Determination of Stroke Volume from Left Ventricular Isovolumetric Contraction and Ejection Times

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SUMMARY

Examination was made of the relationship of left ventricular isovolumetric contraction and ejection times to stroke volume. These studies were performed in humans at cardiac catheterization using the dye dilution technique and in open-chest dogs with electromagnetic flowmeters. The cardiac phases were measured from intracardiac catheters in humans and were calculated from the flow curves in dogs. While the isovolumetric and ejection periods independently gave correlations of only marginal significance with stroke volume, the ratio of these intervals was highly significant: $r=0.92$ for humans and $r=0.86$ for dogs.

Additional Indexing Words:

Cardiac phases Indirect cardiac output

THE relationship between stroke volume and the systolic phases of ventricular contraction was first implied in the frog heart studies of Otto Frank.¹⁾ Subsequent investigations in animal and man have provided evidence that the ejection phase of ventricular systole, under conditions of uniform myocardial contractility, is directly related to stroke volume.²⁾⁻⁹⁾ These investigators also recognized the inverse relationship between the isovolumetric contraction interval and stroke volume. Blumberger¹⁰⁾ reported that a ratio of the ejection and isovolumetric contraction periods reflected changes in stroke volume, but his work was not substantiated by direct stroke volume measurements. In 1965, a report from our laboratory described the use of the systolic intervals for determining stroke volume in dogs.¹¹⁾ The present investigation was undertaken to determine whether the durations of the isovolumetric contraction and ejection intervals, independently or in combination, could be used to estimate stroke volume.

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METHODS

Human Experiments

Data were obtained from 25 subjects who had undergone left heart catheterization and who fulfilled the following criteria of normal left heart hemodynamics: sinus rhythm, normal blood pressure, normal end-diastolic pressure, absence of valvular insufficiency and shunts. Patients with minimal aortic stenosis were included if the gradient was less than 10 mm. Hg. In 9 of these subjects, simultaneous left ventricular and aortic pressures and ECGs were inscribed on a Honeywell oscillographic recorder at a paper speed of 100 mm./sec. In the remaining 16 subjects, ECGs and central aortic pressure tracings were obtained immediately after the catheter was withdrawn from the left ventricle. The isovolumetric contraction period was measured from the R peak of the ECG to the aortic upstroke; the ejection interval was measured from the aortic upstroke to the incisura of the aortic notch. Cardiac outputs were performed using cardio-green dye and the Stewart-Hamilton formula used for computation.

Animal Experiments

Five open-chest normotensive dog experiments were performed using a Statham pulsed-field electromagnetic flowmeter placed at the aortic root². The flowmeter was calibrated with each animal's blood and the instrument calibration was maintained the same in all experiments. The flow curves and Lead II of the ECG were recorded on an Electronics for Medicine oscillographic recorder at a speed of 200 mm./sec.

Measurements of the isovolumetric contraction interval were made from the peak of the "R" wave to the onset of the flowmeter upstroke; the ejection period was measured by the duration of the flow curve. Stroke volumes were calculated by measuring the area under the flow curves transcribed to mm.² paper using the "counting squares" method. Hemodynamic alterations were accomplished by rapid infusion of 100 ml. of blood into the right atrium and by mechanical constriction of the aortic arch, just distal to the site of the flowmeter.

Regression analyses were performed on the data to determine the best-fit formula for estimating stroke volume from the cardiac phases.

RESULTS

Human

The data consisted of 30 measurements made in 25 subjects and are listed in Table I.

The relationship between the ejection intervals (ET) and stroke volume

1. We wish to express our gratitude to Dr. Jeremy Swan, formerly at Mayo Clinic and now Chief of Cardiology at Cedars-Sinai Medical Center, Los Angeles, California, and to Dr. Donald Ritter at Mayo Clinic, Rochester, Minnesota, for cases 1-9; Dr. Oscar Magidson at St. Vincent's Hospital, Los Angeles, California for cases 10-16; Dr. Morton Lee Pierce at Veterans Administration Hospital, Los Angeles, California for cases 17-25.

2. Statham pulsed-field electromagnetic flowmeter Model 0-5000.

(SV) is illustrated in Fig. 1-a. While there is a tendency for the ejection period to be prolonged at higher stroke volumes, no consistent relationship between these parameters is evident ($r=0.14$). A significant inverse relationship ($r=0.74$) was found between the isovolumetric contraction interval (ICT) and SV (Fig. 1-b).

