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ORIGINAL RESEARCH ARTICLE

Data-driven atherosclerotic plaque profiles from QAngio-CT associated with functional impairments assessed with PET-CT

Perfiles de placas ateroscleróticas basados en datos de QAngio-CT asociados con alteraciones funcionales evaluadas mediante PET-CT

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Abstract

Objective: *Although coronary artery disease (CAD) involves progressive atherosclerotic plaque dysfunction, further characterization of different cluster profiles and their impact on myocardial function has not been fully explored. Therefore, this study's pilot aim is to identify data-driven atherosclerotic plaque clusters using coronary computed tomography angiography and correlate types with dysfunction observed by positron emission tomography/computed tomography (PET-CT).* **Methods:** *Myocardial perfusion study images of subjects with a high clinical risk of developing CAD were analyzed with semi-automated atherosclerotic plaque characterization. The K-mean clustering method was performed to detect coronary atherosclerotic plaques. An atherosclerotic plaque score was assigned to each subject according to their arteries cluster profiles and was correlated with a principal component analysis (PCA) score that evaluated myocardial perfusion, volumes, and synchrony from PET-CT.* **Results:** *Three well-differentiated clusters were identified from 95 coronary atherosclerotic plaques of 35 subjects. Cluster 1 (28.2%) was characterized by a high fibro-necrotic atherosclerotic plaque, cluster 2 (59.7%) by predominantly fibrous atherosclerotic plaque, and cluster 3 (11.9%) by a necro-calcified atherosclerotic plaque. The atherosclerotic plaque score displayed a significant correlation with the first (r = 0.42; 95% confidence interval [CI]: 0.049-0.675, p = 0.012) and third (r = 0.36; 95% CI: 0.036-0.626, p = 0.035) PCA score components. These were comprised parameters related to impairments in ventricular volume capacity, mechanical dyssynchrony, filling rates, and calcium scores in PET-CT evaluation.* **Conclusion:** *The atherosclerotic plaque clusters identified in this study could provide a pathophysiological explanation of CAD progression and potentially lead to a better characterization of the developing disease.*

Keywords: *Atherosclerotic plaque. Coronary artery disease. Data-driven clusters. Positron emission tomography/computed tomography.*

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Resumen

Objetivo: *La enfermedad coronaria implica disfunción progresiva de placas ateroscleróticas, pero la caracterización de perfiles de agrupación y su impacto en la función miocárdica no se ha explorado a fondo. Este estudio piloto busca identificar grupos de placas ateroscleróticas mediante angiografía coronaria por tomografía computarizada (TC) y correlacionarlos con la disfunción miocárdica observada por PET-CT.* **Métodos:** *Se analizaron imágenes de perfusión miocárdica de sujetos con alto riesgo de enfermedad coronaria, utilizando caracterización semiautomatizada de placas ateroscleróticas. Se aplicó el método de agrupamiento K-means para identificar placas coronarias y asignar un puntaje a cada sujeto basado en perfiles arteriales. Este puntaje se correlacionó con un análisis de componentes principales (PCA) que evaluó perfusión, volúmenes y sincronía miocárdica mediante PET-CT.* **Resultados:** *Se identificaron tres grupos a partir de 95 placas ateroscleróticas coronarias en 35 sujetos. El grupo 1 (28.2%) con alto contenido fibro-necrótico, el grupo 2 (59.7%) predominantemente fibroso y el grupo 3 (11.9%) por una composición necrocalcificada. El puntaje de placas mostró correlación significativa con el primer (r = 0.42; IC 95%: 0.049-0.675, p = 0.012) y tercer (r = 0.36, IC 95%: 0.036-0.626 p = 0.035) componentes del puntaje PCA que reflejaban parámetros de capacidad ventricular, disincronía mecánica, tasas de llenado y puntajes de calcio en PET-CT.* **Conclusión:** *Los grupos de placas ateroscleróticas identificados en este estudio podrían proporcionar una explicación fisiopatológica de la progresión de la enfermedad coronaria y potencialmente conducir a una mejor caracterización de la enfermedad en desarrollo.*

Palabras clave: *Placa aterosclerótica. Enfermedad de las arterias coronarias. Agrupaciones basadas en datos. Tomografía por emisión de positrones/tomografía computarizada.*

Introduction

Cardiovascular disease (CVD) continues to be the leading cause of mortality worldwide[1,2]. Within the spectrum of cardiovascular diseases, coronary artery disease (CAD) accounts for the most CVD-related deaths[2]. At present, identification and risk stratification are essential in the diagnostic workup of CAD, and it is crucial for making individualized therapeutic decisions to prevent adverse outcomes[3,4]. Most of these approaches have used quantitative and qualitative non-invasive imaging methods, mainly focusing on assessing the structure and function of coronary arteries[5]. However, recent reports have shown that the use of coronary computed tomography angiography (CCTA) for assessing CAD in at-risk populations has increased[4].

