AVIATION MEDICINE VOLUME 27 NUMBER 2 1983

AIR MARSHAL SUBROTO MUKERJEE ORATION—1983

Recent Advances in Diagnostic Techniques in Cardiology

M L BHATIA

I am delighted to join the proceedings of the 25th annual conference of the Aero Medical Society of India and am privileged to be asked to deliver the Subroto Mukerjee Oration for the year.

Air Marshal Mukerjee was the first Indian to become the Chief of the Air Staff of the Indian Air Force after independence. He was keenly interested in the Air Force Medical Services and laid its firm foundations as an organisation to cater to the special needs of the Indian Air Force. The Institute of Aviation Medicine, which is the first of its kind in Asia came into existence because of his farsightedness, patronage and support.

Air Marshal Mukerjee was the first patron of the Aero Medical Society of India when it was formed in 1952 and remained so for the next several years till his untimely demise in 1960. He had taken a very keen and active interest in its development and activities during its formative years. As a mark of its gratitude and appreciation the Aero Medical Society of India instituted, in 1971, an oration named after him, to be delivered during its annual meeting. Since then eleven medical scientists from India and abroad have delivered the oration on subjects of importance to medical scientists in general and the members of the Aero Medical Society in particular. I am privileged to be the twelfth such speaker.

The subject of my discussion is "Recent advances in diagnostic techniques in cardiology". The last three decades have seen phenomenal advances in various fields of scientific thought and action and many ideas considered fictional not many years ago are now a matter of daily practice. Medical sciences have also kept pace with these advances and spectacular advances have taken place on all fronts, conceptional, diagnostic and therapeutic. Progress in cardiovascular medicine and surgery has been specially phenomenal and far reaching; more than perhaps in any other related field. These improvements reflect the needs and capabilities of the present times.

Advances in diagnostic techniques

The most important advance in cardiovascular practice in the past quarter century has been the development of catheterisation of the human heart which is now a matter of routine and undertaken with relative ease and patient safety. it is difficult to imagine what the study of cardiovascular disease would have been today if we had to analyse the problem without the enormous anatomic and physiological knowledge derived by cardiac catheterisation during these years. Dr Andre Cournand who received the Nobel prize in Medicine for his efforts in this field remarked in his Nobel lecture that "the cardiac catheterisation was.................. the key to the lock". By turning the key Cournand and his associates and others who followed him in later years led us into an era of understanding of the normal and abnormal circulatory dynamics. The fifties and sixties witnessed an improvement in the invasive method of cardiovascular diagnosis with better instrumentation, newer techniques and routine use of selective angiography. In recent years invasive investigation has advanced further specially in the fields of investigating ischaemic heart disease by selective coronary angiography and the development of techniques of bedside haemodynamic studies using balloon floatation catheter for pressure measurement and thermal dilution techniques for estimating blood flow. The immense contributions of these two newer methods for an intelligent and precise evaluation and management of seriously sick cardiac patients are well known today.

While the fifties and sixties witnessed advancement of invasive technologies of cardiovascular investigation, non-invasive techniques of investigation have come to the fore front in the seventies and early eighties and will continue to dominate the field in the future also. Non-invasive techniques have the advantage of being without any morbidity or mortality, are generally repeatable and therefore preferred both by the patient and the investigator as an initial investigation as well as to render long term follow up easier and acceptable. Since most of these methods have been validated against more direct and precise data obtained by cardiac catheterisation and angiography as well as at surgery or at autopsy, their sensitivity and specificity are generally well known thereby allowing the physician to give value judgement and appropriate importance to the data so obtained.

