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Chest Pain Characteristics in Cardiac Syndrome X Compared to Coronary Artery Disease

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Abstract

AIM: This study aimed to assess if clinical remarks gained by analysis of the present and past medical history of patients undergoing elective coronary angiography (ECA) due to typical chest pain can help to predict the outcome of ECA.

MATERIAL AND METHODS: One hundred and fifty-four ECA candidates with a history of typical chest were seen on the same day intended for ECA in the cardiac centre of AlShaab Teaching Hospital, Khartoum, Sudan. The details of the present complaints, characteristics of chest pain, past medical and socioeconomic history were recorded from each subject guided by a questionnaire. ECA confirmed CAD in 112 of the studied patients and were considered as the test group. The remaining patients (N = 42) were diagnosed as CSX after exclusion of significant narrowing of the coronary vessels and were considered as the control group.

RESULTS: Univariate analysis of pain characteristics among patients undergoing coronary angiography revealed that pain is less likely to radiate to the neck (OR = 0.44, 95% CI = 0.21 – 0.91, P = 0.027) and the back (OR = 0.48, 95% CI = 0.23 – 1.00, P = 0.049) in patients with CAD. Presence of shortness of breathing and/or dizziness significantly decrease the odds of having abnormal coronary angiography (OR = 0.30 and 0.48, 95% CI = 0.12 – 0.77 and 0.22 – 0.92, P = 0.013 and 0.030 respectively). Past history of diabetes mellitus significantly increases the odds of having abnormal coronary angiography (OR = 3.96, 95% CI = 1.68 – 9.30, P = 0.002). In contrast, past medical history of migraine decreases the odds of having positive finding in ECA (OR = 0.31, 95% CI = 0.13 – 0.72, P = 0.006).

CONCLUSION: Characteristics of chest pain are comparable in CAD and CSX. However, pain is less likely to radiate to the neck and/or the back in the first group. Presence of dyspnea and dizziness during angina attacks as well as the history of migraine significantly decreases the odds of having abnormal coronary angiography.

Introduction

Patients with typical chest pain and positive stress electrocardiography (ECG) or other cardiac tests are not certainly suffering from coronary artery disease (CAD) [1], [2]. Cardiac syndrome X (CSX) is frequently used to diagnose patients with typical chest pain, positive cardiac stress test(s) and normal coronary macrocirculation [3]. Dysfunction of coronary microcirculation [4] and abnormal perception of pain [5], [6] are the most acceptable explanations for CSX in the literature so far. In clinical practice, the relatively high percentage of patients with no significant angiographic findings following elective coronary angiography (ECA) raise a question whether ECA is overused in patients with suspected CAD [7]. Although there are a lot of studies investigating risk factors for CAD [8], [9], researches exploring the predictors of CSX are scarce [2], if any. This study aimed to assess if clinical remarks gained by analysis of the present and past medical history can help to predict outcome of ECA. Special care was given in comparing chest pain characteristics between patients with CSX and CAD.

Material and Methods

The present study was approved from the ethics review committee (ERC), Faculty of Medicine, University of Khartoum, Sudan. All candidates who agreed to join this study signed a written informed consent before being evaluated.

One hundred and fifty-four ECA candidates with a history of typical chest pain were seen on the same day intended for ECA in the cardiac centre of AlShaab Teaching Hospital, Khartoum, Sudan. The details of the present complaints, characteristics of chest pain, past medical and socioeconomic history were recorded from each subject guided by a questionnaire. The body mass index (BMI) and mean arterial blood pressure (MABP) were calculated for each subject by the formulae:

$$\text{BMI (kg/m\^2)} = \text{weight (kg)/(height (m\^2)}$$

and

$$\text{MABP} = \text{Diastolic blood pressure} + \frac{1}{3}(\text{Diastolic blood pressure} - \text{Systolic blood pressure})$$

respectively.

