Evaluation of Left Ventricular Performance and of Its Reserve by Radionuclide Angiocardiography: Comparison with other methods

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This study was performed, i) to compare radionuclide angiocardiography with the other methods, and ii) to evaluate its usefulness in investigating left ventricular performance and its reserve.

Radionuclide angiocardiography*, chest X-ray film, chest X-ray cineangiography*, echocardiography*, two-dimensional echocardiography*, pulsed Doppler flowmetry*, cardiologyography*, myocardial imaging*, contrast ventriculography and coronary arteriography were performed (*: also at exercise) in 105 subjects including various kinds of cardiac patients.

Radionuclide angiocardiography could be performed both at rest and at exercise, contrary to invasive methods. In detailed analysis of left ventricular mechanics in non-ischemic heart disease, echocardiography at rest and at exercise may be appropriate, because of its high image resolution. In evaluation of ischemic heart diseases, radionuclide angiocardiography at rest and at exercise might be appropriate, because of bidirectional informations and its high success rate. Two-dimensional echocardiography with M-mode echocardiography might compensate for it, particularly for continuous informations during exercise. Detection of regional wall motion dysfunction at exercise is more specific than exercise ECG and is more sensitive than exercise myocardial imaging. From many kinds of examinations, appropriate one should be selected according to the purpose of investigators. Much more technical progress in these methods can be expected.

There are now many kinds of examinations to evaluate left ventricular performance and its reserve clinically. One of them is radionuclide angiocardiography. The purpose of the present study is i) to compare radionuclide angiocardiography with the other methods, and ii) to evaluate its usefulness in investigating left ventricular performance and its reserve.

MATERIALS

One hundred and five subjects were divided into two groups. Group I consisted of 38 subjects with or without cardiac diseases other than coronary artery diseases (age 16–74 years, mean 50.7 ± 16.2 years). This group included four controls, 10 patients with mitral valvular dis-

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Key Words:
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Exercise radionuclide angiocardiography
Exercise myocardial imaging

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eases, twelve with aortic valvular diseases, four with idiopathic cardiomyopathy, four with hypertension, and four who had other conditions. Diagnoses were based on physical and laboratory examinations, including chest X-ray film, ECG, phonocardiography, echocardiography and cardiac catheterization. They were various in the severity of the cardiac diseases. Group II consisted of 67 patients with coronary artery diseases (age 42–70 years, mean 59.6 ± 6.3 years). This group included 42 patients suspected of angina pectoris and twenty-five with myocardial infarction.

METHODS

I. Examinations at rest

1) Radionuclide angiocardiology

The subject was placed in a supine position. An 18 gauge Teflon® catheter was inserted into the antecubital or external jugular vein, and it was connected with a three-way stopcock, 20 inch venotube, and a 20 inch syringe filled with normal saline. Then the subject was imaged with a Baired Atomic Autofluoroscope System Seventy-Seven multicroystal gamma camera®. The projection was anterior, as a rule. When compared with echocardiogram, radionuclide angiocardiom was taken at deep left anterior oblique projection (LAO) (60°), and when compared with myocardial imaging, radionuclide angiocardiology was taken from the other projections, too. A bolus of 15mCi technetium-99m pertechnetate was instantaneously injected, and counts were recorded at 50 msec intervals for 30 seconds by first pass method.

The data were stored on magnetic disc, and were processed later. Left ventricular ejection fraction (EF) and regional wall motion was determined according to the standard technique. Briefly, the left ventricular region of interest was identified from an oscilloscope serial display of the entire radionuclide angiocardiology, with each image repeating the sum of 20 individual 50 msec frames. End-diastolic frames, identified as high count peaks in the left ventricular time-activity curve, were used as starting points to sum together counts at corresponding 50 msec intervals over 3 to 6 (average 4) cardiac cycles. A series of regional background frames were chosen directly from the left ventricular time-activity curve at a time point prior to the first discernible left ventricular beat at the beginning of the left ventricular phase, and the summed background was subtracted from the summed cardiac cycle forming a representative cardiac curve. From this curve, EF was calculated by (end-diastolic counts – end systolic count) x 100/ end-diastolic counts. Mean velocity of circumferential fiber shortening of left ventricle by radionuclide (mVcf-R) was obtained by (√end-diastolic counts – √end-systolic count)/√end-diastolic count·ET. ET (left ventricular ejection time) was measured from a carotid pulse tracing obtained through a funnel held manually over the carotid artery. In some cases, it was also tried to measure from the histogram of left ventricular time-activity curve of radionuclide angiocardiogram.

