Association Between Abdominal Aortic Atherosclerosis and Carotid Artery Atherosclerosis

A Prospective Cross-Sectional Study

Carlos Jesus P Haygert[1], Giordano RT Alves[2], Bruna H Suzigan[3], Lucas V de Souza[3], Alexandre Naujorks[4], Juarez Barbisan[5]

ABSTRACT

Atherosclerosis is a prevalent systemic disease, responsible for the greatest number of deaths in developed countries. Clinical events and appropriate treatment depend on the sites involved. Both aortic and carotid atherosclerotic disease may result in grave clinical outcomes; however, the association between these two entities has not been clearly demonstrated yet. We developed a study to look at the association between Abdominal aortic Atherosclerotic Plaque (AAP) and Carotid artery Atherosclerotic Plaque (CAP). A prospective cross-sectional study was performed from March 2011 to April 2012. Consecutive patients who underwent total abdominal Computed Tomography (CT) for several reasons and Ultrasonography (US) of the carotid arteries were included. The independent association between the incidental finding of both AAP and CAP was sought using uni and multivariate analyses. One hundred and eighteen patients were evaluated. AAP was present in 53/118 (44.9%) patients and CAP in 69/118 (58.4%). After performing adjustment by multiple logistic regression with covariables such as sex, smoking, diet, abdominal circumference, Systemic Arterial Hypertension (SAH), diabetes and history of ischemic stroke, we observed that AAP and SAH were associated with CAP, with an OR of 10.75 (CI: 3.95-29.3 and p=0.0001) and 5.65 (CI: 2.06-12.5 and p=0.001), respectively. The presence of AAP at CT scan is strongly associated with CAP at US. In the future, such incidental finding at routine abdominal CT may probably recommend carotid US performance. SAH is also strongly associated with the presence of CAP.

Key words: *Abdominal aorta, carotid artery, atherosclerosis, computed tomography*

Abdominal Aortik Arteroskleroz ve Karotid Arter Aterosklerozu Arasındaki ilişki: Prospektif Kesitsel bir Çalışma

ÖZET

Ateroskleroz gelşmiş ülkelerde ölümlerin büyük çoğunluğundan sorumlu olan yaydın görülen sistemik bir hastalıktır. Klinik olaylar ve uygun tedavi tutulumun olduğu bölgeye göre değişir. Hem aortik hemde karotis aterosklerotik hastalığı ciddi sonuçlara yolaçabilir, bununla birlikte bu iki klinik antite arasındaki ilişki henüz net olarak gösterilmemiştir. Biz abdominal aortik aterosklerotik plak (AAP) ile karotis arter aterosklerotik plağı (CAP) arasındaki ilişkiyi gösterme amaçlı bir çalışma planladık. Mart 2011 den Nisan 2012 ye kadar süren prospektif kesitsel bir çalışma planladık. Çeşitli nedenlerle abdominal komputerize tomografi ve carotis arter ultrasonografisi yapılmış ardışık hastalar çalışmaya dahil edildi. AAP ve CAP arasındaki bağımsız ilişki univariate ve multivariate analizler ile araştırıldı.118 hasta değerlendirildi. AAP 53/118 (44.9%) hastada ve CAP 69/118 (58.4%) hastada mevcuttu. Cinsiyet, sigara içimi, diyet, abdomen çevresi, sistemik arteryel hipertansiyon (SAH), diyabet ve iskemik inme öyküsü gibi değişkenler için multiple logistic regresyon analizi ile düzeltme yapıldığında we AAP ve SAH CAP ile ilişkili bulundu (sırasıyla OR 10.75 (CI: 3.95-29.3 and p=0.0001) ve 5.65 (CI: 2.06-12.5 ve p=0.001). CT incelemesindeki AAP ile ultrasonda görülen CAP kuvvetli ilişki gösteriyordu. Gelecekte rutin abdominal CT de görülen böyle tesadüfi bulgular karotis arter ultasonu ile karotis plağına bakma açısından yönlendirici olabilir. SAH da CAP varlığı ile kuvvetli ilişki gösteriyordu.

