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Association between carotid artery and abdominal aortic aneurysm plaque

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Abstract

Background: The correlation between AAA and carotid artery plaque is unknown and a common etiology and pathophysiology is suspected by some authors. The purpose of this work was to explore the association between the features of a) carotid artery plaque and b) abdominal aortic aneurysm (AAA) plaques using multi-detector-CT Angiography (MDCTA).

Methods: Forty-eight (32 males; median age 72 years) patients studied using a 16-detectors CT scanner were retrospectively analyzed. A region of interest (ROI) ≥ 2 mm^2 was used to quantify the HU value of the plaque by two readers independently. Inter-observer reproducibility was calculated and Pearson correlation analysis was performed.

Results: The Bland-Altman plots showed the inter-observer reproducibility to be good. The Pearson correlation was 0.224 (95 % CI = 0.071 to 0.48), without statistically significant association between HU measured in the carotid artery plaque and in the AAA plaques ($p = 0.138$); after exclusion of the calcified plaques from the analysis, the rho values resulted 0.494 (95 % CI = 0.187 to 0.713) with a statistically significant association ($p = 0.003$).

Conclusion: In this study, we found an association between the features of the non calcific carotid plaque and the features of AAA plaque.

Keywords: Carotid, Aneurysm, Plaque, CTA

Background

Atherosclerotic disease of carotid artery is considered the most important cause of cerebrovascular events [1, 2]; imaging techniques in the last years focused their attention in finding those parameters that are associated with an increased risk of stroke and transitory ischemic attacks (TIA) [3, 4]. The concept of "vulnerable plaque" has thus been introduced, focusing on those atherosclerotic plaques with a high likelihood to cause thrombotic complications [5, 6]. However, atherosclerosis is a process that may affect all the arterial vessels in the body [7] and, commonly, a significant target of this pathology is the abdominal aorta [8, 9].

The most prevalent pathology of the aorta is the abdominal aortic aneurysm (AAA), whose rupture has been recognized to be a significant cause of mortality for adults aged >60 years in the developed world [10]. The pathogenesis of AAA is still poorly understood with some studies suggesting the importance of inflammatory pathways, hemodynamic forces, matrix degradation and thrombosis [11, 12]. Subjects with AAAs have frequently atherosclerosis: Cornuz et al. [13] showed the association of peripheral atherosclerosis with AAAs. Whether the association between atherosclerosis and AAA is simply due to common risk factors or is causal is unknown [14].

In the last few years MDCTA has emerged as an outstanding technique to explore the vascular system [15–18], and by using the Hounsfield Units (HU) sampling it is possible to have quantitative and reproducible information of the analyzed tissue [19].

The purpose of this work was to explore the association between plaques in the carotid artery and abdominal aortic aneurysm by using quantitative data obtained with MDCTA.

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Methods

Patient population

Forty-eight (32 males; median age 72 ± 14 years) patients studied between August 2005 and May 2011 by using a 16-detector CT scanner (Philips Brilliance, Rotterdam, Netherlands) were retrospectively analyzed. Patients with medical history of cardiac output failure, or any contra-indications to iodinated contrast media did not undergo MDCTA exams. Criteria to be included in this study were: 1) Patients underwent MDCTA of carotid and abdominal aorta for AAA. 2) The time interval between the carotid and the AAA studies was not more than 3 months. Each examination was performed when clinically indicated and was ordered by the patient's physician as part of routine clinical care. The patients were all neurologically asymptomatic, without history of TIA or stroke. In accordance with the applicable National Research Ethics Service guidance, ethical approval for the study was not required because the study was performed retrospectively on routinely acquired images and specimens.

MDCTA technique

All patients underwent MDCTA of the supra-aortic vessels using a technique previously described [blinded for peer review].

In our protocol for the analysis of carotid arteries, the angiographic phase is obtained by injecting 80-110 mL of contrast using a power injector at a flow rate of 5 mL/s. A bolus tracking technique is used to calculate the correct timing of the scan. Dynamic monitoring scanning begins 6 s after the beginning of the intravenous injection of contrast material. The trigger threshold inside the ROI is set at + 90 HU above the baseline. The delay between the acquisitions of each monitoring scan is 1 s. CT technical parameters include: matrix 512x512, field of view (FOV) 14–19 cm; mAs 180–220; kV 120–140.

