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NAILFOLD CAPILLAROSCOPY IN PATIENTS WITH ANGINAL CHEST PAIN AND NORMAL CORONARY ANGIOGRAMS – AN OBSERVATIONAL CROSS SECTIONAL STUDY

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ABSTRACT

AIM: To study nailfold capillaroscopy findings in patients with typical anginal symptoms with normal coronary angiograms.

METHODS AND RESULTS: We studied 40 patients with typical anginal chest pain and normal coronary angiograms. Nailfold capillaroscopy was performed with the OITEZ e-scope on the right and left ring fingers. Overall, abnormalities were detected in 30% of the patients. Decreased capillary density (25%) was the most common finding followed by capillary dilatation (17.5%), microhaemorrhages (10%) and bushy capillaries (5%).

CONCLUSIONS: Nailfold capillaroscopic abnormalities are common in patients with anginal chest pain and normal coronary angiograms. These findings suggests a generalized microvascular abnormality that may play a role in the pathogenesis of this syndrome. Further studies are needed to determine whether the abnormality is associated with myocardial flow disturbances, such that the findings can be extended to the heart.

KEYWORDS : Anginal chest pain , normal coronary angiograms, nailfold capillaroscopy, microvascular.

INTRODUCTION

Approximately 20%-30% of patients undergoing diagnostic coronary angiography for typical anginal symptoms have angiographically normal coronary arteries[1]. Microvascular dysfunction has been suggested to play a pathogenic role in at least some of these patients[2].

Nailfold capillaroscopy is a simple, low cost, non-invasive and safe method enabling direct assessment of capillaries of the periungual region by means of stereoscopic microscopy[3]. It is now considered one of the best diagnostic non-invasive imaging techniques capable of studying the microcirculation in vivo. It has been employed in the field of rheumatology and dermatology for last 3 decades and this technique is currently extremely useful in the identification of microvascular involvement in many rheumatic diseases, particularly in systemic sclerosis (SSc) and related disorders[4].Recently, there is increasing interest in the use of this technique in other systemic disorders as well[5,6]. In particular, nailfold capillaroscopic abnormalities have been well documented in systemic hypertension[7].

The aim of this study was to analyse nailfold capillaroscopy findings in patients with typical anginal symptoms with normal coronary angiograms.

MATERIALS AND METHODS:

A total of 40 patients who underwent coronary angiography for typical exertional angina and found to have normal coronary angiograms were studied. Patients having history or physical findings of systemic rheumatic diseases (SLE, systemic sclerosis, rheumatoid arthritis, Sjogren syndrome, MCTD, polymyositis/dermatomyositis, antiphospolipid syndrome, Raynauds phenomenon) were excluded. Also patients with hypertension, diabetes mellitus and acute coronary syndromes (STEMI/NSTEMI) were not included. A written informed consent was taken.

The nailfold capillaroscopy was then performed with the OITEZ e-scope [DP-M17filter e-scope pro] on the right and left ring finger of the selected patients. The images were recorded under polarized light at 20x and200x. The images of the capillaroscopy were stored and the different parameters were noted. The data was then analysed.

RESULTS:

The baseline demographic and clinical characteristics and echocardio graphic findings of these patients are given in table 1.

Table 1. Demographic, clinical and echocardiographic characteristics of the patients

Age	45 ± 6
Male Gender (%)	14 (35)
Hb (g/dl)	11.4 ± 1.2
Total Cholesterol (mg/dl)	205 ± 56
LDL-C (mg/dl)	106.5 ± 45.4
HDL-C (mg/dl)	45.6 ± 6.8
Triglyceride (mg/dl)	147.4 ± 72.6
Creatinine (mg/dl)	0.8 ± 0.1
Heart Rate (bpm)	70 ± 09
Blood pressure- systolic	116 ± 11
Blood pressure- diastolic	74 ± 07
LVID (diastole)	46.2 ± 4.6
LVID (systole)	27.5 ± 6.2
LV Ejection fraction (%)	56 ± 4

Nail fold capillaroscopy findings of are given in Table 2.

Table 2. Nail fold capillaroscopic findings of patients (n= 40)

Normal (%)	28 (70)
Decreased capillary density (%)	10 (25)
Capillary dilatation (%)	07 (17.5)
Microhaemorrhages (%)	04 (10)
Bushy capillaries (%)	02 (05)

Overall, abnormalities in the nailfold capillaries were detected in 30% of the patients. Decreased capillary density was the most common finding followed by capillary dilatation , microhaemorrhages and bushy capillaries.

DISCUSSION:

The phenomenon of anginal chest pain with normal coronary angiograms was clinically characterized by by Harvey Kemp in 1973 who coined the term 'Cardiac syndrome X'[8]. This term is now generally used to describe patients with exertional angina, completely normal coronary angiograms, and a positive ECG response to exercise testing. It excludes patients with coronary artery spasm (Prinzmetal's or variant angina), left ventricular hypertrophy, systemic hypertension, and valvular heart disease.[9] The term "Microvascular Angina" (MVA) (coined by Cannon and Epstein)[10] includes all such patients with coronary microcirculatory derangements but with normal coronary angiograms irrespective of the presence or absence of exercise-induced ST segment depression. However, often the two terms are used interchangeably.

