Evaluation of the Left Ventricular Function in Aortic Regurgitation by Echocardiography and Indicator Dilution Method

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SUMMARY

The left ventricular function and severity of LV volume overload were assessed in 30 patients with aortic regurgitation by a combined use of echocardiography and indicator dilution method.

With decreasing functional capacity of patients, there tended to be greater increase in EDV, and decreases in CO, EF, Vcf, and BAP(DN)/ESV, and shift of LV function curve downward and to the right, reflecting LV myocardial dysfunction.

There was a substantial correlation between functional capacity and the severity of regurgitation as well as LV myocardial function, suggesting the possibility that clinical symptoms may depend upon both the myocardial function and severity of aortic regurgitation. In contrast with many patients with AR of functional class I or II, who had relatively normal LV function, the patients of class III consistently showed substantial LV myocardial dysfunction.

After sublingual administration of ISDN, BAP lowered, EDV and RF decreased. Lowering of BAP and RF were more prominent in class III than in class I.

It has been proved that a combined use of echocardiography and indicator dilution method is of value in assessing the left ventricular function and regurgitant fraction in patients with aortic regurgitation, allowing a better understanding of the disease process and the potential for recognizing patients who may require early valve replacement.

Additional Indexing Words:
Regurgitant fraction LV myocardial function Functional capacity
The severity of diastolic volume overload of the left ventricle in aortic regurgitation (AR) does not always correlate with clinical symptoms. Patients with AR are frequently free of symptoms and may deteriorate rapidly when cardiac decompensation develops, prompting urgent surgical consideration for valve replacement.\textsuperscript{1-6} Surgical replacement of aortic valve, however, is frequently impossible or ineffective because of an irreversible left ventricular (LV) myocardial damage. Therefore, serial and quantitative assessment of left ventricular function in patients with AR is an important clinical problem.

Cineangiography, usually employed in the measurement of cardiac volume and quantitating the severity of regurgitation, is invasive and hardly repeatable.\textsuperscript{7-9} Echocardiography offers a possible alternative and several studies have shown the reliability and usefulness of this noninvasive technique in measuring left ventricular volumes, ejection fraction and mean circumferential fiber shortening velocity.\textsuperscript{10-15}

The purpose of this study is to assess the left ventricular function and the severity of aortic regurgitation by a combined use of echocardiography and indicator dilution method, and to analyze the relation of LV myocardial function and the degree of LV volume overload to the functional capacity of the patient with AR.

\textbf{Materials and Methods}

The study population consisted of 30 patients with AR (20 males and 10 females, mean age of 55±10 years). Diagnosis of AR was made by phonocardiography, echocardiography, and aortography. Etiology of AR was considered to be rheumatic in 13 patients, sclerotic in 5 patients, syphilitic in 2 patients, congenital in 1 patient, and unknown in 9 patients.

The patients were divided into 3 groups according to the functional capacity of NYHA classification, group I for 12 patients of class I, group II for 10 patients of class II, group III for 8 patients of class III. Five patients of group II and all 8 patients of group III were under treatment with digitalis and/or diuretics.

Cardiac output (CO) and effective forward stroke volume (FSV) were determined by indicator dilution method. Arterial cuvette curves were recorded on a Gilford IR 103 cuvette densitometer. Indocyanine green (1 mg) was injected manually into the antecubital vein and arterial blood was drawn from the brachial artery. A recording of septal and left ventricular posterior wall echocardiograms was obtained simultaneously with phonocardiogram (PCG), and direct brachial artery pressure (BAP)
through an Aloka SSD-110 instrument and Honeywell strip-chart recorder, utilizing a 2.25 MHz transducer of 10 mm diameter with a repetition rate of 1,000 impulses per second. As shown in Fig. 1, the left ventricular end-diastolic dimension (Dd) was measured at the beginning of the upstroke of the R wave on ECG and end-systolic dimension (Ds) at the time of the aortic component of the second heart sound on PCG, respectively. Then, total stroke volume (TSV) including regurgitant volume and ejection fraction (EF) were derived from the left ventricular end-diastolic volume (EDV) and endsystolic volume (ESV) which were calculated from Dd and Ds by using the correction formula of Teichholz et al\textsuperscript{14)} \[EDV=7Dd^3/(2.4+Dd), \quad ESV=7Ds^3/(2.4+Ds)\]. Mean circumferential fiber shortening velocity (Vcf) was determined by echocardiography as \[Vcf=(Dd-Ds)/Dd\times ET\] (ET: ejection time). Regurgitant volume (Reg. V) was estimated by subtracting the FSV measured by indicator dilution method from TSV measured by echocardiography and regurgitant fraction (RF) was calculated \[RF=\text{Reg.V}/\text{TSV}\]. LV stroke work (SW) was derived from TSV and direct brachial artery pressure (BAP). LV function curve was obtained by plotting SW against EDV before and after sublingual administration of isosorbide dinitrate (ISDN) (5 mg). LV end-systolic pressure-volume ratio was determined approximately from the