Anahtar kelimeler: *Abdominal aorta, karotis arter, ateroskleroz, komputerize tomografi*

University Hospital of Santa Maria, Division of Radiology, Santa Maria, Brazil[1], Federal University of Santa Maria, Department of Clinical Medicine, Santa Maria, Brazil[2], Cardiology Institute of Rio Grande do Sul, University Foundation of Cardiology, Deparment of Statistics, Porto Alegre, Brazil[3], University Hospital of Santa Maria, Division of Cardiology, Santa Maria, Brazil[4], Cardiology Institute of Rio Grande do Sul, University Foundation of Cardiology, Division of Cardiology, Porto Alegre, Brazil[5]

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Correspondence: *Giordano R. T. Alves , Federal University of Santa Maria, Department of Clinical Medicine*
Roraima Avenue, 1000, Zip-code: 97105-900, Santa Maria, Brazil
Tel.: +55(55)99159009; fax: +55(55)32221024
E-mail: grtalves@gmail.com

INTRODUCTION

Atherosclerosis is a prevalent systemic disease and accounts for the greatest number of deaths in developed countries. Clinical events secondary to it and their individual appropriate treatment depends on the sites involved in each case (1). Several studies have demonstrated that patients with atherosclerotic disease at one site are very likely to present it at another (2-12). Wofford et al showed that patients with atherosclerotic coronary disease are very likely to present atherosclerotic lesions in the carotid arteries (11). Another study using autopsies found a high frequency of fat plaques in the abdominal aorta, both in young adults and children, and correlated abdominal aortic calcifications with coronary calcified plaques (12). Aortic calcifications, especially in the thoracic aorta, are common in the elderly. Moreover, there is large evidence indicating that patients with thoracic aorta calcifications are at greater risk for coronary disease and stroke (3,13,14). Computed Tomography (CT), distinctively after the advent of multi-slice equipment, has been frequently used to evaluate carotid and coronary atherosclerosis. Images of the aorta, however - including the abdominal segment - had received less attention (15). Because of this, although parietal hyperdensities are often seen in the abdominal aorta at CT, the true value of such finding has not been well defined yet (2,10).

Concurrently, carotid Ultrasonography (US) studies are able to provide high-resolution images, which not only supplies the grade of a carotid stenosis, but also the characteristics of arterial walls. Some authors have shown that arterial myointimal thickening is a strong predictor of future cardiovascular events (16), as well as carotid plaques for atherosclerotic systemic disease. Both aortic and carotid atherosclerotic disease may result in very grave clinical outcomes (2,4,5). Early diagnosis can lead to immediate treatment and, consequently, decrease mortality rates (1). However, there are very few evidences proving a clear and significant association between these two entities. Therefore, the aim of our study was to look at the association of atherosclerotic involvement at these two sites using abdominal CT and carotid US.

MATERIAL AND METHODS

Study and patient population

We developed a prospective cross-sectional study from March 2011 to April 2012. A total population of 118 patients was included, after accepting to participate in the research by signing the informed consent form. All patients were submitted to abdominal CT scans for various medical reasons, and were subsequently invited for carotid US performance. Patients who did not undergo both exams and patients with neurological deficits who had no family to answer for were excluded.

CT evaluation of abdominal aorta

CT scans were performed using three single-slice helical equipment: Siemens Somaton Emotion (Siemens Medical Solutions, Malvern, PA, USA), Shimadzu SCT 7000ts (Shimadzu, Kyoto, Japan) and General Electric Hispeed (GE Medical Systems, Milwaukee, WI, USA). Slice thickness of images acquisition protocols varied from 3 to 10 mm. CT scans were obtained from the thoracoabdominal transition to the iliac crests, and soft tissue filters were used. The images were visualized in DICOM (Digital Imaging Communications in Medicine) format, enabling the use of gray tone and zoom adjustment tools. Imaging analysis was done by one radiologist with 10 years of experience (C.J.P.H.), who sought for abdominal aorta hyperdense parietal images (calcifications), from the diaphragm to the iliac bifurcation. Iliac bifurcation calcifications were not included.