In addition, CCTA has proven helpful in identifying atherosclerotic plaque components and subsequent plaque characterization. However, its clinical significance remains in doubt[6-8]. Epidemiological studies have observed that atherosclerotic plaque composition is heterogeneous and may be associated with distinct risk profiles and adverse outcomes[9,10]. Although CCTA can provide highly accurate anatomical images of coronary arteries and identify the composition of atherosclerotic plaques, it cannot assess the functional performance of the heart and the impact of CAD on the myocardial microvascular system[3]. While highly efficient hybrid nuclear imaging methods have been proposed to close the gap between anatomical and functional assessments of CAD, the characterization of atherosclerotic plaque profiles might provide valuable insight into the impact of CAD on myocardial coronary flow and function.

Thus, this pilot study aimed to evaluate the relationship between atherosclerotic plaque profiles derived from a data-driven analysis of CCTA images aided by semi-automated plaque characterization software (QAngio CT [Research Edition V2.1.16.1; Medis Specials]) with functional parameters assessed by myocardial perfusion studies using positron emission tomography/computed tomography (PET-CT). We hypothesized that a hemodynamically unfavorable plaque composition phenotype could predict myocardial flow and function impairment.

Methods

Study design and population

Our retrospective pilot study was based on images from a cohort of adult patients who visited the PET-CT unit at the School of Medicine of the National Autonomous University of Mexico between January 2018 and December 2018. Inclusion criteria to select images from a myocardial perfusion study (MPS) were adult subjects who underwent PET-CT with high clinical risk of CAD defined as the presence of angina, < 5 years since the clinical onset of their symptoms, no history of medication that could alter or modify the atherosclerotic plaque extension (e.g., PCSK-9 inhibitors), history of ≥ 3 years using high-dose statins and left ventricular ejection fraction of ≥ 60% at evaluation[11]. The MPS images of

subjects with prior myocardial infarction, arrhythmias, congenital heart disease, acute infections, or cancer were excluded from the assessment. In addition, illegible or incomplete MPS images extracted from recorded databases were also excluded. All the MPS images were then processed using a semi-automated atherosclerotic plaque characterization (SAPC). The same medical specialist trained and supervised data collectors during the study period.

Clinical assessment

Complete clinical histories of the patients were performed by a physician. Chronic comorbidities and traditional risk factors (history of systemic hypertension, type 2 diabetes mellitus, dyslipidemia, smoking, alcoholism, and obesity) were self-reported during interviews. Medical records of subjects who had incomplete or inconclusive clinical information or whose PET-CT scan images were illegible were excluded from the analysis.

Coronary CTA measurements

A previously validated SAPC software (QAngio CT [Research Edition V2.1.16.1; Medis Specials]) tool for quantification and characterization of the coronary atherosclerotic plaques of each subject was used[8,12,13]. The complete description of coronary atherosclerotic plaques incorporated myocardial perfusion data derived from PET-CT images, which provided information regarding vessel morphology, intensities, plaque burden, and characterization in coronary CT data. 6 ml/sec of non-ionized iodide contrast was used; complete technical details are presented in supplementary material. Briefly, SAPC identified four well-differentiated components within the coronary atherosclerotic plaque: fibrous, fibro-fatty, necrotic, and calcified. These components were calculated as percentages of the global atherosclerotic plaque (Fig. 1). In addition, SAPC could evaluate the lumen and plaque characteristics, which included the degree of stenosis, lesion length, plaque burden, and plaque volume. All SAPC measurements were done by a blinded operator, unaware of any clinical or biochemical data.

PET/CT perfusion procedure

To evaluate myocardial perfusion, ventricular function, coronary flow, and coronary flow reserve, we used a self-produced cyclotron-derived nitrogen13 ammonium ([13N]-NH3), which has a half-life period of 9.9 min. Patients were placed in a PET/CT camera where 10mCi of ammonium was injected, and 3-mm thick slices were obtained during a breath-holding protocol over 10 min. 20 min after the rest phase ended, a pharmacological stress phase was performed, during which adenosine was administered intravenously at a dose of 140 μg/kg/min for 4 min. Afterward, 10mCi of ammonium was injected, and images were obtained over 10 min. Once the image acquisition was completed, intravenous catheters were removed. During the entire test, electrocardiographic activity and blood pressure were monitored.