The comparison of the ET/ICT ratio to SV is shown in Fig. 2. A direct relationship was found with a significantly improved correlation over ICT or ET independently ($r=0.92$).

Table I. Human Data

	AGE	BP	HR	ICT	ET	ET/ICT	SV
1	10	104/71	90	90	300	3.3	43
2	61	100/55	58	60	320	5.3	86
3	62	127/61	80	45	270	6.0	92
4	12	108/78	104	65	260	4.0	59
		105/63	120	40	230	5.8	63
		113/44	126	35	160	4.6	61
5	14	125/65	60	40	320	8.0	160
		106/52	80	30	250	8.3	170
		104/49	130	25	200	8.0	129
6	31	147/86	66	50	300	6.0	108
7	12	104/60	99	45	210	4.7	81
		117/82	140	45	180	4.0	64
8	38	118/76	70	60	350	5.8	76
9	12	125/64	96	55	250	4.5	78
10	18	130/86	88	60	270	4.5	75
11	14	—	89	45	240	5.3	79
12	17	132/100	89	80	280	3.5	49
13	43	—	100	75	360	4.8	49
14	33	122/80	103	40	280	7.0	99
15	42	166/94	75	50	300	6.0	75
16	60	140/90	97	60	250	4.2	73
17	28	123/61	58	70	310	4.7	74
18	47	105/65	60	90	240	2.7	33
19	25	161/58	94	60	280	4.7	78
20	43	120/60	76	50	240	4.8	58
21	49	115/70	94	60	280	4.7	54
22	55	135/80	100	120	240	2.0	28
23	36	140/60	70	80	340	4.2	72
24	18	—	91	60	270	4.5	72
25	54	96/68	143	80	280	3.5	41

BP = Blood Pressure (mm. Hg)

HR = Heart Rate

ICT = Isovolumetric Contraction Time (msec.)

ET = Ejection Time (msec.)

SV = Stroke Volume (ml.)

Fig. 1. In the human, ET was virtually independent of SV, while ICT had a significant inverse relationship.

Fig. 2. The ratio ET/ICT had a significantly improved correlation with SV over the intervals independently. The parabola has its minimum at the Y-axis resulting in no linear term in the equation.

Fig. 3 compares the measured and estimated stroke volumes based on the regression formula:

$$SV = 1.8 (ET/ICT)^2 + 27$$

Most of the predicted stroke volumes fall within 20% of the actual stroke volumes and are equally distributed about the line of identity. The difference between measured and estimated stroke volume and heart rate (Fig. 4-a) indicated that the stroke volume estimate was not significantly influenced by heart rate. Similar observations were made on the arterial pressure (Fig. 4-b).

Animal

The data from the 5 dog experiments, comprising 100 stroke volume and cardiac interval measurements are listed in Table II.