Evaluation of atherosclerosis in the carotid artery

The US exams of the carotid arteries were performed with Envisor HD equipment (Philips Medical Solutions, Malvern, PA, USA), using the multifrequency linear transducer 7-10 MHz. A cardiologist (A.N.) specialized in ultrasonography, with 15 years of experience, classified carotid lesions. Focal lesions greater than 1.4 mm thick were considered plaques. At the time of examination, he was blinded for any information concerning abdominal CT results.

Risk factor estimates

The covariables included in our study correspond to potential risk factors associated with Carotid artery Atherosclerotic Plaques (CAP). Sex, color, smoking, alcohol drinking, diabetes, Systemic Arterial Hypertension (SAH, systolic pressure 140 and diastolic pressure 90), diet, physical activity, abdominal circumference (men:

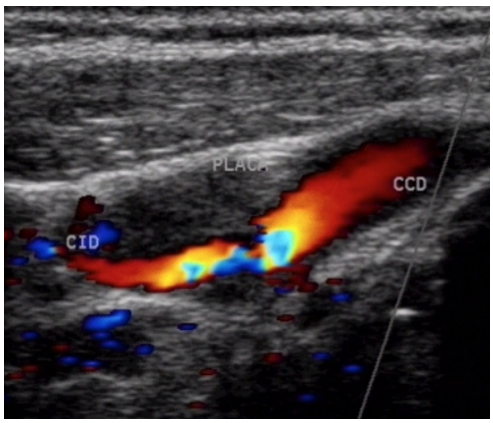

***Figure 1**. Abdominal Computed Tomography (CT) scan showing two foci of aortic calcification. Any hyperdense image with calcium density at CT, regardless its extension, was considered an Abdominal Aortic Plaque (AAP).*

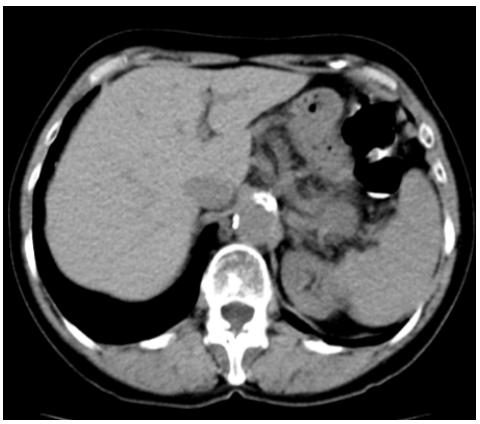

***Figure 2**. Carotid Ultrasonography (US) revealing the presence of a Carotid Atherosclerotic Plaque (CAP), in the same patient of Figure 1. CAP was defined as focal lesions which thick measured more than 1.4 mm.*

normal if 102 cm, altered if >102 cm and women: normal if 88 cm, altered if >88 cm), Body Mass Index (BMI) classification (<24.9: normal; ≥25: altered), family history of cardiovascular disease, ischemic stroke, coronary angioplasty and revascularization surgery.

Statistical analysis

We have applied univariate logistic regression to select possible risk factors associated with carotid lesions to construct the multiple regression model. The univariate regression enabled the estimation of the odds ratio (raw OR) and the respective confidence intervals of 95% (CI 95%). A non-conditional analysis strategy was used for multiple logistic regression analysis, which simultaneously included in the model all the significant independent covariables of univariate logistic regression results, with the forward stepwise method, and a 0.20 level of significance verified by the Wald test. The non-significant covariables were eliminated from the multiple model (p>0.05), and the effect of the exit of each one was verified in the remaining coefficients. Statistical analyses were performed using computational application SPSS 15.0 (SPSS Inc., Chicago, IL, USA).

Ethical aspects

This study was approved by the ethical committees from Federal University of Santa Maria and Cardiology Institute of Rio Grande do Sul – University Foundation of Cardiology, according to the Declaration of Helsinki and the International Committee of Medical Journal Editors. All patients included in the sample were invited to participate in the study and have signed an informed consent form.

