ORIGINAL ARTICLE

PATTERN OF CORONARY ARTERY DISEASE WITH NO RISK FACTORS UNDER AGE 35 YEARS

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Background: Coronary artery disease (CAD) is no more deemed to be an ailment of the 4th or 5th decade; rather an earlier age incidence is not infrequently encountered in our population. However, there are a few data regarding CAD in young adults, and much about its underlying pathology still remains undetermined. The objective of this study was to delineate the coronary arterial disease pattern in adults under the age of 35 years, but having no known coronary risk factors. **Methods:** This prospective study was conducted at the Cardiology Departments of all 3 public sector tertiary care hospitals in Peshawar from Jun 2008 to Dec 2009. After having excluded the traditional risk factors for CAD, patients under the age of 35 years with objective evidence of CAD were subjected to percutaneous coronary angiography. **Results:** Out of a total of 104 patients, 85 (81.73%) patients were men, and 19 (18.27%) were women. The mean age of the whole group was 32.66±3.237 (22–35) years. Significant CAD (>50% diameter narrowing of at least one major coronary artery) was found in 87 (83.7%) patients while 17 (16.3%) patients had non-atherosclerotic coronary artery disease, including 12 (11.53%) patients having normal coronary arteries, 1 (1%) patient had anomalous origin of right coronary artery (RCA), 1 (1%) patient had coronary arteritis, 2 (1.92%) patients had coronary artery ectasia, and 1 (1%) patient had a myocardial bridge over left anterior descending artery (LAD). Among the patients with significant CAD, the prevalence rate of one, two and three vessel disease was 54 (51.9%), 22 (21.2%) and 11 (10.6%) respectively. Almost 50% of the lesions occurred in LAD followed by 25% in RCA and 20% in circumflex, while only one patient (1%) had isolated significant CAD of left main coronary artery. Osteal segments were involved in 10%, proximal in 61%, mid in 21% and distal segments in 7% of the lesions. **Conclusion:** In the younger age group, CAD is mostly a disease of men, single vessel CAD predominates with LAD involvement mostly, predominant osteal to proximal segment involvement of vessels, and a much higher incidence of normal coronaries and non-obstructive CAD is met with.

Keywords: Coronary Artery Disease (CAD), Myocardial infarction (MI), Coronary Angiography, Risk Factors

INTRODUCTION

In the year 2000, cardiovascular diseases (CVDs) accounted for 16.7 million deaths globally.[1] Two thirds of CVD mortality arises from developing countries with a rapid rise expected towards 2020. South Asians are reported to have one of the highest rates of coronary artery disease (CAD),[2] and it is therefore unsurprising that CAD is now the leading cause of death in the Indo-Pak subcontinent.[3] Alarmingly, an earlier age incidence of CAD is not infrequently encountered in the South-Asian population.[3–9] It is a topic of increasing clinical interest due to the potential for premature death and long-term disability. Numerous studies have been carried out in the past aiming to discover the etiopathogenesis, clinical profile, management and prognosis of coronary artery disease in the younger population, yet many aspects are undiscovered.[10–19]

We, therefore, chose to investigate whether or not the pattern of coronary arterial involvement in the younger patients who have CAD under the age of 35 years in our population, is of a similar fashion as in the older patients we commonly come across. The purpose of this multi-institutional study was to investigate the phenomenon of CAD among young patients in a general population. The analysis was sought to identify the anatomic characteristics of the coronary arterial disease pattern, as defined by coronary angiography, using a prospective protocol, so as to determine the anticipated difficulty in revascularization, with particular reference to percutaneous intervention (PCI).

