Pulsus Alternans Determined by Biventricular Simultaneous Systolic Time Intervals

YOSHIYUKI HADA, M.D., CARLA WOLFE, AND ERNEST CRAIGE, M.D.

SUMMARY This investigation was performed to determine the presence of unilateral or bilateral pulsus alternans in the systemic and pulmonary circulations in heart failure and to estimate the prevalence of pulsus alternans in congestive cardiomyopathy. The subjects were 36 adult patients in heart failure due to a variety of cardiopulmonary diseases. We measured left- and right-sided systolic time intervals from simultaneous dual echocardiograms of both semilunar valves. The alternans was left-sided in seven patients, right-sided in one patient and bilateral in six patients. Pulsus alternans was induced by ventricular premature complexes (VPCs), except in one patient with bilateral and persistent alternans. For a VPC to precipitate alternans, the early beat itself must be associated with an abbreviated ejection time.

Echophonocardiographic records of 100 patients with congestive cardiomyopathy were reviewed for evidence of pulsus alternans. We found persistent alternans in 10 patients and VPC-induced alternans in seven patients. We could not measure any difference in severity of disease in patients with pulsus alternans compared with those without.

PULSUS ALTERNANS was first described by Traube more than a century ago. Although hemodynamic studies have been made in humans and efforts to reproduce the condition have been undertaken, its physiologic mechanism is uncertain; nor has its incidence been determined in the deteriorated forms of heart disease in which it is considered to be a useful diagnostic sign. Pulsus alternans is ordinarily recognized from the carotid and peripheral pulse or blood pressure, but hemodynamic studies have revealed its presence in the pulmonary circulation as well. Echocardiography provides a means of observing intracardiac structures continuously and noninvasively. The presence of pulsus alternans can thus be determined by timing semilunar valve movements. This method can be applied to both right- and left-sided events. Right-sided pulsus alternans may be observed by other noninvasive methods such as external registration of pulmonary arterial pulsations, but this method is impractical.

The only reliable method available for determining bilateral alternation has been the simultaneous recording of pressures or flow velocity from the systemic and pulmonary circulations. These invasive methods are unsuitable for observations under physiologic conditions or for repeated observations in the same patient. The development in our laboratory of dual echocardiography, permitting the registration of M-mode echograms from two intracardiac structures, has lowered recording both semilunar valves simultaneously. This method is ideal for determining the presence of symmetrical or asymmetrical pulsus alternans.

Pulsus alternans is a characteristic feature of severe ventricular dysfunction, but its incidence is unknown. Using the computerized recording and retrieval system that has been used in our laboratory for 7 years, we can identify and study the records of a large number of patients with congestive cardiomyopathy and determine the prevalence of pulsus alternans.

Materials and Methods

Definition

Pulsus alternans is a beat-to-beat alternation of strong and weak contractions without significant
cyclic change of RR intervals on the ECG and independent of respiratory influences. It is recognized by alternation in the height of the pulse or systolic blood pressure or, in graphic records, by alternation in the height of the carotid pulse and the duration of the ejection time. The latter can be measured from carotid pulse tracings (fig. 1) or from semilunar valve echograms (fig. 2). Alternation is defined as persistent if it continues without waning throughout the entire recording of the semilunar valve echogram or carotid pulse and is not dependent on induction by premature beats. Pulsus alternans induced by ventricular premature complexes (VPCs) is defined as alternation initiated by the early beat and continues for three or more cardiac cycles. Electrical alternans is an unrelated condition and is not included in the present study.

Prospective Study to Determine the Presence of Bilateral or Unilateral Pulsus Alternans

Selection of Patients for Dual Echocardiography

Thirty-six patients were selected for dual echocardiographic studies from those referred to the Cardiac Graphics Laboratory for diagnostic examination during 12 months beginning in October 1978. Twenty-one were males and 15 females, ages 48.2 ± 15.6 years (mean ± SD). Criteria for inclusion were: (1) Evidence of heart disease (table 1). All of these patients were in heart failure clinically. (2) Exclusion of patients with aortic or pulmonary valvular disease. (3) Exclusion of patients with atrial fibrillation. (4) Adequate simultaneous visualization of both semilunar valves.

