Instantaneous measurement of left and right ventricular stroke volume and pressure-volume relationships with an impedance catheter

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ABSTRACT The feasibility of using continuous on-line recording of intraventricular electrical impedance to measure ventricular stroke volume was assessed in 12 patients at cardiac catheterization with a multielectrode impedance catheter and a 1.3 kHz measuring current of 4 μA. Stroke volumes determined by electrical impedance were compared with stroke volumes determined by the thermodilution technique in 10 patients and correlated with an r value of .95. Directional changes in impedance recordings throughout the cardiac cycle were also compared with volume curves obtained from six patients by radionuclide ventriculography, and in all instances the agreement between the two volume recordings was excellent. For all patients, on-line measurements of impedance showed a beat-by-beat decrease in stroke volume with the Valsalva maneuver and the administration of amyl nitrite, as well as an immediate increase in stroke volume in the contraction following an extra-systolic beat. Similar directional changes in stroke volume were recorded in both left and right ventricles. Left ventricular pressure-volume relationships were assessed with simultaneous left ventricular pressure recordings and volume signals recorded from the impedance catheter to determine if impedance measurements of volume can be used clinically. Pressure-volume diagrams were subsequently plotted, and for all patients these diagrams showed characteristic isovolumetric contraction and relaxation phases as well as typical ejection and filling periods. Moreover, beat-by-beat sequential pressure-volume diagrams constructed for patients during the administration of amyl nitrite revealed a linear end-systolic pressure-volume relationship. We conclude that measurement of intracavitary electrical impedance can be used to monitor instantaneous changes in stroke volume in patients and may be helpful in the construction of pressure-volume diagrams and the assessment of left ventricular end-systolic pressure-volume relationships.

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THE CONTINUOUS on-line recording of intraventricular electrical impedance has been proposed as a means of instantaneously determining stroke volume and cardiac output. Previous studies of animals have found a high correlation between intracardiac impedance measurements and stroke volume determined by standard techniques, but there have been only preliminary reports on the use of impedance measurements in humans. The purpose of our study was to assess the feasibility of monitoring instantaneous stroke volume with an impedance catheter technique in patients studied at cardiac catheterization. The validity of changes of stroke volume measured by the impedance catheter was assessed by comparing impedance recordings with simultaneously measured stroke volumes determined by thermodilution. The ability of the impedance catheter to measure relative changes in volume throughout the cardiac cycle was also assessed by comparing volume signals recorded from the impedance catheter with volume curves obtained simultaneously by radionuclide ventriculography. Beat-to-beat changes in stroke volume induced by the Valsalva maneuver, administration of amyl nitrite, and stimulation of premature ventricular impulses were assessed by impedance measurements in all patients. Moreover,
volume signals recorded from the impedance catheter and left ventricular pressure recordings were used in the construction of left ventricular pressure–volume diagrams and the assessment of left ventricular end-systolic pressure–volume relationships to determine if stroke volume measured by impedance can be used clinically.

**Methods**

**Study group.** Measurements of intracardiac electrical impedance were made at cardiac catheterization in 10 men and two women who had an average age of 52 years old. All patients had been referred for evaluation of chest pain and were scheduled for diagnostic catheterization. After approval of the project by the Beth Israel Hospital’s Committee on Clinical Investigation, all patients gave written informed consent after being informed of the nature and purpose of the study and the potential risks involved. There were no complications for patients as a result of this study.

**Cardiac catheterization.** Coronary angiography was performed in all patients with standard techniques. Left ventriculography was performed via a pigtail catheter with simultaneous biplane cineangiographic recordings in the right and left anterior oblique projections. Right heart catheterization was performed in all patients with a flow-directed thermocatheter that was inserted percutaneously into the right femoral vein and advanced to the pulmonary artery.

In each of five patients tested with atrial pacing (see below), a bipolar, flared, atrial-pacing catheter (Atcri-pacer; Mansfield Scientific, Mansfield MA) was inserted percutaneously into the left femoral vein and advanced to the right atrium.

**Measurements of intracardiac electrical impedance.** Measurement of intracardiac impedance was accomplished with a No. 9F end-hole multielectrode catheter (Cardiac Pacemakers Inc.; St. Paul, MN) that was inserted percutaneously through a No. 9F sheath and advanced retrogradely (over a guidewire under fluoroscopic guidance) from the right femoral artery to the left ventricle. The catheter consists of 12 platinum ring electrodes mounted equidistantly at 1 cm intervals along the distal 12 cm of the catheter (figure 1). Under fluoroscopic guidance, the catheter was positioned along the long axis of the left ventricle with the distal catheter tip placed at the left ventricular apex. Once the catheter was in position, a constant alternating 1.3 kHz current of 4 μA was applied between driving electrodes numbers 1 and 9, while sensing electrode pairs 2–4, 4–6, and 6–8 were used to measure voltage generated by the current and the impedance of blood within the left ventricular cavity. Impedance recordings from sensing electrode pairs 2–4 were inscribed on a Honeywell Electronics for Medicine VR-16 recorder.

