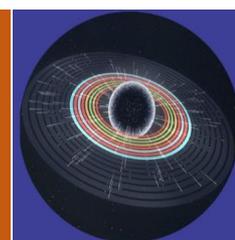


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Original article**Day-to-day glycemic variability and the incidence of complications due to myocardial infarction in the first 72 hours post infarction in patients with diabetes mellitus**Rafael Contreras¹, Guarina Molina²¹Research department Hospital General de la Plaza de la Salud, Santo Domingo, Dominican Republic²Universidad Iberoamericana (UNIBE), Santo Domingo, Dominican Republic

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Abstract

Background: Diabetes is considered an equivalent to coronary artery disease and glycemic variability has been proposed as a factor associated with the occurrence of major adverse cardiovascular events (M.A.C.E).

Objective: The aim of this study is to evaluate the relationship between day-to-day glycemic variability during the first 72 hours after admission for an acute myocardial infarction in diabetic patients, the incidence of myocardial infarction complications during this time and age.

Methods: A retrospective study was conducted evaluating day-to-day glycemic variability and the incidence of myocardial infarction complications in the first 72 hours after admission for an acute myocardial infarction in 38 diabetic patients from the General Hospital of the Health Plaza in Santo Domingo, Dominican Republic. Patients were grouped according to glycemic variability (high/low variability) and age (≤ 64 and ≥ 65 y/o).

Results: In the sample, 16 patients were aged 64 or younger and 22 aged 65 or older (n=38). The group of patients aged 65 or older were found to have the highest incidence of complications as well as higher glycemic variability. Nonetheless, according to statistical analysis the occurrence of MI complications was found to be independent of glycemic variability (p=0.52).

Conclusion: Congestive heart failure (cause being other than arrhythmias) and cardiogenic shock were the most common complications observed. Age was found to be related to glycemic variability and with a negative tendency towards hypoglycemia ($r = -0.53$, $p = <0.05$).

Keywords: diabetes, myocardial infarction, congestive heart failure, glycemic variability, M.A.C.E.

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Introduction

It is currently known that diabetes mellitus (D.M.) is one of the most prevalent chronic diseases that affects adults worldwide and is estimated that about 422 million people aged 18 or older are living with D.M.I. The prevalence of cardiovascular disease is currently on the rise and it is estimated that about 30% of deaths worldwide occur due to cardiovascular disease.² The presence of diabetes is an equivalent to coronary artery disease.

The purpose of this study is to establish a relationship between age, day-to-day glycemic variability (D.D.G.V.) during the first 72 hours after an acute myocardial infarction (A.M.I.) in diabetic patients and the incidence of myocardial infarction (M.I.) complications during this time.

It is of importance to point out that regardless of the importance of glycated hemoglobin (HbA1c), glycemic variability has been proposed as one of the main factors associated with the occurrence of M.A.C.E., both in diabetic and non-diabetic patients. This study was needed to provide for data and evidence that allowed professionals in the medical field to establish patterns of complications in patients that presented such variability after a myocardial infarction, therefore allowing improvement in the strategies of care of such patients, reducing morbidity and mortality.

Several other studies of this nature have been published in the past decade, following a retrospective observational pattern of patients with similar characteristics⁴ while others were performed as prospective observational clinical studies at a single center using continuous glucose monitoring systems (C.G.M.S.).^{5,6,7}

Methods

Using electronic records, the hospital's database was screened for patients meeting the following criteria: 1) Previous diagnosis of D.M., 2) diagnosis of A.M.I. between 2016 and 2017 in the hospital where the study was conducted and 3) having at least 3 blood glucose measurements each day for 3 consecutive days (72 hours). The exclusion criteria included: 1) hospitalization due to an elective procedure, 2) having a diagnosis of atrial fibrillation, congestive heart failure, AV block, ventricular fibrillation, atrial flutter, myocardial rupture, left or right bundle branch block and 3) having a previous admission due to complications of M.I. A total of 38 patients were selected, of which 36% of the subjects were female and 64% male. Female subjects were aged between 32 and 92 years old with an average of 67.2 years. Males were aged between 41 and 80 years old with an average of 62.7 years.

An observational retrospective study was conducted using the aforementioned health records to evaluate the outcomes of interest for this study. These were: 1) the relationship between D.D.G.V. during the first 72 hours after an admission for an A.M.I. in diabetic patients and the incidence of M.I. complications during this time 2) the relationship between age and D.D.G.V. during the first 72 hours after admission for an acute myocardial infarction in diabetic patients.