Several groups ot non-invasive techniques are presently practised. These are :

(1) Electrophysiological techniques :

- (a) Electrocardiography
  - (i) Resting
  - (ii) Ambulatory (dynamic)
  - (iii) Stress testing
- (b) Electrophysiology

  Non-invasive recording of His bundle potentials

(2) Graphic techniques :

- (a) Systolic time intervals
- (b) Apex cardiography
- (c) Cardio kymography
- (d) Phonocardiography
- (e) Transthoracic impedance plethysmography

(3) (a) Echocardiography

  - (i) 'M' Mode
  - (ii) Two dimensional realtime studies

- (b) Doppler studies

(4) Radionuclide studies

- (a) Radionuclide ventriculography
- (b) Infarct imaging technique.
- (c) Perfusion scanning
- (d) Others

(5) X-ray imaging techniques

- (a) Dynamic contrast imaging
- (b) Dynamic spatial reconstruction
- (c) Nuclear magnetic resonance

(6) Laboratory studies

(a) Serum enzymes

(b) Serum lipids and lipid transfer and mechanics

(c) Serum levels of drugs etc.

(d) Special studies eg. renin assays etc.

In the next part of my talk I will not discuss invasive technique but will highlight some of the non-invasive techniques available for and used in current cardiac practice and perhaps of special importance to the present audience.

Ambulatory ECG monitoring

Since its introduction by Holter in 1957 ambulatory ECG monitoring over extended periods of time has rapidly become a widely applied clinical tool. The fundamental principle of the method is a *continuous recording* of ECG information for playback at a later date. It thus differs from continuous ECG monitoring which provides immediate on line display of cardiac rhythm as for example seen in the intensive care areas or in the exercise laboratories.

The components of an ambulatory system include: (a) recorders (b) scanners and (c) data analyser and recorder. The clinical indications for ambulatory monitoring are :—

(a) *Diagnosis :*

Suspected cardiac arrhythmias

Bradyarrhythmias/tachyarrhythmias

Transient myocardial ischaemia

(b) *Evaluation :*

Drug efficacy / safety

Pacemaker function

Post myocardial infarction arrhythmias and for ischaemia.

The following cardiac diagnoses suggest the need for ambulatory monitoring :

(i) Myocardial ischaemia (Angina/MI) with PVCs noted on the ECG or by stress testing.

(ii) Mitral valve prolapse with history of syncope or with prolonged QT interval.

(iii) Prolonged 'QT' syndrome.

(iv) Cardiomyopathy

(v) History of primary ventricular fibrillation

(vi) Pre-excitation syndrome

(vii) Valvular heart disease with symptoms of palpitation and syncope.

Ambulatory ECG monitoring may also be useful for specific symptoms like :

(i) Palpitations

(ii) Dizziness and/or syncope

(iii) Transient ischaemic attacks

(iv) Completed stroke

(v) Seizure disorders.

Interesting results from ambulatory monitoring of 'normal' individuals have been observed and may be of interest to the present audience. Some of these studies are tabulated here :

Author	No of subjects	Age (Years) average	PVC Single	PVC Multiple	PVC Complex	PVC V.Tachycardia
Gilson	37	40	—	—	5	—
Brodsky	50	23-27*	50	2	4	—
Hinkle	283	55	62	9	54	3
Glasser	13	69	all	15	31	—

*(Medical students)

These studies in normal, symptom-free patients demonstrate that :

(a) Infrequent PVCs are common. Frequent PVCs are uncommon, specially in the young.

(b) Frequency and complexity of PVCs increase with age. This may represent an effect of advancing age or be a manifestation of subclinical heart disease.

The finding of a frequent or complex ventricular ectopic activity does not necessarily indicate the presence of significant IHD. Kennedy and associates who evaluated these patients by coronary arteriography reported that in 25 patients in whom these were recorded, the coronary arteries were normal in 14, had minor insignificant disease in 5 and significant disease in only 6 patients. It would thus appear that a majority of apparently healthy subjects with frequent and complex ventricular ectopic activity do not have subclinical IHD and therefore a conservative management is indicated.

Exercise stress testing

Since physical exercise stresses the heart to utilise its reserve capacity it is a useful mechanism of objective evaluation of the heart's performance and specially for delineating any latent problems.

Regular physical exercise increases total body fitness as measured by oxygen uptake at maximum exercise or VO_2 max. This results from improvement in cardiac factors (like an increase in cardiac output) and peripheral factors (i.e., increased peripheral extraction of oxygen with a widened A-VO_2 difference) as highlighted below.