MPS images were obtained in three main axes: short and long, horizontal and vertical. Two certified nuclear cardiologists processed the images. We performed a semiquantitative visual interpretation of tomographic perfusion images, both at rest and in stress, dividing the left ventricle into 17 segments. Each segment was assigned a score of 5 points: 0 (normal), 1 (slight reduction), 2 (moderate reduction), 3 (severe reduction), and 4 (absence of radioactive tracer uptake). The summed rest score (SRS) was considered the summed score of all the segments in the images taken during the rest phase, which depicts perfusion at basal condition, whereas the summed stress score (SSS) was the sum of the points at peak stress, representing the perfusion at the peak of the exercise. Finally, the summed difference score (SDS) was calculated as the difference between the SSS and the SRS and represents the degree of reversibility of myocardial ischemia.

The LVEF, standard deviation (SD) bandwidth and entropy were automatically obtained with the Emory Toolbox software. The ventricular volumes and the ejection fraction were calculated by QGS software.

Finally, we defined decreased coronary flow reserve as < 2.5[14]. Increased plaque charge, stress, and basal coronary flow were determined using the value from the 90th percentile of each distribution.

Cluster variable selection

Variables for our clustering model were selected on the premise that everyone who was evaluated by an MPS could contribute with three main coronary arteries (right, left anterior descending, and circumflex) that could independently provide flow to specific territories of the heart. Under this assumption, each coronary artery was managed as an individual study unit for the composition of its atherosclerotic plaque. Likewise, the dimensions of the circumference of each coronary artery were assumed to vary according to the body composition and anatomy of each subject assessed with PET-CT.