ECA confirmed CAD in 112 of the studied patients and were considered as the test group. The remaining patients (N = 42) were diagnosed as CSX after exclusion of significant narrowing of the coronary vessels and were considered as the control group.

Statistical analysis was performed using Statistical Package for the social sciences (SPSS) for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA). Normal distribution of variables was examined using Shapiro-Wilk test. Unpaired T-test was used to assess statistical difference between mean (SD) of normally distributed scaled variables. Mann-Whitney U test was used to compare median (25^{th} – 75^{th} interquartile) of abnormally distributed scaled variables. Univariate analyses were carried out to evaluate characteristics of chest pain and past medical history as past predictors of CAD. Results of univariate analyses were expressed by odds ratios (OR) and their 95% CI. In all tables expressing results of univariate analysis, OR described the ratio of the odds of an event occurring in patients with CAD to the odds of the same event occurring in subject with CSX. P < 0.05 was considered significant.

Results

Coronary artery catheterization of the studied subjects (N = 154) revealed 112 patients with CAD (P (95% CI) = 72.7% (65.3 –79.3%), mean (SD) of age = 60.58 (10.26) years) and 42 subjects with normal coronary arteries (P (95% CI) = 27.3% (20.7–34.7%), mean (SD) of age = 50.95 (16.46) years).

Table 1 compares age, anthropometric measurements and blood pressures of subjects with CSX and CAD. Age was significantly higher in CAD patients compared to CSX (*P* < 0.001). In contrast, BMI was significantly higher in CSX compared to CAD patients (*P* = 0.004).

Table 1: Comparison of age, anthropometric measurements and blood pressures among patients undergoing ECA

	CSX N = 42 Mean (SD) Median (25 – 75 interquartile)	CAD N = 112 Mean (SD) Median (25 – 75 interquartile)	*P*
Age (years)	50.0 (42.5 – 53.3)	55.0 (60.0 – 68.8)	< 0.001*
Weight (Kg)	80.04 (13.77)	72.39 (13.67)	0.004*
Height (Cm)	164.65 (8.33)	165.38 (8.14)	0.640
BMI (kg/m^2)	29.61 (5.06)	26.32 (4.52)	0.001*
SBP (mmHg)	132.83 (20.16)	129.41 (22.86)	0.379
DBP (mmHg)	79.29 (11.99)	78.21 (11.94)	0.627
MABP (mmHg)	97.14 (12.82)	95.28 (13.92)	0.446

Univariate analysis of chest pain characteristics among patients undergoing coronary angiography revealed that chest pain is less likely to radiate to the neck (OR = 0.44, 95% CI = 0.21 – 0.91, *P* = 0.027) and the back (OR = 0.48, 95% CI = 0.23 – 1.00, *P* = 0.049) in patients with CAD (Table 2). In addition, presence of shortness of breathing and / or dizziness significantly decrease the odds of having abnormal coronary angiography (OR = 0.30 and 0.48, 95% CI = 0.12 – 0.77 and 0.22 – 0.92, *P* = 0.013 and 0.030 respectively).

