Indications, Applications and Future Prospects of Diagnostic Examinations in Clinical Cardiology

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Nowadays there are various kinds of diagnostic examinations in the field of clinical cardiology. In this field, information concerning structure, dimension (hypertrophy and dilatation) and cardiac function is essentially important. For the diagnosis of valvular and congenital heart diseases and of cardiomyopathy, ultrasonic examinations are more useful; for ischemic heart disease, nuclear medicine is superior. Angiocardiology provides us much information but it is invasive.

A combination of an exercise-test with the examinations mentioned above is useful for the detection of left ventricular and coronary reserves. The determinants of left ventricular reserve, being related to the prognosis of the patients, can be analyzed by exercise echocardiography. Exercise echocardiography can reveal instantaneous changes in myocardial ischemia during exercise. Regional and global left ventricular performances revealed by exercise radionuclide angiocardiology can lead us to a new interpretation of an exercise ECG.

THE first device for cardiac evaluation was the invention of the stethoscope by Laennec in 1816. ECG became available in the early 1900s. X-ray film has also been used, and various kinds of valuable examinations have recently been introduced, especially using a computer system.

Here, we will consider the indications, applications and future prospects of these examinations in clinical cardiology.

Characteristics and Indications of Examinations in Clinical Cardiology

Key Words:

Ultrasonics
Nuclear medicine
Invasive methods
Left ventricular reserve
Coronary reserve

What Should Be Examined in Clinical Cardiology

Figure 1 shows the diagrammatic representation of structure and function in normal and abnormal hearts. The heart is composed of structures such as myocardium, cardiac chambers, valves and others, and has electrical and metabolic phenomena related to a characteristic cardiac movement. The functions of the heart can be described as myocardial contractility, pump function as its result and blood flow ejected from the heart as a result of the pump function. The ejected blood flow consists of aortic blood flow for systemic circulation and of coronary blood flow for the myocardium. Each function has a reserve (= functional compensatory mechanism), which will be mentioned later. Cardiac abnormalities, such as valvular stenosis, myocardial ischemia, intracardiac shunt and many other disorders, bring about an overloading

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Fig.1. A diagrammatic representation of structure and function in normal and abnormal hearts.

TABLE I CONCEPTS AND PARAMETERS OF LV PERFORMANCE IN CLINICAL CARDIOLOGY

A. Pump Function	
a)	cardiac output, stroke volume
b)	LV end-diastolic pressure
c)	LV end-diastolic diameter
d)	LV end-diastolic volume
	LV function curve
	pressure-volume relationship
e)	LV asynergy
B. Myocardial Contractility	
a)	isovolumetric phase: dp/dt
b)	ejection phase
	ejection fraction
	fractional shortening
	V_{cf} , mV_{cf}
	stress-velocity relationship
	aortic flow velocity
c)	systolic time intervals
C. Regional Myocardial Function	

condition in the heart. Morphological compensatory mechanisms such as myocardial hypertrophy and chamber dilatation occur, but if the overloading exceeds these compensatory capacities, heart failure takes place.

We are now able to obtain much information from the examinations about 1) primary changes of structure, 2) dimension (hypertrophy and dilatation, as the secondary morphological com-

pensatory mechanisms) and 3) cardiac function, which suggests the degree of heart failure.

Information concerning the structure (valves, hypertrophy and dilatation, etc.) and global cardiac function is useful for an evaluation of non-ischemic heart diseases. On the other hand, ECG, regional myocardial function, myocardial blood flow and morphology of the coronary arteries are valuable for ischemic heart disease.

At present, we have various methods to obtain this information. They are a) routine examinations such as ECG and X-ray films, b) non-invasive ones such as ultrasonics and nuclear medicine and c) invasive ones such as cardiac catheterization and angiocardiography.

Table I shows the concepts and parameters of left ventricular (LV) performance in clinical cardiology. LV performance was expressed at first by intracardiac pressure, but recently imaging methods, such as ultrasonics, nuclear medicine and angiocardiography, play a major role in this field. The parameters which are now often used are ejection phase indices, such as the global function in non-ischemic heart disease, and the regional myocardial function in ischemic heart disease. There may be some gap between experimental and clinical cardiology in the evaluation of cardiac function. Experimental study is often carried out using pressures and dimensions obtained by devices attached directly on the cardiac surface. However, clinical studies often depend on non-invasive methods, which may

TABLE II CLINICAL USEFULNESS OF EXAMINATIONS IN THE STRUCTURAL DIAGNOSIS OF CARDIAC DISEASES (MODIFIED FROM REF. 3)