Regional wall motion was evaluated from composite images (perimeters) formed by superimposing a composite generated end-diastolic contour upon the end-systolic image. The change rates of count at each part of left ventricle, from end-diastole to end-systole, were also analyzed. The regions of radionuclide angiocardiogram of left ventricle were classified into 5 segments: septal, apical, anterolateral, posterior and inferior. When end-systolic perimeter was of a shape similar to end-diastolic, it was interpreted homogenous contraction; on the other hand, when there were akinetic or hypokinetic regions, it was interpreted heterogenous contraction. (Only when the dysfunction was accounted for most part of a segment, the region was interpreted akinetic or hypokinetic.)

In 13 cases, radionuclide angiocardiology was performed twice, in order to investigate the reproducibility of EF obtained by this method.

2) Chest X-ray film

Chest X-ray film was taken at postero-anterior projection as a routine examination.

3) Chest X-ray cinegram

Plain X-ray cinegram of heart was taken with a 35 mm camera at 60 frames/sec at antero-posterior projection. ECG was superimposed on the film.

4) Echocardiogram

Echocardioogram was recorded by standard methods, using an Aloka SSD 110 ultrasonoscope, with a 3.5 MHz, 13 mm diameter transducer focused at 7.5 cm. The transducer was placed in the 3rd or 4th left intercostal space and the left sternal edge where the characteristic echo from the anterior cusp of the mitral valve could be identified. Then the transducer was angled to demonstrate the interventricular septum and the left ventricular posterior wall just below the tip of the mitral leaflets at the level of the chorda.

Fig. 1. A comparison of EF between the first and the second radionuclide angiocardiography obtained at rest in 13 cases.

Fig. 2. Relationship between the clinical courses and the changes of EF obtained by radionuclide angiocardiography. 
left panel: the cases who improved 
right panel: the cases who deteriorated

Fig. 3. A comparison of EF determined by radionuclide angiocardiography and by echocardiography at rest.

tendinea. Echocardiogram was photographed on light sensitive paper (Kodak Linagraph, 1895) at a paper speed of 50 mm/sec, using a Honeywell 1956 strip chart recorder. An ECG lead and a carotid pulse tracing were recorded on the echogram. End-diastolic and end-systolic left ventricular diameters (Dd and Ds) were measured by the standard method. Left ventricular end-diastolic and end-systolic volumes (LVEDV and LVESV) were calculated using the equation of Gibson. EF by echocardiogram was calculated as (LVEDV - LVESV) \times 100/LVEDV. Mean Vcf was calculated as (Dd - Ds)/Dd \times ET. ET was obtained from carotid pulse tracing.

5) Two-dimensional Echocardiogram

Two-dimensional echocardiograms were recorded using a sector scanner (Hitachi). Images from various directions, including cross-sectional and longitudinal images, were obtained.

6) Pulsed Doppler Flowmeter

Blood flow velocity of ascending aorta was measured by an Aloka pulsed-Doppler flowmeter, and was recorded by a Honeywell 1956 strip chart recorder, just as echocardiogram.

7) Cardiokymography (CKG)

This was measured by Cardiokymograph (Ran Vas), and was recorded by San-ei visigraph recorder.