Table 2: Univariate analyses of pain in patients undergoing ECA

	OR	95% CI	*P*
Duration since first chest pain attack > 2years	0.86	0.39 – 1.86	0.695
Duration of pain attack > 30 minutes	0.95	0.38 – 2.39	0.950
Severity of pain	0.92	0.56 – 1.52	0.750
Pain radiation			
Retrosternal	1.24	0.51 – 2.00	0.631
Left sided chest pain	0.70	0.32 – 1.55	0.378
Radiation of pain to the neck	0.44	0.21 – 0.91	0.027*
Radiation of pain to the right shoulder	0.74	0.35 – 1.53	0.410
Radiation of pain to the left shoulder	0.52	0.25 – 1.09	0.082
Radiation of pain to the right upper limb	1.19	0.52 – 2.70	0.686
Radiation of pain to the left upper limb	0.64	0.31 – 1.32	0.230
Radiation of pain to the Back	0.48	0.23 – 1.00	0.049*
Radiation of pain to other areas	1.16	0.55 – 2.42	0.702
Aggravating factors			
Exercise	1.34	0.57 – 3.15	0.503
Cold	0.56	0.26 – 1.23	0.148
Food intake	1.05	0.46 – 2.42	0.902
Others	0.75	0.13 – 2.24	0.743
Relieving factors			
Rest	1.07	0.35 – 3.25	0.905
Sublingual nitrates	1.05	0.52 – 2.12	0.883
Others	1.64	0.44 – 6.14	0.461
Associated factors			
Sweating	0.61	0.27 – 1.39	0.242
Nausea	0.80	0.38 – 1.67	0.552
Vomiting	0.92	0.42 – 2.02	0.841
Palpitation	0.58	0.28 – 1.20	0.143
Shortness of breathing	0.30	0.12 – 0.77	0.013*
Dizziness	0.45	0.22 – 0.92	0.030*
Loss of consciousness	0.84	0.34 – 2.11	0.714

Table 3 shows the results of univariate analyses of past medical and socioeconomic history in patients undergoing coronary angiography. Past history of diabetes mellitus significantly increases the odds of having abnormal coronary angiography (OR = 3.96, 95% CI = 1.68 – 9.30, P = 0.002). In contrast,

past medical history of migraine decreases the odds of having positive finding in ECA (OR = 0.31, 95% CI = 0.13 – 0.72, P = 0.006).

Table 3: Univariate analyses of past medical and socioeconomic history for patients undergoing ECA

	OR	95% CI	*P*
Past medical history			
Hypertension	1.29	0.63 – 2.63	0.490
Diabetes mellitus	3.96	1.68 – 9.30	0.002*
Peptic ulcer	0.45	0.11 – 1.76	0.249
Esophageal disease	0.50	0.23 – 1.07	0.072
Respiratory disease	0.87	0.21 – 3.52	0.841
Migraine	0.31	0.13 – 0.72	0.006*
Raynaud's phenomenon	0.37	0.02 – 6.01	0.482
Chronic inflammatory disease	0.58	0.18 – 1.89	0.366
Socioeconomic history			
Smoking			
- Active smoking	1.64	0.80 – 3.39	0.178
- Passive smoking	1.20	0.55 – 2.64	0.650
Socioeconomic status	0.97	0.54 – 1.76	0.923

Discussion

Univariate analysis of pain characteristics, namely onset and duration of pain attacks, severity, radiations, aggravating and relieving factors reveals only a few predictors for positive coronary angiography findings in patient undergoing ECA because of typical chest pain. According to the current results, distributions of chest pain are comparable in both studied groups. However, pain is less likely to radiate to the neck and/or the back in patients with CAD. Also, presence of shortness of breathing and/or dizziness significantly decreases the odds of having abnormal coronary angiography. Although previous reports on CSX patients suggest enhancement of their pain perception [10], the current study failed to demonstrate a significant difference in pain severity, duration or aggravating factors when CAD and CSX patients were compared. The special attention paid by cardiologists while evaluating the need of patients with chest pain for diagnostic coronary angiography may explain the limited difference in chest pain characteristics of studied groups. This is because typical features of angina are carefully evaluated by cardiologists while selecting patients who are in real need of diagnostic coronary angiography.

At least two previous studies explain the radiation of chest pain in patients with CSX [11], [12]. The first study was conducted by Lanza and his group in the late nineties of the last century [12]. Lanza *et al.* demonstrated cardiac adrenergic nerve dysfunction in 75% of patients with CSX patients suggesting cardiac origin of chest pain in these patients. Five years later, Rosen *et al.* used positron emission tomography (PET) and stress echocardiography studies to assess origin of pain in patients with CSX [11]. According to Rosen *et al.,* results, chest pain and ECG changes during attacks were not accompanied by demonstrable myocardial dysfunction. However, there was altered central neural handling of afferent signals suggesting that CSX might be a cortical pain syndrome. The hypotheses suggested by either Lanza *et al.,* or Rosen *et al.* can explain the great similarities in the areas of chest pain radiation in patients with CSX and CAD targeted by this study.

