Air Marshal Subroto Mukherjee Oration

Ischaemic Heart Disease - The Symptoms, Diagnosis and Management

Dr. M. Khalilullah

Chief of Air Staff, Air Chief Marshal DA La Fontaine, Lt Gen K.D. Kapur, Director General Armed Forces Medical Services, Ladies and Gentlemen :

I feel greatly honoured and privileged to have been invited as guest speaker of 30th Meeting of Indian Society of Aerospace Medicine. I am indeed extremely grateful to Air Marshal S.K. Bhalla DGMS(Air), the President of the Society and other members of the Society for having invited me. I am fully aware of the philosophy of late Air Chief Subroto Mukerjee for his care and concern for the Staff of Indian Air Force. Therefore, I have chosen this topic which I feel will be befitting to the memory of late Air Marshal Subroto Mukerjee. During the course of next 50 minutes or so, the task before me is to present a brief bird's eye view on the recent trend on diagnosis and management of IHD and silent myocardial ischaemia.

Customary evaluations in the IHD are consideration of symptoms, assessment of risk factors and diagnostic tests which provoke myocardial ischaemia, evaluation of ventricular functions and visualisation of coronary arteries. With advent of improved optics and superb technique available in the hands of experts, it has been possible to do coronary angiography with negligible morbidity and mortality.

Technique of evaluation of IHD consists of assessment of electrical alteration which include stress electrocardiography, ambulatory monitoring, perfusion scintigram using Thallium 201, contractile function of the heart assessed by exercise echocardiography and recently introduced radio-nucleide vest, which is similar to ambulatory electrocardiography but tests the ambulatory ventricular function rather than the electrical signal of the heart. Metabolic function can be assessed by Catscan using FOG (Fluride Oxy Glucon) to see degree of perfusion and ischaemia operating in a particular individual. Anatomy of the coronary arteries can be seen by coronary angiography. In addition to this, coronary angioscopy can be used to visualise lumen of the coronary arteries directly on the table just like endoscopy of the gastrointestinal tract.

Ventricular perfusion can be studied by myocardial perfusion scintigraphy which show the sequence of patho-physiological changes during myocardial ischaemia by selective reduction in perfusion at ischaemic sites leading to anaerobic metabolism.

The exercise electrocardiography begins with legendary Master's Two Step Test, unfortunately of very low sensitivity because of very low workload involved especially if persons of the Armed Forces are being evaluated. The sensitivity of treadmill test has now increased to 70 to 85%. Interpretation of the treadmill test, however, depends on various theorems. It is considered that if an individual's pre test likelihood of IHD is 10% and if the treadmill test is positive in his case, the likelihood of coronary Artery disease in him may be upto 18% whereas if the pre test likelihood of IHD is 80%, a positive treadmill test augers of confirmation of IHD in almost upto 90 to 95% and a negative test lowers the chance of disease to 60%. Done with adequate care and precaution and in presence of medical personnel, the chances of misadventure in treadmill testing is very little, there being not a single mortality in our

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set-up where over 6000 treadmill tests have been done during a period of 9 years.

The response of an asymptomatic individual to stress test has a fractional value of only about 20% as obtained from our pooled data of 6000 tests. Relative risk of developing coronary artery disease in future in these 20% cases is 5 to 10 times higher as compared to the normal population.

Most commonly employed sequence is to repeat stress electrocardiography with Thallium 201 study following a positive stress test. An individual with a pre-test diagnosis of IHD with 20% possibility would have about 45% to 50% possibility of IHD following positive stress test and as high as 90% likelihood of IHD if his Thallium 201 study is also positive. In our study of 191 cases who showed abnormality in treadmill test, 14% had coronary artery disease when the Thallium study was negative but 74% had coronary artery disease in those with Thallium 201 positive report.

ECG stress test in asymptomatic individuals especially those whose occupation concern the safety of public, those with high lipid profile and those with equivocal test, therefore, should be subjected to Thallium 201 scintigraphy. Persons showing normal Thallium study should be cleared and returned to their duties whereas those with gross abnormality should be evaluated with coronary angiography.

It is also necessary to mention that asymptomatic individuals with positive stress test who have high abnormal lipid profile stand far greater risk of CAD as compared to others. In a primary prevention trial, 3806 men had high serum cholesterol; out of which 2299 had abnormal stress test. The ten year follow-up in these men showed 5 times higher death rate in the subjects with high cholesterol and positive stress test.