Technique of Dual Echocardiography

Two experienced operators were required, each manipulating a separate transducer. One located the aortic valve and the other the pulmonary valve. Depending on the echocardiographic beam direction, simultaneous visualization was accomplished from different intercostal spaces or, if necessary, from the same space. All tracings were taken at a paper speed of 100 mm/sec by an Irex 101 strip-chart recorder with an accompanying lead 2 of the ECG and phonocardiogram from two locations, the cardiac apex and base. Recordings were made in each patient during relaxed respiration or, if possible, during expiratory apnea. Care was taken to avoid pseud alternation, which can result from respiratory variations.

The following measurements were made in each case, with time intervals measured to the nearest 5 msec: (1) RR interval and heart rate. (2) Ejection time (ET), the interval from the opening point of each semi-
### Table 1. Clinical and Dual Echocardiographic Findings

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*The value in parenthesis is the number of the beats showing alternans.

Abbreviations: HR = heart rate; PEP = prejection period; ET = ejection time; CM = congestive cardiomyopathy; HT = systemic hypertension; MVR and TVR = mitral and tricuspid valve replacement; CABG = coronary artery bypass graft; CAD = coronary artery disease; ASD = atrial septal defect; P-PDA = postop patent ductus arteriosus; L and R = left- and right-sided pulsus alternans; s = strong beat; w = weak beat.
lunar valve to its closing point. The onset of opening of the pulmonary valve was determined as the onset of sharp downward movement of the posterior cusp (fig. 3). Timing of the pulmonary component (P₂) of the second heart sound in the phonocardiogram recorded simultaneously was helpful in confirming the point of the closure. (3) Preejection period (PEP), the interval from the onset of the QRS complex of the ECG to the opening point of each valve. (4) Electromechanical systole (QA₂ and QP₂), the interval from the onset of the QRS complex to the aortic and pulmonic components of S₂.

Retrospective Study of the Incidence of Pulsus Alternans in Congestive Cardiomyopathy

Selection of Patients

A series of 100 patients with congestive cardiomyopathy was obtained from the computerized files and retrieval system used in our cardiac graphics laboratory during the past 7 years (table 2).

Criteria for inclusion were as follows:

(1) Clinical aspects. Patients were classified as having congestive cardiomyopathy if they had evidence of a large heart with dilated ventricles, without primary valvular, coronary or congenital heart disease. Patients who had undergone cardiac surgery or had persistent systemic hypertension were excluded. Almost all patients were taking medications such as digoxin and diuretics but were in a sufficiently stable state for dual echo- or phonocardiographic study. However, the nine patients whose echocardiograms were recorded in the intensive care unit were severely ill and were inadequately controlled by medical therapy.

(2) Echocardiographic criteria. Left ventricular end-diastolic dimension (Dd) at the onset of the QRS complex ≥ 55 mm; left ventricular end-systolic dimension (Ds) at the time of A₂ ≥ 40 mm; left ventricular posterior wall motion ≤ 10 mm; and sum of the amplitude of movement of left septal echo and posterior endocardial echo ≤ 15 mm. Cases with pericardial effusion of more than minimal dimensions were excluded.

(3) ECG. Patients with ECG consistent with myocardial infarction or atrial fibrillation were excluded.

(4) Catheterization and angiography. Congestive cardiomyopathy was diagnosed by this technique in 28 of the 100 patients included in this series.

Technique of Echophonocardiography

The 91 patients who could be studied in the cardiac graphics laboratory were studied by echophonocardiography — simultaneous registration of valvular or ventricular events with phonocardiograms from two locations at a paper speed of 50 or 100 mm/sec. These patients also had, during the same investigation, a routine phonocardiogram with carotid pulse tracing at a 100 mm/sec paper speed. The other nine patients were too ill to be brought to the cardiac graphics laboratory and were studied with a portable echo machine that did not have phonocardiographic capability.

In this series, observations were confined to left-sided events. The pulmonary valve was recorded in 53 of the patients, but because of the inconsistency with which both opening and closing points were identified, we could not accurately observe right-sided systolic time intervals.

Left-sided pulsus alternans was determined from either the aortic valve echogram or from the carotid pulse tracing, where ejection time could be measured from onset of the upstroke to the dicrotic notch (figs. 1 and 2).