*Fig. 1. Measurement of the left ventricular volume and regurgitant volume by echocardiography and indicator dilution method. ACW=anterior chest wall; IVS=interventricular septum; PW=posterior wall of the left ventricle; BAP=direct brachial artery pressure; ECG=electrocardiogram; PCG=phonocardiogram; Dd=LV dimension at end-diastole; Ds=LV dimension at end-systole.*
direct BAP at dicrotic notch (BAP(DN)) and ESV. Statistical analysis was made by using analysis of variance.

RESULTS

Fig. 2 and Table I show mean values and one standard errors of the mean of CO, EDV, BAP, RF, EF, and Vcf in the 3 groups of patients with AR.

Average CO was $5.30 \pm 0.38$ l/min in group I, $4.13 \pm 0.42$ l/min in group II, and $4.08 \pm 0.35$ l/min in group III, and was significantly lower in group III than in group I, though remained within normal range in most cases. On the other hand, EDV was significantly larger in group III than in group I and II, as indicated by averages of $159 \pm 14$ ml in group I, $169 \pm 13$ ml in group II, and $221 \pm 33$ ml in group III.

Systolic and diastolic BAP averaged $161 \pm 8$ and $70 \pm 3$ mmHg in group I, $161 \pm 8$ and $58 \pm 4$ mmHg in group II, $157 \pm 12$ and $56 \pm 5$ mmHg in group III, respectively. Diastolic BAP was significantly lower in groups II and III than in group I, though there was no significant difference in systolic BAP among the 3 groups.

RF was $22 \pm 5\%$ in group I, $34 \pm 4\%$ in group II, and $36 \pm 6\%$ in group II.
Table I. Hemodynamic Parameters in 30 Patients with AR

<table>
<thead>
<tr>
<th>Group</th>
<th>CO (l/min)</th>
<th>LVEDV (ml)</th>
<th>BAP (mmHg) syst</th>
<th>RV (ml)</th>
<th>RF (%)</th>
<th>EF (%)</th>
<th>Vcf (cm/sec)</th>
<th>RAP (mmHg) LVEDV (mmHg)</th>
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<tr>
<td>I</td>
<td>5.30 ± 0.30</td>
<td>159 ± 14</td>
<td>161 ± 29</td>
<td>28</td>
<td>22</td>
<td>5.9 ± 1.0</td>
<td>1.09 ± 0.14</td>
<td>1.98 ± 0.14</td>
</tr>
<tr>
<td>II</td>
<td>4.12 ± 0.42</td>
<td>169 ± 13</td>
<td>161 ± 50</td>
<td>33</td>
<td>34</td>
<td>4.5 ± 2.0</td>
<td>0.95 ± 0.16</td>
<td>1.53 ± 0.16</td>
</tr>
<tr>
<td>III</td>
<td>4.06 ± 0.35</td>
<td>221 ± 12</td>
<td>157 ± 56</td>
<td>38</td>
<td>36</td>
<td>4.8 ± 4.0</td>
<td>0.75 ± 0.06</td>
<td>1.12 ± 0.08</td>
</tr>
</tbody>
</table>

Each value shows mean and one standard error.

Patients were divided into 3 groups according to the NYHA functional classification (class I—group I, class II—group II, class III—group III).