After the impedance catheter had been properly positioned along the long axis of the left ventricle, baseline left ventricular impedance signals, pressure tracings, and cardiac output by the thermodilution method were obtained in all patients. Each patient was subsequently tested with these maneuvers, including Valsalva maneuver, inhalation of amyl nitrite, and stimulation of premature ventricular impulses, while continuous on-line recording of the intraventricular impedance signal and left ventricular pressure was performed. After each maneuver, left ventricular pressure and impedance measurements were allowed to return to their baseline state before further interventions were done.

In five patients, the impedance catheter was introduced into the left femoral vein and was placed (under fluoroscopic control) along the long axis of the right ventricle; again, after the measurement of right ventricular pressure and volume in the impedance catheter, each patient was tested by the Valsalva maneuver, inhalation of amyl nitrite, and stimulation of premature ventricular impulses.

**Measurement of stroke volumes.** Previous researchers doing animal studies using the impedance principle have reported accurate ventricular stroke volumes by determining a calibration factor of impedance based on a measurement in vitro of blood resistivity, a known distance between sensing electrodes, and a difference in measurements of end-diastolic and end-systolic impedance. Because of theoretical considerations that are discussed below, no attempt was made in our study to determine absolute ventricular volumes; rather, changes in stroke volume were determined by comparing impedance measurements and thermodilution measurements in each patient at two different steady states. Accordingly, in each of 10 patients, baseline intraventricular impedance signal, left ventricular pressure, and cardiac output determined by the thermodilution method were measured, followed either by the sublingual administration of 0.15 mg of nitroglycerin or atrial pacing at a heart rate of 120 beats/min. After a new steady state had been achieved, repeat measurements of intraventricular impedance, left ventricular pressure, and cardiac output by the thermodilution method were made. The change in the stroke volume determined by the thermodilution method was calculated for each patient from the change in the heart rate and the cardiac output determined by the thermodilution method; change in volume as measured by impedance was subsequently correlated with the change in stroke volume determined by thermodilution measured in each patient.

**Measurement of relative chamber volumes throughout the cardiac cycle.** In six patients, intraventricular impedance measurements were made simultaneously with gated radionuclide ventriculography. Each patient was injected with 20 mCi of red blood cells labeled in vitro with technetium-99m and was subsequently scanned in the modified left anterior oblique position over 5 min. A total of at least 10 million counts per study was collected with a 30 degree slant-hole collimator and a portable small field-of-view camera (Technicare 410) with an on-board computer. The degree of obliquity (35 to 45 degrees) was individualized to best visualize the septum in each patient. Relative left ventricular volumes vs time curves were derived from each study from an operator-defined, fixed, left ventricular region of interest and a computer-selected background region of interest.

Impedance signals obtained from a minimum of 6 consecutive beats (representing the range of impedance measurements
Results

Cardiac catheterization. All 12 patients who were studied had significant coronary obstructive disease, with eight patients having obstruction of three vessels and four having obstruction of two vessels. Six patients had a history of prior myocardial infarction, and in each patient left ventriculography revealed a localized regional wall abnormality corresponding to the infarct. Left ventricular ejection fractions ranged between 52% and 76%. No patient had significant valvular regurgitation.

Waveform of intraventricular impedance signal. For all 12 patients, impedance measurements from the left ventricle were recorded as continuous on-line waveforms that resembled ventricular volume signals. An example of a typical left ventricular impedance tracing is shown in figure 2 along with simultaneously recorded left ventricular pressure. The impedance tracing shows a maximum "volume" at end-diastole following a discrete wave, presumably representing atrial systole. Throughout the respiratory cycle obtained at the midpoint of the radionuclide scan were subsequently digitized and averaged by a 4052 Tektronix computer to obtain an average left ventricular impedance signal. For each patient the recording of the intraventricular impedance signal and the time-activity (volume) curve obtained from the radionuclide scan were subsequently superimposed to assess the agreement between the two methods in measuring volume changes throughout the cardiac cycle.

