ORIGINAL ARTICLE

Particularities of the cardiovascular risk factors patterns and cervical arterial ultrasound findings related to the coronary angiography lesions significance in patients with ischemic heart disease

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Abstract: **Background** – Carotid artery stenosis (CAS) is related to the extent of coronary artery disease (CAD) and multi-vessel CAD is an independent predictor for CAS. Simultaneous ATS lesions of the carotid arteries (carotid intima-media thickness-CIMT) increases and extracranial cervical stenosis due to carotid plaques) and coronary circulation indicates the extent of ATS burden. **Aim** – study of comparative cardiovascular risk factors (CVRF) profile, CIMT, CAS, and CAD patterns in acute coronary syndrome (ACS) and in stable CAD patients. **Method** – laboratory tests for CVRF, arterial cervical US parameters measurements, and coronary angiography evaluation. **Results** – ACS patients had more diabetes mellitus (72.2% DM) and hypertriglyceridemia (56.4% HTgl), while stable CAD patients were more smokers (53.5%) and hypertensive (78.7% HT). ACS patients had increases CIMT (1.07±0.26 mm vs. 0.7±0.2 mm). Stable CAD patients had more CAS (63.7% vs. 33.3%), but in ACS patients, the severity of CAS increases with the number of coronary artery lesions. **Conclusions** – CAD patients have particular CVRF profile, different for ACS patients and stable CAD patients and these could be related to their specific CAS-CAD patterns. In ACS patients, increased CIMT, and carotid stenosis are associated with the presence, the extent, and the severity of coronary stenosis, and might be useful in estimating ATS burden in patients with multi-vessel disease, in particular with left anterior descending coronary artery lesion.

Keywords: coronary artery disease, carotid artery stenosis, carotid intima media thickness, cardiovascular risk factors.

Rezumat: **Introducere** – Există o legătură între ateromatoza carotidiană şi extensia bolii coronariene aterosclerotice (ATS), afectarea coronariană multitronculară fiind un factor predictiv independent pentru stenozele carotidiene. Leziunile ATS concomitente ale arterelor carotide (creşterea grosimii intimă-medie (GIM) şi stenozele carotidiene) şi ale arterelor coronare reprezintă un indicator al încărcării ATS. **Scop** – Studiul profilului factorilor de risc cardio-vasculari (FRCV) şi ale pattern-urilor ATS carotidiene şi coronariene la pacienţii cu sindrom coronarian acut (SCA) comparativ cu pacienţii cu boală coronariană stabilă (BCS). Metodă-analize de laborator pentru evaluarea FRCV, ultrasonografie carotidiană şi angiografie coronariană. **Rezultate** – Pacienţii cu SCA au avut mai mult diabet zaharat (72,2% DZ) şi hipertrigliceridemie (56,4% HTgl), la pacienţii cu BCS prevalenţa fumatului (53,5%) şi a hipertensiunii arteriale (78,7% HTA) au fost mai mari. GIM a fost mai mare la pacienţii cu SCA comparativ cu pacienţii cu BCS (1,07±0,26 mm vs. 0,7±0,2 mm). Pacienţii cu BCS au avut mai multe stenoze carotidiene (63,7% vs. 33,3%), dar la pacienţii cu SCA, severitatea acestora a fost mai mare în relaţie cu creşterea numărului de leziuni coronariene. **Concluzie** – Pacienţii cu SCA, respectiv cu BCS au pattern-uri specifice ale ATS carotidiene şi coronariene, probabil în relaţie cu profilurile particulare ale FRCV. La pacienţii cu SCA, ateromatoza carotidiană semnificativă se asociază cu extensia şi cu severitatea leziunilor coronariene şi poate reprezenta un indicator util în estimarea încărcăturii ATS la pacienţii cu afectare coronariană multitronculară, în particular cu leziune la nivelul arterei coronare descendente anterioare.

Cuvinte cheie: boală coronariană, stenoză arterială carotidiană, grosimea intimă-medie, factori de risc cardiovasculari.

