Comorbid conditions in individuals assessed by SPECT: Study of a reference cardiology center in Mexico City

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Background. **There is an increasing prevalence of comorbidities in patients with ischemic heart disease (IHD) in developing countries. The aim of this work is to assess the prevalence of comorbidities and associated factors for IHD among patients at a reference cardiology center.**

Design and Methods. **This was a cross-sectional study. A complete clinical history which focused on the main comorbidities, previous myocardial infarction, and the main reason of referral was assessed. A single-photon emission computed tomography (SPECT) myocardial perfusion study (MPS) with two protocols was performed.**

Results. **We included 1998 patients, 64.2% male, median age 63 (I.R.: 56–71) years. 1514 (75.8%) subjects had at least one associated comorbidity. The main comorbidity was diabetes (T2D) (772: 38.6%), followed by systemic hypertension (737: 36.9%), smoking (518: 25.9%), and dyslipidemia (517: 25.9%). 806 (40.3%) had histories of previous myocardial infarctions. The main cause of referral was angina (923: 46.2%). We identified 1330 (66.5%) abnormal MPS. 460 (23%) had ischemia, 292 (14.6%) infarction, and 578 (28.9%) ischemia and infarction.**

Conclusion. **An increased prevalence of comorbidities was found in patients who were studied in the Nuclear Cardiology Department (NCD): most of them had traditional risk factors attributable to myocardial infarction. A great percentage were newly diagnosed with both ischemia and infarction.**

Key Words: Traditional risk factors • myocardial infarction • myocardial ischemia • nuclear cardiology • epidemiology

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Abbreviations	
CVD	Cardiovascular diseases
T2D	Type 2 diabetes
ENSANUT	National Health and Nutrition Survey
PTCA	Percutaneous coronary angioplasty
MPS	Myocardial perfusion study
SPECT	Single-photon emission computed tomography
NYHA	New York Heart Association
NCD	Nuclear Cardiology Department
IHD	Ischemic heart disease
CMD	Coronary multivessel disease

INTRODUCTION

Cardiovascular diseases (CVD) are the main causes of mortality worldwide.[1] In the United States, the prevalence of CVD in people over 30 years or older was 6.3% in the overall population, with a higher rate in black men.[2] In recent years, the World Health Organization reported an increase of CVD in developing countries, mostly attributable to non-communicable diseases like type 2 diabetes (T2D), obesity, dyslipidemia, and systemic hypertension.[3] These risk factors have risen worldwide, leading to a transitional change in the burden of non-communicable diseases.[1] In Mexico, the 2016 National Health and Nutrition Survey (ENSANUT) reported a rise in the prevalence of non-communicable diseases in Mexico, including T2D, systemic hypertension, and obesity; nevertheless, this survey does not include a detailed description of these comorbidities in patients with ischemic heart disease (IHD).[4] In Mexico City, a report estimated a mortality rate of CVD in 2008 of 45.85 for every 100,000 habitants showing higher results than other countries like the United States.[5] An imaging method like single-photon emission computed tomography (SPECT) is an excellent technique for the diagnosis and stratification of patients with IHD. An analysis of the main comorbidities in patients who seek assessment of ischemic heart disease (IHD) using SPECT can help to understand the increasing burden of comorbidities in these patients, especially in the Mexican population. The aim of this work is to assess the prevalence of comorbidities and reasons of referral in patients coming for evaluation at a Nuclear Cardiology Department (NCD) in Mexico City. Furthermore, we aimed to assess the factors associated with the myocardial perfusion study SPECT results.

METHODS

Population of Study and Clinical Evaluation

The National Institute of Cardiology Ignacio Chavez is a teaching, healthcare hospital and a center of reference for patients with diseases specifically of the heart. We designed a cross-sectional study, which included all patients who came to the NCD for study between January 2017 and December 2017. A professional physician performed a complete clinical history of comorbidities of the evaluated patients. We directly asked for self-reported history of systemic hypertension, dyslipidemia, smoking, obesity, and previous myocardial infarction together with the reported image method used in the diagnosis of previous myocardial infarctions in these patients. Additionally, we directly reported other comorbidities associated with the heart including arrhythmias, coronary multivessel disease (CMD), atrial fibrillation, aneurysms, heart failure, myocardial dilatation, heart block, deep vein thrombosis, and valve diseases. All the previous diagnoses were taken from the electronic clinical records according to their ICD-10 codification. The clinical records of subjects who had incomplete information or those whose reports were inconclusive were excluded from the analysis. Blood pressure was assessed using a calibrated manual sphygmomanometer, after 5 minutes of rest, with previous indications to stop smoking, alcohol, or caffeine. Blood pressure was registered immediately before performing the myocardial perfusion study SPECT (MPS-SPECT).