Table II. Animal Data

SV	ICT	ET	ET/ICT	HR	SP	SV	ICT	ET	ET/ICT	HR	SP
3.4	45	120	2.7	140	69	3.0	75	105	1.4	180	83
4.1	65	110	1.7	188	70	3.0	75	100	1.3	180	83
4.2	65	110	1.7	170	75	3.5	72	105	1.5	180	91
4.4	60	115	1.9	166	76	4.3	72	110	1.5	160	97
6.3	50	125	2.5	166	76	4.3	65	115	1.8	165	97
6.8	50	170	3.4	145	76	4.5	60	125	2.1	165	94
6.9	55	160	2.9	136	70	4.7	60	125	2.1	165	90
7.2	47	170	3.6	140	77	4.8	75	120	1.6	160	97
7.3	47	160	3.4	133	90	5.2	65	115	1.8	165	97
7.4	52	165	3.2	133	76	5.4	62	125	2.0	165	97
7.4	45	175	3.9	133	80	2.0	70	135	1.9	140	
8.0	45	170	3.8	133	76	2.2	80	137	1.9	133	
8.0	50	160	3.2	130	75	2.4	70	135	1.7	145	
8.3	47	175	3.7	133	85	2.7	65	140	1.9	140	
9.3	50	180	3.6	133	76	4.0	75	150	2.2	140	
10.0	45	170	3.8	133	94	4.2	67	150	2.3	130	
10.2	45	170	3.8	136	110	5.3	60	150	2.5	140	
10.6	45	175	3.9	130	85	5.3	55	160	2.9	140	
10.8	42	180	4.3	185	85	5.4	56	154	2.7	133	
11.0	45	170	3.8	133	110	5.7	65	165	2.3	133	
4.8	70	160	2.3	135	70	5.7	55	165	3.0	130	
4.8	65	175	2.7	140	63	5.7	55	170	3.1	133	
5.0	70	150	2.1	140	100	6.2	50	155	2.8	140	
5.4	55	175	3.2	127	90	6.5	50	170	3.4	140	
5.5	65	165	2.5	145	110	6.5	55	170	3.1	133	
5.6	55	170	3.1	143	134	6.5	50	170	3.4	133	
5.7	60	160	2.7	143	134	6.5	50	170	3.4	135	
5.7	60	165	2.8	143	120	7.0	54	174	3.2	128	
5.7	62	185	3.0	143	126	9.0	51	185	3.6	130	
5.8	60	185	3.1	127	120	11.8	41	180	4.4	130	
6.0	60	170	2.8	143	134	4.0	75	130	1.7	155	80
6.2	55	175	3.2	127	120	4.3	70	140	2.0	175	80
6.2	60	185	3.1	143	120	4.3	70	145	2.1	160	80
6.2	60	185	3.1	145	110	4.5	60	150	2.5	155	80
6.5	57	190	3.3	143	126	4.8	70	135	1.9	175	80
6.5	55	175	3.2	132	130	5.0	55	130	2.4	150	90
6.6	50	175	3.5	143	134	5.2	70	145	2.1	160	90
6.6	50	170	3.4	120	128	5.3	65	150	2.5	160	90
7.2	55	175	3.2	127	90	5.6	50	150	3.0	170	105
8.0	60	170	2.8	132	130	6.3	70	145	2.1	160	90
1.4	80	90	1.1	180	63	6.6	60	150	2.5	160	97
1.5	80	90	1.1	180	63	6.8	55	150	2.7	170	105
1.6	75	90	1.2	180	63	7.4	52	150	2.9	170	110
1.8	75	100	1.3	180	63	7.5	60	150	2.5	175	130
1.8	70	110	1.6	180	63	7.8	50	150	3.0	160	134
2.0	75	110	1.5	180	63	8.1	50	150	3.0	170	170
2.0	75	95	1.3	180	63	8.9	70	150	2.3	150	130
2.6	77	100	1.3	180	83	9.1	60	160	2.7	160	130
2.9	70	105	1.5	180	85	9.6	50	150	3.0	150	130
3.0	80	110	1.4	180	85	10.0	50	150	3.0	160	130

SV = Stroke Volume (ml.)
ET = Ejection Time (msec.)

ICT = Isovolumetric Contraction Time
HR = Heart Rate
SP = Systolic Pressure

Fig. 3. Most of the predicted SV's determined from the regression equation were within 20% of the measured SV with equal scatter about the line of identity.

Fig. 4. A comparison of the measured—predicted stroke volume difference showed that heart rate and mean arterial pressure did not influence the ratio—SV relationship.

An example of a record obtained during infusion is shown in Fig. 5. As the stroke volume is increased by rapid infusion of blood into the animal's right atrium, there is progressive shortening of the isovolumetric and lengthening of the ejection intervals.

A comparison of ET and ICT to SV is illustrated in Fig. 6-a. In contrast to the human data, a significant correlation was found between ET and SV ($r=0.73$). The ICT was inversely related to stroke volume with a correlation similar to that found in the human ($r=0.77$). The ET—ICT ratio (Fig. 7) had a direct relationship to SV with an improved correlation over the

Fig. 5. An example of a flowmeter record obtained from an animal. Note the prolongation of ejection time (ET) and abbreviation of the isovolumetric contraction period (ICT) as stroke volume is augmented by infusing blood into the right atrium.

Fig. 6. Both ET and ICT were significantly related to SV in the animal experiments.

use of either interval independently ($r=0.86$).

