients with DM.

Furthermore, this research found that the non-administration of reperfusion therapy was significantly associated with complications, a finding consistent with Diaz ⁽²³⁾, who observed that patients with AMI who underwent thrombolysis, including those with DM, had a higher probability of no reperfusion.

The echocardiographic results of the present study partially align with the findings reported by Acosta et al. ⁽²⁴⁾ and Ramón et al. ⁽²⁵⁾, who stated that variables such as WMSi,

LAP and systolic dysfunction are related to altered glycemia parameters.

Additionally, Rosabal et al. ⁽²⁶⁾ reported that echocardiographic parameters such as LAV > 34 ml/m² were prevalent among patients experiencing DM adverse events.

The reviewed literature ⁽²⁵⁾ further suggests that echocardiographic abnormalities among patients with DM seem to be related to glycemetic control, whereby reductions in blood glucose levels are correlated to improvements in both systolic and diastolic functions of both ventricles. In this regard, Jairo et al. have also reported similar results ⁽²⁷⁾.

The findings of the present research underscore that the risk of cardiac complications among patients with DM and AMI should not be assessed solely based on traditional risk factors. Instead, echocardiographic parameters such as LVEF, LAP and WMSi should also be considered.

Regarding the multivariate analysis related to the association between DM and coronary events, Valdés-Álvarez ⁽²⁸⁾ reported that variables such as duration of diagnosis of DM and history of HTN, among others, are related to the onset of ischemic heart disease.

Finally, the study's main limitations include the small sample size, as well as the lack of modern humoral markers and advanced echocardiographic techniques. Factors such as psychosocial elements, multimorbidity, frailty in cardiovascular disease and medium- to long-term functional status were also not addressed. Future research should explore these aspects, since they could offer crucial insights in the management of patients with DM. In conclusion, the study identified six independent clinical risk factors for cardiac complications among patients

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with DM and AMI, with the most significant being glycemic control on admission, decreased LVEF, increased LAP and non-administration of reperfusion therapy.

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