MATERIAL AND METHODS

This was a descriptive cross-sectional study carried out in all the 3 tertiary care hospitals of Peshawar (i.e., Hayatabad Medical Complex, Lady Reading Hospital, and Khyber Teaching Hospital). All patients, of both genders with age lesser than 35 years, admitted into the

cardiology units of these three hospitals with the diagnosis of CAD (unstable angina, stable angina, STEMI or non-STEMI) were enrolled. Between June 2008 and December 2009, a total of 132 patients were entered into the registry. Only patients with no evidence of traditional risk factors for CAD (i.e., hypertension, diabetes mellitus, smoking, positive family history, hyperlipidemia, obesity) formed the basis of the present analysis. After a prior informed consent, they were subjected to coronary angiography at Cardiac Cath Lab in Lady Reading Hospital, Peshawar.

Conventional coronary angiography was performed via right femoral or right radial artery approach using 5F or 6F Judkins catheters according to the local standard protocol. Coronary angiograms were visually assessed by two independent observers (cardiologists) blinded to the identity and clinical characteristics of the patients. Significant lesions (>50% diameter reduction) were described in a single angiographic view at the end-diastole, in which the lesion appeared most severe. The severity of stenosis was defined as the maximum percentage narrowing calculated from the minimum diameter of the involved segment and the diameter of an adjacent normal coronary segment in a single projection, which was as perpendicular as possible to the axis of the radiographic beam.[13] Prior approval for conducting the study was sought from the local ethical committee of Hayatabad Medical Complex, Peshawar.

Data so obtained was entered into and analyzed using SPSS version 15 software. The data has been presented as mean with standard deviation for the continuous variable, i.e., age. Frequency and percentages were calculated for the categorical data such as the gender, the number of vessels and the site involved.

RESULTS

The study Algorithm has been shown in Figure-1.

Mean age of the patients was 32.66±3.237 years (range 22–35 years). Eighty-five patients (81.73%) were male, while 19 (18.27%) were female. Mean age of male patients was 32.52±0.367, while that of female was 33.32±0.557. There were 6 patients in the age group below 25 years, 21 patients between 26 and 30 years, and 77 patients 31 years and older.

As revealed by the coronary angiography, there were 17 (16.3%) patients with non-atherosclerotic coronary arteries. Significant CAD was found in 87 (83.7%) patients, the pattern of distribution of which is shown in Figre-2 and Table-1.

Of all the total 131 lesions found in these patients, 14 (10.68%) lesions occurred in the osteal segment, 80 (61.06%) in the proximal, 28 (21.37%) in the mid, and 9 (6.87%) in the distal segment.