Left ventricular pressure-volume relationships. For all 12 patients, intraventricular impedance signals and left ventricular pressure tracings were synchronized to end-diastole with the peak of the R wave on each patient's electrocardiogram and digitized with a 4052 Tektronix computer; pressure-volume diagrams were subsequently plotted from 32 pressure-volume points throughout the cardiac cycle. In five patients, sequential pressure-volume diagrams were constructed from every fourth beat after the inhalation of amyl nitrite to assess sequential changes in pressure and volume in response to short-term alteration in loading conditions.

FIGURE 2. Simultaneous recording of left ventricular (LV) pressure, intracardiac electrical impedance (V), and electrocardiogram (EKG). The impedance tracing shows a maximum at end-diastole following a discrete wave, presumably representing atrial systole.

FIGURE 3. Correlation between impedance volume and time-activity (volume) curve throughout the cardiac cycle. Open circles, radionuclide points; closed circles, impedance points.

FIGURE 4. Correlation between the change in impedance stroke volume (SV) and thermodilution stroke volume in five patients treated with nitroglycerin and five patients undergoing atrial pacing at 120 beats/min. The correlation was excellent with r = .95 and SEE = 10.5.
dance waveform and a time-activity (volume) curve obtained simultaneously by radionuclide ventriculography in the same patient. Both are plotted as percent of end-diastolic values. As is apparent from the superimposed volume curves, the agreement between the two methods in plotting relative volume changes throughout the cardiac cycle is excellent. Similar agreement was noted in the five other patients in whom a comparison of time-activity curves was undertaken.

**Measurement of stroke volume changes.** Figure 4 shows the correlation between changes in stroke volume measured by the impedance catheter technique and by the simultaneous thermodilution technique in 10 patients. In five of the patients treated with sublingual nitroglycerin, left ventricular stroke volume determined by the thermodilution method decreased to a mean of 92 ± 5%, while in an additional five patients who underwent atrial pacing at 120 beats/min, stroke volume (determined by thermodilution method) decreased to approximately 63 ± 7%. The correlation between stroke volume measurements determined by the thermodilution and impedance methods was $r = .95$.

**Continuous on-line measurement of left ventricular stroke volume.** Figures 5A through 7 show typical simultaneous impedance volume measurements and left ventricular pressure tracings in a patient during the Valsalva maneuver (figure 5A), inhalation of amyl nitrite (figure 6A), and the induction of a premature ventricular contraction (figure 7). With Valsalva maneuver, left ventricular systolic and diastolic pressures increased initially with the onset of increased intrathoracic pressure and then fell progressively until the Valsalva release; the impedance waveform showed a progressive decrease in end-diastolic and end-systolic volumes as well as a beat-by-beat decrease in stroke volume, until the release of the Valsalva when both end-diastolic and end-systolic volumes rose. With inhalation of amyl nitrite, left ventricular systolic and diastolic pressure decreased progressively as did end-diastolic, end-systolic, and stroke volumes. With the induction of a premature ventricular contraction, both left ventricular pressure and stroke volume decreased substantially during the premature contraction, but increased to above control levels in the beat following the premature contracture.

Similar directional changes were observed in right ventricular impedance waveforms in the five patients that were tested. Figure 8 shows simultaneous right ventricular pressure and impedance recordings immediately before, during, and after the Valsalva maneuver.

**Left ventricular pressure–volume diagrams and end-systolic pressure–volume relationships.** Beat-by-beat pressure–volume diagrams constructed from simultaneous left ventricular pressure recordings and intraventricular impedance tracings from all 12 patients showed characteristic isovolumetric contraction and relaxation.

**FIGURE 5A.** Simultaneous measurement of left ventricular (LV) pressure and intracardiac impedance (V) during Valsalva maneuver.

**FIGURE 5B.** Summary of beat-to-beat changes in left ventricular (LV) pressure and impedance volume during the Valsalva maneuver when baseline impedance stroke volume was calibrated to thermodilution stroke volume.
phases as well as typical filling and emptying periods. Figure 9 shows pressure-volume diagrams constructed from every fourth beat after the inhalation of amyl nitrite in one patient. Of note is the fact that the end-systolic relationship is linear.

Discussion

Our study indicates that intraventricular impedance measurements can track beat-to-beat changes in both left and right ventricular stroke volume. Our results suggest that impedance recordings can measure changes in absolute stroke volumes with reasonable accuracy if baseline impedance measurements are calibrated to standard techniques of measuring stroke volume (e.g., thermodilution). In addition, our results suggest that impedance measurements agree very well with radionuclide determinations of chamber volume changes throughout the cardiac cycle. However, while the impedance catheter technique appears to be accurate for measuring relative volumes, additional investigation will be needed before it can be accepted for the accurate determination of absolute volumes.