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INTRODUCTION

Atherosclerosis (ATS) is a systemic, extensive, diffuse, and progressive inflammatory, metabolic, and immune vascular disorder, involving multiple arterial beds. Progressive carotid lesions are reportedly a stronger predictor of imminent myocardial infarction (MI) than of future stroke events[1,2]. Carotid stenosis is related to the extent of CAD and multi-vessel coronary lesions had shown to be an independent predictor for CAS[3]. The presence of symptoms of carotid disease is alarming and certainly correlates with poor outcome, but the absence of symptoms is not a particular security for a good outcome[4].

ATS changes in carotid morphology include CIMT increases, correlated with endothelial dysfunction, carotid plaque formation and deposition leading to arterial stenosis, also present simultaneous in the coronary arteries territory. Concomitant ATS lesions of the extracranial carotid and coronary circulation indicates the extent of ATS burden and portend an adverse prognosis in various clinical settings, including asymptomatic individuals, stroke patients, and patients undergoing coronary artery bypass surgery (CABG)[1]. There are limited studies focused on the prevalence of asymptomatic carotid disease in association with CAD other than candidates for major cardiac surgery, indicating a strong link with multi-vessel CAD[5]. We did not found specific observations from studies regarding particularities of the relationship between coronary and cervical arteries lesions in patients admitted with ACS and comparative differences with stable CAD patients.

SUBJECTS AND METHODS

The study was performed in the Cardiology Department of Emergency County Clinical Hospital of Cluj-Napoca. After signing an informed consent, we enrolled 167 consecutive patients (pts.) without any anamnestic clinical carotid artery symptomatology, and without any documented history of established or transient stroke: 87 with ACS [10 p. with ST elevation (STEMI) and 77 p. without ST elevation (NSTEMI)] and 80 with stable CAD. The NSTEMI criteria according to guidelines[6] definition were: acute chest pain [prolonged (>20 min) angina pain at rest, or new onset (de novo) angina, or recent destabilization of previously stable angina (crescendo angina)], and elevation of cardiac troponin cTnI above the 99th percentile of the laboratory cut-off value (0.02 ng/l). The stable CAD patients selected had inducible ischemia during exercise stress tests and no elevation of cTnI. In all patients we performed clinical evaluation, 12 lead electrocardiogram (ECG), hemodynamic monitoring, and laboratory tests for CVRF (glucose, cholesterol, triglyceride serum levels). CVRF were defined according to the criteria in the current guidelines. Smoker status referred to the active smoker. The presence of dyslipidaemia was defined by increased >200 mg of total cholesterol and/or increased >150 mg of triglycerides serum levels[7]. Diabetes diagnosis was made prior to inclusion in the study.

All patients underwent imaging vascular duplex ultrasound (US) evaluated cervical arterial lesions, topography and hemodynamic significance of CAS. The US scan was made on Hewlett Packard HP Sonos 4500 machine using a 7.5 MHz linear transducer, by a single specialist doctor examiner (certified for cardiovascular US competence) who was blinded to clinical and coronary angiographic data, using a described below protocol The patients with ACS followed coronary angiography evaluation and the cervical arteries US evaluation was made in the first 24-72 hours from admittance.

Arterial cervical US parameters were measured: CIMT measurements were made in the bilateral common carotid artery (CCA), in longitudinal projection (the lumen intima and media-adventitia interfaces were clearly defined), between two parallel echogenic lines corresponding to the distance between the leading edge of the luminal echo (first bright line) and the leading edge of the media-adventitia echo (second bright line), on the posterior-medial wall, standard 2 cm before the bulb carotid bifurcation, in a free of plaque region, using manual reading system. CIMT was calculated as the average of the CIMT for left and right CCA. The average values measured were compared with normal values considered <0.75 mm[8]. The CCA-IMT value >1.2 mm was considered as ATS plaque6. The estimation of hemodynamic significance of CAS or the degree of luminal narrowing was assessed using the following elements: morphology criteria provided by duplex color cross-section carotid luminal planimetry in B-mode US with the calculation of the stenosis area (%) by the formula: total vessel area-duplex color permeable area/total vessel area, and hemodynamic criteria: peak-systolic velocity (PSV), end-diastolic velocity (EDV), intra-stenosis/pre-stenosis PSV ratio[9-12]. Stenosis between 50-70% was considered moderate CAS and was defined by the follow arterial US parameters: PSV=1.25-2.3 m/s, EDV <0.4 m/s, PSV intra-stenosis/pre=2-3, and by corresponding percentage