(a) *Cardiac mechanisms :*

Increased cardiac output

Increased stroke volume.

Increased venous return

Increased myocardial contractility.

Reduced heart rate at rest and at any given workload.

(b) *Peripheral mechanism* :

Reduced systemic vascular resistance.

Increased capacity for aerobic metabolism.

Since stress testing is specially useful for evaluation of patients with ischaemic heart disease (IHD) factors governing myocardial oxygen consumption and coronary blood flow should be appreciated. These are :

Principal determinants of myocardial oxygen consumption (MVO_2) :

Heart rate

Myocardial contractility

Ventricular wall tension

Peak ventricular systolic pressure

Ventricular volume.

Determinants of coronary blood flow :

Coronary perfusion pressure

Coronary vascular resistance (auto regulated)

Myocardial oxygen tension (dependent on MVO_2)

The use of exercise to evaluate patients with suspected IHD dates back to over 50 years. The test has evolved over the years and most recently treadmill testing or bicycle exercise have been used to provide standardised, strenuous and regulated exercise. Exercise protocols requiring leg muscle activity are preferred. Graded multistage protocols are commonly used with gradually increasing workloads at 2 to 3 minutes intervals, the most common such protocols being those reported by Bruce or Ellestad. While early protocols utilised only a single ECG monitor lead (viz.,CM_5) to detect changes of myocardial ischaemia presently multiple lead systems are preferred since these enhance the sensitivity of the exercise test (from 56 to 88%) without reducing the predictive value of a positive test (90%). While the recommended degree to which the patient should exercise remains controversial a submaximal test is common but a maximal or symptom limited stress test is more physiological and is not any more unsafe as compared to the submaximal test.

Recent evaluation has resulted in better understanding and clearer indications for noninvasive exercise stress test. These are :

(i) as an aid in diagnosis of chest pain,

(ii) to determine the severity and prognosis of cardiac disease especially IHD,

(iii) to evaluate cardiac arrhythmias,

(iv) to guide rehabilitation after acute myocardial infarction or cardiac surgery specially coronary artery bypass,

(v) to evaluate medical and surgical therapy of cardiac disease,

(vi) to screen high risk professionals (airline pilots, train drivers etc.),

(vii) to assess coronary risk factors in an asymptomatic person, and

(viii) as a safety checkup prior to prescribing a physical fitness programme.

Exercise testing is contraindicated in patients with acute myocardial infarction, unstable angina pectoris, myocarditis, pericarditis, advanced congestive heart failure, serious arrhythmias, high grade A - V block and severe resting hypertension (BP ≥220/150 mm Hg). Severe obstructive valvular disease (e.g., aortic stenosis), marked pulmonary hypertension, severe postural hypotension, severe anaemia and thyrotoxicosis are other relative contraindications for undertaking this procedure.

Stress testing as a method of noninvasive diagnosis specially for IHD is valuable only when applied to an appropriate population. The number of true positive tests is high in symptomatic patients with only a small number of false positive as against a high false positive and a low true positive rate of stress testing in asymptomatic patients so tested as confirmed by coronary arteriography. The predictive accuracy of the test increases exponentially with increasing disease prevalence in the tested population. The predictive value is also related to the criteria used for a positive diagnosis. With use of stringent criteria (e.g. ≥2.5 mm ST segment depression) even at a low disease prevalence the test may be highly predictive of IHD. The greatest value of the test lies not so much in detecting IHD but rather in evaluating the severity of the disease and the prognosis of patients with known IHD. The stress test is particularly useful in identifying patients with this disease who are in need of further evaluation and therapy.

Several features of the exercise test response are helpful in interpreting the stress test and for determining the severity of IHD. These are :

(i) the degree of ST depression and its morphology,

(ii) 'ST' segment elevation,

(iii) time of onset of 'ST' change,

(iv) duration of exercise tolerance,

(v) persistence of 'ST' change after exercise,

(vi) changes in 'R' wave amplitude,

(vii) response of blood pressure specially hypotension, and

(viii) exercise provoked arrhythmias and conduction abnormalities.