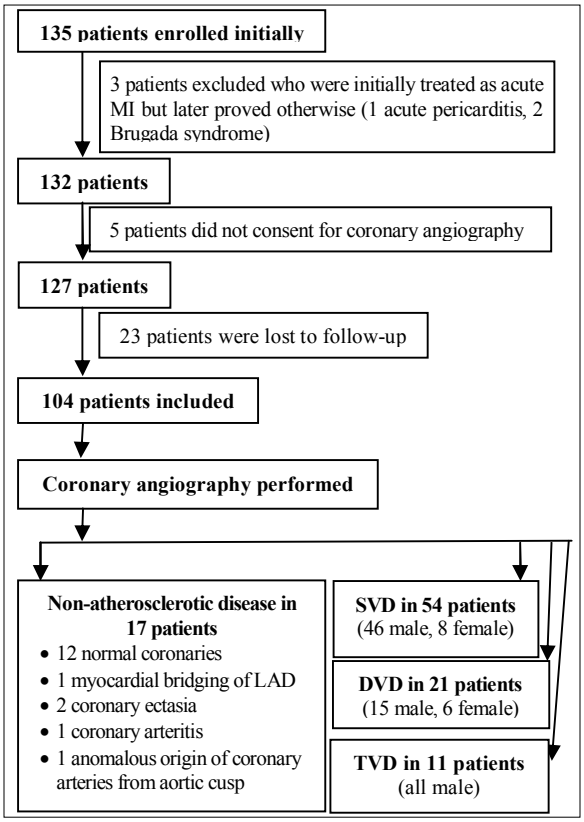

Figure-1: Algorithm of the study

Figure-2: Frequency of the diseased vessels among all study patients gender-wise

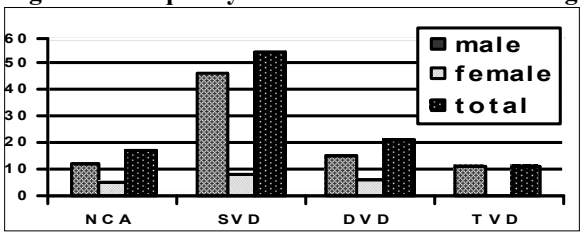

Table-1: Involvement of major epicardial vessels

Name of vessel(s)	Number (n=104)	Frequency (%)
Normal coronary arteries	17	16.3
LMS	1	0.96
LAD	36	34.61
RCA	11	10.57
LCx	7	6.7
LAD + LCx	9	8.6
LAD + RCA	9	8.6
LCx + RCA	2	1.9
LAD + RI	1	0.96
LAD + RCA + LCx	9	8.6
LAD + RCA + RI	1	0.96
LMS + LAD + LCx + RCA	1	0.96
Total	**104**	**100.0**

LMS: left main stem artery, LAD: left anterior descending artery, CIRC: left circumflex artery, RCA: right coronary artery, RI: ramus intermedius artery, NCA: normal coronary arteries

Non-atherosclerotic disease was found in 17 (16.3%) patients on the whole. Of these, 12 (11.53%) had angiographically normal coronaries. These included 12 male (14.11% of the total male patients) and 5 female (26.31% of the total female patients). Among the other 6 patients with non-atherosclerotic disease, 1 (1%) patient had anomalous origin of RCA, 1 (1%) patient had coronary arteritis, 2 (1.92%) patients had coronary artery ectasia, and 1 (1%) patient had a myocardial bridge over LAD.

DISCUSSION

The steady increase of mortality due to coronary artery disease in the 1940's and 1950's was followed by a declining trend in the United States, Australia, and several European countries since the late 1960's. This was attributed to the increasing awareness among the population about the modification of risk factors. However, during this period, a disturbing shift of coronary mortality towards younger age group and a diminishing male/female ratio was observed.[20,21] An increasing trend of smoking, cocaine abuse and unhealthy dietary habits, caused an increase in the prevalence of CAD among the younger ones, while in females an increasing trend of use of OCPs contributed even further to CAD in a younger age group.

The 104 patients we studied prospectively revealed that CAD was predominant in young men (82%); women represented 18% of our series. But this was surprisingly one of the highest percentages of females reported yet. Previously, it has been reported as low as 3% by Al-Khadra[5] in Saudi Arabia, 5% by Siwach[7] in India, 6% by Fournier[12] in Spain, 7% by Rumboldt[19] in Croatia, 9% by Wolfe[16] in Kansas, 11% was reported by Cole[10] in Georgia, 13% by Ahmed[4] in Punjab, to as high as 19% by Kanitz[13] and 25% by Doughty[11] in Michigan. However, in most of these studies, the age group under study was up to 40 to 45 years of age, while our study included patients who were 35 years and lesser of age. Wolfe *et al*[16], however, studied patients under 35 years of age, but they reported a female frequency of only 9%. This implies that in our population, a very high percentage of females have CAD in a younger age, as also previously reported by Khan *et al*[20] in the same population in 2006. In our society where smoking, cocaine use, or OCPs use is very infrequent in women; other factors like coronary vasospasm, coronary artery dissection, and coronary artery occlusion resulting from hypercoagulable states, or vasculitis are more likely to be implicated.[20,22]

The distribution of lesions in our patients, with a high incidence of normal coronary arteries and single vessel disease, is in accordance with previous studies as is the paucity of patients with left main coronary artery disease.[9,12–16] In these studies, normal coronary arteries ranged from 10% to 20%, SVD from 36% to 62%, DVD from 17% to 36%, and TVD from 6% to 15%. LMS was found diseased in approximately 2% of our patients, similar to a frequency of 2% and 2.8% LMS disease as reported by Fournier *et al*[12] and Wolfe *et al*.[16]

Most studies have shown LAD to be the vessel most commonly involved,[15–17] in agreement with our study showing the predilection for LAD followed by RCA. The LCx was the least involved artery. Some of the previous studies have disagreed with regard to this point. In the population of young patients studied by Fournier *et al*[12] and Kanitz *et al*[13], RCA disease was most commonly observed, while other studies[14] revealed even distribution of coronary arterial involvement.

