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Stenosis Level, Plaque Morphology and Intima-Media Thickness of Internal Carotid Artery in Chronic Stable Angina and Acute Coronary Syndrome; A Comparative Study

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Background: Ischemic heart disease (IHD) is the most common cause of cardiovascular diseases and divided into two main categories as acute coronary syndrome (ACS) and chronic stable angina (CSA). These two groups have stenosis and atherosclerosis in the coronary artery, but are more severe in patients with ACS.

Objectives: We aimed to find the association between coroner and internal carotid artery, also comparing prospectively stenosis level, plaque morphology and intima-media thickness of internal carotid between patients with acute coronary syndrome (ACS) and chronic stable angina.

Patients and Methods: In this study, 60 patients were enrolled as ACS group chosen from those admitted in CCU or referred to clinic. Forty-five patients of CSA group were chosen from those referred to clinic. All 105 patients underwent color Doppler sonography, and stenosis, plaque morphology and intima media thickness (IMT) were measured.

Results: In 60 patients with ACS, 49 (81.7%) had no stenosis in ultrasonography and 11 (18.3%) had some degrees of stenosis; also 28 (46.7%) and 16 (26.7%) of patients had plaque and IMT, respectively. In the rest 45 patients of CSA group, just 4 (8.9%), 17 (37.8%) and 8 (17.8%) patients had stenosis, plaque and IMT, respectively. Therefore, there was no statistically significant difference between the two groups regarding stenosis ($P = 0.171$), plaque morphology ($P = 0.362$) and IMT ($P = 0.283$) (Power = 90%).

Conclusions: According to the results, there were no significant and meaningful differences comparing ACS and CSA groups of patients by ECDS using three indicators of stenosis, plaque morphology and IMT as indicators of atherosclerosis. Results also display that patients with ACS had more stenosis, more plaque and thicker intima–media, but these differences were not statistically significant ($P < 0.05$).

*Keywords:*Acute Coronary Syndrome; Chronic Stable Angina; Doppler Ultrasonography; Stenosis; Intima-Media Thickness

1. Background

Cardiovascular-related diseases such as Ischemic heart disease (IHD) are the most common causes of death worldwide (1-3). Patients with IHD are divided into two major groups of patients with chronic coronary artery disease who most present with chronic stable angina (CSA) and those with acute coronary syndrome (ACS). The latter group has three subtypes of unstable angina, non ST-segment elevation myocardial infarction (MI) and ST-segment elevation MI (4).

It is proved that ACS patients have poor prognosis according to much clinical and laboratory variables (5-8). Atherosclerosis plaque rupture in coroner is one of the primary motivating factors in ACS and the most important cause of disease severity in patients (9).

In recent clinical trials, IMT (intima media thickness) has been introduced as a surrogate end point for assessing the progression of atherosclerosis (10). Carotid plaque is reported as another predictable factor to evaluate the risk of CAD, but not still discovered whether there is any strong association with cardiovascular events in patients with CAD (11).

Non-interventional and interventional methods for detection of atherosclerosis of vessels are widely used in clinical practice. Carotid intima-media thickness (CIMT) measurement is recommended by the American Heart Association as the most scholastic and useful method to identify atherosclerosis (12). CIMT can be measured by B-mode ultrasonography.

Carotid Doppler sonography is a noninvasive, simple and cheap method to investigate stenosis, plaque morphology and IMT of internal carotid as indicators of atherosclerosis. As atherosclerosis is a systemic disease, probably carotid atherosclerosis is the reflex of coroner diseases. We could use these tests to study the coroner

atherosclerosis indirectly. By this test, coroner atherosclerosis can be estimated approximately. Probably, carotid vessels are the mirror of coroner vessels.

In Ischemic heart disease spectrum, patients with ACS have more atherosclerosis, wider involvement of coroner and more intensive clinical symptoms in comparison to CSA. Therefore, it is possible that their carotid involvement would be more significant. For example, carotid stenosis would be more serious, IM has more thickness or more plaque would be detected in their carotid (13), but there is no reliable data. By proving this hypothesis, we would use carotid as a mirror of coroner and observed coroner atherosclerosis in the mirror of carotid.

2. Objectives

We performed this study to compare these three factors in both ACS and CSA patients and assess whether there is any association between carotid and coroner involvement.