To evaluate the relationship between D.D.G.V. during the first 72 hours after an A.M.I. in diabetic patients and the incidence of M.I. complications during this time, a mean value of glucose for the first 72 hours after an M.I. was obtained for each subject in the study. This value was obtained after averaging all the blood glucose measurements performed during this period.

The mean value of glucose and the standard deviation (SD) for the entire sample were obtained. Using the corresponding formula ($[\text{Mean of subject} - \text{Mean of sample}] / \text{SD}$) the Z-score was obtained for each of the participants in the study and this was used as a surrogate for glucose variability around the sample mean. Z-score between -1 and 1 was defined as low variability and a Z-score < -1 or > 1 was defined as high variability. Each of the subjects were then grouped as having low glycemic variability or high glycemic variability based on their Z-score and the incidence of complications from an A.M.I. during the first 72 hours of admission was determined within each group.

To evaluate the relationship between age and D.D.G.V. during the first 72 hours after admission for an acute myocardial infarction in diabetic patients, study subjects were grouped by age as having “64 or less years” or “65 or more years”. Incidence of M.I. complications during the first 72 hours after admission for an A.M.I and the glycemic variability during this time was then observed for each of the subjects within each age group. A secondary outcome measured was the incidence of MI complications within the different age groups.

Results

The software EpiInfo (AMPLIAR DETALLES) was used to perform statistical analysis of the outcomes of interest. Using the Z-score of each subject as a surrogate for glycemic variability, a logical regression model was employed to determine the relationship between D.D.G.V. during the first 72 hours after admission for an A.M.I in diabetic patients and the incidence of M.I. complications within each group of glycemic variability.

A linear regression analysis was used to evaluate the relationship between age and glycemic variability during the first 72 hours after admission for an A.M.I. in diabetic patients as expressed by the Z-score of each study subject. In both cases a p-value <0.05 was deemed as statistically significant.

After evaluating the relationship between D.D.G.V. during the first 72 hours after an admission for an acute myocardial infarction in diabetic patients and the incidence of myocardial infarction complications during this time, we found the sample had a mean blood glucose concentration of 184.7 mg/dL with a standard deviation (SD) of 54.3 mg/dL. The Z-score for each of the subjects was calculated using this observation (Table 1).

From the 38 subjects, 29% (n=11) were grouped as having a high glycemic variability (Z-scores <-1 or >1). Within this group, 45.5% were females with a mean age of 71 years old and the remaining 54.5% were males with a mean age of 63 years old. The remaining 71% (n=27) of the study subjects was grouped as having a low glycemic variability (Z-scores between -1 and 1), of these 33% were females with a mean age of 65 years and the remaining 67% were males with a mean age of 62.5 years.

From the 38 study subjects included, 23 suffered from a M.I. complication during the first 72 hours after admission. Of these, 56.5% were males. When examining each group of glycemic variability, 63.6% of patients from the high glycemic variability group (n=11) suffered a complication, meanwhile 59.3% of those with low glycemic variability (n=27) had complications.

The logical regression model used in the statistical analysis of the relationship between glycemic variability and the occurrence of AMI complications within the first 72 hours of admission for an AMI revealed a correlation coefficient $r = -0.21$ (OR = 0.8, 95% CI: 0.92 – 2.24, $p = 0.52$), and a likelihood ratio of 0.4, $p = 0.54$

Analysis of the relationship between age and D.D.G.V. during the first 72 hours after admission for an A.M.I in diabetic patients, revealed that from the study sample (n=38), 42.11% (n=16) were aged 64 years or younger and 57.9% were aged 65 years or older. Of the 16 subjects grouped as 64 years or younger, 31.3% was found to have a high glycemic variability as determined by the Z-score, meanwhile of those aged 65 or older (n=22), only 27.8% was found to have a high glycemic variability. (Table 2)

Table 1: Z-score of subjects

Subject	Mean blood glucose concentration in 72hrs (mg/dL)	Z-score
#1	304.3	2.2
#2	278.3	1.7
#3	275.7	1.7
#4	260.7	1.4
#5	256.7	1.3
#6	244.6	1.1
#7	237.0	1.0
#8	236.2	0.9
#9	221.3	0.7
#10	220.3	0.7
#11	219.7	0.6
#12	216.0	0.6
#13	213.2	0.5
#14	204.7	0.4
#15	195.0	0.2
#16	193.7	0.2
#17	193.4	0.2
#18	192.1	0.1