Patients with angina with normal coronary angiograms show a distinct female preponderance implying a possible pathogenic role for estrogen deficiency [9]. Other proposed mechanisms behind this phenomenon are functional or anatomical abnormalities in the coronary microcirculation, a metabolic disorder which affects the handling of energy substrates by the heart, insulin resistance and a

neurological component affecting pain perception[11].

Histopathological changes in coronary microcirculation have long been demonstrated in patients presenting with anginal chest pain and normal coronary angiograms. Mosseri et al [12] studied right ventricular endomyocardial biopsies in which revealed pathological small coronary arteries with fibromuscular hyperplasia, hypertrophy of the media, myo-intimal proliferation, and endothelial degeneration and capillaries with swollen endothelial cells encroaching on the lumen. Suzuki et al[13] using electron microscopy of myocardial biopsies found that the capillaries of these patients were irregular in shape with chromatin margination of the endothelial nuclei and basal lamina thickening.

Several studies indicate microvascular ischemia as the most likely cause of chest pain in these patients. Syedi-Shirwania et al[14] observed a significant increase in malodialdehyde (MDA) levels and decrease in GSH levels indicating increased oxidative stress due to coronary microvascular dysfunction. Buffon et al[15] demonstrated a large cardiac release of two lipid peroxidation products namely lipid hydroperoxidases and conjugated dienes (both sensitive and independent markers of ischemia-reperfusion oxidative stress) after pacing induced tachycardia, indicating microvascular ischemia in the presence of normal coronary angiograms. Buchthal et al [16] used Phosphorus-31 nuclear magnetic resonance spectroscopy to identify metabolic evidence of myocardial ischaemia. They found that 20% of their patients with chest pain and normal coronary angiograms had evidence of myocardial ischemia in response to handgrip exercise indicating microvascular ischemia. Similarly, Panting et al[17] demonstrated subendocardial hypoperfusion using cardiovascular magnetic resonance imaging during the intravenous administration of adenosine associated with intense chest pain in upto 90% of these patients suggesting an ischemic origin of chest pain.

Multiple studies suggest that patients presenting with anginal chest pain and normal coronary angiograms may not only have abnormalities of the coronary microvasculature, but rather a more generalized systemic microvascular abnormality. Studies by Sax et al[18], Pedrinelli et al[19], Botker et al[20] and Buus et al[21] have demonstrated a significantly higher minimal forearm vascular resistance than normal controls, indicating impaired vasodilatory capacity. Of particular interest is the observation by Sax et al that the magnitude of the vasodilator impairment of the peripheral bed correlated closely with that of the coronary bed, indicating a relationship between central and peripheral vascular abnormalities.

Yuksel et al[22] studied nailfold capillaroscopic findings in patients in patients undergoing coronary angiography with normal coronary flow (24 patients) and coronary slow flow phenomenon (25 patients). Abnormalities were detected in 21% of patients in the normal coronary flow group which is consistent with our findings. Interestingly, abnormalities were even more common (60%) in the group of patients with coronary slow flow phenomenon.

Nailfold capillaroscopic findings patients with typical anginal chest pain, positive exercise testing and normal coronary angiograms were studied by Antonios et al[23]. A total of 49 patients (out of which 27 were normotensive and 22 were hypertensive) were compared with 50 controls without history of anginal chest pain (29 normotensive and 21 hypertensive subjects). Skin capillary density was significantly lower in patients with chest pain and normal coronary angiograms compared to normotensive controls. The finding of decreased capillary density in our study is consistent with this finding. However, there was no statistically significant difference in skin capillary density between subjects with chest pain and normal coronary angiograms and hypertensive controls indicating the presence of microvascular abnormalities in the hypertensive controls also.

Coronary microvascular disease exists in patients with essential hypertension in whom it can cause both a reduction of coronary flow reserve and a shift to the right of the coronary flow autoregulation curve[24]. Previous studies have demonstrated a reduced peripheral vasodilatory capacity in patients with essential hypertension[25]. Recently rarefaction of skin capillaries in essential hypertension has been demonstrated to be a primary or a very early abnormality that antedates the onset of sustained hypertension[26]. A proportion of patients with syndrome X are known to develop systemic hypertension during long-term follow up[9] and this may be one possible explanation for the capillaroscopic findings.

Insulin resistance has also been demonstrated in these patients[27]. Since insulin resistance has been linked to impaired capillary recruitment in essential hypertension, a similar pathogenic role may be attributed to insulin resistance in the microvascular abnormalities observed in these patients [28-30].

In conclusion, nailfold capillaroscopic abnormalities are common in patients with anginal chest pain and normal coronary angiograms. Structural rarefaction of capillaries in these patients suggests a generalized microvascular abnormality that may play a role in the pathogenesis of this syndrome. Further studies are needed to determine whether the abnormality is associated with myocardial flow disturbances, such that the findings can be extended to the heart. New therapeutic approaches for patients with chest pain and normal coronary angiograms targeting capillary angiogenesis and improving capillary reserve warrant future investigation.

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