3. Patients and Methods

In this prospective cross-sectional study, 60 patients with ACS and 45 CSA ones were enrolled at internal clinic of Vali-Asr hospital, a tertiary health care center affiliated with Fasa University of Medical Sciences, Fasa, Iran from September 2010 to February 2011. Patients were included according to the American Heart Association criteria of diagnosing cardiovascular disease (14). Patients with ACS were those who had typical chest pain accompanied with abdominal pain, shoulder pain, vertigo, palpitation, dyspnea, nausea, vomiting and cold sweating. The patients who had typical chest pain as described above with a positive history (hx) of at least one time hospital admission (CCU and Post CCU of Vali-Asr hospital) entered the research. Patients whose chest pain was due to non-cardiac reasons or did not have hospital admission, were excluded from our study. The other group was patients with chronic stable angina whose chest pain initiated with an exact limit of activity. Their chest pain was not very severe, lasting below 15 minutes and resolving with rest and sublingual nitroglycerin consumption. Results of cardiac enzymes were normal and electrocardiography (ECG) might have normal or abnormal finding. Patients were selected from those referred to Vali-Asr hospital clinic. Carotid color Doppler sonography was performed for all patients. As Electronic Control Devices sonography (ECDS) do not measure atherosclerosis directly, we used three indicator of stenosis, plaque morphology and intima-media thickness to evaluate carotid atherosclerosis indirectly. After preparation of ECD sonography, their information was gathered in a studied checklist. This data included demographic information, history of Transient Ischemic Attack (TIA), history of Cerebrovascular Accident (CVA), ECG on admission, ECD sonography findings, ECG findings, Bruit, history of peripheral vascular disease, risk factors including (diabetes mellitus, hypertension, smoking and hyperlipidemia) and CK-MB enzyme. According to PASS software ($\alpha = 0.05$, power = 80% and D = 15%), the number of samples in each group was calculated as at least 45 subjects. Rout of sampling in this research was sequential.

The study was approved by the Ethics Committee of Fasa University of Medical Sciences and all participants signed a written informed consent (Approval number: 29637/A/23). The protocol of the study was approved by the Institutional Review Board of the University.

3.1. Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive results were expressed as mean value ± standard deviation for 95% confidence interval. Chi-square test and independent sample t-test were used for comparison between the groups. A two-tailed $P < 0.05$ was considered statistically significant.

4. Results

Overall, we enrolled 60 patients including 26 (43.3%) malesand 34 (56.7%) femalesin ACS group (15 ones excluded) and 45 patients including 21 (46.7%) males and 24 (53.3%) females as CSA group (14 ones excluded) referred to internal clinic of Vali-Asr hospital (Fasa, Iran). Among patients with ACS, 45 (75%) had unstable angina pectoris. Fifteen patients (25%) had the impression of MI. The mean age of patients in ACS and CSA groups were 64.7 ± 12.3 and 63.5 ± 9.7 years, respectively. (P = 0.574).

Table 1. Internal Carotid Artery Parameters of 60 Patients With Acute Coronary Syndrome Compared to 45 Patients With Chronic Stable Angina [a,b]

Internal Carotid Parameters	Acute Coronary Syndrome Group (n = 60)	Chronic Stable Angina Group (n = 45)	P Value
Stenosis	11 (18.3)	4 (8.9)	NS
Plaque	28 (46.7)	17 (37.8)	NS
Calcified Plaque	6 (10)	1 (2.2)	NS
IMT	16 (26.7)	8 (17.8)	NS

[a] Abbreviations: IMT, intima-media thickness; NS, not significant.
[b] Data are presented as No. (%).

Table 2. Severity and Site of Stenosis of Internal Carotid Artery in Patients With Chronic Stable Angina and Acute Coronary Syndrome [a]

Internal Carotid Parameters	Acute Coronary Syndrome Group (n = 60)	Chronic Stable Angina Group (n = 45)
Stenosis Severity		
No stenosis	49 (81.7)	41 (91.1)
Beneath 50%	9 (15.1)	3 (6.7)
50-70%	0	1 (2.2)
Over 70%	2 (13.3)	0
Stenosis Site		
Left carotid	6 (10)	1 (2.2)
Right carotid	2 (5)	2 (4.4)
Left and Right	3 (3.3)	1 (2.2)

[a] Data are presented as No. (%).

Therefore, there was no statistically significant difference between demographic data of the two groups. Results of stenosis, plaque morphology and IMT of the two groups are available in Table 1.

In CSA group, four patients (8.9%) had stenosis, 17 patients (37.8%) had plaque and eight patients (17.8%) had intima-media thickness of the internal carotid artery; these values for ACS patients were 18.3%, 46.7% and 26.7%. ($P = 0.171$, $P = 0.362$, $P = 0.283$, respectively). We also considered the severity of stenosis. In CSA group, three patients (6.7%) had severity up to 50%. One patient (2.2%) had severity of 50-70% and there was no patient with severity over 70%. However, in ACS group, nine patients (15.1%) had stenosis below 50% and two patients (13.3%) had stenosis over 70%. In summation of the two groups, 90 patients (85.7%) had no stenosis, 12 patients (11.4%) had stenosis below 50%, one patient (1%) had 50-70% stenosis and two patients (1.9%) had stenosis over 70%. Stenosis severity and the site of stenosis are presented in Table 2.

We expected that patients with ACS have more involvement in their carotid. Statistical analysis between these two groups showed that patients with ACS had more stenosis, more plaque and thicker intima–media, but these differences were not statistically significant ($P > 0.05$). For example, 8.9% of patients with CSA had stenosis in their carotid. This number was 18.3% for patients with ACS. Although stenosis level of patients with ACS was 2 times more than those with CSA, it was not considered meaningful ($P = 0.171$).