For the analysis of AAA, the angiographic phase is obtained by injecting 80-110 mL of contrast medium into a cubital vein (usually the left side was used), using a power injector at a flow rate of 4-5 mL/s and an 18-gauge intravenous catheter. The scan starts at the level of the diaphragm up to the pubic symphysis. For the study of AAA a bolus tracking technique similar to the procedure described for the carotid arteries is used.

Image analysis

In the first phase two experienced radiologists independently measured the HU value of the carotid artery plaques. A region of interest (ROI) ≥ 2 mm^2 was used to quantify the HU value of the plaque. After two weeks, the same radiologists independently measured the HU value of the AAA plaque (Fig. 1). Images were blinded and randomized. MDCTA images were analysed with a varying magnification from 120 to 400 % in comparison to the acquisition.

Window parameters (width and level) were freely modifiable but the parameters from another article [20] were followed. To quantifiy the HU value, a circular or elliptical region of interest cursor in the predominant area of plaque was used. Regions of beam hardening in calcified areas were excluded and areas showing contamination by contrast material or calcification were avoided.

Statistical analysis

Continuous data were described as the mean value ± standard deviation (SD). In order to evaluate the inter-observer reproducibility in HU quantification, Bland-Altman analysis with 95 % limits of agreement (mean difference ± 1.96 SDs) was performed and the differences between the measured values were plotted against the mean of the 2 measurements to assess the relationship between the difference and the magnitude of the measurement. Mann-Whitney test was used to test the differences between groups. For the analysis of correlation (Pearson Rho correlation) between HU measured in the carotid artery and AAA plaques, the HU values between the 2 observers were averaged. *R* software (www.r-project.org) was employed for statistical analyses.

Results

General results

Three patients were excluded from the final analysis because of sub-optimal image quality due to movement artifact. Therefore the final number of analyzed patients was 45 (29 males; median age 72 ± 13 years). Demographic characteristics are summarized in Table 1. The total number of carotid artery plaque measured were 79 because in 11 carotid arteries no evidence of plaque was found. The ROI value was between 2 mm^2 and 5 mm^2 (mean value 2.56 mm^2).

Bland-Altman analysis

We analyzed the inter-observer reproducibility of HU measurement of the plaque in the 79 carotid arteries and in the 45 patients with AAA and the plots are given in the Fig. 2. The plots showed that the inter-observer reproducibility is good for both analysis and the best agreement is obtained in the carotid artery plaque HU quantification (with 95 % CI from −25.5 % to 20.3 %.

Mann-Whitney analysis

We tested the differences between HU values in carotid arteries and AAA also by using the Mann-Whitney test and we found that there were no differences in HU analysis between the two observers in the carotids ($p = 0.836$)