#19	191.0	0.1
#20	178.8	-0.1
#21	178.0	-0.1
#22	175.7	-0.2
#23	172.2	-0.2
#24	165.6	-0.4
#25	155.2	-0.5
#26	155.0	-0.5
#27	154.3	-0.6
#28	149.7	-0.6
#29	134.7	-0.9
#30	131.2	-1.0
#31	130.3	-1.0
#32	129.5	-1.0
#33	128.3	-1.0
#34	123.2	-1.1
#35	115.0	-1.3
#36	106.2	-1.4
#37	97.8	-1.6
#38	84.8	-1.8

Table 2: Variability and Z-Score by Age Group

	Age 64 > (n=16)	Age 65 < (n=28)
High Variability	31.3%	27.8%
Low Variability	68.7%	72.7%
Z-score mean	0.5	0.35

The Z-score of those aged 64 or younger ranged between -1.4 and 2.2 with a mean of 0.5; In those aged 65 or older the Z-score ranged from -1.8 and 1.3 with a mean of -0.35 (Table 2)

Lineal regression analysis showed a correlation between age and glycemic variability, with a correlation coefficient of -0.043 (95% CI -0.066 and -0.020 p = <0.05). (Figure 1)

When examining the incidence of complications by age group, of those aged 64 years old or less, 56.25% suffered a complication secondary to the acute M.I. of which 33% had a high glyceic variability. In the group of 65 or older group, the affected were 63.63% with 28.4% presenting high glyceic variability.

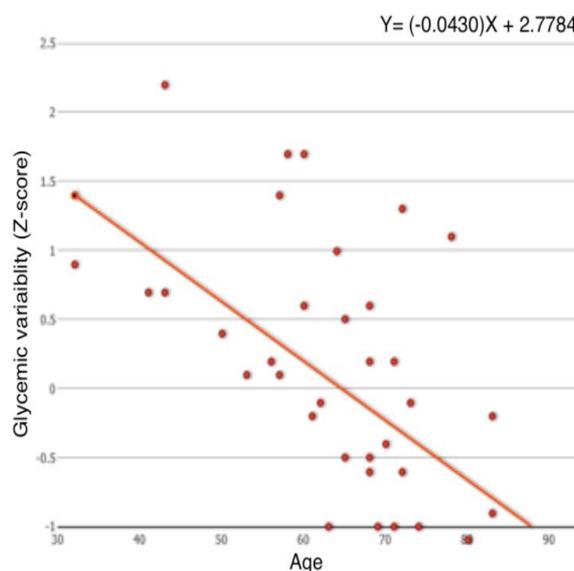


Figure 1. Relationship glyceic variability and age

Discussion

The results of the study showed that although most subjects had a low glyceic variability, the incidence of AMI complications was greater in those with a higher glyceic variability.

Statistical analysis failed to reveal any statistical significance in the relationship between glyceic variability and the incidence of complications during the first 72 hours of admission for an A.M.I. in diabetics. This finding differs from what has been previously observed in other studies where a greater glyceic variability has been linked with the occurrence of major adverse cardiovascular outcomes in patients following an acute myocardial infarction^{4,5,6,7}. This occurrence is likely explained by the small sample size used in this study, a point that should be addressed and worth noting for future research.

The analysis of the interaction between age and glyceic variability found an association between age and glyceic variability. These findings are consistent with those reported by Gude F et. al. who observed a link between age and glyceic variability, independently of other cofounders.⁸

Measures of central tendency of Z-score in those aged 64 years or less was found to have a positive skew while in those aged 65 or older a negative skew was seen. Therefore, we are able to conclude that younger subjects have a tendency towards hyperglycemia, while older subjects usually have a tendency towards hypoglycemia. This finding is consistent with the results from the lineal regression that showed the correlation between age and glyceic variability where age was associated with a negative tendency of the variability. We were able to observe that although most subjects in this study had a low glyceic variability, the magnitude of the variability was greater in those subjects aged 64 or less years

Is also worth noting that the incidence of myocardial infarction complications in the first 72 hours post MI in the diabetic patients was found to be greater in those subjects aged 65 or older, which is congruent with the findings reported by Hanefeld M et. al.⁹ where hypoglycemia was associated with the occurrence of negative cardiovascular outcomes.

Nonetheless, is worth noting that these findings may be compromised due to the characteristics of the sample used in this study.

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Conclusion

As a result, the risk of complications increases in diabetic patients compared to non-diabetic patients, especially within the first 72 hours after myocardial infarction.

Conflict of interest

No

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