According to the results of the present study, the presence of dyspnea and dizziness in patients with typical chest pain significantly increases the probability of having normal rather than abnormal coronary angiography. This finding is not necessarily contradictory to what was reported before that dyspnea and dizziness are common during angina attacks of CAD patients [13], [14]. In contrast, it may indicate the higher frequency of these symptoms in patients with a separate pathology that causes typical angina in the presence of patent coronary vessels. Patients with CSX are at higher risk of neuroticism like anxiety and depression [15], [16]. Neuroticism could perpetuate to somatoform disorder with physical symptoms like shortness of breathing and dizziness; however, however, the present literature lacks scientific proof for this hypothesis and further researches are desirable to explore this area.

It is worth mentioning that previous studies suggested that patients with angina and normal coronary angiography may have a diffuse disorder of smooth muscle tone [17]. Cannon *et al.,* studied forced expiratory volume in the first second (FEV1) in the basal state and after methacholine inhalation to determine whether the bronchial smooth muscle is affected in CSX patients [18]. Fourteen per cent of patients with CSX had a basal FEV1 of less than 70% of that predicted and did not receive methacholine. Also, the product of the methacholine dose inhaled and the magnitude of decline in FEV1 from baseline was significantly lower in patients with CSX than in normal volunteers suggesting airway smooth muscle hyperresponsiveness in CSX patients. Cannon *et al.* findings may explain the shortness of breathing in patients with angina and normal coronary angiography during chest pain attacks. This is because the initiator of microvascular smooth muscle dysfunction, and hence angina, may at the same time trigger shortness of breathing by inducing airway hyperresponsiveness.

Previous researches that compare features of chest pain in patients with obstructive, non-obstructive and normal coronary vessels are scarce [19], [20]. The current study findings on the major differences of chest pain in patients classified according to ECA outcome are probably naïve and deserved to be explored further by additional researches.

Evaluation of past medical history in patients undergoing ECA shows that the odds of having CAD increases about four times in the presence of diabetes mellitus but decreases to about one-third if migraine exists. The results of the present study failed to link positive angiographic finding and common CAD risk factors like past medical history of hypertension [21], [22], Raynaud's phenomenon [23], chronic

inflammatory diseases [24], smoking [25] and socioeconomic status [26]. The current data also failed to demonstrate decreased odds of having positive angiographic finding in patients with past medical history of peptic ulcer, oesophagal or respiratory diseases, whose clinical presentations may mimic angina pain [27], [28].

The prevalence of migraine is significantly increased in either subject with spastic or normal coronary arteries compared with patients with CAD [29], [30]. Koh *et al.* conducted a prospective study on the prevalence of migraine in Korean patients with proven variant angina compared to two control groups: one group with CAD and another one with subjects without heart disease [30]. According to the results of Koh *et al.*, migraine was diagnosed in 40.0%, 20.0% and 38.7% of patients with variant angina, CAD and no heart diseases respectively. Five years later, a comparable study was conducted by Nakamura *et al.,* in Japanese [29]. The data of Nakamura *et al.,* showed that the prevalence of migraine in Japanese patients with vasospastic angina, angina with effort and subjects without known ischemic heart disease are 23%, 4% and 11% respectively. Although it is evident from the works of Koh *et* al., and Nakamura *et al.,* that there is possible link between migraine and normal coronary arteries, gender and age-specific prevalence of migraine mismatch with that of CAD, which could explain low risk of CAD in migraineurs [23]. This possible explanation for low prevalence of migraine among CAD patients warrants additional investigations and studies.

In conclusion, characteristics of chest pain are comparable in CAD and CSX, however, pain is less likely to radiate to the neck and / or the back in the first group. Presence of shortness of breathing and / or dizziness during angina attacks as well as history of migraine significantly decreases the odds of having abnormal coronary angiography.

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