reduction of the duplex color area reported to the functional duplex values[9-12]. Stenosis >70% was defined by the follow values: PSV >2.3 m/s, EDV >0.4 m/s, PSV intra-stenosis/pre-stenosis ratio >3 and by corresponding percentage reduction of the functional area reported to the functional duplex values[9-12]. Arterial luminal occlusion was defined by the presence of a total occluding mass with the absence of color and pulsate duplex flow. Stenosis >70% and occlusion were considered severe CAS[9-12]. Variation coefficients of the measurements for the examiner were <5%.

Coronary angiography was performed in emergency for STEMI patients and in an emergency elective manner for NSTEMI patients in the first 24-72 hours after admittance. The stable CAD patients were selected having positive inducible myocardial ischemia on treadmill exercise stress electrocardiogram test and they underwent coronary angiography. By coronary angiography, we evaluated the topography and the hemodynamic significance of coronary artery lesions. Coronary angiography was performed by standard techniques on Siemens angiography system 2000. The severity of coronary lesions was determined by visual estimation at the discretion of the interventional cardiologist performing the procedure. Clinically significant CAD was defined as the presence of a coronary lesion resulting in a lumen diameter stenosis >70% in a major epicardial artery (left anterior descending artery (LAD), left circumflex artery (Cx), right coronary artery (RC) or one of its major branches). Clinically significant left main disease (LMD) was defined as a lumen diameter stenosis >50%. Patients were stratified according to the number of involved vessels as follows: normal coronaries or non-obstructive CAD (individuals not meeting the criteria for clinically significant CAD), and 1VD, 2VD, 3VD/LMD (significant lesions in 1, 2, and 3 vessels or left main disease, respectively). The study methodology was approved by the Ethical Committee. Data was analyzed using SPSS version 2.0. Categorical variables were expressed as proportions and percentages and continuous variables were expressed as means ± standard deviation. Student T-test was used to compare PSV, EDV, and intra/prestenosis PSV ratio. For categorical variable Chi-square test was used. p<0.01 was consider statistically significant.

RESULTS

Descriptive characteristics established for the two groups and for all subjects and the CVRF profiles are

Table 1. Demographic and cardiovascular rick factors (CVRF) profile in our study group

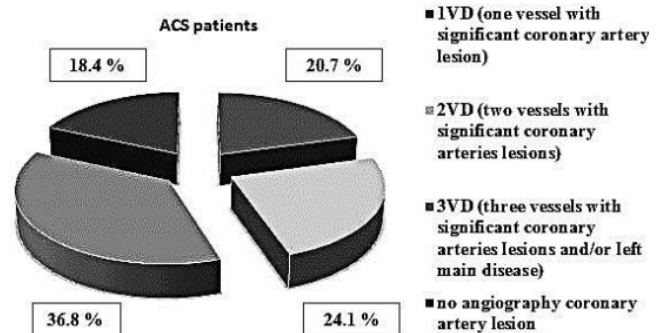| Demographic characteristics and CVRF	ACS patients	Stable CAD patients	Statistical significance
Age (yrs.)	60.±9.7	61.4±8.9	ns
Malke gender	65.6%	71.2%	ns
Smoker	35.8%	53.5%	p<0.001
Diabetes mellitus (DM)	72.2%	21.9%	p<0.001
Hypertension (HT)	64.4%	78.7%	p<0.01
Hypercholesterolemia (HCst)	66.5% 216±55	64.6% 220±42.2	ns
Hypertriglyceridemia (HTgl)	56.4% 192±121	21.8% 126±30.2	p<0.001

Figure 1. Coronary artery lesions repartition in ACS patients.

presented in Table 1. The distribution of coronary arteries lesions diagnosed by angiography examination in ACS patients is represented in Figure 1.