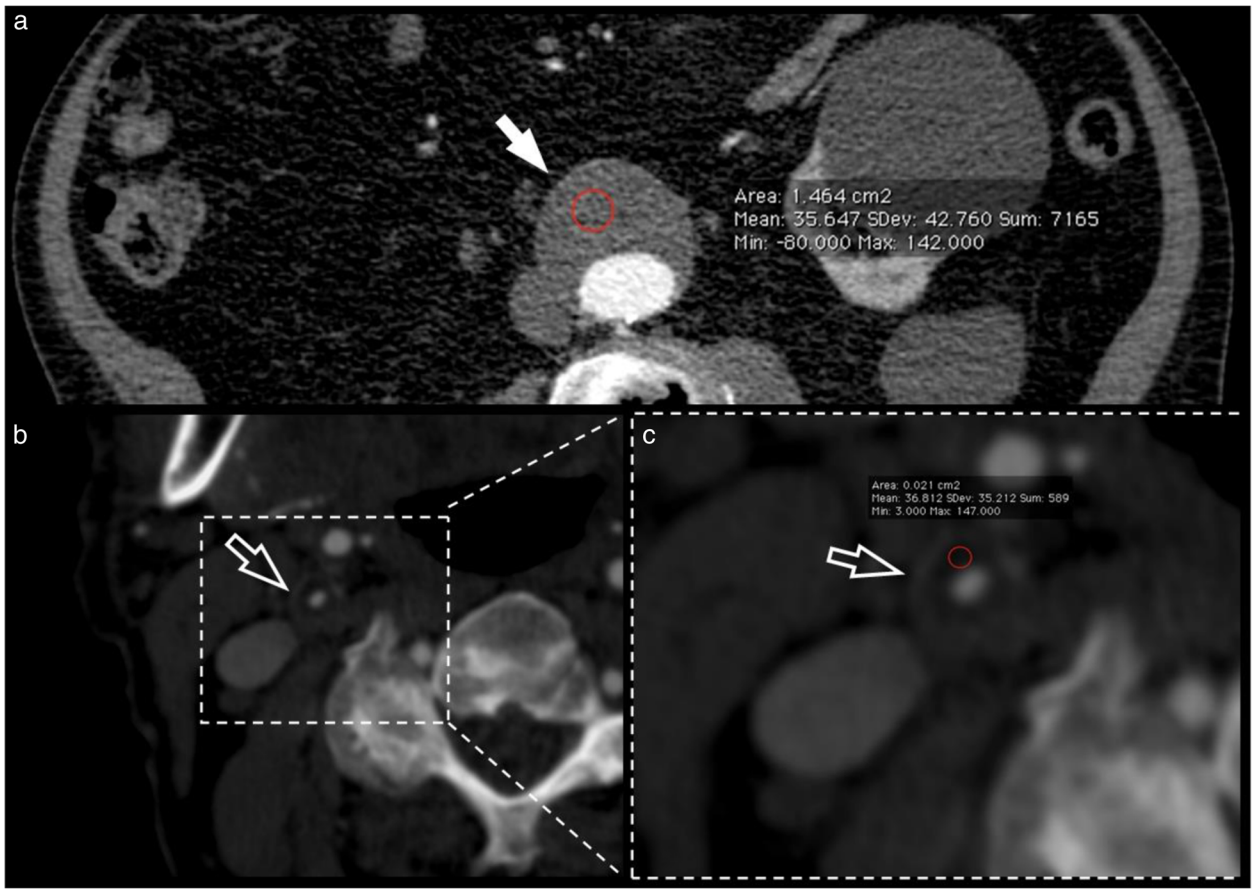

Fig. 1 MDCTA axial images of AAA (**a**) and carotid arteries (**b**, **c**). The AAA is indicated by the white arrow (**a**) and the circle represents the analyzed ROI. The carotid artery plaques is indicated by the open white arrow (**b**, **c**) and the circle represents the analyzed ROI. Panel **c** represent the 200 % zoom of the panel **b**

and in the AAA ($p = 0.353$). Summary statistic is given in Table 2. These results demonstrate that the HU measurement performed by the 2 observers in the carotid and AAA plaques are not statistically different.

Pearson correlation analysis

The correlation coefficient rho was 0.224 (95 % CI = 0.071 to 0.48) and there was no statistically significant association between HU measured in the carotid artery plaque and HU measured in the AAA plaque ($p = 0.138$). The scatter-plot with 95 % confidence interval is shown in Fig. 3. We analyzed also the correlation between carotid and AAA plaques by excluding the calcified plaques (namely those plaques with HU value > 130 HU) and we performed a further analysis by obtaining a coefficient rho of 0.494 (95 % CI = 0.187 to 0.713) with a statistically significant association ($p = 0.003$).

Table 1 Patients characteristics

Age[a]	72 y (SD[b] 13 y)
Sex (male)	65 % (n = 31)
Hypertension	53 % (n = 25)
Smoker	62 % (n = 30)
CAD	59 % (n = 28)
Diabetes	15 % (n = 7)
Dyslipidemia	61 % (n = 29)

[a]Mean age
[b]*SD* standard deviation

Discussion

In the last few years several papers demonstrated that the plaque composition of the carotid arteries plays a significant role in the "vulnerability" of the plaque and in the risk of develop cerebrovascular events.

In the carotid artery (as well as in the coronary arteries), it is possible to find different types of plaque [3, 4] and the very hypodense regions (<30 HU) in the center of atherosclerotic carotid plaque are associated with the presence of a lipid core (i.e., lipid, hemorrhage, or necrotic debris) [21, 22]; this kind of plaques are associated with the development of cerebrovascular events [19].