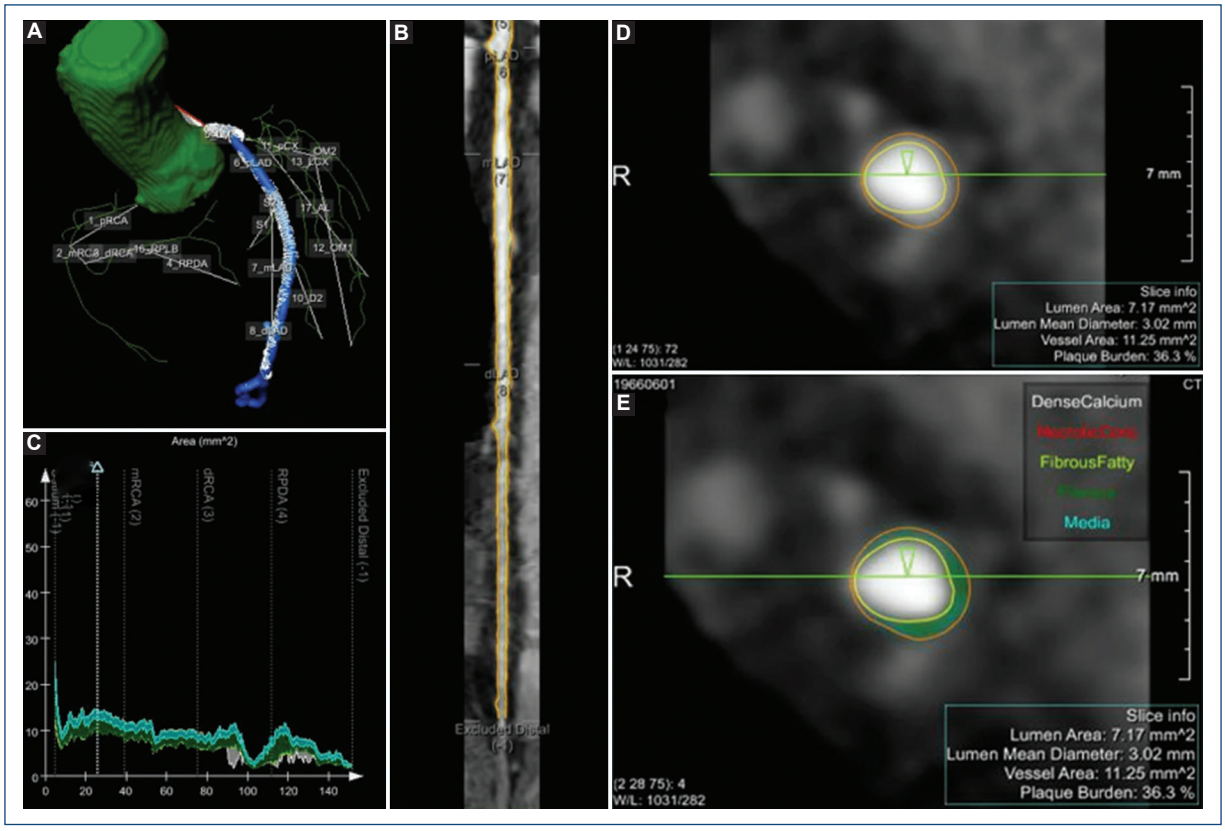

Figure 1. Example of coronary artery tree analyzed by semi-automated atherosclerotic plaque characterization-coronary computed tomography angiography. **A:** automatically extracted coronary tree. The left anterior descending coronary artery is highlighted in blue; **B:** plaque burden analysis in the left anterior descending coronary artery. The area between the yellow line and the orange line represents the volume of arterial media and atherosclerotic plaque; **C:** virtual histology analysis in the left anterior descending coronary artery. Blue color, dark green, light green, red, and white represent media, fibrous plaque, fibro-fatty plaque, necrotic plaque, and calcified plaque, respectively; **D:** cross-section of the artery with plaque burden analysis at that level; **E:** the same cross-section of the artery with virtual histology analysis.

Thus, the relative percentages of fibrotic, fibro-fatty, necrotic, and calcified percentage content reported from each coronary artery were extracted for analysis.

Statistical analysis

All analyses were performed using R software (Version 1.3.2), whereas a $p < 0.05$ was considered a statistically significant threshold.

Descriptive characteristics

Continuous data were presented as means and SD or medians and interquartile range (IQR), wherever appropriate. Categorical data of clinical comorbidities were presented as relative frequencies with their respective percentages. All the characteristics were presented for all the subjects in the study population and for the grouped atherosclerotic profiles derived from our cluster analysis.

K-mean analysis

Cluster analysis was performed using a K-means algorithm with standardized centered values with a mean value of 0 and a SD of 1. Coronary arteries with extreme outliers were defined as > 5 SDS from the mean in the selected variables. Those arteries with no detected atherosclerotic plaques were excluded from the final model selection. The k means runs function with a k value of 3, and a 100-run selection from the fpc package of R was used. Cluster stability and selection were assessed by resampling the dataset 1,000 times and computing the Calinski-Harabasz criterion. Labels of each cluster were assigned according to the cluster variable means.

Association of data-driven clusters with PET-CT variables

We performed logistic regression models to prove that our data-driven clusters were associated with PET-CT score parameters related to arterial dysfunctionality. We used decreased coronary flow reserve and increased plaque charge, basal, and stress coronary flow as our endpoints to define arterial dysfunctionality. Adjustment covariates were plaque volume, lesion length, and arterial stenosis. To evaluate the adjustment, we extracted the Bayesian Information Criteria.

Atherosclerotic plaque score

PET-CT can also evaluate the volume capacity of heart chambers and the synchrony of ventricular rhythm. However, since comparing these parameters between clusters could potentially introduce a multicollinearity bias, the parameters were collected at a patient-based level.

To study the implications of atherosclerotic plaque clusters of coronary arteries in a patient-centered approach, an atherosclerotic plaque score was assigned to each patient according to the clustered artery profiles everyone had. The score was assigned under the assumption that each cluster provided a different adverse profile using CCTA and PET-CT.

Principal component analysis (PCA) score

A PCA was performed in an exploratory fashion to extract a pooled score of PET-CT measurements that explained the maximum variability of myocardial function for each subject. PCA was performed using the centered and scaled matrix of the selected variables. The optimal number of components was evaluated using elbow graphs, and those with ≥ 1 eigenvalue were selected. Finally, a Pearson correlation matrix was performed to evaluate the correlation coefficient with the atherosclerotic plaque score and PCA score adjusted for sex and number of comorbidities.

Results

Study population

After excluding and eliminating individuals according to the selection criteria, a sample population of 35 subjects was included for analysis of MPS images using the CCTA-SAPC algorithm. Of 35 subjects, 62.8% were men, 20% reported living with diabetes, 42.8% hypertension, 27.4% dyslipidemia, and 37.1% smoked. 91.4% were assigned a NYHA-I functional class. The median basal LVEF was 71% (IQR: 64.3-74.5), a SDS of 2.5 (IQR: 0-8.25), and a CRF of 2.52 (± 0.83). The clinical and PET-CT characteristics of the patients are presented in table 1.