Heart diseases	Phonocardiography Mechanocardiography	Ultrasonics	Myocardial imaging	Radionuclide angiocardiology	Angiocardiography
Valvular heart diseases	+++	++ ~ +++	—	— ~ +	(+++)
Congenital heart diseases	++ ~ +++	++ ~ +++	—	— ~ +	(+++)
Cardiomyopathies	+ ~ ++	+++	— ~ +	— ~ +	(+++)
Exertional angina	— ~ +	+	+++	+++	(+++)
Myocardial infarction	— ~ +	++	+++	+++	(+++)

—: not useful, +: occasionally useful, ++: useful diagnostic tool, +++: best diagnostic method, ( ): invasive

decrease the accuracy of the measurements.

Indication of Examinations

Which method should be chosen for the evaluation of each cardiac disease? We have tried various kinds of examinations in various kinds of cardiac patients.^{1,2}

Table II shows how each examination can contribute to the diagnosis of cardiac diseases mainly through a detection of structural abnormalities other than secondary changes such as hypertrophy and dilatation. Phonocardiography is useful in valvular and congenital heart diseases. Ultrasonics is also useful in valvular or congenital heart disease and in cardiomyopathy. This is because ultrasonics reveals a structure by a reflection of the echo beam from the structure itself. A major difficulty in standard M-mode echocardiography is its "ice-pick" view. Viewing the heart through this narrow window has a potentiality for error in cases of segmental wall motion abnormalities. Two-dimensional echocardiography may compensate this demerit, but it can view only one cross-section. Ultrasonics can be applied to patients with angina pectoris during exercise, as mentioned later, but this may not always be possible. In myocardial infarction, ultrasonics can not always reveal the apical region. Nuclear medicine seems to have been intended for ischemic heart disease. It has the merit of expressing three-dimensional elements on a two-dimensional plane, but it cannot detect delicate structural changes in the valves, etc. Myocardial imaging by Tl-201 detects the presence of myocardial hypoperfusion, and it is the only method available for that purpose. In the cases of multi-vessel diseases, however, its usefulness decreases because this method can detect only relative distribution. In these cases, the detection of regional mechanical abnormalities

using ultrasonics or radionuclide angiocardiology may be more sensitive. Angiocardiography can yield clear images in all kinds of heart diseases, but non-invasive methods are preferable to invasive ones, because the patients undergoing non-invasive examinations are usually subject to no or very low risk even from repeated studies. Invasive methods should be carried out only when it is indispensable for the treatment of the patient. However, no method can substitute for coronary arteriography to evaluate the morphological changes of the coronary arteries.

For the evaluation of the dimension or size (hypertrophy and dilatation) and motion (cardiac function) a rather quantitative expression is needed. For this purpose, ultrasonics, nuclear medicine and angiocardiography can be used, but they have merits and demerits respectively. From the point of view of internal medicine, non-invasive methods should be performed. M-mode echocardiography provides an accurate assessment of the diameter, wall thickness and their changes during each cardiac cycle, on the basis of which cardiomechanical parameters about myocardial contractility, preload and afterload can be calculated. LV volume calculated by M-mode echocardiography correlates well with the angiographically estimated volume, but two-dimensional echocardiography greatly underestimates the volume.⁴ As mentioned above, there is a difficulty in the case of asynergy in M-mode echocardiography. Two-dimensional echocardiography is not yet useful for the quantitative measurement. We tried a subxiphoid approach in these cases and showed its validity.⁵ Radionuclide angiocardiography can detect cardiac dilatation and myocardial imaging may detect myocardial hypertrophy, but there are still methodological problems in minute details. Angiocardiography is accurate but is invasive.

Fig. 2. Changes of LV peak stress-velocity relations during exercise in the patients with LV diseases of various severities. (exercise echocardiography)

Fig. 3. a: Changes of SV during exercise on the relation between $\% \Delta mVcf$ and $\% \Delta Dd$. b: Relations among $\% \Delta SV$, $\% \Delta mVcf$, $\% \Delta Dd$ and severities of LV diseases. (exercise echocardiography)

In obtaining hemodynamic or cardiomechanical parameters from these various kinds of measurements, we should always be careful about the range of errors of each parameter. We should not evaluate the changes which are within the range of error. For instance, the measurement of the dimension by M-mode echocardiography has an error of about 2 mm. Therefore, the relative error of LV diameter may be about 0.2 cm/5.0

cm (= 4%), that of wall thickness about 0.2 cm/1.0 cm (= 20%) and systolic stress about 24%.