8) Myocardial Imaging

Two mCi of $^{201}$Tl was injected intravenously. Imaging was begun 15 to 20 min following isotope injection. A Searle Pho Gamma IV Scintillation Camera was used for the studies. Scintigrams

formed, and selective coronary arteriogram and left ventriculogram were taken with a 35 mm camera at 60 frames/sec. ECG was superimposed on the film.

II. Examinations at exercise

Among the examinations performed at rest, the followings were performed also at exercise: X-ray cineangiocardiography, two-dimensioned echocardiography, pulsed-Doppler flowmetry, cardiokymography, radionuclide angiocardiography and myocardial imaging. The exercise at these examinations was performed by the same method, using the same bicycle ergometer and at the same exercise level. In the exercise study, patients were chosen whose cardiac disease was not so advanced that it prevented the performance of a degree of ergometer exercise sufficient to raise the heart rate to 100 beats/min (method described below) without subjective complaints. Thus, severe cases were excluded.

The graded exercise was performed by electrodynamic bicycle ergometer (Siemens) in a supine position with electrocardiography monitored by oscilloscope by telemeter system. The intensity of the initial exercise level was 20 to 40 Watts/min, depending on age, sex and clinical conditions, and it was then increased by 10 Watts/min every 1 or 2 minutes. The end point of the exercise was i) in Group I, the attainment of heart rate up to 100 beats/min, except in some controls in whom exercise was graded up to increase heart rate to 130 beats/min, and ii) in Group II, appearance of typical anginal pain, depression of ST segment more than 2 mm or life threatening dysrhythmias in ECG or the attainment of target heart rate, which was 85% of the predicted maximal heart rate for their age.

Radionuclide angiocardiogram at exercise was taken more than 10 minutes after taking one at rest, by injecting higher dose of isotope than at rest. When any one of the criteria of end point of the exercise, as mentioned above, occurred during exercise, the thchnetate was injected and the exercise was stopped.

Echocardiography was performed during exercise (Dynamic Exercise Echocardiography), as described in our previous study. The subjects
performed ergometer exercise in a supine position. The subject was fixed at shoulder level by attachments of a special table. In order to obtain the true minor dimension of the left ventricular cavity both at rest and during exercise, the left ventricle was scanned along its major axis at every time of taking echogram. During the exercise, the recording was performed continuously every 30 seconds.

For exercise myocardial imaging, the isotope was injected 60 sec prior to the termination of the exercise estimated from a prior exercise test. Image defects in the exercise study were defined as discrete, regional decrease in activity compared to the patients own rest scintigram.

**RESULTS**

1) Global function of left ventricle

a) at rest

Clear radionuclide angiocardiogram was taken in all the subjects, except a few cases who were in severe heart failure.

Fig. 1 is a comparison of EF between the first and second radionuclide angiocardiogram obtained at rest in 13 subjects. It reveals a good reproducibility. Mean Vcf was also reproducible.

Fig. 2 reveals the relationship between the clinical course and the changes of EF obtained by radionuclide angiography. In the cases, who improved, as shown in the left panel, EF increased; and in those who deteriorated, as...
shown in the right panel, EF decreased.

Chest X-ray film, generally speaking, reveals normal cardiothoracic ratio (CTR) in control and mild cardiac patients, and reveals large CTR in severe patients, and it suggests the degree of cardiac function and its reserve.

Fig. 3 shows a comparison of EF determined by nuclide angiocardiology and by echocardiography at rest. Almost identical values were obtained by the two methods, except in the cases of ischemic heart diseases. Mean Vcf obtained

**Fig. 8.** A comparison of the changes of EF at exercise, determined by exercise radionuclide angiocardiology and by exercise echocardiography.

**Fig. 9.** The changes of left ventricular mechanics, revealed by exercise echocardiography. a) stress-velocity relationship, and b) diameter-velocity relationship. 1: mild, 2: moderately severe, and 3: severe cases.

**Fig. 10.** A resting and exercise two-dimensional echocardiograms in a control.

*Japanese Circulation Journal Vol. 45, January 1981*
Fig. 11. A resting and exercise pulsed Doppler flow pattern in a control.

by the two methods showed also the same tendency, but mVcf-R calculated from ET measured from histogram of time-activity curve had a tendency to scatter.

