The Relationship between Uric Acid/Albumin Ratio and Carotid Intima-Media Thickness in Patients with Hypertension

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To the Editor,

We carefully read the article entitled: *"The relationship between the uric acid/albumin ratio and the carotid intima-media thickness in patients with hypertension"*, whose objective was to investigate the association of the uric acid/albumin ratio (UAR) and carotid intima-media thickness (CIMT) in hypertensive patients.[1] Although the present study demonstrated a significant correlation between UAR and CIMT, with UAR showing greater discriminatory capacity for increased CIMT values than uric acid and albumin alone and than the other inflammatory markers analyzed in the study, such as the systemic immune inflammation index (III), the neutrophil/lymphocyte ratio (NLR), the platelet/lymphocyte ratio (PLR) and the C-reactive protein/albumin ratio (CAR),[1] some aspects observed, when reading the article, are worthy of note.

The classification of patients into groups of increased and normal CIMT used, as a cutoff point, a value of 0.9mm, in line with the normal value recommended in the guidelines of the European Society of Cardiology (ESC).[2,3] This simplification, however, can lead to classification errors in different populations and age groups, in which similar values may be within the normal range.[2] This was evidenced by Homma et al.,[4] through the finding that in aging, the increase in CIMT may be due to a process of diffuse intimal thickening and not necessarily the formation of atherosclerotic plaques. Given this, we consider it important to stratify the studied population by sex, age, and ethnicity, given the existence of variability among these individuals, which may influence an underestimation of the results.

In the Vascular Ultrasonography positioning of the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology – 2019,[5] it is recommended that after acquiring numerical CIMT data, the average values should be compared with already existing reference values in accordance with the normative tables of the ELSA-Brazil, CAPS or MESA studies. The decision on which table to use will depend on the individual's gender, age, and ethnicity. It should be added in the conclusion whether the measurement is above or below the 75th percentile, in addition to the table used with its bibliographic reference. Therefore, the cutoff point used in the methodology may lead to confusion bias.

However, the presence of atheromatous carotid plaque was not described in the groups since plaque identification is the main reclassifier of cardiovascular risk. Furthermore, the classification of the stage of hypertension in the selected group, according to the 2020 Arterial Hypertension Guideline,[6] confers a greater risk for target organ damage the higher the blood pressure levels, in addition to greater endothelial dysfunction and arterial vascular remodeling.

As evidenced in the methodology, patients with congestive heart failure, secondary hypertension, moderate to severe valvular heart disease, coronary artery disease, chronic kidney or liver disease, malignancy, active infection, and chronic inflammatory disease, in addition to those taking medications that affect serum levels of uric acid and/or albumin and those with malnutrition.[1] However, we observed that individuals affected by peripheral arterial obstructive disease were not included in the research exclusion criteria, which may confuse the results presented since the evidence regarding the correlation between atherosclerotic deterioration of the arterial wall in peripheral vascular territories and the increase in CIMT, have already been demonstrated for some decades.[7] It is, therefore, necessary to consider this comorbidity among the exclusion criteria for a better analysis of the results obtained in the study.

We also understand that it is necessary to stratify the diabetic patients included in the study in relation to the antidiabetic therapy used, given its potential to reduce CIMT. This effect was demonstrated, by way of illustration, in studies that analyzed drugs such as liraglutide[8] and metformin.[9] Due to these aspects, stratifying individuals in relation to the hypoglycemic agent used, the duration of treatment, and the dose used emerges as a relevant factor for a better interpretation of the association between UAR and CIMT.

Finally, the correlation between diabetes mellitus and vascular calcification[10,11] is well established, which occurs, among other aspects, due to prolonged exposure of the smooth muscle fibers of the tunica media to hyperglycemia.[12]

Keywords

Cardiovascular Diseases/complications; Uric Acid; Human Serum Albumin; Carotid Intima-Media Thickness; Hypertension

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Due to this, it is inferred that the duration of illness presented by individuals affected by diabetes mellitus can be a predictor of this process, in addition to the fact that calcifying sclerosis of the media can be another confounder of the results presented, thus justifying the need for stratify diabetic patients according to the duration of illness.

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Reply

Dear Editor,

We thank to authors for their valuable comments regarding our study entitled "The relationship between the uric acid/albumin ratio and the carotid intima-media thickness in patients with hypertension".[1]

We agree with the authors on the issue that age is correlated with carotid intima-media thickness (CIMT) irrespective of the formation of atherosclerotic plaques,[2] and the high CIMT group in our study was older than the low CIMT group. However, we eliminated this confounding factor by adding this variable in the multivariable model to get an adjusted odds ratio for uric acid/albumin ratio (UAR) for a high CIMT. Since there was no difference between the groups in terms of gender and such a parameter was also not associated with a high CIMT based on the univariable logistic regression analysis, we did not input that variable in the multivariable model. Finally, the population in our study consisted of only white Caucasian ethnicity, and there were no patients from other ethnic groups.

The cutoff value for the discrimination of high and low CIMT groups was 0.9 mm, as suggested by the guidelines of the European Society of Cardiology.[3] Because this cutoff value was also used to determine the patients having high cardiovascular risk in the literature, we applied this cutoff value in our study.[4]

It is a well-known issue that the presence of atheromatous plaque is an independent predictor of cardiovascular risk.[5] The study aimed to evaluate the relationship between the UAR and CIMT. Thus, we did not investigate the presence of atheromatous plaque and its predictive role in cardiovascular risk.

We agree with the authors on the relationship between the stage of hypertension and the risk of target organ damage, including vascular remodeling and endothelial dysfunction.[6] However, the vast majority of patients had already had hypertension diagnosed before enrollment in the study and were on anti-hypertensive treatment for a while. With the aid of anti-hypertensive drugs, blood pressure values were normalized in most patients. With this, the classification of hypertension based on recommended guidelines was not applicable in our study. Therefore, we could not evaluate the impact of the degree of hypertension on CIMT in this study. As mentioned by the authors, there is strong evidence regarding peripheral arterial deterioration and higher CIMT.[7] Thus, we excluded the patients with peripheral arterial disease from the study. However, we did not mention it in the exclusion criterion.

The frequency of patients with and without diabetes mellitus (DM) was similar between high and low CIMT groups

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in our study (p-value = 0.280). Additionally, DM was not associated with high CIMT in the univariable logistic regression analysis. Thus, there was no impact of DM with having a high CIMT in our study. Additionally, diabetic patients with longer disease duration might develop micro- and macro-vascular complications. Due to the difficult calculation of CIMT in such patients, we did not include these patients in this study. We acknowledge that anti-diabetic drugs, including liraglutide and metformin, might have effects on CIMT.[8,9] On the other hand, GLT-1 inhibitors such as liraglutide have been recently used for the treatment of DM in our country. As we described above, because of the homogeneous distribution of diabetic patients between the study groups, we did not consider that DM had a biased impact on CIMT in this study. However, we did not collect data regarding the duration of DM as well as dosage and the duration of anti-diabetic drugs. Thus, these limitations might be added in the limitations part of the text.

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