In ACS patients, the median value of CIMT was significantly higher than in stable CAD patients, in which CIMT values were around normal range. CIMT was significantly higher in 3VD patients than in 2VD of ACS patients. CIMT was similarly increased in 1VD patients and 2VD patients, as well as in patients without significant coronary stenosis. Some of the ACS patients had a "normal" CIMT value (i.e. Fig. 2).

The prevalence of overall CAS >50% was higher in stable CAD pts. than in ACS pts. Both prevalence of CAS=50-70% and prevalence of CAS >70% or carotid occlusion were higher stable CAD pts. in comparison with ACS pts. (i.e. Table.2). The prevalence of multi-vessel coronary stenosis (2VD and 3VD) was higher in stable CAD patients comparative with ACS patients, while the prevalence of LAD coronary artery lesions was higher in ACS patients (75.8%) in comparison with stable CAD. CAS >50% was significant higher in stable CAD patients comparative with ACS patients. (i.e. Table 2).
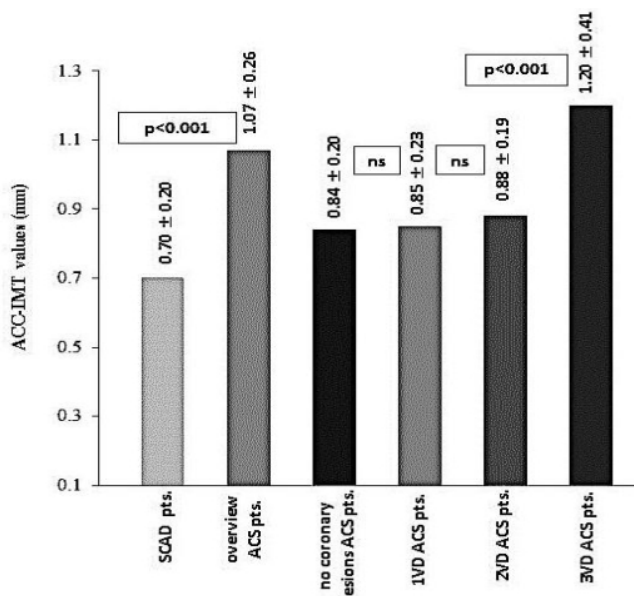
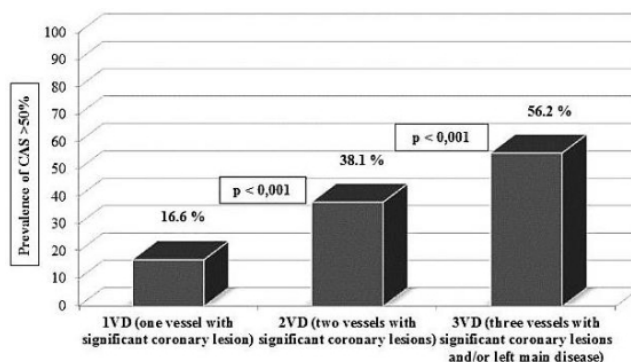**Figure 2.** Comparative IMT values measured on CCA in study group.

Figure 3. Comparative repartition of overall CAS >50% related to the disposition of coronary arteries lesions in ACS patients from our study group.

Figure 4. The prevalence of CAS >50% was significant higher in 1VD and 2VD of ACS patients with a LAD coronary involvement, than in those with Cx and/or RC lesions (i.e Fig.5)

In unadjusted linear regression analysis cholesterol, HT, smoking status and age were positively associated with the lesions in stable CAD patients. Cholesterol, triglycerides serum levels, the presence of diabetes,
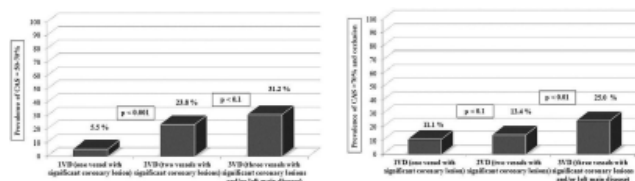
Table 2. Repartition of coronary and cervical arteries lesions in our study group