Myocardial Perfusion Study

A Symbia Siemens gamma chamber with a Cardiocentric Smartzoom collimator was used. We employed ^{99m}Tc-MIBI-Gated SPECT in patients with normal ventricular function, middle and moderate ventricular dysfunction, or ^{201}Thallium if patient had a severe ventricular dysfunction.

Resting and rest-gated images were acquired with photopeak 20% in 120 keV, matrix 128 × 128, 16 frames, 12 seconds/images and for stress and stress-gated images, 9 seconds/image. Stress phase with pharmacological stress (dipyridamole) or physical stress on a treadmill was performed according to the physical and clinical characteristics of the patients.

The dose of radiotracer was administered according to the guidelines published in 2016 and 2017.[6,7] The processing of images was made using QPS-QGS Cedars-Sinai software. The MPS-SPECT images were interpreted by a nuclear cardiologist as a semiquantitative visual representation of 5-point score for each of the 17 segments, (Figure 1).

Patients were divided according to the presence of ischemia, infarction, or both conditions.[6,7] The results were classified as normal or showing the presence of ischemia, infarction of both.

The Human Research Ethics Committee of the National Institute of Cardiology Ignacio Chavez approved the study

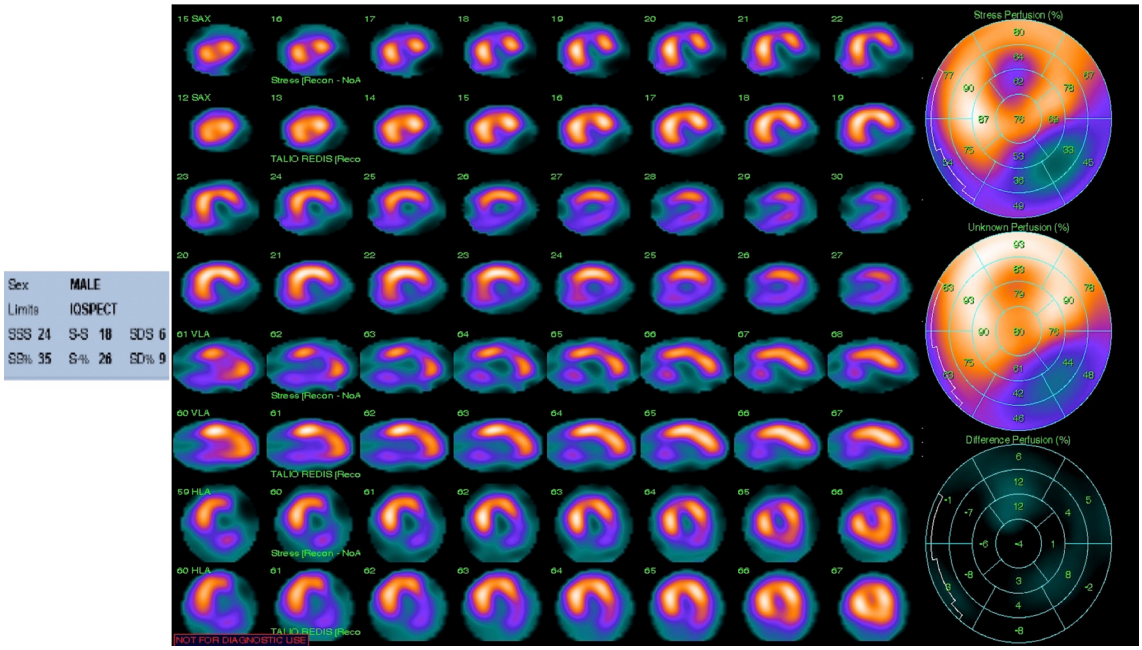

Figure 1. This is the case of a 55-year-old male with T2D, systemic hypertension, without previous history of IHD, who was referred for angina. The MPS-SPECT showed multivessel disease with non-transmural inferolateral myocardial infarction with mild ischemia and anterior moderate ischemia.

with the number PT-17-072. Patients signed an informed consent before MPS-SPECT.