The measured and estimated stroke volumes based on the formula $SV=2.53(ET/ICT)-0.82$ are compared in Fig. 8. Slightly more scatter was found than in the human data; however, most predicted SV's fell within 20% of the actual SV. As in the human, heart rate and blood pressure alterations did not appear to influence the ET/ICT ratio—stroke volume relationship (see data).

Fig. 7. The ET/ICT ratio showed an improved correlation with SV over the intervals alone.

Fig. 8. A comparison of measured SV and SV obtained by the regression formula showed equal scatter about the line of identity with most predicted SV's within 20% of the actual SV.

DISCUSSION

Investigations relating the duration of ventricular phases to stroke volume have largely been performed on the experimental animal, relatively few having been obtained in man.

Wiggers,⁵⁾ studying the intact dog heart, found that ICT was diminished by factors which increased the stroke volume (augmented venous return or end diastolic pressure), while the ejection period was prolonged. Similar observations were made on the isolated dog heart by Katz and Feil.²⁾ Wallace, et al.⁴⁾ confirmed that ICT was inversely and ET directly related to stroke volume and concluded that, because of these opposing variations, total systole remained relatively constant even while stroke volume underwent marked variations. In man, Weissler, Peeler and Roehill¹²⁾ have found a direct relationship between ejection time and stroke volume at rest for both the failing and non-failing heart. Jones and Foster⁹⁾ however, when examining these relationships both at rest and exercise, found that the ejection phase was only slightly influenced by stroke volume.

These investigations indicate that ICT is diminished by those factors which increase stroke volume. The relationship of ET to SV, however, varies with the experimental condition. Simple expansion of blood volume, as in heart-lung studies, results in a direct ET—SV relationship, but when cardiac contractility is altered, as occurs in exercise, the ejection period can be diminished even though stroke volume is unchanged or even increased. ET may then be unrelated or inversely related to SV. For ET to be correlated with SV under all conditions, compensation for altered contractility must be made. Since ICT is in large part a function of the rate of ventricular pressure rise, its duration can be used as an index of contractility.^{6), 13)} By using ICT in the denominator of the ratio ET/ICT, the ejection interval is corrected for changes in contractility. The high correlation of the ratio with stroke volume in the human, despite the independence of ET and SV may thus be explained. Where ET is inversely related to SV, the ratio may also be applicable, for if the percentage decrease of ICT is greater than that of ET, an increased ratio will result. Since the validity of the ratio is based on a true isovolumetric contraction and an ejection phase in which forward ventricular outflow represents the total stroke volume, the method would not be applicable to conditions of valvular insufficiency, shunts, etc.

It is certain that there are other factors not considered here which modify the interval—SV relationship. This is evident from the animal data where stroke volume could change independently of the intervals. That heart rate did not account for this scatter is not surprising, since ET and HR are highly correlated and thus any effects of heart rate are manifested through the duration of ET. The absence of a blood pressure effect in the human is not understood, although in the animal, the rigidity of the experimental condition (infusion of blood) may account for this finding. Further study is required to test the importance of arterial pressure, since it reflects peripheral resistance and should

thus influence the ratio—SV correlation.

Several of the human subjects in this study manifested unusual ventricular hemodynamics: subject 18 had a cardiac output of approximately 2 L. per min. and subject 12 exhibited a heart rate of 140 beats per min. While some question can be raised as to the normalcy of these individuals, their interval—SV relationships were not different from the other subjects in this study.

The quadratic regression equation obtained from the human data is highly dependent upon the inclusion of three stroke volumes from one subject. For this reason, a linear regression analysis was performed on the data exclusive of these three values. While the correlation coefficient of the linear equation was reduced from 0.92 to 0.86, the standard deviation after regression ($SV = 14.44 (\text{ratio}) + 0.51$) varies with the quadratic equation a maximum of only 5% between stroke volumes of 35 and 100 ml. The quadratic equation does not provide for stroke volumes below 27 ml. and may not be applicable to states of severely depressed circulation. The linear equation, however, while adequate for low stroke volumes, most likely underestimates at levels over 100 ml. and would not be useful in conditions of severe stress.

Despite these limitations, the correlations were sufficiently high to justify use of the ET—ICT ratio for the prediction of stroke volume in the intact left heart under average conditions. Better understanding of other factors involved may extend the usefulness of this method.

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