Fig. 4 shows a representative cycle (relative volume curve) formed by summing activity from individual cardiac cycles. The white space above the curve can be interpreted to reveal the ejection pattern of the blood into aorta. Fig. 5 shows a representative blood flow pattern obtained by pulsed Doppler flowmeter at ascending aorta.

b) at exercise

Fig. 6 shows the end-diastolic and end-systolic perimeters of a normal control at rest and at exercise. Effective wall motion is noted in all the segments of left ventricle both at rest and at exercise. In all the cases of this exercise study, clear radionuclide angiocardiograms were obtained both at rest and at exercise. In controls, EF increased by exercise at the heart rate of 100 beats/min and increased more at the heart rate of 130 beats/min. In mild cardiac patients it also increased at exercise, but in moderately severe patients it tended to decrease. Mean Vcf showed a similar tendency at exercise.

Plain chest X-ray cinegram could reveal the movement of the cardiac silhouette. The movement was more active in control and mild patients, but it was not sensitive.

Fig. 7 shows a resting and dynamic exercise echocardiogram in a control. In controls and pa-
patients, EF and mVcf obtained by echocardiography, changed at exercise, almost similarly to those obtained by radionuclide angiography.

Fig. 8 shows a comparison of the changes of EF at exercise, determined by exercise radionuclide angiography and by exercise echocardiography. It reveals a good correlation, except in the cases of ischemic heart diseases. The changes of mVcf showed a similar tendency.

Fig. 9 shows the changes of stress-velocity relationship (a) and of diameter-velocity relationship (b) in some cases during exercise, obtained by exercise echocardiography. On the other hand, it was not easy to obtain such relationship by exercise radionuclide angiography, because of the difficulty in obtaining accurate absolute values of diameter or of stress by that method.

Fig. 10 shows a resting and exercise two-dimensional echocardiograms in a control. Two dimensional information can be obtained.

Fig. 11 shows a resting and exercise Doppler flow patterns in a control. It reveals an increase of aortic blood flow velocity at exercise.

In the cases of mitral stenosis, left atrial image revealed by radionuclide angiography increased in size at exercise. This phenomenon is coincident with an increase of left atrial diameter revealed by dynamic exercise echocardiography.

2) Regional function of left ventricle

a) at rest

In the cases of myocardial infarction, regional dysfunction was revealed by radionuclide angiography. And it was similar to that revealed by contrast ventriculography. Echocardiography can reveal regional wall motion abnormality in posterior wall and in interventricular septum. Two-dimensional echocardiography could offer two-dimensional information.

b) at exercise

Fig. 12 shows the end-diastolic and end-systolic perimeters of a case of exertional angina pectoris, at rest and at exercise. At exercise, wall motion dysfunction occurred.

Fig. 13 shows a comparison of the existence of abnormal findings in coronary arteriography, exercise ECG, exercise myocardial imaging, exercise radionuclide angiography and exercise echocardiography, in the patients complaining of chest pain. In the cases showing abnormal coronary arteriography, the other examinations also revealed abnormal, but in several cases, only
Exercise ECG was abnormal. In most cases, the regions of wall motion dysfunction detected by exercise radionuclide angiocardiography and of hypoperfusion detected by exercise myocardial imaging coincided, but in some cases the areas of wall motion dysfunction were larger than those of hypoperfusion. A coincidence was also revealed between the regions of abnormal wall motion detected by exercise radionuclide angiocardiography and those by exercise echocardiography. CKG also revealed systolic bulge at exercise in angina.

Fig. 14 shows a representative time course of posterior wall and interventricular septum excursions (PWE and IVSE) detected by echocardiography during exercise. In this case, IVSE decreased and PWE increased gradually with an increase of blood pressure. At 1 min and 30 sec ST in ECG depressed, and at 3 min chest pain occurred.