Parameters	ACS patients	Stable CAD patients	Statistical significance
Prevalence of 2VD/3VD coronary arteris lesions	60.9%	80.0%	p<0.001
Prevalence of LAD coronary artery lesion	75.8%	50.0%	p<0.001
CIMT (median value in mm)	1.07±0.26	0.70±0.20	p<0.001
Prevalence of overall CAS >50%	33.3%	63.7%	p<0.001
Prevalence of CAS = 50-70%	18.4%	40.0%	p<0.001
Prevalence of CAS >70% and occlusion	14.9%	23.7%	p<0.01

Figure 4. Relationship between the prevalence of moderate, respectively severe CAS, and coronary arteries lesions significances in ACS patients from our study group.
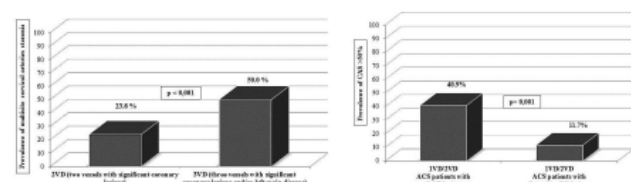

Figure 5. The prevalence of multisite CAS related to the multi-vessel coronary arteries lesions significances in ACS patients and the higher prevalence of CAS >50% in 1VD and 2VD of ACS patients with LAD lesions from our study group.

The prevalence of overall CAS >50% in 3VD, 2VD and 1VD of ACS patients is represented in Table 3 and Figure 3.

The prevalence of moderate and severe CAS in 3VD, 2VD and 1VD of ACS patients are presented in

Table 3. Repartition of cervical arteries lesions related to the disposition and significance of coronary arteris lesions in ACS patients from our study group

Parameters of ACS	1VD	2VD	Statistical significance (1VD vs. 2VD)	3VD	Statistical significance (3VD vs. 3VD)
CIMT (median value in mm)	0.85±0.23	0.88±0.19	ns	1.20±0.41	p<0.001
Prevalence of overall CAS >50%	16.6%	38.1%	p<0.001	56.2%	p<0.001
Prevalence of CAS = 50-70%	5.5%	23.8%	p<0.001	31.2%	p<0.01
Prevalence of CAS >70% and occlusion	11.1%	14.3%	p<0.1	25.%	p<0.01

Table 4. Analysis of correlation/prediction between the presence of certain cardiovascular risk factors and the presence/extension of carotid ATS lesions

Variables	Univariate		Multivariate		Univariate		Multivariate	
	r	p-value	β	p-value	r	p-value	β	p-value
Cholesterol	0.326	0.37	0.23	0.04	0.347	0.034	0.29	0.038
Triglycerides	0.218	0.052	0.02	0.056	0.432	0.026	0.34	0.040
DM	0.369	0.001	0.103	0.040	0.378	0.000	0.163	0.037
Smoker status	0.412	0.0448	0.17	0.042	0.432	0.024	0.15	0.035
HT	0.314	0.044	0.132	0.001	0.256	0.051	0.19	0.54
Age	0.375	0.002	1.43	0.001	0.383	0.001	1.67	0.001

and smoking status were positively associated with the carotid lesions in ACS patients (i.e. Table 4).

DISCUSSIONS

The data from studies shows that the patients with coronary-carotid tandem lesions are at middle age (45-64 yrs.) and with a slightly prevalence of female gender, especially for the patients with critical CAS[13]. Patients from our study were majority male, and not very elderly, with similar values of median age years. ACS patients had more DM, and hypertriglyceridemia, while stable CAD patients were more smokers and had more HT. The prevalence of hypercholesterolemia was almost equally high. The data regarding the prevalence of multiple CVRF are very different in various study, explain by the diversity of patients groups. In REACH registry the proportion of multiple CVRF was 18.3%, less than in our group[14,15]. There are studies emphasized that none of these CVRF (HT, DM, dyslipidemia, obesity, smoking, family history) can be a potential predictor of CAS. Other studies showed that peripheral vascular disease (PAD), previous ischemic stroke, smoking, and female gender, are markers associated with important CAS[16,17].