When we study the pattern of coronary arterial involvement of our study patients, we come across a very high frequency (11%) of angiographically normal coronary arteries. This important finding of our study conforms with the previous prospective and retrospective analyses[4,5,10–17] of patients <35 years old having described angiographically normal coronary arteries in 9% to 17%. Studies of young women <45 to 50 years old have described angiographically normal coronary arteries in 7% to 32%.[22–25] The actual prevalence of angiographically normal coronary arteries with myocardial infarction has been difficult to determine because some reports have included patients with up to 50% coronary stenosis as well as those free of lumen narrowing. Others have distinguished patients with moderate disease from those with angiographically normal arteries. Possible mechanisms include coronary vasospasm, coronary embolism from the heart endocardium or valves, platelet aggregation, spontaneous lysis of a coronary thrombus, and angiographically indiscernible coronary lesions. Moreover, there is a possibility that the real incidence can be influenced by thrombolysis which was not taken into account in our study. Normal coronary arteries have been demonstrated after resolution of coronary thrombosis subsequent to lytic treatment.[26]

Despite the rather compelling body of evidence that the evaluation of patients after an cute coronary event should be based on non-invasive studies, the evaluation of the young patient after myocardial infarction is controversial and generally geared towards invasive evaluation by cardiac catheterisation, regardless of left ventricular function or ischemic threshold, for 'prognostic' reasons. Kapoor's[27] review reached the following conclusion: 'coronary angiography is highly effective in

demonstrating a prognostic spectrum of coronary artery disease even in asymptomatic young patients after infarction'. Warren *et al*[18] believed that cardiac catheterisation of the patient suffering myocardial infarction before the age of 36 years was indicated in all patients secondary to the fact that these investigators found a significant number of patients with normal coronary arteries (13%) and congenital coronary arterial anomalies (4%).

We suggest that features suggestive of CAD should always be taken seriously not just in younger males but also females. Also, we should bear in our mind the possibility of the conditions which mimic acute MI in their clinical presentation like Brugada Syndrome, acute pericarditis, acute myocarditis.[28] Overlooking acute MI in a young patient or taking some other condition as acute MI can bear serious consequences in a young individual. We strongly suggest that coronary angiography ought to be mandatory for any young patient sustaining acute coronary event, keeping in view the predilection for the involvement of proximal LAD segment. A particular challenge remains for the clinician in the management of the young patient with CAD who anticipates a life expectancy measured in decades rather than years.

STUDY LIMITATIONS

Our study has certain limitations. There was no control group of older patients; comparison was therefore not possible except by historical references. Some of the patients did not consent to the angiographic procedure, while others were lost to follow-up, which could have influenced our results. Also, the patients who reach hospital are by definition 'survivals'. Therefore, our study population might not be a true representative of the population. Assessment of percent diameter stenosis was visual in which could have been subject to inter-observer bias. Utilization of thrombolytic therapy could have potentially affected our results as far as the higher incidence of normal coronary arteries is concerned.

CONCLUSIONS

We found that very young (age <35 years) patients who have CAD, have less extensive coronary artery disease, with a high incidence of angiographically normal vessels and relative paucity of left main coronary arterial involvement. CAD is also quite prevalent in the female population in a younger young. The diagnosis of CAD must not to be over-looked by the patients' young age. Also, conditions which mimic acute MI (Brugada syndrome, pericarditis, myocarditis) should be kept in mind in young patients presenting with features suggestive of acute MI.

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