RESULTS

The examinations of 118 patients who underwent total abdominal CT and carotid US were evaluated. The mean age was 55 ±13 years (ranging from 30 to 70) and 66/118 (55.9%) were female (versus 52 men - 44,1%). Table 1 summarizes the demographic characteristics and all covariables in the study, as well as the results of univariate logistic regression analysis.

Abdominal aortic Atherosclerotic Plaque (AAP) was diagnosed at CT in 53/118 (44.9%) patients (Figure 1). Additionally, there were 69/118 (58.4%) individuals with detected CAP at US (Figure 2). We observed that 46/53 (86,8%) with AAP at CT concomitantly presented CAP at US examination, or that 46/69 (66%) with CAP at US also had AAP at CT. After multiple logistic regression analysis, we obtained an OR of 10.75 for the association between AAP and CAP (CI: 3.95-29.3 and p=0.0001). Other covariables like sex,

***Table 1**. Descriptive analysis of risk factors for carotid atherosclerosis and univariate logistic regression, with carotid plaque occurrence as being the outcome (n = 118).*

Independent variables	*Carotid lesion*		*Raw OR*	*CI (95%)*	*P*
	No (%)	*Yes (%)*			
Sex					
Male	*25(48.1)*	*27(51.9)*	*1*	*0.773-3.396*	*0.193 **
Female	*24(36.4)*	*42(63.6)*	*1.62*		
Color					
White	*44(42.3)*	*60(57.7)*	*1*	*0.414-4.212*	*0.638*
Non-White	*5(35.7)*	*9(64.3)*	*1.320*		
Alcoholism					
Non drinker	*42(44.2)*	*53(55.8)*	*1*	*0.682-4.808*	*0.229*
Drinker	*7(30.4)*	*16(69.6)*	*1.811*		
Smoking					
Non smoker	*36(46.8)*	*41(53.2)*	*1*	*0.853-4.191*	*0.114**
Smoker/ex-smoker	*13(31.7)*	*28(68.3)*	*1.891*		
Diabetes Mellitus					
Non - diabetic	*48(47.5)*	*53(52.5)*	*1*	*1.729-30.067*	*0.002**
Diabetic	*1 (6.2)*	*15(93.8)*	*13.585*		
Hypertension					
Normal	*40(58.0)*	*29(42.0)*	*1*	*2.664-15.113*	*0.001**
Hypertensive	*8(17.4)*	*38(82.6)*	*6.552*		
Diet					
With controlled diet	*46(48.9)*	*48(51.1)*	*1*	*1.874-24.020*	*0.001**
Without controlled diet	*3(12.5)*	*21(87.5)*	*6.708*		
Physical Activity					
Performs physical activity	*35(39.3)*	*54(60.7)*	*1*	*0.299-1.614*	*0.396*
Does not perform physical activity	*14(48.3)*	*15(51.7)*	*0.694*		
Abdominal Circumference					
Normal	*29(50.0)*	*29(50.0)*	*1*	*0.951-4.207*	*0.066**
Altered	*20(33.3)*	*40(66.7)*	*2.000*		
Family History					
Absent	*25(46.3)*	*29(53.7)*	*1*	*0.605-2.764*	*0.507*
Present	*22(40.0)*	*33(60.0)*	*1.293*		
BMI Classification					
Normal	*21(38.9)*	*33(61.1)*	*1*	*0.392-1.710*	*0.593*
Overweight	*28(43.7)*	*36(56.3)*	*0.818*		
Ischemic stroke					
No	*48(43.6)*	*62(56.4)*	*1*	*0.645-45.553*	*0.084**
Yes	*1(12.5)*	*7(87.5)*	*5.419*		
Coronary angioplasty					
No	*49(42.6)*	*66(57.4)*			
Yes	*0(0.0)*	*3(100.0)*			
Revascularization surgery					
No	*49(42.2)*	*67(57.8)*			
Yes	*0(0.0)*	*2(100.0)*			
Aortic calcification					
No	*42(64.6)*	*23(35.4)*	*1*	*4.670-30.837*	*0.001**
Yes	*7(13.2)*	*46(86.8)*	*12.000*		

OR: Odds ratio; BMI: Body Mass Index; Raw OR = 1: Reference category; CI 95%: 95% Confidence Interval; * p 0.20

smoking, diabetes, SAH, diet, abdominal circumference and history of ischemic stroke have also reached at univariate analysis a level of significance <0.20. However, after adjustment in the multiple logistic regression model, only AAP and SAH continued to have independent association with CAP (Table 2).