The prevalence of smoking and HT did exceed 80% in CAD population from some studies[13,17]. In others, variables such as HT, or hyperlipidemia were not statistically different[3]. The REACH registry revealed also high prevalence of HT (80.3%), hypercholesterolemia (77%), DM (38.3%), but not so high prevalence of obesity/ hypertriglyceridemia (29.9%) and smoking (13%) in CAD patients[14,15]. These differences could result from the ethnic variety of REACH patients enrolled from many countries, from the fact that CAD patients were not separated in ACS and stable CAD, implying particular different CVRF patterns, and from some specific CVRF exposure in Romanian citizen.

The smoking, HT, hypercholesterolemia and DM are associated with ATS of extracranial carotid arteries. Diabetic patients with CAD often have a combi-

nation of elevated triglycerides and low level of HDL than high-level of LDL cholesterol[3,13,17,18]. We might make the assumption that the higher prevalence of DM in our ACS patients might be prone to a more pro-inflammatory, and pro-thrombotic status associated with the worsening of endothelial dysfunction and increases CIMT, while smoking and HT seems to be more related to a progressive fibro-calcific ATS evolution. These hypotheses do not suggest a one to one correspondence between carotid and coronary artery lesions formation and development. The correlated presence of tandem carotid and coronary artery lesions do not necessarily share the same associations with similar CVRF. Differences in ATS lesions prevalence and incidence in both arterial systems may be related also to marked morphologic, hemodynamic and geometric differences between coronary and carotid arteries[19].

Some studies have shown that CIMT could be a reliable marker for CAD and might improve the prediction ability for CV events risk over and above conventional CVRF[20]. The use of CIMT for assessment of CV event risk has a number of limitations too. Although increased CIMT has been shown to be a strong predictor of incident MI in overall population >55 years, it is not a good predictor for the extent and the severity of CAD. The normal CIMT cannot predict the absence of significant CAD. There are several explanations like: considerable heterogeneity among various studies regarding the characteristics of the participants, CIMT methodology and measurement protocols, and the interpretation of the results[21-23].

The uppers values of normal CIMT varies with the site of carotid measurement, increasing from ICA to ACC, but not significant (0.62 to 0.74 mm)[21-23]. The majority of CIMT studies agree that a CIMT value >0.75 mm could be accepted as pathological increases. On other hand a CIMT value >1.2 mm (1.1-1.5 mm in different studies) can be considered as an ATS deposition (carotid plaque)[22]. In European countries,

it is recommended that measurement of CIMT should be performed in a region free of plaque and the distinction between CIMT and carotid plaque should be clearly made. CIMT normal value increases with progression of age, but this interval values between 0.7-1.2 mm are mostly accepted as normal regardless of age[21-24].

We did not found significant studies regarding the particularities of CIMT values significances and CAS profiles in ACS patients comparative with stable CAD patients. CIMT values significant increases in CAD patients with multi-vessel lesions (≥2VD)[25]. In this context, we can stipulate the fact that increases values of CIMT in ACS patients (with an slowly ascending trend from 1VD to 2VD and respectively with a significant increasing bound to 3VD) might reflects a more" aggressive" coronary and carotid arteries ATS evolution, possible related to the high presence of DM, inflammation and to the endothelial dysfunction linked to arterial stiffness, which, by itself, is associated with adverse CV outcomes. In ACS patients, there is a stepwise increase in carotid lesions with the increasing severity of CAD, and carotid lesions may reflect a diffuse CAD. The extent of non-obstructive CAS lesions has been found to be a strong predictor of coronary events, independent of severity and the number of flow-limiting coronary lesions[21]. In support of what has been already stipulated, even our ACS patients with no significant coronary lesions had CIMT values higher than normal. In opposition, stable CAD patients seems to have a more slowly and progressive coronary and carotid ATS evolution, which "allows" the development of an extensive and multisite vessels ATS lesions possible related to their particular metabolic risk profile (smoking, HT, HCst).

