Effect of aortic valvular regurgitation upon the impedance cardiogram¹

RICHARD M. SCHIEKEN, MAHENDRA R. PATEL, HERMAN L. FALSETTI, ROBERT W. BARNES, AND RONALD M. LAUER

From the Division of Pediatric Cardiology, Department of Pediatrics, the Division of Cardiology, Department of Internal Medicine, and the Division of Thoracic-Cardiovascular Surgery, Department of Surgery, University of Iowa Hospitals, Iowa City, IA, USA

SUMMARY The first derivative thoracic impedance cardiogram, phonocardiogram, and electrocardiogram were recorded in three groups of 22 subjects each. In Group 1 (control), simultaneous impedance cardiogram, phonocardiogram, and aortic valve echocardiograms showed that the X point of the impedance cardiogram occurred synchronously with the aortic second heart sound and with echocardiographic aortic valve closure. In group 2 (clinical diagnosis of aortic regurgitation) the scalar magnitude of the impedance cardiogram O wave and the ratios of the impedance cardiogram wave form $X/dz/dt_{max}$ and $O/dz/dt_{max}$ were different from control. In addition, the early diastolic ($\bar{X}$) and systolic portions ($\bar{S}$) of the impedance cardiogram wave form of group 3 patients were planimeted and expressed as the ratio $\bar{X}/\bar{S}$, called the impedance cardiographic aortic regurgitant fraction (aortic RF_I). The aortic RF_I was increased by handgrip, a manoeuvre which acutely increases the magnitude of aortic regurgitation. The difference between Fick cardiac output and left ventricular angiographic output was used to calculate aortic valvular regurgitant fraction, which related closely to the impedance cardiogram. These data suggest that it is useful in the noninvasive assessment of aortic regurgitation.

The impedance cardiogram was developed by Kubicek *et al.* (1966) as a noninvasive system to monitor cardiac output. This instrument applies a constant current across the chest and the impedance to the current is recorded. Typical records of the impedance cardiogram are shown in Fig. 1 and 2.

A previous study from our laboratory, which recorded the impedance cardiogram and the phonocardiogram simultaneously, showed that the impedance cardiogram X point occurs synchronously with the aortic component of the second heart sound (Lababidi *et al.*, 1970). We have observed the X point to be deeper in subjects with aortic regurgitation than in normal subjects. A study previously reported from our laboratory indicated that though the impedance cardiogram could estimate cardiac output in children, in patients with aortic regurgitation, the impedance cardiogram overestimated the Fick cardiac output (Lababidi *et al.*, 1971). These observations suggested that the impedance cardio-

gram was affected both in contour and magnitude by aortic regurgitation and might reflect the total left ventricular systolic output, including the regurgitant fraction.

The impedance cardiogram ratio $X/dz/dt_{max}$ appears to correlate with the severity of aortic regurgitation (Schieken *et al.*, 1975). To confirm these observations, we induced experimental aortic regurgitation in dogs using a specially designed catheter. The aortic regurgitant fraction was calculated using an electromagnetic flowmeter integrated forward and reverse aortic flows. These animal data suggested that the ratio of the area under the X wave divided by the area under the dz/dt_{max} herein called the impedance cardiogram aortic regurgitant fraction (aortic RF_I) correlated well with the regurgitant fraction ($r = 0.87$) computed from the flowmeter measurements in these animals (Patel *et al.*, 1976).

With these observations in mind, we planned this clinical study to investigate further the temporal relation of the X point to echocardiographic aortic closure and to determine the correlation of the impedance cardiogram aortic RF_I to the aortic

¹Supported in part by an NIH grant

Received for publication 9 May 1977

Fig. 1 Simultaneous recording of the electrocardiogram (ECG), phonocardiogram (phono), echocardiographic aortic valve tracing (echo), and the impedance cardiogram (ICG) in a 10-year-old boy (group 1) with a clinical diagnosis of innocent pulmonary flow murmur. The echocardiographic aortic valve closure occurs shortly before the aortic component of the second heart sound (A_2), but synchronously with the nadir of the ICG X point (x).

regurgitant fraction calculated in patients undergoing cardiac catheterisation.