DISCUSSION

Calcification in blood vessels is known to be part of a complex atherosclerotic process and tends to appear later than the so-called atheromas. In this context, aortic calcification reveals to play a role in an actively regulated process (17,18), usually denoting the presence of aortic atherosclerosis. Therefore, the presence

***Table 2**. Multiple logistic regression analysis with carotid atherosclerotic plaque as being the outcome.*

Independent variables	Adjusted OR *	CI (95%)	P
Hypertension			
Normal	1		0.001*
Hypertensive	5.653	2.063–15.490	
Aortic Calcification			
No	1		0,0001*
Yes	10.752	3.944–29.307	

* Odds ratio adjusted for the other covariables in the table by means of multiple logistic regression; adjusted =1: reference category; CI 95%: 95% Confidence Interval.

of calcified vascular foci at routine examinations cannot be considered antique or resolved entities, and should always gain proper consideration. In our research, we have cross-matched several covariables with the presence of imaging pathological findings. In the Rotterdam population base study, Kardys et al have evaluated coronary calcification, carotid wall thickness, carotid plaque and abdominal aortic calcification using different imaging modalities (19). In that study, the authors have concluded that carotid plaques occur more frequently in males. On the other hand, our results have shown a higher occurrence of carotid atherosclerosis in women. Nevertheless, after performing multiple regression statistical analysis, the variable gender was not significantly associated with CAP. There is also a well-known association between SAH and atherosclerotic carotid alterations. Allison et al have proved that SAH is an important risk factor for carotid atherosclerosis (OR: 3.2) (20). Interestingly, in our study, the occurrence of carotid lesion in hypertensive patients was approximately six times greater than its occurrence in non-hypertensive patients (OR: 5.653). Moreover, we have found that the concomitant presence of AAP and CAP was almost two times more likely to occur (OR: 10.752) than the presence of SAH and CAP, a result that had not yet been described in the literature.

When regarding to radiological findings, several authors have found strong associations between two specific sites of atherosclerosis occurrence. Reaven et al have described the association between coronary artery atherosclerosis and abdominal aortic calcification, as well as an increased risk of cardiac events in patients with type 2 diabetes (7). In the present study, although diabetes apparently revealed to be associated with CAP at univariate analysis, such correlation was not confirmed after applying multiple regression analysis. Other studies had already identified an important correlation between carotid wall alterations and thoracic aortic plaques (6,9,10). Kallikazaros et al have demonstrated a consistent association between carotid artery atheromas and atheromas of the ascending aorta by using mode B of transesophageal ultrasonography (6). As we initially postulated, our study indicated a similar correlation, now showing that CAP is also strongly associated with atherosclerotic disease of the abdominal aortic segment. It is mandatory to state that our research has limitations, which may have somehow influenced the final outcome. Most of these difficulties are attributed to technical and institutional issues, such as not disposing of multi-slice CT. However, since most data was minimally and individually collected, and considering the rigorous statistical process throughout results were submitted, we believe that the conclusions we have obtained are very unlikely to be only occasional.

Parietal calcifications in the abdominal aorta are often incidentally identified at CT exams, and we believe that such finding has not been sufficiently dimensioned in daily medical practice. Our study shows a strong independent association of incidentally found AAP at CT with the presence of CAP at US. To our knowledge, the present study is one of the first statistically corroborating this association. As well, we have found a significant correlation between the diagnosis of SAH and CAP, although this correlation had been previously described. Even admitting that more evidences are necessary to support ours, we believe that in the future the incidental finding of AAP may recommend additional investigation at other sites looking for atherosclerotic disease, with special attention to the carotids. This information will probably allow early diagnoses of atherosclerosis, reducing potential risks for major cardiovascular events in future.

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