Theory of impedance volume measurement. The technique of electrical impedance measurement of intravascular volume has been studied for over 30 years, but has only recently been applied to determination of intracardiac volume in humans. In 1953, Rushmer et al.¹ attached electrodes to the walls of both right and left ventricles to dogs and recorded changes in impedance during contraction. In 1966, Geddes et al.² used electrodes sutured to the epicardium of a dog and measured impedance at 80 kHz during the injection and withdrawal of blood from its heart with valves sutured closed in vitro. More recently, Baan et al.³ used an eight-ring catheter with a frequency of 20 kHz and recorded in dogs a high degree of correlation between left ventricular impedance measurements and stroke volume determined simultaneously by an electromagnetic flowmeter. In addition, in a preliminary report, Baan et al.⁴ has recently described the ability of a catheter to continuously record ventricular impedance and relate it to volume in six patients.

The theoretical basis of volume determinations from impedance measurements has been previously described by Baan et al.⁴ As a first approximation the
FIGURE 7. Simultaneous measurement of left ventricular (LV) pressure and stroke volume during premature impulse stimulation (PVC); baseline stroke volume was calibrated with thermodilution.

volume of blood that is measured between any two sensing electrodes can be considered to be a cylinder with boundaries defined by the endothelial surfaces of the cardiac walls and by the equipotential surfaces through the electrodes. The total volume of blood within the left ventricular cavity can be considered to be a column of these cylinders stacked together. The change in impedance sensed during ventricular contraction in any one of these cylinders is caused by a change in resistance between the two sensing electrodes as a result of a change in the cross-sectional area of the cylinder. The relationship between resistance and cross-sectional area is given by

\[ R = \frac{\rho L}{A} \]  \hspace{1cm} (1)

where \( R \) = resistance, \( \rho \) = resistivity of blood, \( L \) = distance between sensing electrodes, and \( A \) = cross-sectional area. For a cylindrical volume where volume \( (V) \) is equal to cross-sectional area times length \( (A \times L) \), equation 2 may be substituted for resistance.

\[ R = \frac{\rho L^2}{V} \]  \hspace{1cm} (2)

Resistance at end-diastole and end-systole can now be defined as

\[ R_{ed} = \frac{\rho L^2}{V_{ed}} \]  \hspace{1cm} (3)

and

\[ R_{es} = \frac{\rho L^2}{V_{es}} \]  \hspace{1cm} (4)

where \( ed = \) end-diastole and \( es = \) end-systole. By combining these two equations and subtracting we get

\[ V_{ed} - V_{es} = \frac{\rho L^2 (R_{es} - R_{ed})}{(R_{es})(R_{ed})} \]  \hspace{1cm} (5)

Thus, for a given cylinder of blood between any two sensing electrodes, the change in volume that occurs with ventricular contraction can be determined from difference in impedance at end-systole and end-diastole. Moreover, since each cylinder of blood within the left ventricle can be thought of as a resistor in series between the driving electrodes, volume measurements for individual cylinders can be added to determine the stroke volume of the whole ventricle.

Use of the impedance catheter in vivo. As a diagnostic

FIGURE 8. Simultaneous measurement of right ventricular (RV) pressure and impedance volume (V) with Valsalva maneuver.
tool, use of the impedance catheter should add no significant risk to the patient undergoing cardiac catheterization. The catheter is inserted percutaneously through a No. 9F sheath and does not require a femoral artery cutdown. In spite of the No. 9F shaft, the distal tip of the catheter has a flexible No. 8 to No. 7F taper that minimizes risk of ventricular perforation or induction of ectopy when the catheter is positioned in the ventricle. Since the 4 μA measuring current of the catheter is far below the ventricular fibrillation threshold measured by other investigators,7 the use of the catheter offers no significant electrical risk to the patient.

Difficulties in the measurement of absolute volumes. The theory of impedance volume measurement presented above is an oversimplification that requires considerable modification when impedance measurements are used to assess absolute volumes.