Subjects and methods

The impedance cardiograms of 22 control subjects (group 1) with a normal cardiac examination, 22 patients with a clinical diagnosis of mild to moderate aortic regurgitation (group 2), and 22 patients with a cardiac catheterisation diagnosis of aortic regurgitation (group 3) were recorded on a Minnesota impedance cardiogram Model 202 simultaneously with a phonocardiogram and electrocardiogram. The mean age of group 1 was 22.8 years (range 5 to 52), that of group 2 was 23.8 years (range 5 to 71), and that of group 3 was 31.4 years (range 18 to 56). In group 2 patients, the diagnosis of aortic regurgitation was established clinically by the typical auscultatory findings of an early diastolic decrescendo murmur, loudest at the left sternal border. Of 22 group 2 patients, 8 had both ab-

normal electrocardiograms with left ventricular hypertrophy, T wave changes, and chest x-ray films showing increased heart size. The impedance cardiogram was recorded in the following manner. Four coated aluminium Mylar strips with an adhesive tape backing were placed around each subject; two strips were placed around the neck and two around the lower thorax (Lababidi *et al.*, 1971). The upper electrodes on the thorax were placed at the level of the xiphoid process. The electrodes on the neck and trunk were placed at least 3 cm apart. The outer two electrodes were attached to a constant current oscillator supplying alternating current at 100 KHz. The first derivative of the electrical impedance between the inner two electrodes was continuously recorded. Echocardiograms of the aortic valve were recorded using a Smith Kline Ekoline 20 ultrasonoscope with a 2.2 or 3.5 mHz transducer with a 1 μ s transmission time and a repetition rate of 1000/s. Simultaneous phonocardiograms, with a frequency filter set from 50 to 100 Hz, were recorded from the second right intercostal space.

The wave form of the impedance cardiogram was recorded simultaneously with the echocardiogram, phonocardiogram, and standard lead II of the electrocardiogram on an Electronics for Medicine DR12 modified for echocardiographic recording in 10 subjects from group 1. The intervals from the Q wave of the electrocardiogram to the X point of the impedance cardiogram and the Q wave to the echocardiographic closure of the aortic valve were measured. The uniformity and accuracy of the paper speed (100 mm/s) were measured from 0.04 s time lines generated within the recorder. All impedance cardiographic tracings were recorded in held midexpiration to minimise respiratory variation. The maximal deflection of $dz/dt_{\max}$, O point, and depth of the X point were measured in ohm/s (Fig. 2). Two ratios $dz/dt_{\max}$ and $O/dz/dt_{\max}$ were calculated.

Group 3 patients with aortic valvular regurgitation underwent cardiac catheterisation. Oxygen consumption was measured using a Wright respirometer and a Beckman E_2 oxygen analyser. The expired air volumes were measured for 3 minutes. Cardiac output was measured by the Fick method. Left ventricular cineangiograms were performed in the right anterior oblique position. All data were analysed randomly without previous knowledge of patient identification. Ventricular volumes were computed using the formula:

$$\text{volume calculated (V}_c\text{)} = \frac{\pi}{6} M^2 L (CF)^3, \text{ where } M =$$

minor axis in centimetres, perpendicular to a major

Fig. 2 The left panel shows the electrocardiogram (ECG), the impedance cardiogram (ICG), and phonocardiogram (phono) of a control subject. Before the ICG, a calibration of 1 ohm/s is recorded. The maximum upward deflection occurs during systole ($dz/dt_{\max}$). The nadir of the X wave, the X point, occurs with the aortic component of the second heart sound. The smaller positive deflection, the O wave, occurs during rapid diastolic filling. The right panel shows a similar recording in a patient with an aortic regurgitant fraction of 48 per cent. The striped area ($\bar{S}$) defines the area under $dz/dt_{\max}$ or the systolic portion of the ICG. The stippled area $\bar{X}$ is the early diastolic portion. The area boundaries are (B° to B' and B' to X') the intersections of these wave forms with a line drawn through the B° of two successive ICG wave forms. The area $\bar{X}$ divided by the area $\bar{S}$ is called the impedance cardiogram aortic regurgitant fraction (aortic RF_1).

axis at mid point, L = major axis in centimetres, taken from the left atrioventricular intersection to apex, and CF = correction factor (Greene *et al.*, 1967). This volume was further corrected using the formula (Kennedy *et al.*, 1970): volume = $V_e \times 0.81 + 1.9$.