Data-driven atherosclerotic plaques characterization

After excluding extreme outliers and arteries without atherosclerotic plaques, information was obtained from 92 (87.6%) coronary arteries to perform cluster analysis. Three well-defined atherosclerotic plaque groups were identified using K-means analysis, which displayed a defined component delimitation and an optimal variance according to the Calinski-Harabasz criterion (Supplementary fig. 2). Cluster 1, which included 26 (28.2%) coronary arteries, was characterized by a relatively high percentage of fibrous content, this group had the highest fibrofatty and necrotic percentages of the three identified groups and a null percentage of calcified components. This group was labeled as fibro-necrotic atherosclerotic plaque (FNAP). Cluster 2 included 55 (59.7%) coronary arteries and was characterized by a high fibrous component, a relatively low percentage of fibrofatty and necrotic structure, and an almost null percentage of calcified elements. This group was labeled as predominantly fibrous atherosclerotic plaque (PFAP). Finally, cluster 3, which included 11 (11.9%) coronary arteries, was characterized by the lowest fibrous and fibrofatty content but with a moderate accumulation of necrotic material and the highest content of calcified components. This group was labeled as necro-calcified atherosclerotic plaque (NCAP) (Fig. 2).

Comparison of coronary profiles among data-driven atherosclerotic plaque clusters

Previously identified coronary artery clusters also showed differences in the lumen and plaque characteristics provided by the CCTA-SAPC algorithm. Arteries labeled as NCAP arteries had the highest plaque burden, followed by PFAP and FNAP arteries. This finding could reflect progressive dysfunction attributable to the progression of CAD. This hypothesis also correlated with PET-CT-derived parameters since NCAP arteries displayed the highest basal coronary flow, followed by

Table 1. Clinical and PET-CT characteristics of the study population

Characteristic	n = 35
Male sex, n (%)	22 (62.8)
Arterial hypertension, n (%)	15 (42.8)
Dyslipidemia, n (%)	13 (37.4)
Diabetes, n (%)	7 (20)
History of smoking, n (%)	13 (37.1)
Alcohol consumption, n (%)	9 (25.7%)
NYHA functional class I (%) II (%) III (%)	 32 (91.4) 2 (5.7) 1 (2.85)
Basal-LVEF, n (%)	71 (64.3-74.5)
Stress-LVEF, n (%)	70.5 (65.3-75.5)
Basal-ESV (mL)	28 (20-37.5)
Stress-ESV (mL)	30 (23.3-37.8)
Basal-EDV (mL)	92.5 (66.8-103.3)
Stress-EDV (mL)	97 (77.5-115.5)
Basal-Systolic-Vol (mL)	61 (44.5-68)
Stress-Systolic-Vol (mL)	68 (55-74)
Basal-Band width (º)	162 (69-180)
Stress-Band width (º)	165 (43-184)
Basal-entropy (º)	43.1 (± 12.2)
Stress-entropy (º)	40.1 (± 9.15)
Basal-total calcium score (pts)	0.83 (0.65-0.95)
Stress-total calcium score (pts)	2.03 (1.8-2.4)
Summed difference score (pts)	2.5 (0-8.25)
Basal-peak filling rate (mL/seg)	2.32 (± 0.46)
Stress-peak filling rate (mL/seg)	2.34 (± 0.67)
Basal coronary flow (mL*min/gr)	0.80 (± 0.26)
Stress coronary flow (mL*min/gr)	2.04 (± 0.70)
Coronary flow reserve (mL*min/gr)	2.52 (± 0.83)

LVEF: left ventricular ejection fraction; EDV: end-diastolic volume; ESV: end-systolic volume; PET-CT: positron emission tomography/computed tomography.

arteries affected by PFAP and FNAP. Despite the observed differences in basal coronary flow, all three phenotypes had the same coronary flow during the PET-CT stress phase, which reveals a marked difference in coronary distensibility in response to oxygen demand. Finally, a progressive decrement in coronary flow reserve was observed; NCAP arteries had the lowest score for this parameter, followed by PFAP and FNAP arteries (Fig. 3).