Fig. 15 shows a change of regional force-velocity relationship at exercise in a case. Regional wall velocity was obtained by wall excursion divided by ejection time, and regional wall stress was obtained by left ventricular pressure × regional radius/2 wall thickness. Wall thickness was obtained from echocardiogram. But this was not always possible, because of the difficulty in quantitation and calibration by radionuclide angiocardiography.

Fig. 16 shows the frequency of exercise-induced asynergy in the patients with positive exercise ECG. Those who had only positive exercise ECG are more frequent in female than in male.

DISCUSSION
There are now many kinds of examination methods to investigate cardiac performance. They are often classified into two groups: non-invasive and invasive. Formerly, non-invasive methods were considered only for screening the subjects as one step before invasive methods. But recently many kinds of non-invasive, useful and accurate methods have been developed, and some of them are even superior to invasive ones in obtaining informations.

Table 1 shows the concepts and parameter of left ventricular performance, and the methods to
TABLE I CONCEPTS AND PARAMETERS OF LEFT VENTRICULAR PERFORMANCE, AND THE METHODS TO MEASURE THEM

<table>
<thead>
<tr>
<th>Concepts and Parameters</th>
<th>Methods</th>
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<td><strong>A. Pump function</strong></td>
<td></td>
</tr>
<tr>
<td>a) CO, SV</td>
<td>2, 5, 9, 10)</td>
</tr>
<tr>
<td>b) LVEDP</td>
<td>1)</td>
</tr>
<tr>
<td>c) LVEDD</td>
<td>5, 6, 10)</td>
</tr>
<tr>
<td>d) LVEDV</td>
<td>5, 6, 10)</td>
</tr>
<tr>
<td>EF</td>
<td>5, 6, 9, 10)</td>
</tr>
<tr>
<td>LV function curve</td>
<td>1, 2, 5, 6, 10)</td>
</tr>
<tr>
<td>P-V relationship</td>
<td>1, 5, 6, 8, 10)</td>
</tr>
<tr>
<td>e) Synergism of LV contraction</td>
<td>5, 6, 8, 9, 10)</td>
</tr>
<tr>
<td><strong>B. Myocardial contractility</strong></td>
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<tr>
<td>a) Isovolumetric phase:</td>
<td></td>
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<tr>
<td>dp/dt</td>
<td>1)</td>
</tr>
<tr>
<td>b) Ejection phase:</td>
<td></td>
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<tr>
<td>Vcf, mVcf</td>
<td>5, 6, 9, 10)</td>
</tr>
<tr>
<td>Tension-velocity-length relationship</td>
<td>1, 5, 6, 10)</td>
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<tr>
<td>Aortic flow velocity</td>
<td>7)</td>
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<tr>
<td>c) Systolic timing</td>
<td>4, 5, 6)</td>
</tr>
<tr>
<td><strong>C. Compensatory mechanisms</strong></td>
<td></td>
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<tr>
<td>Hypertrophy: wall thickness</td>
<td>3, 5, 6, 10)</td>
</tr>
<tr>
<td>Dilatation: diameter, volume</td>
<td>3, 5, 6, 10)</td>
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| CO: cardiac output, SV: stroke volume, LV: left ventricle, ED: end-diastole, P: pressure, D: diameter, V: volume |

TABLE II PRINCIPLES OF THE MEASUREMENTS OF LEFT VENTRICULAR PERFORMANCE

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Cardiac catheterization</th>
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<tbody>
<tr>
<td>Blood flow volume</td>
<td>Fick or dilution method</td>
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<tr>
<td>Blood flow velocity</td>
<td>Pulsed Doppler flowmeter</td>
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<tr>
<td>Dimension</td>
<td>X-ray film or cinegram</td>
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<tr>
<td>shape, image</td>
<td>Echocardiography</td>
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<td>T</td>
<td>Two-dimensional echocardiography</td>
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<tr>
<td>Timing</td>
<td>Systolic time intervals</td>
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<td>CKG</td>
<td>Radionuclide angiography</td>
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<td>Contrast ventriculography</td>
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measure them. Table II shows the principles of the measurements. From these methods, at present, we can select those, which seem appropriate to our purpose to measure the parameters of left ventricular performance.