Coronary multivessel disease (CMD) was defined as the involvement of more than one coronary vessel.

Statistical Analysis

Frequency distribution of categorical variables was reported as frequencies and percentages. Demographic data were described as mean and standard deviation or with median and interquartile range as appropriate. Chi-squared, Student's t, and Mann-Whitney U tests were used where appropriate. A logistic regression analysis was performed to evaluate the association between the factors and comorbidities related to myocardial infarction, ischemia, or both conditions. The goodness of fit of the model was assessed by the Hosmer-Lemeshow test. In addition, to evaluate the performance of the model, the area under the receiver operator curve (AUC) with its respective 95% confidence interval was applied. Statistical analyses were performed using Statistical Package for Social Science (SPSS Inc, Chicago, IL, Version 21.0) and GraphPad Prism, version 7.0. A P value of <0.05 was taken as statistically significant.

RESULTS

Characteristics of the Patients

There was a total of 2,153 patients who were assessed for MPS-SPECT: 155 (7.2%) patients were excluded due to inconclusive results or illegible reports, leaving a total of 1998 reports for the statistical analysis. Male patients were accounted for 1282 subjects (64.2%), while 715 (35.8%) were female. Median age was 63 (I.R.: 56-71) years for the entire group, with 62 (54-69) years for men and 65 (57-72) years for women. Median systolic and diastolic blood pressure were 120 (110-140) mmHg and 80 (70-80) mmHg, respectively (Table 1).

Prevalence of Associated Comorbidities

Of the total patients, 802 (40.2%) had at least one associated comorbidity, 514 (25.7%) two, 163 (8.2%) three, and 34 (1.7%) four or more comorbidities. The main comorbidity was T2D in 772 (38.6%) cases, followed by systemic hypertension in 737 (36.9%) cases, smoking in 518 (25.9%) cases, and dyslipidemia in 517 (25.9%) cases; 371 (18.6%) had other types of comorbidities (Figure 2A). Dividing our study population by gender, we found that women were older ($P < 0.001$). Both genders had an equal distribution of number of comorbidities. Nevertheless, more men had

Table 1. Characteristics and comorbidities in the study population in the period of January 2017 to December 2017

Parameter	Frequency (*n*; %) (*n* = 1997)	Men (*n* = 1282)	Women	*P* value
Sex (%)	-	1282 (64.2%)	715 (35.8%)	<0.001
Age (years)	63 (56-71)	62 (54-69)	65 (57-72)	<0.001
SBP (mmHg)	120 (110-140)	125 (110-140)	120 (110-140)	0.212
DBP (mmHg)	80 (70-80)	80 (70-80)	80 (70-80)	0.063
Comorbidities				
T2D	772 (38.6%)	481 (37.5%)	291 (40.7%)	0.162
Systemic hypertension	737 (36.9%)	454 (35.4%)	282 (39.4%)	0.074
Active smokers	518 (25.9%)	418 (32.6%)	99 (13.8%)	<0.000
Dyslipidemia	517 (25.9%)	337 (26.3%)	180 (25.2%)	0.586
Obesity	196 (9.8%)	114 (8.9%)	82 (11.5%)	0.064
Others	371 (18.6%)	179 (14.0%)	191 (26.7%)	<0.001

T2D, type 2 diabetes; *SBP*, systolic blood pressure; *DBP* diastolic blood pressure

histories of active smoking ($P < 0.001$). Women had other comorbidities ($P = 0.001$) and tended to have more T2D and dyslipidemia, but did not reach statistical significance ($P = 0.129$) (Table 2; Figure 2B).

Associated Cardiovascular Diseases

We found that myocardial infarction was reported in 806 (40.3%) patients. The main diagnostic and therapeutic method was coronary angiography with percutaneous coronary angioplasty (PTCA) in 164 (20.3%) cases, followed by electrocardiographic findings in 152 (18.85 %), previous MPS in 101 (12.5%) and only coronary angiography in 91 (11.2%). Nevertheless, in 170 (21.1%) cases, there was no specified method of diagnosis. We also reported other cardiovascular diseases (Supplementary Table 1).