Association of dysfunctional arteries among data-driven atherosclerotic plaque clusters

Arteries labeled as NCAP had an increased likelihood of having decreased coronary flow reserve (odds ratio [OR]: 6.28, 95% confidence interval [CI]: 1.21-32.69, p = 0.003) along with an increased plaque burden (OR: 15.9, 95% CI: 1.72-146.1, p = 0.01) and basal coronary flow (OR: 19.2, 95% CI: 1.08-340.41, p = 0.04) compared with plaques classified as FNAP, after adjusting for plaque volume, stenosis, and length. Plaques classified as PFAP displayed no significant association with our evaluated outcomes (Fig. 4).

Atherosclerotic plaque score description

An attempt was made to determine whether atherosclerotic plaque clusters could impair the myocardial functionality of each patient by creating a composite atherosclerotic plaque score. Arteries labeled as NCAP were assigned an atherosclerotic plaque score of 3, PFAP a score of 2, and FNAP a score of 1. Coronary arteries without detectable atherosclerotic plaque were assigned a score of 0, and arteries with extreme outliers were excluded from this analysis. The median value of the atherosclerotic plaque score for the evaluated sample was 5 (IQR: 4-6) points.

Correlation of atherosclerotic plaque score with myocardial function

As an exploratory analysis, a PCA score was performed on the PET-CT measurements. The first six dimensions explained 86.2% of the cumulative variance of overall myocardial function (Supplementary Fig. 3). The contribution of each variable in these first six PCA score components is shown in supplementary figure 4. A positive correlation existed between the atherosclerotic plaque score and the first PCA component (r = 0.42; 95% CI: 0.049-0.675, p = 0.012), comprised of increased end-systolic and diastolic ventricular volumes and decreased LVEF. The first PCA component could be interpreted as an increased volume overload with decreased mechanical functionality. Finally, the