Horizontal or downsloping 'ST' depression is highly predictive of multivessel IHD as compared to slowly upsloping ST depression or 'J' point depression. The degree of 'ST' segment depression also has diagnostic significance for the number of coronary vessels involved. Almost 60% patients with no 'ST' segment change have normal coronary arteries by coronary angiography while marked 'ST' segment depression (≥ 2.5 mm) is almost invariably associated with severe 2 or 3 vessel disease. Moreover the disease in those with a negative or mildly positive test is rarely, if present, multivessel.

The persistence of 'ST' segment depression in the post exercise period also reflects the severity of IHD. Over 40% patients in whom the changes reverse within one minute have normal vessels or single vessel disease while changes persisting for 9 minutes or more identify those with severe multivessel disease.

The value of 'ST' elevation during a stress test has been well studied. In patients with known preceding myocardial infarction such a change reflects the existence of an underlying ventricular aneurysm. However, in those without antecedent myocardial infarction the test reflects the existence of severe multivessel IHD and hence the need for further invasive evaluation. The role of vasospasm in some patients with raised 'ST' segment response to exercise is yet controversial.

Exercise-induced changes in 'R' wave amplitude are a useful marker for patients with IHD and underlying ventricular dysfunction. The amplitude of 'R' wave reportedly varies with the ventricular volume and hence decreases in normal subjects with exercise. Patients with significant IHD frequently develop LV dysfunction and hence increased LV volume with exercise. The 'R' wave in such patients therefore increases in amplitude. It has been reported that analysis of exercise-induced 'R' wave amplitude changes enhances stress test sensitivity (48 to 63%) and specificity (59 to 79%) as compared to conventional 'ST' segment analysis.

The exercise-induced hypotension is generally suggestive of severe underlying IHD with patients having 2 or 3 vessels disease at coronary angiography.

Unlike the above variables the value ot exercise-induced arrhythmias or conduction defects is less well defined. Significant ventricular ectopic activity with exercise is likely to be associated with significant IHD but not universally so. The significance of exercise-induced multiventricular or A-V conduction block is even more controversial. The development of RBBB does not mask 'ST' segment changes but of LBBB masks an ischaemic response and thereby precludes accurate interpretation of 'ST' response.

Based on the many changes which develop in response of exercise in patients with IHD a multivariate approach to the analysis of exercise test performance has been attempted. In one such study the predictive value of the positive stress test increased from 78% when only 'ST' segment depression was evaluated to 97% when any two of the following variables were additionally present: peak double product less than 23×10^{-3}, exercise duration (Bruce protocol) less than 6 minutes or ST segment depression persisting for more than 3 minutes into the recovery period. Such data have also been used to stratify patients into a low or high risk category on basis of a 4 year survival study.

Exercise testing, in experienced hands is quite safe. An analysis of 170,000 tests in one study revealed a mortality rate of 1 per 10,000 and morbidity of 4 per 10,000.

Echocardiography

This pulse reflected ultrasonic method of cardiac examination was introduced in 1954. In the three decades since then, specially during the last 10 years, its growth as a key clinical procedure has been phenomenal. This safe, reliable, repeatable and painless technique currently plays an important role in evaluation of almost all forms of heart disease and is a procedure of choice in many. It has relatively few d'sadvantages.

The reflected echocardiographic signal is displayed in a number of modes of which 'M' mode and two dimensional (2-D), also called cross sectional, sector scan or realtime, are commonly employed. The past few years have specially witnessed the evolution and dissemination of two dimensional echocardiography which has the advantage of demonstration of the actual lateral relationship of cardiac structures to one another which is only inferred in 'M' mode echocardiography. Increasingly sophisticated electronic devices with use of microcomputers are becoming availablo for rapid analysis of echocardiographic data like chamber size, volume, ejection fraction and other functional parameters.

Another ultrasonic technique Doppler ultrasound is also being increasingly used. Its potential clinical applications include measurement of flow through great vessels for determining cardiac output and the magnitude of shunts, for evaluating valvular regurgitation and for identifying turbulent blood flow and thereby the site of valvular obstruction.