5. Discussion

In this study, we investigated stenosis level, plaque morphology and IMT of internal carotid artery of patients with ACS and CSA and compared their atherosclerosis together to find any significance difference. In addition, we aimed to assess whether there is any association between coroner and carotid involvement in these patients. Our instrument was color Doppler sonography.

Cicorella et al. (15) investigated usefulness of carotid atherosclerosis ultrasound evaluation (intima-media thickness, unstable carotid plaques and severe carotid stenosis) to predict the presence and the extent of coronary artery disease in a consecutive series of 1337 patients. They retrospectively evaluated coronary angiography and carotid ultrasound of patients. IMT more than 0.90 mm, unstable plaque and severe stenosis ($\geq$ 70%) were considerable. On the other hand, presence of at least one lesion more than 50% within the main branches of coronary arteries was considered as significant CAD.

They found that IMT more than 0.90 mm, unstable plaque and severe carotid stenosis were associated with odds ratio of coronary artery disease of 2.28 (1.8-2.9) ($P < 0.0001$), 3.6 (2.3-5.7) ($P < 0.001$) and 4.2 (2.0-8.7) ($P = 0.0001$), respectively. According to these results, they confirmed usefulness of carotid ultrasound evaluation to predict the presence and extent of coronary artery disease.

In another similar study, Komorovsky et al. (10) tried to find an association between carotid ultrasound findings and occurrence of coronary artery disease. They believed that screening patients with diagnosed CAD for carotid atherosclerosis is very important. However, prognostic effect of ultrasound characteristics of carotid plaques on cardiovascular outcomes of patients with CAD remains controversial.

In a Turkey study, Demircan et al. (16) compared carotid intima-media thickness of patients with stable angina pectoris and patients with acute coronary syndrome. In this prospective study, they found carotid artery atherosclerotic plaques more frequent and more increased carotid IMT in patients who had early-onset CAD compared to control subjects. (40% *vs.* 11%, $P < 0.001$, and 0.73 ± 0.10 *vs.* 0.60 ± 0.10 mm, $P < 0.001$, respectively). Besides, they deduced that patients who had CAD and presented with an acute coronary syndrome had significantly increased carotid IMT compared to patients with CSA in the form of stable angina pectoris (0.76 ± 0.10 *vs.* 0.70 ± 0.10 mm, $P < 0.05$). Therefore, their main conclusion was to find greater carotid IMT in patients with acute coronary syndrome

compared to patients with stable angina pectoris.

In one of the recent studies, Ciccone and his Italian team (17) evaluated common carotid artery IMT (CCA-IMT) in acute and chronic coronary artery diseases. The ACS group showed an upper CCA-IMT than the chronic CAD group (0.94 ± 0.22 *vs.* 0.86 ± 0.15 mm, P = 0.027); also there were no differences regarding the extension of coronary atherosclerosis on angiograms. CCA-IMT confirmed its importance and necessity in predicting coronary artery disease by showing significantly upper values in patients in ACS group compared to those in the chronic CAD group.

Rosa EM and his assistants (18) held a case-control study to determine the association between coronary artery atherosclerosis and common carotid artery IMT measured on ultrasonography. They conducted the study with two groups of patients with coronary artery disease and normal individuals using ultrasonography. As a result, they found that IMT of the common carotid artery was significantly greater in patients with CAD.

You and Lu (19) studied the association of myocardial ischemia and carotid atherosclerosis in patients with hypertension. Eighty-five patients with hypertension did exercise test and divided into two groups according to test; myocardial ischemia group and ischemia free group. In this research, patients undergone carotid doppler sonography. Results showed that plaque formation was the most important indicator to predict ischemia in patients. The other result was that myocardial ischemia group had more plaques in their sonography. The last result was that IMT is not a good marker to predict ischemia in patients.

According to our results and some other related researches, we could mention some important points; first: we supposed that these three indicators were good and suitable, the result of this research showed there is no association between coroner and carotid arteries. There is no reason the more atherosclerotic the coroner is, the more atherosclerotic the carotid must be.

Second, it is not exactly and obviously vivid that coroner of patients with ACS has more atherosclerosis than those with CSA. It means that severe symptoms of patients with ACS may not be relevant to more coroner atherosclerosis. Genetic and environmental causes may be responsible for presenting severe symptoms in patients with ACS.

Finally, patients in this research did not undergo angiography. If ACS group do not have more atherosclerosis in their coroner, there is no reason to detect more atherosclerosis in their carotid.

5.1. Limitations

Because of limited time and equipment, our sample may not be adequate. If our sample size was larger, the result of research would be different probably. Some other researches have been performed up to now comparing IHD patients with normal population, but we could not find an exact research like ours. Thus, we could not judge decisively about correctness of the results of our research.

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