Early post-infarction exercise stress testing especially in persons of Army, Navy and Air Force is a matter of concern because the authorities would like to find out whether residual angina /ischemia still persists, whether there is any objective variation in ischaemia and what would be the long term progress. If the post-infarction stress test shows no ST depression of significance, the one year mortality rate is only 2.1% but this rises to 27% if the ST segment shows ischaemic depression. Such cases with positive stress test, therefore, must be taken up for coronary angiography to evaluate the coronary arterial anatomy for further treatment as the one year mortality in them is 10 times more than those with stress test negative.

Those post-infarction subjects who show positive stress test have almost invariably multivessel disease (81%) and more than half of them have triple vessel disease. It should also be emphasised that these post infarction subjects who show ischaemic ST depression at a lower heart rate (less than 70% of age predicted maximal heart rate) have more chances of left main disease or a triple vessel disease.

A pharmacological method of stress testing is available especially for those who are unfit for carrying out the exercise on medical, neurological or orthopedic grounds. Such subjects can be given Dipyridemole orally or IV. This drug causes maximal coronary vaso-dilatation allowing maximal blood flow in the normal myocardium and producing a relative ischaemia in the narrowed coronary artery zone. This ischaemic zone gets further augmentation of ischaemia and unmasks the latent ischaemic heart disease in ECG.

Exercise echocardiography has also been introduced where 2D and M Mode cardiac evaluation and left ventricular function study can be simultaneously done in an individual performing supine bicycle ergometry exercise or upright TM exercise. By this both the ventricles can be studied, detection of regional wall motion abnormality can be made and global ejection fraction can also be ascertained. It is a non-invasive, easy, repetitive and reproducible

test and results can be comparable to stress testing with radionucleide studies.

Ambulatory Holter monitoring electrocardiography, especially the modern equipment with advanced two channel continuous recording for 24 to 48 hours, holds a great promise for evaluation of IHD in our country. Holter monitoring for ST segment analysis must satisfy the technical requirements for providing isoelectric base line recordings without any artefact.

Ambulatory monitoring has the advantage over treadmill exercise in recording the ischaemic response to an anginal attack at any time, occurence of variant angina, nocturnal chest discomfort, emotion-precipitated chest pain or silent ischaemia. The sensitivity of treadmill test and Holter monitoring is ranged between 67 to 80% and 62 to 78% respectively, whereas the specificity ranges between 61 to 82% and 75 to 88% respectively. Thus Holter monitoring is shade less informative than TM test but has the advantage of picking up ischaemia which is not reproducible in the stress laboratory.

Exercise radionucleide imaging is a better technique and more informative than stress test alone. The techniques used for diagnosis of coronary artery disease are myocardial perfusion imaging with Thallium 201 and radionucleide angiography using Technetium. Indications for use of these isotope studies are evaluation of patients with left main artery block, patients on digoxin where electrocardiographic evaluation is faulty as patients are not able to attain any increase in heart rate in the first instance and ST segment is already modified by digitalis effect. Exercise radionucleide imaging is also helpful in confirming the diagnosis following positive stress test, in prognostication of already existing IHD and for study of progress following drug therapy, balloon angioplasty or coronary bypass surgery. 1.5 to 2 millicurrie of the isotope is injected during exercise and post exercise imagings are obtained at 10 min, 1 hour and 2½ hours in lateral view and 45 degree to 75 degree LOA. Delayed imaging is taken for differentiating between scar and ischaemia. Normal Thallium imaging has homogeneous distribution of radio-activity within the left ventricular myocardium with decreased activity in the central zone. Perfusion defect present at rest or redistribution phase suggest a previous myocardial infarction.

Radionucleide angiography can be useful in assessment of left ventricular ejection fraction and regional wall motions. This can be carried out in both fast paced and equilibrium rated exercises and the sensitivity and specificity are same as Thallium scintigraphy.

Cardiac vest is the recent innovation in the diagnostic armamentarium for IHD. This is like continuous 24-48 hours Holter monitoring with the difference that it records the ejection fraction of left ventricle at period of stress and strain instead of recording the electrocardiogram.

Coronary angiography is used as an invasive procedure to study the anatomy of coronary circulation. The latest procedure, rather an improvement on coronary angiography, is coronary angioscopy. This is still in the initial stage of clinical application. This has certainly added advantage over coronary angiography as the investigator can directly see and study the degree of obstruction and nature of thrombus/ plaque. It has been recently demonstrated that patients with unstable angina usually have complex plaques blocking the coronary artery which could not be imaged by coronary angiography but could only the visualised and recognised by angioscopy. Coronary angioscope consists of a fibro-optic fiber 0.9 mm in diameter which can be put inside a catheter and pushed into the coronary artery for direct visualisation as well as photography.

Management of ischamic heart disease includes risk factor modification like lowering of lipid level, control of diet, physical exercise and secondary prevention of myocardial infarction with

anticoagulants, anti-platelet aggregants anti-arrhythmic drugs, thrombolytic therapy and betablockers. Coronary angioplasty and coronary bypass graft surgery are interventional and surgical techniques.