One of the major difficulties that previous studies have encountered with impedance determination of absolute volumes has been in factoring out the contribution of myocardial tissue to measurements of intracardiac electrical impedance. The impedance method of determining ventricular cavity volumes depends on a higher electrical resistivity of myocardial tissue than blood. As a result, the measuring current is primarily contained within the ventricular chamber, and impedance changes should predominantly reflect the time-varying quantity of intracavitary blood. Under ideal conditions, if the tissues were a perfect insulator, all of the measuring current would pass only through the ventricular cavity, and extremely accurate volume measurements could be made. Support for this concept is derived from impedance measurements of blood volumes contained within a rubber bulb in which correlations of impedance with absolute volumes have been found to be .99.4

Some success in separating myocardial impedance from intraventricular blood impedance has been achieved by taking advantage of the fact that the contribution of tissue impedance diminishes as the frequency of the measuring current decreases.8 At frequencies of 20 kHz or greater, the resistivity of the myocardium is less than 400 Ω-cm, which is only 2.5 times greater than that of blood (150 Ω-cm). However, at 1.3 kHz, the frequency at which our studies were conducted, the resistivity of the myocardial tissue is greater than 1000 Ω-cm, and thus a much smaller percentage of the measuring current escapes the ventricle. Several previous investigations have found that impedance measurements generally underestimate ventricular stroke volume.1,2 The decrease in current leakage that occurs at this driving frequency may reflect both the improved accuracy of volume measurements reported in this study as well as the tendency to slightly overestimate stroke volumes (figure 4).

In addition to the contribution of myocardial impedance to impedance volume measurements, there are other potential problems in the determination of absolute chamber volumes. One such problem concerns the resistivity of blood, which is not constant and has been shown to vary with temperature,9 hematocrit,10 and blood velocity11; moreover, it is possible that changes in electrolyte concentrations alter resistivity as well. Perhaps of greater importance is that technical considerations in the use of the catheter need further study. For example, it is not known what differences and potential errors in volume measurements are created by variations in the catheter position in the left ventricle. Also, although the most accurate volume measurements should presumably be obtained by choosing driving electrodes that span the ventricular cavity (i.e., just below the aortic valve and at the ventricular apex), it is not clear exactly how many intermediate electrodes are needed to span the ventricular cavity. Furthermore, the effect of an open mitral valve and the contribution of left atrial volume to impedance measurements have not been determined. Finally, measurement of absolute volumes presumably depends on the geometry of the ventricle, in which the left ventricle is assumed to be a prolate ellipsoid that is approxi-
mated by a stack of cylinders in which individual measurements of impedance are added to determine the changes in impedance in the whole ventricle. Difficulties in this model exist because of both the existence of papillary muscles and chordae and possible regional wall abnormalities that may make impedance measurements inaccurate. In addition, although a stacked cylindrical model of volume may accurately approximate left ventricular volume, the geometry of the right ventricle does not represent a prolate spheroid and the accuracy of impedance volume measurements between any two right ventricular sensing electrodes needs to be determined.

Although this study suggests that impedance measurements can accurately track changes in absolute stroke volume, it is notable that in several individual patients the correlation between stroke volumes determined by impedance and those determined by thermodilution differed significantly (figure 4). Whether these discrepancies were related to problems in terms of the myocardial contribution of impedance measurements or to other technical problems described above is not certain. Until these technical problems are solved, the accuracy and value of impedance measurement of absolute volume cannot be assessed fully.

Measurement of relative volumes. While previous investigators have focused on the ability of impedance measurements to determine absolute volumes, it is clear that use of the catheter to measure relative volume changes has both theoretical appeal and potential clinical use. To begin with, measurement of relative changes in volume greatly simplifies the use of impedance measurements. Difficulties in determining the contribution of myocardial impedance to the intraventricular impedance measurement, in determining the absolute resistivity of blood, and in determining the accuracy of geometric models of the left and right ventricle are all avoided. As a diagnostic tool, impedance measurements could prove valuable in the characterization of left ventricular contractile function on a beat-by-beat analysis of end-systolic pressure-volume relationships and in the determination of the effects of drugs and other interventions on end-diastolic, end-systolic, and stroke volumes. For the clinician, impedance measurements could potentially revolutionize monitoring capabilities in the setting of the intensive care unit, with continuous monitoring of both left ventricular filling pressures and an index of right ventricular stroke volume; in this regard, our laboratory is currently testing a No. 7F balloon-tipped, flow-directed, impedance catheter that can be percutaneously inserted and advanced to the pulmonary artery to measure pulmonary artery and pulmonary capillary wedge pressures — this catheter also has appropriately placed ring electrodes to simultaneously assess measurements of right ventricular impedance.

Given the potential advantages that impedance measurement offers over standard techniques of determining volume and the apparent safety and simplicity of the method as far as the patient is concerned, it seems clear that the technique merits further investigation.

References
Instantaneous measurement of left and right ventricular stroke volume and pressure-volume relationships with an impedance catheter.

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