There is another important problem in the significance of the parameters of cardiac function. Nowadays we can easily obtain various parameters of cardiac function. In basic medicine, they are useful for the analysis of pathophysiology, but clinically, they should contribute to the treatment of the patient. We should consider which parameter will be useful in each case.

Applications of Examinations in Clinical Cardiology

Examinations are usually performed at rest. In daily life, however, the heart has to eject blood against various loads due to every day activity, and the functional compensatory mechanism, designated "reserve", operates. This is an important factor in the evaluation of cardiac function. In order to evaluate cardiac reserve, stress tests are used, because it reveals when and how the compensatory mechanism fails. To detect latent abnormalities in structure, stress tests can also be applied. For instance, phonocardiogram under the administration of drugs is used to detect mild valvular diseases.

There are two main reserves for cardiac function: reserve of LV function and reserve of coronary circulation. When the former reserve decreases, symptoms such as dyspnea appear during exertion, and the patient lapses into heart failure. When the latter reserve decreases, symptoms such as anginal pain appear during exertion, and myocardial ischemia occurs. Stress tests have been used for evaluation of these two reserves.

There are two types of stress tests: by drugs and by exercise. By drug administration and so on, which can change only one single factor relating to cardiac function (e.g., changes of myocardial contractility by isoproterenol, those of preload by isosorbide dinitrate, those of afterload by methoxamine and those of heart rate by cardiac pacing), the analysis of reserve becomes simple. On the other hand, exercise induces changes of all the determinants relating to reserve. However, exercise is directly related to daily life, and so it is an important test and is widely used. The exercise test is, of course, not necessary in these patients who have symptoms even at rest.

Left Ventricular Reserve

As mentioned above, even asymptomatic patients, who usually exhibit normal LV perfor-

Fig. 4. Relation between the changes of mVcf during exercise and later clinical courses. Group I = patients who showed no aggravation for 2 years; Group II = patients who showed aggravation during the 2 years. (exercise echocardiography)

mance at rest, may manifest functional abnormalities when the heart is subjected to stress.^{6,7} A functional classification according to the New York Heart Association (NYHA) has often been used to estimate cardiac reserve, but it is based only on subjective complaints. An objective criteria has been desired.

The role of LV performance is the ejection of blood (cardiac output, CO). CO is determined by heart rate (HR) and stroke volume (SV); SV, which expresses pump function, is determined by myocardial contractility, preload and afterload. LV reserve is also considered to be composed of the reserves of each of these components.

It has been demonstrated that even in patients with heart diseases, who exhibit normal cardiac function at rest, dysfunction becomes apparent only when their functional reserve is exhausted by exercise. These stress-induced abnormalities have been demonstrated using invasive techniques, which are impractical for routine or repeated evaluation.⁸⁻¹⁰

We have developed a method of dynamic exercise echocardiography.¹¹ Other investigators have also tried similar methods in normal per-

sons.¹²⁻¹⁶ We demonstrated that the mean velocity of LV circumferential shortening (mVcf) measured by this method can detect abnormalities of LV performance, not apparent at rest, in apparently healthy old persons and in patients with LV diseases.^{2,11,17,18}

Figure 2 shows the LV peak stress-velocity relations during mild exercise in which HR increased up to 100 beats/min in patients with LV diseases of various severity. In those with functional class I (NYHA), mVcf increased with a slight change of LV peak systolic stress (σ); in NYHA class II mVcf and σ showed only slight changes; in NYHA class III mVcf decreased with an increase of σ .

Figure 3a shows the changes of SV during exercise by the relation between $\% \Delta mVcf$ (ordinate) and $\% \Delta Dd$ (abscissa) (Dd = end-diastolic LV diameter, which suggests preload). Points are located in the order of $\% \Delta SV$ from right upper to left lower. In Fig. 3b, all the points are grouped according to $\% \Delta SV$ in 10% increments. It suggests that, in NYHA I, SV showed either no change or an increase during exercise by an increase of mVcf, suggesting an increase of myocardial contractility, in NYHA II, SV showed no change by an increase of Dd (increase of preload) or by an increase of mVcf; and in NYHA III, SV decreased with a decrease of mVcf, although there are overlappings among the changes. These changes suggest the mechanisms of LV reserve. We have also studied diastolic reserve by this method.^{19,20}

We have followed these patients up for 2 years after dynamic exercise echocardiography. They were divided into 2 groups: group I who showed no aggravations for 2 years and group II who showed an aggravation during the 2 years. Figure 4 shows that those having an increase or no change of mVcf during exercise belonged to group I and those having a decrease of mVcf belonged to group II. These results show that the prognosis of the patients may be indicated by an evaluation of LV reserve.