Various agents have been used to lower the serum lipid levels in subjects with myocardial infarction. Six trials covering 10000 patients with follow up of 36 to 60 months, however, have revealed no statistically significant difference in re-infarction between the group with treatment and controls. Thus there is no role of lipid lowering agents. Physical exercise has also been studied in 3052 patients with a follow up of 12 to 48 months and results do not show any significant difference between the group. Oral anticoagulant therapy studied in five different trials covering 2246 patients with follow up of 24 to 36 months showed no significant difference in mortality between the group with treatment and the control.

Three different platelet active drugs viz. Aspirin, Dipyridemole and Sulphinpyrezone have been used in 8 different studies covering 1400 patients with a follow up of 12 to 41 months. Only Aspirin showed a favourable trend but this also did not reach to a level of statistical significance. The trial using the two other drugs show no improvement in the treated group as compared to control. Antiarrhythmic agents studied in 1675 patients followed up upto 6 to 12 months also have shown no significant difference in morbidity and mortality in the treated group and controls. Betablockers alone have shown significant improvement in the morbidity and mortality. Four different series covering 560 to 3837 patients and using practolol and propranolol have brought out this important fact. Thus it can be said that secondary prophylaxis of myocardial infarction can be achieved with any degree of statistical significance by administration of betablockers only. Almost 75% of all patients with myocardial infarction can benefit by betablockers. Whereas other pharmacological agents do not improve survival.

Thrombolytic therapy in acute ,stage of infarction holds promise. Injection of streptokinase in a dose of 2000 to 4000 IU per Kg of body weight given by the coronary route has shown dramatic response with relief of pain and rapid return of ST elevation to base line. Reperfusion rate of IV streptokinase therapy ranges between 39 to 96%. Coronary angiograms done after 60 minutes to 90 minutes in 5 different series have shown the recanalisation rate between 44-62%. However, our studies have shown that if coronary angiogram is done after 2 to 2½ hours of streptokinase administration, almost 100% subjects show recanalisation. The disadvantage of intracoronary thrombolytic therapy is the fact that a cardiac cath lab must be available and the administration of streptokinase through catheter must be done as early as possible following the onset of pain.

The pooled data of streptokinase therapy has shown 90% reduction in mortality within six weeks of infarction. However one year follow up does not show any significant difference in mortality in either IV or intracoronary streptokinase therapy as compared to controls.

The procedure of streptokinase therapy followed by us is as follows : IV Corticosteroid administration followed by baseline coronary angiography in the cardiac cath lab as early as possible, IV streptokinase 5 lac units over a period of 30 minutes and repeat angiogram at 15 to 30 minutes intervals till 2½ hours are elapsed. We have found that out of 110 patients treated with streptokinase, 92% showed recanalisation, whereas only 18.5% of untreated cases (30 subjects) showed recanalisation. Ejection fraction in the treated group was 59% whereas that in the untreated group was 42%. Streptokinase therapy should be given within 4 hours, preferably within 2 hours of onset of pain, to get best results.

Coronary Artery Bypass Graft (CABG) surgery is extremely effective in the treatment of IHD. It provides symptomatic relief and increased longevity. The indication of coronary artery

bypass surgery are (1) stable angina refractory to medical treatment (2) disabling angina (3) high risk professional subjects like fliers (4) failure of thrombolytic therapy (5) acute MI during coronary angiography (6) acute MI with cardiogenic shock (7) patients with myocardial infarction and recurrent anginal attacks and (8) failure of PTCA (Percutaneous Transluminal Coronary Angioplasty).

CABG is also indicated in cases with proximal left main disease, triple vessel disease, and in subjects with myocardial infarction associated with LV dysfunction and cardiac failure. CABG should not be recommended in all those cases with single vessel disease who show relief with medical therapy.

Coronary Angioplasty (PTCA) is a very useful technique for recanalisation of coronary artery. The procedure followed is to introduce a balloon catheter with guide-wire to rotate and approach the obstruction in the affected coronary artery. Using an inflator, the balloon is inflated upto 4 to 6, even upto 10 atmospheric pressure and pushed into the stenosed segment of the artery. The atheromatous plaque ruptures and is thrown out resulting in recanalisation of the vessel. Fresh angina preferably of less than three months old, especially in younger individuals, gives best results following PTCA. Single vessel disease is ideal for PTCA, but two vessel and three vessel disease with multiple obstructions may also be subjected to PTCA when only the main affected artery may be dilated. Ostial and left main disease are not yet amenable for dilatation. Re-stenosis of the dilated artery has been reported between 17% to 47% cases.