Myocardial Perfusion Study Results

In 1854 (92.5%) cases, the MPS-SPECT was performed using ^{99m}Tc MIBI-Gated SPECT; in 138 (6.9%) using ^{201}Thallium Gated-SPECT; and in 6 (0.3%) with both. The 38.7% of patients underwent to pharmacological stress, because of left bundle branch block and physical limitations, and the rest underwent to physical stress test.

The reasons for referral included angina in 923 (46.2%) cases, asymptomatic in 624 (31.3%), dyspnea in 359 (18%), impairment of New York Heart Association (NYHA) functional class in 48 (2.4%), palpitations in 33 (1.7%), and syncope in 9 (0.5%). New ischemic heart disease was diagnosed in a total of 1,330 (66.5%) cases, in which 460 (23%) were classified as myocardial ischemia, 292 (14.6%) as myocardial infarction, and 578 (28.9%) as both myocardial ischemia and infarction (Figure 3). Furthermore, we made a stratification among age groups of ages and found that in patients younger

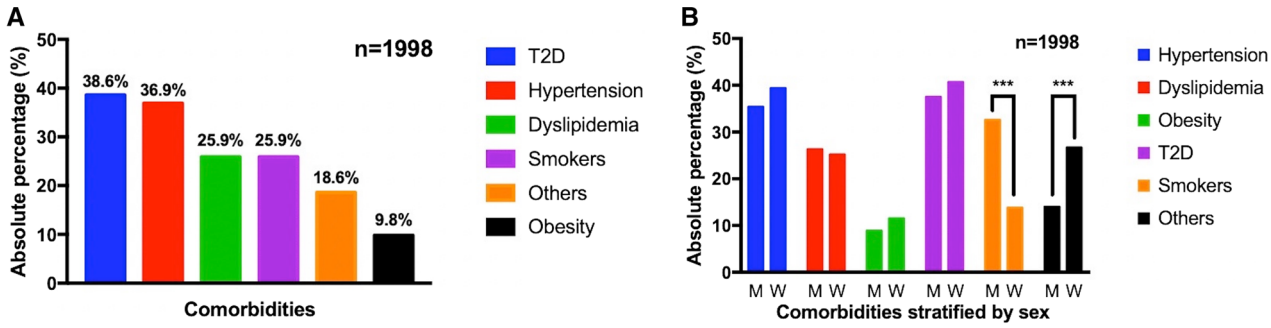

Figure 2. Absolute percentages of comorbidities (**A**) and absolute percentages of comorbidities stratified for sex (**B**). *T2D* Type 2 diabetes, *M* men, *W* women.

Table 2. Characteristics of patients undergoing image perfusion in the study population in the period from January 2017 to December 2017

Parameter	Frequency (%) (n = 1998)
Type of protocol	
^{99}m Tc MIBI-Gated SPECT	1854 (92.8%)
201-Thallium-Gated SPECT	138 (6.9%)
Reason for referral	
Angina	923 (46.2%)
Asymptomatic	626 (31.3%)
Dyspnea	359 (18%)
Impairment of NYHA functional class	48 (2.4%)
Palpitations	33 (1.7%)
Syncope	9 (0.5%)
Result of the study	
Normal	668 (33.4%)
Ischemia + infarction	578 (28.9%)
Ischemia	460 (23%)
Infarction	292 (14.6%)

Tc, Technetium; *SPECT*, single-photon emission computed tomography; *NYHA*, New York Heart Association

than 34 years the predominant result of MPS-SPECT was normal (48%; 12 cases), in the group of 35-45 years the main result was normal (32.1%; 25 cases), in the group of 45-54 years the main result was ischemia and infarction (18.2%, 105 cases), in the group of 55-64 years, also the combination of both conditions (37.7%: 218 cases) as well, and in the group of >65 years the presence of infarction (45.5%; 133 cases).