And in evaluating cardiac patients, it is important to be able to estimate left ventricular reserve. This can be done by measuring various parameters at exercise. However, reliable and easily available methods have been lacking for it. Left ventricular catheterization, which is an invasive method, cannot be easily performed during exercise.

Chest X-ray film reveals the degree of dilatation of cardiac chambers and it is related to cardiac performance. X-ray cinegram can be applied
during exercise. But it can not discriminate cardiac chambers.

Now, there are two useful methods for evaluation of left ventricular performance; echocardiography and radionuclide angiography. Radionuclide angiography has been already applied to exercise test, and we have also applied echocardiography to exercise test. The reproducibility of EF and mVcf obtained by these methods, the coincidence of the parameters obtained by the two methods, and the clinical usefulness of the parameters as indices of clinical status has been ascertained.

These two methods, radionuclide angiography and echocardiography, have merits and demerits respectively. Radionuclide angiography can be performed in almost all the cases at rest and at exercise. In the cases of severe heart failure with prolonged circulation time, first pass method of radionuclide angiography may not offer good imaging, and in such cases equilibrium method might be more useful.

Radionuclide angiography can offer indices such as E' from relative values of isotope count, but the problem still remains in obtaining absolute values of dimension, such as LVDd or LVEDV, because of the problems of image resolution and of calibration. So, radionuclide angiography seems not so good for the detailed analysis of left ventricular mechanics, such as myocardial contractility, preload or afterload. For these analyses, echocardiography seems more useful, as echocardiography is based on the measurement of length by the passing time of ultrasonic beam.

Radionuclide angiography can express three-dimensional information on a two-dimensional plane. So it can offer regional information about each part of the whole left ventricle, and this point is very useful in evaluating ischemic heart disease. On the other hand, echocardiography can offer the informations only about posterior wall and interventricular septum. Two-dimensional echocardiography is now being tried to make up for this demerit.

Radionuclide angiography can not offer continuous information during exercise, as echocardiography can do in Fig. 14. This continuous information may be beneficial in rehabilitation of cardiac patients.

Radionuclide angiography can be performed in any subjects; on the contrary, echocardiography is known not always offer good image in all subjects even at rest. When a clear echocardiogram was obtained at rest, we could obtain acceptable recordings during exercise in 83% of our patients. CKG was also useful in detecting systolic bulge induced by myocardial ischemia, although there remains a problem in quantitative expression by it.

The informations obtained by pulsed Doppler flowmeter are different from those obtained by radionuclide angiography or by echocardiography, as the principle of Doppler method is based on flowmetry, but not on the cardiac dimension. It can offer different kind of useful informations about left ventricular performance. As shown in Fig. 4, radionuclide angiography can reveal phasic aortic blood flow pattern, but it can not reveal aortic regurgitant flow pattern, in contrast to Doppler flowmeter.

In conclusion. i) Radionuclide angiography can be performed both at rest and at exercise, contrary to invasive methods. ii) In detailed analysis of left ventricular mechanics in non-ischemic heart diseases, echocardiography (at rest and at exercise) may be appropriate, because of its high image resolution. iii) In evaluation of ischemic heart diseases, radionuclide angiography (at rest and at exercise) might be appropriate, because of its bidirectional informations and its high success rate, although not so reliable in quantitation. Two-dimensional echocardiography with M-mode echocardiography might compensate for it, particularly for continuous informations during exercise. As detection of regional wall motion dysfunction at exercise is more specific than exercise ECG and is more sensitive than exercise myocardial imaging, the methods may be applied in the diagnosis of myocardial ischemia. iv) From many kinds of examinations for cardiac performance, appropriate one should be selected according to the purpose of investigators. iv) Much more technical progress can be expected in these methods in future.

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