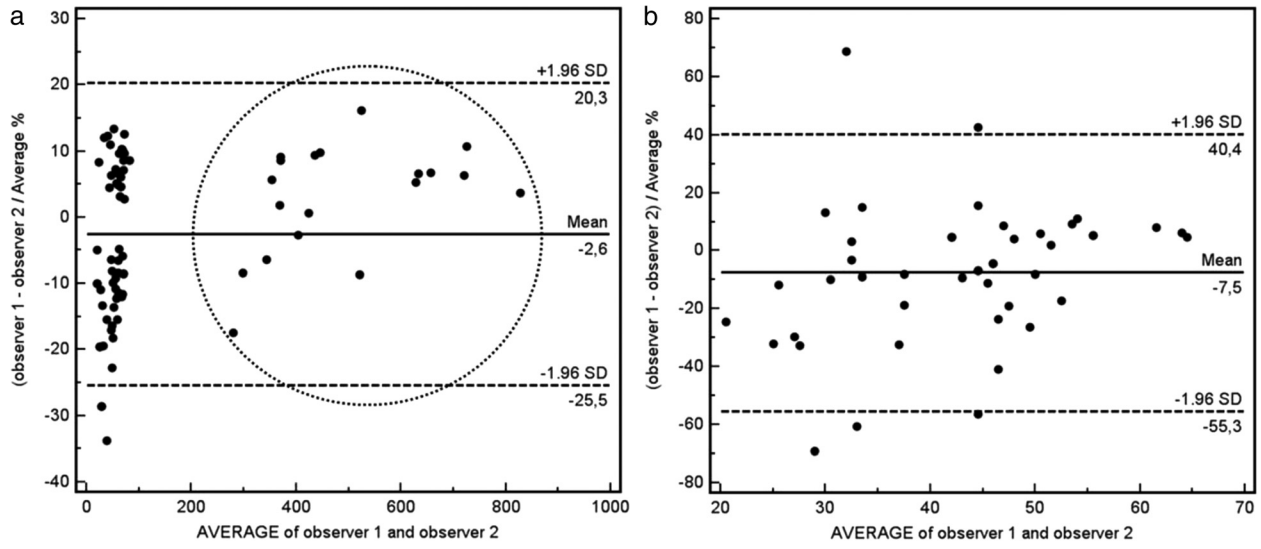

Fig. 2 Bland-Altman plot graphs for the inter-observer reproducibility in the HU measurement of the carotid artery plaque (**a**) and AAA plaque (**b**). In panel a the dotted circle represents the carotid calcified plaques

The presence of atherosclerotic pathology and plaque development in the AAA is well described but if this association is simply due to common risk factors or is causal, is still unknown [14]. In this study, our purpose was to evaluate whether there was an association between the HU values measured in the carotid artery plaque and the HU values measured in the AAA plaque.

By analyzing the correlation between HU values in carotid plaques and AAA plaques a rho value of 0.224 (95 % CI = 0.071 to 0.48) was found with the absence of significant *p*-value ($p = 0.138$). We analyzed the morphology of the scatter-plot and we found that the calcified plaques of carotid plaques represent, for this kind of analysis, a confounding factor. In the Fig. 3a the calcified plaques of carotid are clearly visible (dotted circle) and by excluding this kind of plaques the coefficient rho changed to 0.494 (95 % CI = 0.187 to 0.713) with the presence of a statistically significant association ($p = 0.003$). This is an interesting point to discuss because the presence of carotid calcified plaques are considered a protective factor for the development of cerebrovascular events [23, 24]. Nandalur et al. [23], demonstrated that calcified plaques are 21 times less likely to be symptomatic than non-calcified plaques ($p = 0.030$) whereas no significant predictive value was found between fatty ($p = 0.23$) or mixed ($p = 0.18$) plaque type for the occurrence of symptoms. The results of this study were further confirmed by Saba et al. [19] that showed that carotid calcified plaques are less frequently associated with cerebrovascular symptoms. In that paper the non calcified plaques were found to be associated with the presence of stroke-TIA.

Previous studies have attributed the development of AAA to atherosclerosis [25] because these conditions share risk factors, such as hypertension, smoking, and hypercholesterolemia [26, 27]. The presence of atherosclerotic process in the aneurismal wall is a common finding in AAA patients but several patients with advanced atherosclerosis do not develop AAA [28, 29].

The results of this study suggest that the atherosclerotic process involved in the carotid artery plaques and in the wall of the AAA is of a different nature: in fact in the carotid plaques may show a calcified type (HU value > 130)

Table 2 Mann-Whitney analysis

	HU carotid artery plaque		HU AAA plaque	
	Observer 1	Observer 2	Observer 1	Observer 2
Sample size	79	79	45	45
Lowest value	19	21	18	21
Highest value	843	812	66	63
Median	62	63	43	45
95 % CI for the median	54.88 to 67	57 to 66.12	35.27 to 46.1	40 to 49
Interquartile range	45 to 82.75	49.5 to 76.75	32 to 49	34.5 to 52