III, tending to increase, though not statistically significant, as functional capacity decreased. In contrast, EF and Vcf tended to reduce significantly, with decreasing functional capacity, showing substantial reduction in group III. EF averaged 63±2% in group I, 57±2% in group II, 48±4% in group III and so did Vcf 1.00±0.14 (circ/sec), 0.95±0.05 (circ/sec), 0.75±0.06 (circ/sec), respectively.

As shown in Fig. 3, significant correlations were found between EDV and EF (r = -0.58, p < 0.001) as well as between EDV and RF (r = 0.64, p < 0.001) in the whole patients with AR with a wide spectrum of severity. Although EF in the entire group tended to reduce as RF increased as indicated in the right panel of Fig. 3, EF was maintained fairly normal and relatively constant between 55 and 65% in group I as displayed by open circles, despite a
marked variation of RF, contrasting with group III displayed by closed circles in which EF reduced progressively as RF increased.

Fig. 4 shows the average left ventricular function curves in the 3 groups. With decreasing functional capacity, LV function curve shifted to the right and downward and the slope of the curve tended to diminish.

The average values of BAP(DN)/ESV were $1.98 \pm 0.14$ mmHg/ml in group I, $1.53 \pm 0.16$ mmHg/ml in group II, and $1.12 \pm 0.08$ mmHg/ml in

Fig. 4. Relationship between SW and LVEDV before and after ISDN in patients with AR of NYHA functional classes I, II, and III (so-called left ventricular function curve). SW = left ventricular stroke work; LVEDV = left ventricular end-diastolic volume; ISDN = sublingual administration of isosorbide dinitrate (ISDN) (5 mg).

Fig. 5. Changes in BAP, LVEDV, Reg. V, before and after ISDN, in patients with AR of NYHA functional classes I, II, and III. Each bar shows mean and one standard error. * $p < 0.05$, ** $p < 0.01$. N.S. = not statistically significant.
group III as shown in Table I. This value tended to reduce with decreasing functional capacity, showing marked decrease in group III.

In Fig. 5 and Table II were shown changes in BAP, EDV, and Reg. V in the 3 groups before and after sublingual administration of ISDN (5 mg). Systolic BAP was lowered significantly after ISDN from 161±8 to 151±9 mmHg in group I, 161±8 to 145±4 mmHg in group II, 157±12 to 136±11 mmHg in group III, while diastolic BAP remained unchanged. Similarly, EDV was reduced from 159±14 to 142±12 ml in group I, 169±13 to 158±12 ml in group II, 221±33 to 197±33 ml in group III, all of which were statistically significant. In addition, ISDN decreased Reg. V from 28±9 ml to 23±8 ml in group I, 33±5 ml to 29±4 ml in group II, 38±9 ml to 26±6 ml in group III, resulting in reduced RF as presented in Table II. These lowering of systolic BAP and RF after ISDN administration was most prominent in group III. The ratio of the amount of decreased regurgitant volume to that of decreased EDV was 9% in group I, 35% in group II and 42% in group III which was the largest among the 3 groups.

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<tr>
<td></td>
<td></td>
<td>LVEDV(ml) before</td>
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<td>BAP(syst)(mmHg) before</td>
<td>after</td>
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<td>±30</td>
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**DISCUSSION**

Popp et al\(^{32}\) has estimated the regurgitant flow through aortic valve by subtracting forward stroke volume determined by the Fick method from total stroke volume determined by echocardiography. Danford et al\(^{33}\) calculated aortic regurgitant flow by the arithmetic difference of aortic valvular total flow as computed from LV minor-axis dimension changes and mitral valvular flows estimated from the opening velocity of the anterior mitral leaflet. These calculations of regurgitation correlated reasonably well with the degree of valvular regurgitation estimated from angiographic method. However, no studies have been performed to estimate the severity of aortic regurgitation by a combined use of echocardiography and indicator dilution method which is

### Table II. Changes in Hemodynamics before and after ISDN in 3 Groups

<table>
<thead>
<tr>
<th></th>
<th>LVEDV(ml)</th>
<th>BAP(syst)(mmHg)</th>
<th>BAP(diast)(mmHg)</th>
<th>RV(ml)</th>
<th>RF(%)</th>
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<tr>
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<td>159</td>
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<td>161</td>
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<tr>
<td>SD</td>
<td>±14</td>
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<td>mean</td>
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<tr>
<td>SD</td>
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</table>
routinely used for the measurement of cardiac output.