The natural history, risk factors patterns, and cardiac and cerebral events prediction are different for "carotid plaque", which is a focal structure en-croaching into the arterial lumen, and the "traditional" IMT, which is measured in a region free of plaque, whereas both share some common ATS risk factors[20]. The presence of carotid lesion is associated with incident positive and more rapid and diffuse calcification progression of coronary artery lesions and, from a statistical point of view, more significant than DM and smoking[18]. Like CIMT, carotid plaque reflects the overall ATS burden, and, as compared with IMT, better predicts CV death and nonfatal MI[22]. The assumptions aforesaid could explain also the particularities of CAS in our group study. The stable CAD patients had a higher prevalence of CAS >50% comparative with ACS patients, probably due to their longer ATS evolution. Further stable CAD patients had significant more moderate CAS than ACS patients, but regarding severe CAS, there was only a moderate prevalence in favor of stable CAD patients. In stable CAD patients group we found more moderate than severe CAS, while in ACS patients was a relatively similar proportion of moderate and severe CAS.

The prevalence of asymptomatic CAS in CAD patients is variable in different studies: 10% in REACH registry (started in 2003)[13,14], 7-18% in ESC PAD guidelines (2017)[24], in others 17-22%[13], but this proportion can be greater>30% in high-risk CAD patients prone to ACS. But in discrepancy, the prevalence of CAD in CAS patients is higher: 39-61% in ESC PAD guidelines (2017)[24], 28-40% in other studies[26] so the relationship is reciprocal unequal and need further studies. However the overall rates for CAS in CAD patients varies from 5% to 30. In REACH registry, at 4-year follow-up, the presence of carotid ATS was associated with a 22% increase in the risk of coronary events; consistent finding across all patient subsets, including patients with or without pre-existing CAD[27]. The presence of carotid plaque at baseline is associated with a 7-fold increase in the risk of cardiac death and a 2-fold increase in the rates of the composite end point (all-cause mortality, MI, and stroke)[28].

The presence of carotid ATS is directly related to the extent of CAD, though the prevalence of moderate and severe CAS in patients with CAD is variable, but in general lower than our findings[1]. There are several explanations: first that in many studies the percentage of CAS is calculated by B-mode US longitudinal diameter narrowing, not by transversal planimetry area reduction (which is more accurate)[8-11]. Second, from our previous observations, we found that carotid PSV between 1.25-1.7 m/s can indicate sometime no significant stenosis (<50%), that why is better to add carotid EDV and PSV intra/pre-stenosis ratio[16,29-33]. Third, there is a discrimination between carotid ATS (non-stenotic carotid plaque <50%) and CAS (stenotic carotid plaque >50%). The prevalence of CAS>50% in our SCAD patients was 63.7%, in other studies has varied from 5,8% to 80%, depending if carotid ATS or CAS (defined both as well as carotid disease) was taken into consideration[15,20]. Moreover there are some differences regarding the calculation of CAS hemodynamic significance in USA (NASCET, PSV intra/post-stenosis ratio[34]) and in Europe (ECST, PSV

intra/pre-stenosis ratio[35]) and depends which one was used in the studies. Four, the definition of "significant" CAS was different across the studies, in many studies were reported the overall carotid plaque, irrespective to the stenosis degree, while in others moderate CAS (50-70%) or only CAS >70% were considered. In fifth place, beside the difference in methodologies, there was inhomogeneity in studies group, sample size and in the various ethnic compositions. There were very different categories of studies inclusion criteria like: asymptomatic individuals, patients undergoing CABG with or without prior MI or stoke, so with stable CAD, but rarely ACS patients[36].

The proportion of CAS increases with the number of coronary lesions: 5-14% (from studies) in CAD patients with 1VD (16.6% CAS >50% in our study), 13-21% in 2VD (38.1% in our study), 17-36% in 3 VD, and 31-40% in LMD (56.2% in our study including 3VD and LMD)[1,37-39], although there are studies who found that CAS is correlated with LMD, and it is not correlated with multi-vessel CAD[15]. There are studies showing that LMD patients had more CAS than 3VD patients[1,15,25], in others the proportion of CAS was similar in LMD and 3VD CAD patients[36]. Multiple CAS was found in 23.8% of 2VD and 50% of 3VD ACS patients, so often multisite CAD means multiple CAS. But we have to mention that our study percentages are related to ACS patients and they are 1 fold greater than the reported numbers, probably related to the same imbalanced CVRF profile and to the modality of ATS evolution in ACS patients. Another thing is that the greater percentage of CAS arrives from older studies (around 2000)[37], while the smaller percentage is from more recent studies (2005-2010)[1,38,39]. The explanation might be better and intensive prevention medical therapy of CVRF[1].