Follow up assessment of PTCA therapy include (1) clinical evaluation (2) Stress testing (3) Thallium study (4) Radionucleide cineangiography and (5) coronary angiography.

Laser has been a recent addition to the recanalisation of coronary artery in IHD. A fibro-optic catheter is introduced for visualisation of the plaque and the laser energy is delivered to vaporise the plaque and recanalise the blocked coronary artery.

Silent myocardial infarction is an area of tremendous importance to Air Force Personnel. It can be defined as electrocardiographic evidence of myocardial ischaemia in absence of symptoms including chest pain. Spectrum of this entity includes (1) silent myocardial infarction (2) asymptomatic post infarction angina (3) positive stress test without symptoms (4) asymptomatic ischaemia detected by Holter monitoring and (5) evidence of coronary artery lesions in patients without any symptoms - detected by coronary angiography.

The abnormal ECG patterns in silent ischaemia include (1) ST depression (2) ST elevation (occasionally) and (3) T wave inversion.

Silent ischaemia can be classified into the following types :

(1) Type I - Totally asymptomatic stage. Personnel of Air Force, Army and Navy may belong to this type.

(2) Type II - Asymptomatic patients following myocardial infarction.

(3) Type III - Patients with typical angina but periods of intermittent silent ischaemia as detectèd by Holter monitoring.

The mechanisms of silent ischaemia are (1) It is a less severe ischaemia not enough to reach pain threshold (Type I and Type II) and (2) Difference in pain perception threshold or central termination of painful stimuli.

Silent ischaemia picked up by Holter monitoring is different from that detected during stress test, because most of the time Holter monitoring picks it up at relatively lower heart rate, often in sedentary conditions and many times in a day.

Silent ischaemia can be picked up in 45% patients by treadmill exercise, in 75% of cases during Holter recording and in as high as 80% of patients in hospital bedside monitoring. The average heart rates for detection of this type of ischaemia in our series are 122± 16 BPM by stress test and 97± 19 BPM during Holter recording.

Thus silent ischaemia occurs usually at much lower heart rates both in Holter recording and TM exercise as compared to painful ischaemia which occurs at higher heart rate.

In management of silent ischaemia, (1) one should establish the diagnosis of both silent as much as manifest ischaemia; (2) extent of silent ischaemia should be assessed with stress test and Holter recording; (3) goals of management is to abolish all ischaemia either silent or painful by medical treatment and if necessary by PTCA of CABG. Trials of nitrate, betablockers and calcium antagonists are very useful in the medical management of silent ischaemia.

Investigative approach should include coronary angiography in all cases of silent ischaemia as in our experience this investigation may be negative in as high 64% of cases who could thus be bailed out and cleared of IHD. Air Force pilots with this diagnosis will benefit and return to full flying once the coronary angiography is normal. As the Chief of Air Staff had said the aim should be to find out "the truth behind the game". Some of these patients may have abnormality in the left ventriculogram. Metabolic requirement of the myocardium of these patients may be too high and abnormal and therefore the ECG is abnormal without any abnormality in the coronary arteries. The prognosis in these cases is excellent, three year follow up showing less than one per cent mortality.

We have studied 50 officers from the Armed Forces, all of whom were asymptomatic and had ECG abnormality as positive exercise test. Coronary Angiogram showed only 36% had significant disease; 18% had single vessel disease, 14% had 2 vessel disease and only 4% had triple vessel disease, suggesting that only 4% to 18% had significant coronary artery disease. It is also emphasised that these 4% to 18% patients with disease could be salvaged by intervention therapy and prevented from getting major attack.

In our study, silent ischaemia has been detected at an average heart rate of 80 BPM by Holter monitoring. 50% of the cases detected had the ischaemia at resting condition and the rest during the day-to-day activity. Coronary angiogram carried out in these cases showed triple vessel disease in 19%, two vessel disease in 32% and single vessel disease in 7% cases. Thus unlike Armed Forces Personnel, our patients who had established CAD showed a higher percentage of positivity following angiography.

I had given a bird's eye view of what we have at the moment in the diagnosis and management of IHD. I think the answer to the problem in the individuals in Armed Forces is wide open. We know that the disease in the Forces occurs in a very small fraction of persons. Therefore large number of them can be sent back to flying or can go back to active services. Some who have the disease need certain intervention. A part of the study needs extrapolation by doing ventricular function and also metabolism of the myocardium to find out why do we get ST segment changes in these subjects, whether the myocardium is demanding more oxygen than normal to produce a relative ischaemia in a situation of normal coronary flow. This has to be found out in the study I propose to carry out with the help of people in your own Force.