While most cardiac disease abnormalities are currently evaluated by echocardiography, it has a special role in the following situations.

(i) Evaluation of mitral valve disease specially mitral stenosis, mitral valve prolapse and infective endocarditis.

(ii) Evaluation of aortic valve disease specially aortic stenosis, aortic regurgitation and infective endocarditis.

(iii) Evaluation of the aortic root for dilatation, aneurysm and dissection.

(iv) Evaluation of prosthetic valves in the aortic and mitral position.

(v) Evaluation of tricuspid stenosis and other abnormalities of tricuspid valve.

(vi) Evaluation of pulmonary valve, specially for study of pulmonary hypertension.

(vii) Evaluating the size of left atrium and the presence of LA clots.

(viii) Evaluating the size and function of left ventricle, its wall thickness and functional parameters like volumes, ejection fraction etc. LV clots can also be visualized.

(ix) Evaluation of congenital heart disease. The method, specially 2 D studies, have been found to be invaluable for study of neonates for important decision making.

(x) Study of pericardial disease specially for detection and quantification of pericardial effusion.

Echocardiography is currently unable to provide significant help in detection of coronary arterial disease although it is able to detect the functional effects of such a disease on the heart. There are also problems of obtaining reliable, reproducible and accurate echocardiograms in all patients. This has become specially important in the recent years since many self-trained individuals have started, using this technique without adequate knowledge of the proper use of equipment and the conceptual, mechanical and electronic limitations of the technique.

Radionuclide studies

Radioisotopes have been used in medical (including cardiac) practice for a long time. Availability of newer isotopes and better technical capabilities, specially the rapid development of imaging techniques has resulted in a rapid and widespread use of radionuclide techniques for investigating cardiovascular disease states. Two main avenues of investigation are used :

(a) Radionuclide ventriculography

(b) Myocardial perfusion and infarct imaging.

Radionuclide ventriculography (RNV) is a dynamic visualisation of the cardiac chambers by detection of gamma radiation emanating from the cardiac blood pool and is analogous to the use of other forms of contrast angiography (e.g. conventional cine angiography using iodinated contrast media). The applications of RNV continue to be defined. These presently include :

(i) assessment of regional and global LV functions,

(ii) assessment of the response of LV function to stress and drugs,

(iii) assessment of RV function and the response of exercise and drugs,

(iv) measurements of LV volumes,

(v) identification of wall motion abnormalities of the left ventricle, and

(vi) evaluation of aortic and mitral regurgitation.

RNV has advantages over conventional contrast angiography because :

(i) it is noninvasive, atraumatic and safe,

(ii) ventricular ectopic activity is not produced,

(iii) contrast does not affect cardiac function,

(iv) a single study allows situation of biventricular function,

(v) geometrical considerations do not limit accurate calculation of ventricular volume, and

(vi) with equilibrium gated studies as single injection allows serial views and repeated images over several hours.

Two methods of RNV are currently utilised :

(1) First pass method.

(2) Equilibrium gated RNV.

First pass method offers the following advantages :

(i) right and left heart are temporally visualised separately,

(ii) there is minimal background radioactivity,

(iii) the study is short and hence possible in seriously sick patients without danger or discomfort to the patients.

The equilibrium gated method is advantageous because of :

(i) integrated information from many cardiac cycles is available,

(ii) time activity curves comprise many points affording greater temporal resolution and facilitating calculation of ejection rate, time and fraction,

(iii) there is a better evaluation of regional wall motion changes, and

(iv) repeated studies are possible with a single tracer injection.

Radionuclide ventriculographic studies are currently being used by us for assessment of global and regional ventricular function in patients with chronic ischaemic heart disease, acute myocardial infarction, cardiomyopathy and other causes of congestive heart failure, studies being conducted at rest, with exercise and after use of drugs or subsequent to surgery like coronary artery bypass grafting (CABG). We find it particularly useful in identifying ventricular aneurysms and other wall motion changes in patients with ischaemic heart disease.