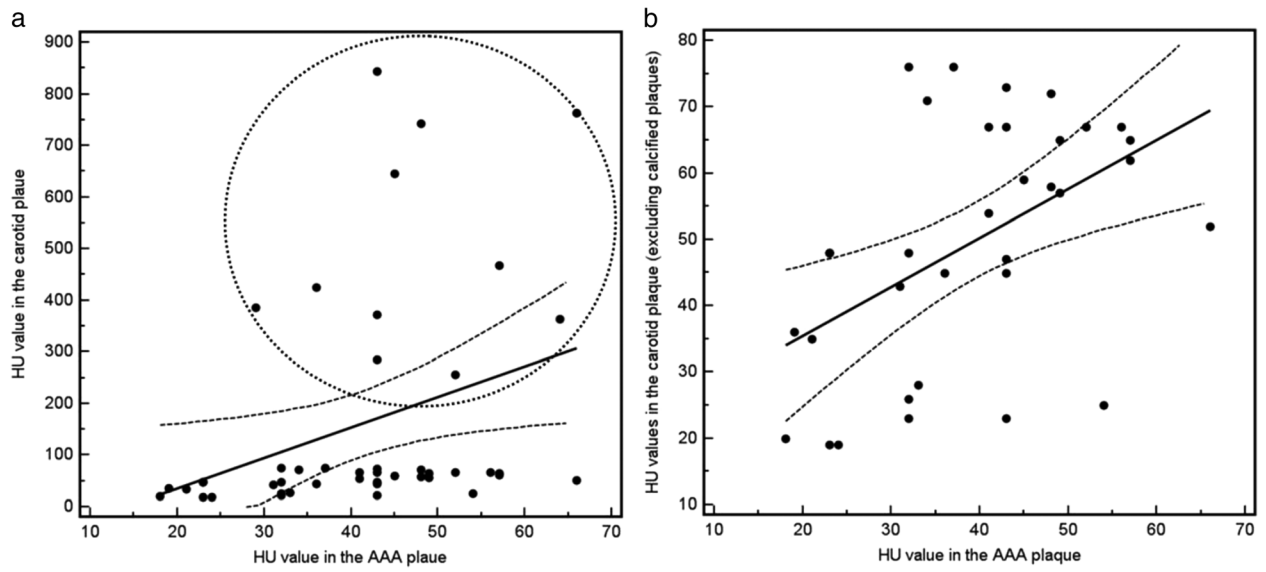

Fig. 3 Regression analysis with 95 % CI (Dashed lines) between HU value of carotid artery plaque and AAA plaque (**a**) the dotted white circle represent the calcified carotid artery plaques; in panel (**b**) is reported the regression analysis with 95 % CI (Dashed lines) between HU value of carotid artery plaque and AAA plaque by excluding the carotid calcified plaques

that is not present in the AAA. Nonetheless, when the carotid calcified plaques are excluded, a significant correlation is found between the HU values in the carotid and in the AAA.

From a pathological point of view authors reported that AAA is characterized by transmural infiltration of lymphocytes and macrophages and by the destruction of elastin and collagen in the media and adventitia loss of medial smooth muscle cells with thinning of the vessel wall [30, 31] and these pathological elements are quite similar in those found in the carotid (and coronary) artery "vulnerable" plaques [3, 4, 32, 33]. A study by Zweig et al., demonstrated that the calcifications of the abdominal aorta correlated with the presence of calcifications in the coronary arteries and even suggested abdominal aortic as a possible tool to help exclude obstructive coronary disease and improve the selection of patients that may benefit from further risk stratification [34].

In this type of study the analysis of reproducibility in the HU measurement is important and Bland-Altman plot analysis showed that the inter-observer reproducibility is good for both analysis and the best agreement is obtained in the carotid artery plaque HU quantification (with 95 % CI from −25.5 % to 20.3 %. In the HU quantification of the carotid artery plaque our results are concordant with previous observations [35, 36] whereas, on the best of our knowledge no previous analysis of concordance in the HU quantification of AAA plaque was found. These results were also confirmed by the Mann-Whitney test where we found no differences in HU analysis between the two observers in the carotids ($p = 0.836$) and in the AAA ($p = 0.353$).

In this paper there are some limitations. First, we quantified the HU values in the carotid and AAA by using a circular ROI; a more precise system like manual drawing of the plaque would be more reliable and this fact may introduce a bias in the data analysis: however we think that this can be considered a minor limitation because the predominant area of the plaque was selected. Second, the total number of analysed patients was forty-five and this represents a relative small population: therefore the obtained results should be further verified in larger cohort.

Conclusion

In this study, we found an association between the features of the non calcific carotid plaque and the features of AAA plaque.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors read and approved the final manuscript.

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