Radionuclide angiocardigraphy may also give these hemodynamic parameters during exercise,^{1,21,22} but there are still methodological problems regarding minute details.

Coronary Reserve

It is well known that myocardial ischemia in ischemic heart disease is induced by an imbalance between the demand and the supply of oxygen in the myocardium, and that the existence of

Fig.5. Time courses of LV parameters during exercise in a case of exertional angina (exercise echocardiography). BP = blood pressure

Fig.6. ECGs and radionuclide angiograms at rest and during exercise in a patient with exertional angina. ST depressed and EF decreased during exercise.

myocardial ischemia influences on myocardial metabolism, ECG, myocardial function, chest pain and vasoactive substances.²³ Chest pain is so simple an index that we need no device for its detection, but it is too subjective. An ECG has usually been used to detect myocardial ischemia, especially a stress-ECG for patients with exertional angina. However, it may not always be

accurate, because of the presence of false positive exercise tests.²⁴⁻²⁷ The detection of anaerobic metabolism is impractical.

We have shown that LV asynergy induced by exercise in patients with exertional angina can be recognized using dynamic exercise echocardiography.¹¹ Figure 5 shows a time course of the posterior wall and the interventricular septum

Fig.7. ECGs and radionuclide angiograms at rest and during exercise in a patient with exertional angina. ST elevated and EF decreased remarkably during exercise.

Fig.8. Changes of EF during exercise in patients with exertional angina in whom ST depressed or elevated, or negative T became positive during exercise.

excursions (PWE and IVSE) detected echocardiographically during exercise. In this case, IVSE decreased and PWE increased gradually with an increase of blood pressure. One min and 30 sec after the beginning of exercise ST was depressed on the ECG, and after 3 min chest pain occurred. It has been shown that in experimental myocardial ischemia mechanical change appears earlier than electrophysiological change. Thus, echocardiography can reveal the time course of myocardial ischemia during exercise, but the diagnostic success rate is not so high.

We have also tried exercise radionuclide angiography in the patients with exertional angina^{1,2}. We have revealed that exercise radionuclide angiography may be more sensitive than exercise myocardial imaging in detecting the ischemic region¹. The success rate of exercise radionuclide angiography was higher than exercise echocardiography in exercise-induced angina, and the former can express three-dimensional elements on a two-dimensional axis, but the latter can detect only 1 or 2 axes.

Figure 6 shows ECGs and radionuclide angiograms at rest and during exercise in a 49 year-old female with exertional angina. During exercise ST was depressed and EF decreased with a wall motion dysfunction at the apex.

In a 59 year-old male with exertional angina, ST elevated and EF decreased remarkably with a

wall motion dysfunction at the apex and other regions during exercise (Fig. 7).

The changes of EF obtained by exercise radionuclide angiocardigraphy are summarized in Fig. 8. EF changed variously in patients with ST depression during exercise, but it decreased in patients with two or three vessel diseases on a coronary arteriogram or in older patients. In patients with ST elevation during exercise, EF decreased remarkably, and they were considered to have severe myocardial ischemia. In those, in whom the negative T wave became positive during exercise, EF elevated, and thus, a new interpretation of these changes is needed.

Here, the applicability of examinations to stress-tests should be evaluated by the following points: 1) whether it can be measured even when the body or the heart moves, 2) whether comparison is possible after the intervention, that is, whether the same point of the heart can be examined and 3) whether the stress-induced changes are outside the range of error in that method.

Future Prospects of Examinations in Clinical Cardiology

Nowadays we have various kinds of examinations as mentioned above. In the future, examinations will be developed which have a higher quality imaging of cardiac and vascular structures and which can measure their functions.^{3,28} More extensive applications of computer techniques for data analysis, for graphical imaging to ascertain normal or abnormal function and for aiding in complex decisions, seem likely. The future problems will be what should be examined and their interpretation. Non-invasive measurement of intracardiac pressure is desired. Information about histology and metabolism is expected.

Higher level examinations will be developed in the future, and we shall be able to analyze the cardiac phenomena more precisely. However, they will be more expensive, for example, costing as much as 1,000,000,000 yen. These extremely expensive devices can be utilized only in limited institutions, and they will benefit few patients. We should apply our acquired knowledge to help many patients. As one such attempt, we have presented the feed-back of the results of exercise radionuclide angiocardigraphy to the interpretation of exercise ECG in the present paper.

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