The Fick angiographic aortic regurgitant fractions were expressed as the difference between the cineangiographic left ventricular volumes and Fick cardiac output divided by the cineangiographic left ventricular volumes (Kubicek *et al.*, 1966). Impedance cardiograms were performed at cardiac catheterisation during the measurement of oxygen consumption. The planimetered areas $\bar{X}$ and $\bar{S}$ were measured using a Keuffel-Esser hand planimeter (Fig. 2). The baseline was established by drawing a line between the B° of two successive beats. The B° which marks the beginning of isovolumetric contraction was identified by the first

high frequency component of the first heart sound (Lababidi *et al.*, 1970). The X wave of the impedance cardiogram was identified and boundaries of that wave which crossed the drawn baseline were B' and X' (Fig. 2). The planimetered areas B' to X' ($\bar{X}$) and B° to B' ($\bar{S}$) were used to compute the ratio $\bar{X}/\bar{S}$. This ratio was called the impedance cardiographic aortic regurgitant fraction (aortic RF_1).

For each subject in group 3, a correlation was sought between the impedance cardiogram $\bar{X}$ and the Fick angiographic regurgitant volume. In addition, a correlation was sought between the impedance cardiogram $\bar{S}$ and the cineangiographic left ventricular stroke volume.

Because our data showed a high correlation between $\bar{X}$ and regurgitant volume and a similar high correlation between $\bar{S}$ and left ventricular stroke volume, by substituting $\bar{X}$ and $\bar{S}$ into the standard formula for cardiac catheterisation deter-

mined aortic regurgitant fraction (AR_{tx}), we derived aortic RF_1

$$AR_{tx} = \frac{\text{Cineangiographic LVSV} - \text{Fick stroke volume}}{\text{Cineangiographic LVSV}} \times 100\%$$

Then substituting the impedance cardiogram equivalents of regurgitant volume ($\bar{X}$) and a cineangiographic left ventricular stroke volume ($\bar{S}$) the formula becomes

$$AR_{tx} = \bar{X}/\bar{S}.$$

To test whether indeed the $\bar{X}/\bar{S}$ is a measure of regurgitant fraction it was compared with the catheterisation-measured regurgitant fraction.

After cardiac catheterisation 8 patients of group 3 were asked to perform maximal sustained handgrip, and were then allowed to rest. The impedance cardiogram was measured at rest and during 25 per cent of maximal handgrip during held mid-expiration.

All data are expressed as the mean ± 1 standard deviation. The significance of difference between the means was calculated by employing either group or paired *t* tests.

To test the reliability of the aortic RF_1 , we measured an additional 3 beats the next day in 10 patients from group 3. These 3 beats were compared one with another and their average with the previous average aortic RF_1 . The reliability between beats within the same individual and between the averages of two different sets of beats was determined for the impedance cardiogram. This was calculated using a 2 factor (randomised block) analysis of variant design.

Results

The X point of the impedance cardiogram is an event that occurs nearly synchronously with aortic valve closure. In 10 of 22 control subjects who had echocardiograms of the aortic valve, the Q to aortic closure time (0.36 ± 0.08 s) was not significantly

different from the Q to X point on the impedance cardiogram (0.34 ± 0.06) (Fig. 1). An analysis of variance indicated no significant difference between these intervals ($r = 0.87$).

The impedance wave for scalar measurements in both group 2 and group 3 were compared with group 1 (Table 1). There was no significant difference between the measurement of the height of dz/dt_{max} or the depth of the X point between the groups. None the less, the X point appeared to be increased in subjects with aortic regurgitation. The O point was diminished ($P < 0.01$) in subjects with aortic regurgitation. The ratio $\bar{X}/dz/dt_{max}$ was increased ($P < 0.001$) and the ratio $O/dz/dt_{max}$ was diminished ($P < 0.01$) in subjects with aortic regurgitation.

The catheterisation measurements in group 3 patients of left ventricular stroke volume, aortic regurgitant stroke volume, regurgitant fraction, and the impedance measurements, $\bar{S}$, $\bar{X}$, and ratio $\bar{X}/\bar{S}$ are given in Table 2. In group 3 patients (Table 2), there was a range of angiographic stroke volumes of 32 to 156 ml. The impedance area $\bar{S}$ correlated ($r = 0.96$) with left ventricular stroke volume; while $\bar{X}$ correlated ($r = 0.89$) with aortic regurgitant volume. The ratio $\bar{X}/\bar{S}$, the aortic RF_1 , correlated highly with the angiographic aortic regurgitant fraction ($r = 0.90$). This relation is shown in Fig. 3.