Comorbidities Associated with the Results of MPS

In the logistic regression analysis, we found that in the case of infarction and ischemia, the associated factors were T2D (OR: 1.76, 95% CI 1.42-2.18), CMD (OR: 4.48, 95% CI 2.32-8.67), previous ischemia or infarction (OR: 3.31, 95% CI 2.68-4.10), and male sex (OR: 2.42, 95% C.I.: 1.89-3.09). For ischemia, the associated factors were T2D (OR: 1.50 95% C.I.: 1.21-1.84), heart failure (OR: 3.37, 95% CI 1.18-9.69), CMD (OR: 2.80 95% C.I.:1.27-6.17), male sex (OR: 2.78 95% CI 2.24-3.46), dilated cardiomyopathy (OR: 2.86 95% CI 1.31-6.24), previous ischemia or infarction (OR: 5.36, 95% CI 4.33-6.64), asymptomatic at arrival (OR: 1.28 95% CI 1.01-1.61), dyspnea (OR: 1.58 95% CI 1.19-2.09), and palpitations (OR: 0.41, 95 CI: 0.18-0.95). Finally, infarction was associated to T2D (OR: 1.60, 95% CI 1.32-1.94), CMD (OR: 4.67, 95% CI 2.21-9.85), male sex (OR: 1.98, 95% CI 1.62-2.42), and previous ischemia or infarction (OR: 1.98, 95 CI: 1.62-2.42) (Table 3).

DISCUSSION

This study compiles the frequency and prevalence of the main comorbidities and other cardiovascular-related disorders in a sample of patients that arrived at the NCD between the period of January 2017 and December 2017 in a national referral center of cardiology in Mexico City. Furthermore, it reports the main reasons of referral and the results of the MPS-SPECT in these patients. In our study population, we found that at least 75.8% of the patients had at least one reported comorbidity at the moment of the study in which T2D, arterial hypertension, dyslipidemia, and active smoking were the most prevalent. Also, we found in our logistic regression analysis that the factors that were associated with ischemia and infarction were T2D, CMD, a history of a prior ischemia or infarction, and male sex.

Evidence confirms that cumulative risk factors increase the risk of incident myocardial infarction and mortality.[8] Similar results have been reported in other countries, in which up to 10.5% of the sample population does not have any traditional risk factor.[9] There has been a consistent increase in the trends of IHD in developing countries like Mexico, compared to the United States. It is noteworthy that in the United States, a series of Cardiac Stress Testing over two decades of follow-up, showed that the frequency of abnormal MPS-SPECT was 40.9%, while we found that in 66.5% of our cases had a diagnosis of IHD. Their decreasing trends could be explained by the reduction of traditional risk factors, favorable changes in lifestyle and the progressive use of cardiac medications over the period of study in their population.[10] In developing countries, the increasing trend of traditional risk factors mean that subjects at risk, especially women, have an increased trend in the prevalence of IHD. In the stratification for sex, women tend to have more traditional risk factors than men at the same age.[11] In our population, women have a higher prevalence of systemic hypertension, dyslipidemia, and other types of comorbidities, but men have an increased prevalence of smoking.

Evidence confirms that, these four comorbidities have shown an increased prevalence in recent years, especially in Latin American populations.[12] Other reports from the same institution of patients who were diagnosed with coronary artery disease by coronary angiography showed that the prevalence of systemic hypertension, T2D, dyslipidemia, and smoking was also

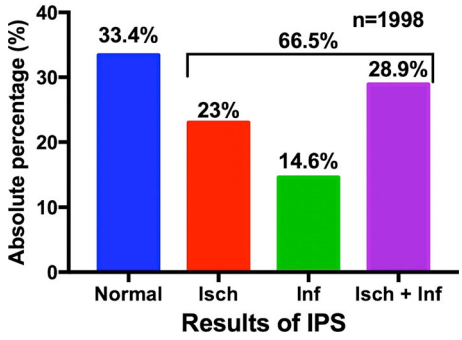

Figure 3. Results of myocardial perfusion study SPECT stratified by age categories. *Isch*, Ischemia; *Inf*, infarction; *Isch + Inf*, ischemia and infarction.

increased.[13] This could be attributed to the demographic transition to non-communicable diseases, reported in recent years and caused by multiple genetic and demographic factors.[14]

The risk factors contributing to myocardial infarction have been reported in other studies, in which an association between history of T2D and male sex for developing myocardial infarction was found.[15] We also found that a great number of patients had prior myocardial infarctions, diagnosed with other methods. This can be explained by the cost and high specialization of MPS, which limits its use to situations in which clinical decisions about the treatment and probable outcome require knowledge about the degree of damage caused by ischemia or infarction.