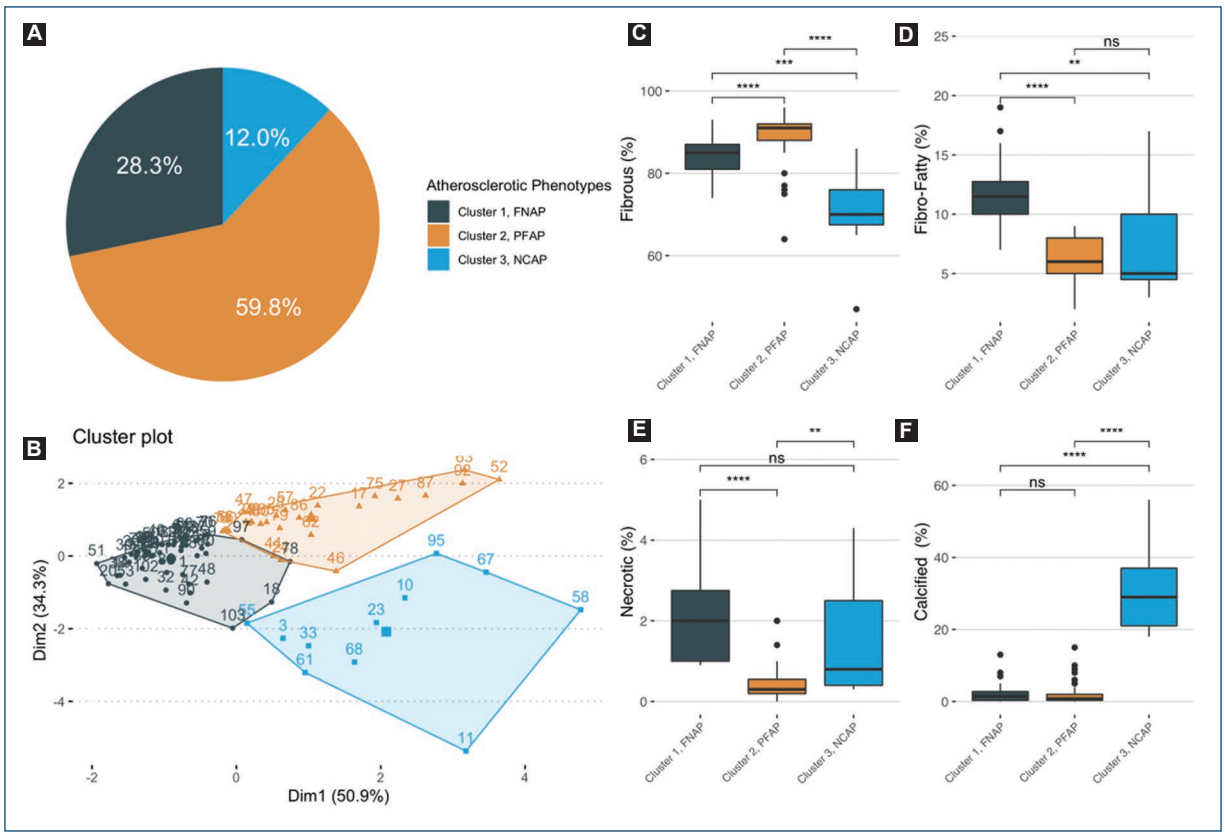

Figure 2. The proportion of fibro-necrotic (FNAP), predominately fibrous (PFAP), and necro-calcified plaque (NCAP) clusters were identified using the k-means algorithm. **A:** boxplots of the content of fibrous, **B:** fibro-fatty; **C:** necrotic; and **D:** calcified percentage of the three identified atherosclerotic plaque clusters. FNAP: fibro-necrotic atherosclerotic plaque; PFAP: predominantly fibrous atherosclerotic plaque; NCAP: necro-calcified atherosclerotic plaque.

third component displayed a significant correlation (r = 0.36; 95% CI: 0.036-0.626, p = 0.035) with the atherosclerotic plaque score, mainly associated with increased entropy, peak filling rate, total calcium volume, and decreased systolic volume. The third PCA component could potentially explain increased myocardial dyssynchrony with increased time of coronary flow fill and decreased systolic volume. The complete correlation matrix with the first six components appears in supplementary figure 5.

Discussion

This study identified three well-differentiated data-driven clusters of plaque lesions evaluated using CCTA-SAPC software QAngio CT and PET-CT in a sample of individuals at high clinical risk of developing CAD. Arteries classified as NCAP displayed the highest plaque burden and the lowest blood flow, followed by arteries classified as PFAP and FNAP. Furthermore, these findings led to the creation of an atherosclerotic plaque score, in which individual values were assigned based on previously observed atherosclerotic plaque features. Individuals with higher scores had significant correlations with impairments in ventricular volume capacity, mechanical dyssynchrony, filling rates, and calcium scores. The data-driven atherosclerotic clusters could make it possible to recognize the pathophysiological progression before the onset of myocardial infarctions in subjects living with CAD.

The results of this study can be explained by the progressive dysfunction observed in CAD associated with an increased accumulation of chronic cardiometabolic risk factors in the Mexican population now of clinical assessment and the physiological loss of arterial elasticity in the adult population[15-17]. In addition, the accumulation of lipid-rich particles under the endothelial lumen can cause tissue oxidation associated with inflammation and accumulation of polymorphonuclear cells that