CAS was more severe in 1VD and 2VD ACS patients, while 3VD ACS patients had more moderate CAS. Moreover 1/2 of the 3VD and 1/3 of the 2VD ACS patients had multiple CAS, aspects that might be related to cyclic (inflammation-calcification) progressive evolution of ATS. Not least, we found another interesting correlation between the presence of predominant LAD lesions and the prevalence of CAS in 1VD and 2VD ACS patients: ACS patients with LAD lesions had 2 fold higher CAS than ACS patients with Cx and/or RC lesions. We did not found this observation in other studies and we just can stipulate that LAD lesion-CAS correlation could be related probably to the pattern of ATS evolution in ACS patients

and maybe to some hemodynamic particularities of LAD coronary circulation.

It is unclear why ATS lesions progress silently for extended periods of time and then suddenly undergo changes leading to plaque instability, rupture, thrombosis, and acute clinical syndromes. These are not limited to a single "culprit" site, they are part of a multi-centric inflammatory process with many triggers and involving simultaneous multiple additional plaques instability at distantly locations in the entire arterial system[21,40]. Inflammation may be the link between coronary and carotid plaque destabilization, reflected in elevated high sensitivity serum C-reactive protein (hsCRP), interleukin-6, adhesion molecule-1[21]. The acute phase reactants reflect the systemic inflammation, but they are also active participants to the process of ATS plaques formation, and may be modulated by focal changes in the carotid arteries[21]. Maybe other new biomarkers related to coronary ischemia and increased incidence of CV events (neutrophil /lymphocyte ratio, plasma leptin, resistin, TNF-α, adiponectin) or to cardiovascular stiffness in HT patients (serum ST-2 soluble) could be more specific for carotid and coronary ATS inflammation and might be added to the clinic, metabolic, and imagistic evaluation of ATS in order to increase prognostic value in polyvascular patients[41-45].

LIMITATION OF THE STUDY

A limitation is the small number of subjects. Despite the fact that noninvasive assessment of CIMT and carotid plaque burden is a marker for future coronary events, and although current guidelines on CVD prevention consider the presence of any degree of CAS a high-risk marker of cardiovascular events, routine carotid US Doppler screening is not currently endorsed. Our data, however, did not propose to resolve the existing controversy regarding the reciprocal relationship between CAD and CAS, but some particular aspects of CVRF profile and US carotid elements, in ACS patients in comparison with stable CAD have been highlights in our study. The prognostic relevance of US characteristics of carotid plaques in patients with CAD, possibly in association with inflammatory markers, needs to be further clarified.

CONCLUSIONS

In our study, we found that CAD patients have particular CVRF profiles, different for ACS patients (more DM and hypertriglyceridemia), and for stable CAD pa-

tients (more smoking and HT) and these specific findings could be related to their specific CAS-CAD patterns. Stable CAD patients had more moderate than severe CAS, while in ACS patients was a relatively similar proportion of moderate and severe CAS. This is one of the first studies focused on CAS particularities in ACS patients. Increased CIMT, and carotid stenosis were associated with the presence, the extent, and the severity of epicardial coronary stenosis in ACS patients, and might be useful in estimating ATS burden in those patients with multi-vessel disease. Our study shows a direct correlation between increasing CIMT values and severity of coronary lesions in ACS patients, as a surrogate marker of acute CV events, and also for revascularization. We find that the high prevalence of CAS increases in parallel with the number of the involved coronary arteries in ACS patients and had a specific correlation with LAD lesions. Independent predictors of severe CAS were: the presence of LMD or 3VD, increasing age, smoking status, DM. Although CAS is known as a risk factor for future adverse CV events in CAD patients, it might be a marker for diffuse ATS disease burden rather than a direct etiologic factor.

Conflict of interest: none declared.

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