Sustained handgrip of 25 per cent maximum grip increased the aortic RF_1 in all 8 patients. The aortic RF_1 rose from a resting level of 0.48 ± 0.09 to 0.71 ± 0.1 ($P < 0.01$).

Statistical analysis of the reproducibility of the impedance cardiogram measurements ($\bar{X}$, $\bar{S}$) showed that the intraclass correlation coefficient was 0.94 between beats within the same individual and 0.85 between the averages of two different sets of beats in the same individual recorded on the next day.

Discussion

The data presented confirm the temporal relation of the impedance cardiogram X point to aortic closure. This temporal relation allows the impedance cardiogram X point to be a useful marker

Table 1 First derivative impedance cardiogram measurements in control subjects and patients with aortic regurgitation

Subjects	No.	dz/dt_{max} (Ω/s)*	X point (Ω/s)*	O point (Ω/s)*	X	O
					dz/dt_{max}	dz/dt_{max}
Group 1	22	2.64 ± 0.95	0.93 ± 0.36	0.42 ± 0.24	0.35 ± 0.02	0.16 ± 0.08
Group 2	22	2.50 ± 1.08	1.20 ± 0.51	$0.17 \pm 0.09^\dagger$	$0.51 \pm 0.19^\dagger$	$0.08 \pm 0.07^\dagger$
Group 3	22	2.73 ± 0.96	1.57 ± 0.49	$0.15 \pm 0.08^\dagger$	$0.46 \pm 0.12^\dagger$	$0.08 \pm 0.08^\dagger$

*These values are the means and standard deviations of the maximal heights or depths of these points.

†Indicates a significance level of $P < 0.01$, comparing group 1 measurements (control) with group 2 or group 3 by group *t* tests.

Table 2 Cardiac catheterisation and impedance cardiogram data in group 3 subjects ($n = 22$)

$\bar{S}$ (Ohms)	Angiographic left ventricular stroke volume (ml/beat)	$\bar{X}$ (Ohms)	Fick angiographic regurgitant volume (ml)	Fick angiographic regurgitant fraction (%)	Aortic RF_1 $\bar{X}/\bar{S}$ (%)
3.86	192	1.0	42.24	22	26
3.19	160	0.56	32.0	20.3	18
4.02	200	2.13	92.0	46	52
2.3	120	0.60	36.0	30	26
2.5	130	1.65	81.9	63	66
5.5	231	2.02	103.95	45	37
2.3	120	1.0	40.8	34	43
1.8	90	1.0	48.6	54	55
6.6	260	3.4	114.4	44	51
8.4	265	4.8	129.85	49	57
4.8	230	2.6	138	60	54
5.7	240	3.8	156	65	66
4.1	190	2.7	119.7	63	65
1.73	65	1.2	44.2	68	69
2.95	150	1.35	54	36	45
5.3	220	1.9	77	35	36
2.9	145	1.6	63.8	44	55
3.9	195	2.3	109.2	56	58
1.9	90	1.1	54	60	57
3.1	174	1.78	87	50	57
5.4	210	1.8	94.5	45	33
2.8	140	1.5	64.4	46	53

Fig. 3 Relation of the impedance cardiogram aortic regurgitant fraction (aortic RF_1) to the angiographically determined regurgitant fraction. The dotted lines represent the 95 per cent confidence limits.

for the aortic component of the second heart sound.

The physical principles that govern changes in the impedance cardiogram are not completely understood. Kubicek and others using simultaneous recordings of impedance and aortic flow in dogs showed the relation of peak dz/dt_{max} to the

peak aortic ejection rate (Kubicek *et al.*, 1974).

We have shown that the systolic portion of the impedance cardiogram ($\bar{S}$) has a strong correlation with the left ventricular stroke volume as determined by cineangiography. In patients with aortic regurgitation, the cineangiographic left ventricular stroke volume exceeds the Fick calculated cardiac output. The regurgitant volume within the left ventricle is responsible for this discrepancy.

The early diastolic portion of the impedance cardiogram ($\bar{X}$) correlates highly with the per beat volume regurgitated across the aortic valve. This explains the deepened X point observed in subjects with aortic regurgitation. Moreover, the impedance cardiogram ratio $\bar{X}/\bar{S}$, the aortic RF_1 , correlates with the resting aortic regurgitant fraction found at cardiac catheterisation.