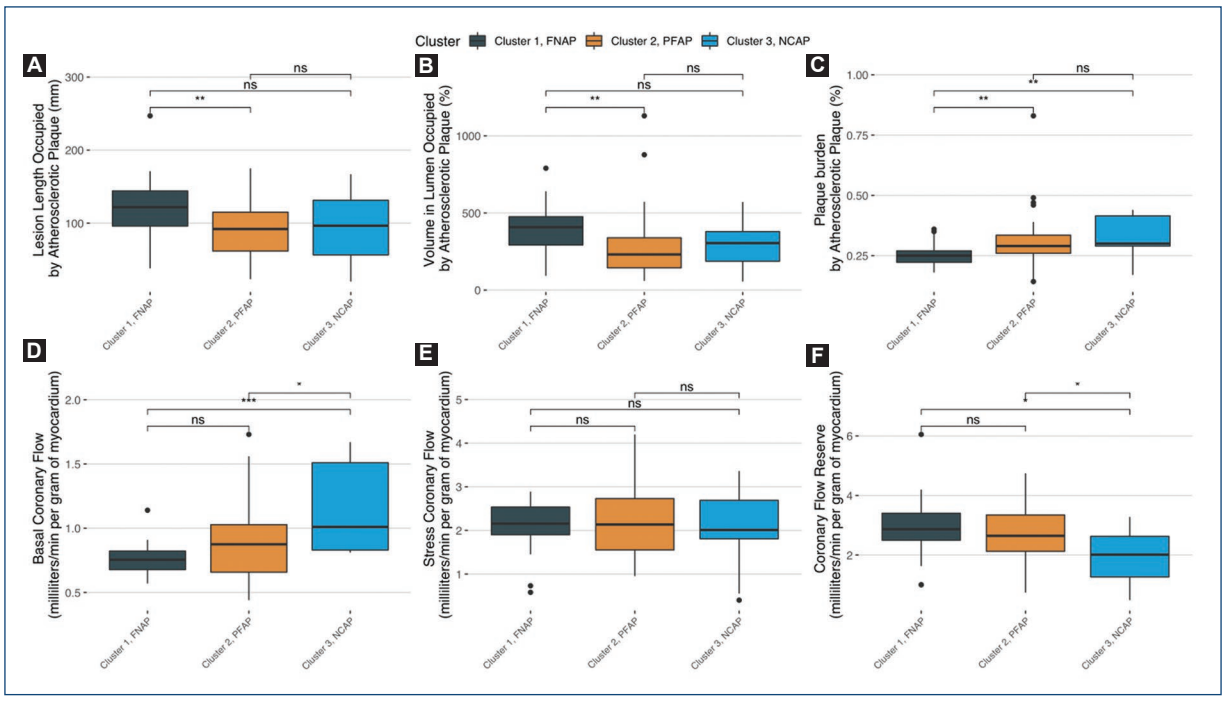

Figure 3. Coronary flow reserve. **A:** characteristics of QAngioCT plaque by data-driven clusters. Boxplots of the lesion; **B:** volume; **C:** plaque burden; **D:** obtained from semi-automated atherosclerotic plaque characterization-coronary computed tomography angiography and basal; **E:** stress, and **F:** coronary flow reserve measurements extracted from positron emission tomography/computed tomography according to the three data-driven atherosclerotic plaque clusters. FNAP: fibro-necrotic atherosclerotic plaque; PFAP: predominantly fibrous atherosclerotic plaque; NCAP: necro-calcified atherosclerotic plaque.

lead to the growth of fibrotic tissue[17,18]. Subsequently, connective tissue restructuring occurs, and a fibrotic layer covers the atherosclerotic plaque. Finally, the atherosclerotic plaque will undergo a process of degradation that generates necrotic tissue with associated calcification[19].

In addition, CAD has been reported to be related to a progressive decrease in ventricular oxygen supply during the early stages of the disease[20]. As the coronary flow drops, the myocardium may experience a toxic accumulation of lactic acid and reactive oxygen species, leading to an abnormal microvascular reconfiguration[18,21,22]. Furthermore, changes in the myocardium translate into dysfunctional contractions and reduced stroke volume. This hypothesis could explain the differences between the reduced coronary flow reserve of NCAP, PFAC, and FNAP arteries. However, caution is advised when interpreting this result, considering the relatively small sample size of the NCAP cluster.

When applied to the PET-CT evaluation, the atherosclerotic plaque score showed an association with mechanical dysfunction in volume capacity, dysrhythmia, and an increase in coronary calcium in the PCA score analysis. Overall, these findings provide evidence that CAD has pathophysiological implications in myocardial function before the onset of major cardiovascular events. However, more studies that could differentiate between the risk of prior myocardial infarction and overall survival attributable to atherosclerotic plaque profiles are warranted.

The results of our study highlight the strengths of diverse MPS parameters obtained from CCTA and PET-CT to better characterize the atherosclerotic plaques of patients living with CAD. Nevertheless, some limitations should be acknowledged. The sample size to evaluate the potential progression of CAD using data-driven characterization was small. Moreover, as the sample population came from a referral center, it may not entirely represent the Mexican population. Finally, it was not possible to assess the potential contribution of genetic and lifestyle-related factors to the evolution of CAD. Nevertheless, this study constitutes an original approach that combines CCTA plaque characterization with PET-CT measurements and lays the groundwork for further analyses.

Figure 4. Association of positron emission tomography/computed tomography scores with atherosclerotic plaque clusters. Forest plot displaying odds ratios and 95% confidence intervals for decreased coronary flow reserve (blue), increased plaque burden (orange), increased stress-coronary flow (green), and increased basal-coronary flow (pink) across fibro-necrotic (FNAP) and predominantly fibrous (PFAP) plaque clusters. The dashed vertical line represents an OR of 1.0. FNAP: fibro-necrotic atherosclerotic plaque; PFAP: predominantly fibrous atherosclerotic plaque.

Conclusion

Three data-driven atherosclerotic plaque clusters were identified with marked differences in myocardial blood flow, mechanical rhythm, and ventricular volume capacities evaluated through CCTA and PET-CT. These atherosclerotic plaque clusters could provide a pathophysiological explanation of CAD progression and ultimately better characterize high-risk patterns in its development.

Supplementary data

Supplementary data are available at DOI: 10.24875/ACM.24000170. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare to have followed the ethical standards of the relevant experimentation committee, according to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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