As expected, many patients do not report any symptoms before the MPS, due to the stabilization of the cardiac function. We also report that a large percentage of patients have a combination of ischemia and infarction which is to be expected considering the capacity of this method for differentiating the two conditions.[16]

Table 3. Logistic regression model for infarction, ischemia, and the presence of both conditions

Model	Parameters	*B*	SE	Wald	OR	95% CI	*P* value
Ischemia and infarction	T2D	0.569	0.108	27.596	1.767	1.42-2.18	<0.001
*R*2 = 0.194	Multivessel disease	1.501	0.336	19.896	4.486	2.32-8.67	<0.001
Hosmer and Lemeshow = 0.749	Deep vein thrombosis	1.760	0.810	4.727	5.815	1.18-28.42	0.030
P = 0.186	Previous ischemia or infarction	1.199	0.109	121.963	3.315	2.68-4.10	<0.001
AUC = 0.664	Male sex	0.884	0.126	49.276	2.421	1.89-3.09	<0.001
(95% CI 0.640-0.688)	Constant	−2.368	0.129	338.941	0.094		<0.001
Ischemia	T2D	0.405	0.107	14.482	1.500	1.21-1.84	<0.001
*R*2 = 0.300	Heart failure	1.217	0.538	5.118	3.377	1.18-9.69	0.024
Hosmer and Lemeshow = 6.29	Multivessel disease	1.030	0.404	6.514	2.801	1.27-6.17	0.011
P = 0.614	Dilated cardiomyopathy	1.051	0.398	6.958	2.861	1.31-6.24	0.008
AUC = 0.654	Previous ischemia or infarction	1.681	0.109	237.883	5.368	4.33-6.64	<0.001
(95% CI 0.630-0.678)	Asymptomatic at arrival	0.246	0.119	4.310	1.279	1.01-1.61	0.038
	Dyspnea	0.459	0.143	10.362	1.583	1.19-2.09	<0.001
	Palpitations	-0.883	0.427	4.267	0.414	0.179-0.95	0.039
	Male sex	1.026	0.110	87.125	2.789	2.24-3.46	<0.001
	Constant	−1.574	0.115	187.499	0.207		<0.001
Infarction	T2D	0.472	0.097	23.81	1.604	1.32-1.93	<0.001
*R*2 = 0.111	Multivessel disease	1.542	0.381	16.39	4.673	2.21-9.85	<0.001
Hosmer and Lemeshow = 0.183	Previous ischemia or infarction	0.664	0.098	46.24	1.943	1.60-2.35	<0.001
AUC = 0.663	Male sex	0.684	0.103	43.721	1.982	1.62-2.42	<0.001
(95% CI 0.639-0.686)	Constant	−1.204	0.097	153.55	0.300		<0.001

T2D, type 2 diabetes; *AUC*, area under the curve; *CI* confidence interval; *OR* odds ratio, *B* Bertha coefficient; *S.E.*, standard error

Strengths and Limitations to be Acknowledged

First, our study was designed as a cross-sectional study with a great number of patients who were diagnosed using MPS-SPECT, which has a great sensitivity for detecting myocardial ischemia and infarction.[14] Furthermore, the great number of patients captured during the period of time gave us a sample who were at risk of myocardial infarction. Among the limitations are the fact that all the data were collected in a national center of reference, which could lead a reference bias that does not reflect the population outside the center of Mexico. We also did not assess the laboratory measurements due to a delay between our records on the day of MPS-SPECT and laboratory measurements in our institution.

CONCLUSION

Patients who were studied in the NCD had a high prevalence of T2D, arterial hypertension, smoking, and dyslipidemia. Systemic hypertension and T2D were more prevalent in women and smoking in men. The presence of T2D, CMD, male sex, and previous history of infarction or ischemia in these patients were conditions associated with ischemia, infarction, or both.

NEW KNOWLEDGE GAINED

Patients studied in the NCD had a high prevalence of cardiovascular risk factors. The presence of diabetes mellitus type 2, coronary multivessel disease and male sex were conditions associated with ischemia, infarction, or both.

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Author Contributions

NEAV: Research idea, study design, data acquisition, data analysis, statistical analysis, manuscript drafting. NEZ: Research idea, study design, data analysis, statistical analysis, manuscript drafting, supervision, and mentorship. ICJ: Research idea, study design, data analysis, manuscript drafting. ANGF: Research idea, study design, data analysis, manuscript drafting. EAR: Research idea, study design, data analysis, statistical analysis, manuscript drafting, supervision, and mentorship.

Disclosures

The authors declare that they have no conflict of interests.

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