Myocardial perfusion imaging has become very important since newer techniques of treatment of patients with ischaemic heart disease have become available making it necessary to detect, localise and quantitate the extent of coronary artery disease. Myocardial perfusion imaging with thallium 201 is a valuable technique which can supplement the available information. The clinical utility of the procedure depends upon the ability of the viable myocardial cells of concentrating thallium 201. Scar tissue is unable to extract the injected thallium from the blood and will therefore not fill in and will be seen as a 'cold spot'. Perfusion defects which fill in on delayed images represent viable but underperfused myocardium while those which do not fill in delayed images represents scar tissue or acutely infarcted myocardium.

Initial images are recorded soon after injecting the tracer while the delayed images are recorded 2 to 4 hours later. The current clinical indications for thallium 201 perfusion imaging are :

(a) Evaluation of patiants with known or suspected IHD.

(i) Asymptomatic patients for detection of IHD.

(ii) Patients with severe IHD for resting perfusion deficits.

(iii) Patients with ECG abnormalities requiring clarification.

(iv) Patients with uninterpretable exercise tests.

(v) Selection of patients for CABG.

(vi) Localisation of IHD.

(vii) Evaluation of functional significance of coronary stenosis seen at angiography.)

(b) Evaluation of patients with myocardial infarction (localisation, extent, LV function and for post MI rehabilitation programme.

(c) Evaluation of results of CABG.

(d) Evaluation of coronary spasm.

(e) Evaluation of cardiomyopathies.

(f) Evaluation of patients with myocardial infiltrative disorders.

Myocardial infarct scintigraphy using radiopharmaceuticals which are sequestered by the acutely necrotic myocardium resulting in regions of increased radiotrace uptake is also receiving significant attention. It is now being increasingly utilised for detection, localisation and quantitation of acute myocardial infarction. While the ideal radiotracer for infarct imaging is yet not available, technitium 99m stannous pyrophosphate is most commonly used and provides a 'hot spot' of radioactivity in the infarcted area.

Positive scans are detected in most patients with acute infarcts imaged 2 to 3 days after infarction. Transmural infarctions are diagnosable in 90% patients but small infarcts may be missed. Non-transmural infarcts are not detected as reliably. Serial scanning over a number of days improves the detection rate to some degree. However, data need to be carefully evaluated and other causes of uptake (e.g., breast tumours, LV aneurysm, fractured ribs, cardioversion, valvular calcification etc.) should be excluded.

Scintigraphy is specially likely to be useful for evaluating patients admitted several days after acute infarction when enzyme and ECG changes are non-diagnostic. Imaging may then be useful. It is also useful if the initial results are equivocal or contradictory. Imaging is also useful for diagnosis of RV infarction. It is equally useful for diagnosis of myocardial infarction after cardiac surgery, suspected infarction with LBBB, new infarctions or infarct extension in patients with old or recent myocardial infarctions and in myocardial contusions.

And.........

While the above described techniques have been tested and found varyingly useful in clinical practice many more techniques are being actively tested in the laboratory and have either been recently introduced or are likely to be so in cardiac practice. These include intravenous digital subtraction angiography, computed axial tomography of the heart, dynamic spatial reconstruction techniques and nuclear magnetic resonance. Of these listed methods, digital subtraction angiography is now available for clinical use. It consists of the principles of computer application to the well known method of photographic subtraction of radiographic images. High speed computers digitalise high resolution fluoroscopic images of vascular structures before and after introduction of standard radiographic contrast materials. Ultimately this results in images of the heart or blood vessel without the overlapping of soft tissues or bone density. The technique is currently successfully practised for visualisation of the great vessels in the neck, renal arteries and pelvic vessels. The application to the heart and coronary arteries is being explored. It is currently possible to determine ventricular volumes, wall motion abnormalities and identify graft patency. Many changes will result from future improvements in technology but the technique is already a reality.

In the last decades of the twentieth century we are moving fast in terms of technological advancement for betterment of the quality of life of the community. Investigative techniques based on such advances are keeping pace with the needs of the time and give hope to patients with cardiovascular disease.

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