To test the response of the impedance cardiogram ratio $\bar{X}/\bar{S}$ to acute changes in the regurgitant volume, we employed isometric handgrip exercise, which has been shown to increase the amount of aortic regurgitation (Lind *et al.*, 1964; Kivowitz *et al.*, 1971). Because the aortic RF_1 did increase with handgrip, the impedance cardiogram appears to respond concordantly to an acute change in regurgitant volume.

The noninvasive assessment of the severity of aortic regurgitation is difficult. Bounding peripheral pulses are unreliable markers for severe aortic regurgitation (Demany and Zimmerman, 1966). Early mitral valve closure is found by echocardiography with severe aortic regurgitation (Botvinick *et al.*, 1975). Left ventricular dysfunction associated with severe aortic regurgitation correlates with

change in fraction of shortening of the echocardiographic minor axis (McDonald, 1976). Moreover, Boughner has found transcutaneous Doppler assessment to relate closely to the regurgitant fraction (Boughner, 1975). Despite these techniques, the clinical assessment of aortic regurgitation remains difficult.

Our findings, both clinical and experimental, suggest that the impedance cardiogram may prove to be a sensitive noninvasive measure of the severity of aortic regurgitation.

References

- Borvinick, E. H., Schiller, N. B., Wickramasekaran, R., Klausner, S. C., and Gertz, E. (1975). Echocardiographic demonstration of early mitral valve closure in severe aortic insufficiency. *Circulation*, **51**, 836-847.
- Boughner, D. R. (1975). Assessment of aortic insufficiency by transcutaneous Doppler ultrasound. *Circulation*, **52**, 874-879.
- Demany, M. A., and Zimmerman, H. A. (1966). Marked aortic regurgitation without peripheral vascular signs. *Diseases of the Chest*, **49**, 61-66.
- Greene, D. G., Carlisle, R., Grant, C., and Bunnell, I. L. (1967). Estimation of left ventricular volume by one plane cineangiography. *Circulation*, **35**, 61-69.
- Kennedy, W. J., Trenholme, S. E., and Kasser, I. S. (1970). Left ventricular volume and mass from single-plane cineangiogram. A comparison of anteroposterior and right anterior oblique methods. *American Heart Journal*, **80**, 343-352.
- Kivowitz, C., Parmely, W. W., Donoso, R., Marcus, H., Ganz, W., and Swan, H. J. C. (1971). Effects of isometric exercise on cardiac performance, the grip test. *Circulation*, **44**, 994-1002.
- Kubicek, W. G., Karnegis, J. N., Patterson, R. P., Witsoe, D. A., and Mattson, R. H. (1966). Development and evaluation of an impedance cardiac output system. *Aerospace Medicine*, **37**, 1208-1212.
- Kubicek, W. G., Kottke, J. F., Ramos, M. U., Patterson, R. P., Witsoe, D. A., Labree, J. W., Remole, W., Layman, T. E., Schoening, H., and Garamella, J. T. (1974). The Minnesota impedance cardiograph theory and applications. *Biomedical Engineering*, **9**, 410-416.
- Lababidi, Z., Ehmke, D. A., Durnin, R. E., Leaverton, P. E., and Lauer, R. M. (1970). The first derivative thoracic impedance cardiogram. *Circulation*, **41**, 651-658.
- Lababidi, Z., Ehmke, D. A., Durnin, R. E., Leaverton, P. E., and Lauer, R. M. (1971). Evaluation of impedance cardiac output in children. *Pediatrics*, **47**, 870-879.
- Lind, A. R., Taylor, S. H., Humphreys, P. W., Kennelly, B. M., and Donald, K. W. (1964). The circulatory effects of sustained voluntary muscle contraction. *Clinical Science*, **27**, 229-244.
- McDonald, I. G. (1976). Echocardiographic assessment of left ventricular function in aortic valve disease. *Circulation*, **53**, 860-871.
- Patel, M. R., Rogers, J. P., Falsetti, H. L., and Schieken, R. M. (1976). Thoracic impedance cardiogram in acute experimental aortic regurgitation. In *Proceedings of 29th ACEMB, Boston, Massachusetts, 6-10 November*.
- Schieken, R., Patel, M., Jordan, H., and Lauer, R. (1975). Quantitative assessment of aortic regurgitation using thoracic impedance cardiogram. In *American Academy of Pediatrics Proceedings, Subsection Cardiology, October*, p. 28.

Requests for reprints to Dr Richard M. Schieken, Division of Pediatric Cardiology, University of Iowa Hospitals, Iowa City, Iowa 52242, USA.