The increased work load imposed on the left ventricle by aortic valve insufficiency consists of an augmentation in stroke volume, leading to a dilatation and hence a hypertrophy of the left ventricle. This compensatory hypertrophy and dilatation permits the heart with AR to maintain normal output and filling pressure for years. An augmented stroke volume, dilatation and hypertrophy of the left ventricle increase oxygen demand of the left ventricle. Low diastolic aortic pressure and a Venturi effect caused by either large forward or regurgitant flows interfere with coronary blood flow, and hence, myocardial oxygen supply. Reduction of oxygen supply may be more prominent in AR when associated with coronary artery sclerosis. As a result of chronic dilatation and hypertrophy of the left ventricle as well as imbalance between oxygen demand and supply of the left ventricle, intramyocardial fibrosis and alteration in ventricular geometry and ultrastructure develop, leading to left ventricular dysfunction.

In this study, left ventricular function as well as the severity of LV volume overload was assessed and compared with functional capacity of the patients with aortic regurgitation. With decreasing functional capacity, there tended to be greater decreases in EF, Vcf, Emax, BAP(DN)/ESV, and shift of LV function curve downward and to the right, with reduction of its slope, all of which could be signs of impaired LV function. The ratio of LV end-systolic pressure to volume appears to be an index of myocardial contractility independent of afterload and preload. Several studies have shown that the slope of end-systolic LV pressure-volume line (Emax) and the value of end-systolic pressure-volume ratio are increased by positive inotropic agents and decreased by negative inotropic agents. Aortic dicrotic pressure just above the aortic valve correlated well with dicrotic BAP (r=0.99, p<0.001). Therefore, end-systolic LV pressure-volume ratio was derived approximately from direct brachial artery pressure at dicrotic notch and ESV by echocardiography, and compared with functional capacity. Significant association was found between these values and functional capacity. It has been shown that the ability of LV to pump blood can be depicted by LV function curve showing SV or SW plotted against EDV, EDP or mean left atrial pressure. A family of such curves reflects a spectrum of contractile states and the relative position of a given curve provides a description of ventricular contractility. LV function curves showed a shift to the right and downward with decreasing functional capacity, reflecting myocardial dysfunction.

This study has shown that there is a significant correlation between NYHA functional classification and LV myocardial function reflected by LV function curve, Emax, BAP(DN)/ESV, EF, and Vcf. In particular, the pa-
tients of NYHA functional class III showed substantial LV myocardial dysfunction, whereas most measures of LV function remains relatively normal in many patients of functional class I and II. Moreover, RF tended to increase, though statistically insignificant, as functional capacity decreased and there was a substantial correlation between ventricular function and the severity of the aortic regurgitation, suggesting the possibility that clinical symptoms may depend upon both the myocardial factor and valvular regurgitation itself. Reduction of EDV and EDP after ISDN administration is considered to be resulted from a combination of reduced venous return and regurgitant volume,\textsuperscript{28,29} as confirmed by our data. The ratio of the decrement of regurgitant volume to that of EDV was larger in group III than in groups I and II. This result might show that afterload reduction by ISDN tended to be more prominent in group III than in group I or II, probably due to the depression of increased sympathetic activity by ISDN in patients with more severely impaired LV function.

Only careful longitudinal studies of LV hemodynamics before and after aortic valve replacement will be able to answer the questions of reversibility of LV size and performance and the optimal time for aortic valve replacement.\textsuperscript{5,6} Our data suggest that lowered functional capacity is consistently associated with various degrees of LV myocardial dysfunction.

This new relatively noninvasive method allows one to successfully evaluate both left ventricular function and regurgitant fraction in patients with aortic regurgitation, allowing a better understanding of the disease process and the potential for recognizing patients who may require early valve replacement.

\textbf{References}