The 100 patients were divided into three groups:

Group A. Patients with persistent alternans detected throughout the whole recording, either from the aortic valve echogram or the carotid pulse.

Group B. Patients with alternans limited to a brief period after a VPC.

Group C. Patients without alternans.

We wished to compare ventricular function among these three groups and therefore obtained, where available, the following measurements from M-mode echocardiograms and phonocardiograms:

Echocardiographic Measurements

(1) PEP/ET. PEP was calculated in the conventional manner (QA₂ - ET) from phonocardiograms if the aortic valve echogram was unsuitable for measurement. In both the prospective and retrospective studies, PEP/ET in cases without pulsus alternans was taken as the average from measurement of three cardiac cycles, but in cases with VPC-induced alternans, PEP and ET were measured in the beat just before the VPC. In cases with persistent pulsus alternans, PEP and ET of stronger beats were measured and compared.

(2) Dd and Ds.

(3) Percent shortening of left ventricular dimension (Dd - Ds/Dd = %ΔD).

### Table 2. Clinical Summary of 100 Patients with Congestive Cardiomyopathy

| Age: 46.4 ± 14.8 years (mean ± SD) | 66 |
| Sex: Male | 34 |
| Alcohol abuse | 24 |
| Peripartum | 5 |
| Unknown | 71 |
| Pulsus alternans | 17 |
| Persistent | 10 |
| VPC-induced | 7 |
| Phonocardiogram and pulse tracings (available in 91 cases) | 18 |
| Mitral regurgitation | 26 |
| Tricuspid regurgitation | 5 |
| Both AV valves regurgitant | 8 |
| Dicrotism | 18 |

Abbreviations: VPC = ventricular premature complex; AV = atrioventricular.
Phonocardiograms and Pulse Tracings

(1) Presence of mitral or tricuspid regurgitation. Mitral regurgitation was diagnosed when a pansystolic murmur was heard and recorded at the cardiac apex or axillary area in cases with marked left ventricular enlargement. Tricuspid regurgitation was reflected in graphic records by a pansystolic murmur at the lower sternal border accompanied by a positive systolic wave in the jugular phonogram. In some instances there was echocardiographic evidence of right ventricular diastolic overload manifest by paradoxical septal movement and right ventricular dilatation. Nine cases with mitral regurgitation, three with tricuspid regurgitation and two with both lesions were confirmed by ventriculography.

(2) Dicrotic pulse (exaggerated amplitude of the dicrotic wave as defined by Orchard and Craigie).

Results
Dual Echocardiographic Study

Results are shown in table 1 and figures 3-6. Fourteen of 36 patients had pulsus alternans. One patient had bilateral and consistent pulsus alternans. The other 13 cases were induced by VPCs and persisted for three to 15 beats. Isolated left-sided alternans was present in seven patients, isolated right-sided alternans in one patient and bilateral pulsus alternans in the other six. The other 22 patients did not have pulsus alternans on either side of the heart, including three patients with VPCs.

In three of six cases with bilateral alternans, the alternation continued in one circulation after its disappearance in the other.

Each sequence of alternation after a VPC tended to diminish in successive beats until finally extinguished and then reappear after the next VPC.

The RR intervals after VPCs showed slight variation in cyclic length of 20 msec between two consecutive beats, except for two patients (patients 1 and 13 in table 1) who had cyclic variation of up to 60 and 40 msec, respectively, with slight shortening in the stronger beats.

In the patients with pulsus alternans induced by VPCs, the first beat after the compensatory pause (strong beat) had a short PEP and a long ET, with a relatively low PEP/ET ratio. The next weak beat was characterized by a longer PEP and shorter ET with therefore a higher PEP/ET ratio. In subsequent beats this sequence was repeated, although with diminishing contrast. Electromechanical systole also alternated in parallel with ET, although its degree of variation was smaller than that of ET. In a case with bilateral and persistent alternans, similar cyclic changes were observed without diminishing in both circulations.

The severity of left ventricular dysfunction was indicated by the ratio of PEP/ET, which was increased in almost all instances (table 1), with a mean of 0.57 ± 0.15 (± sd). However, this ratio was not statistically different in patients with or without left-sided alternans (0.62 ± 0.13 vs 0.55 ± 0.15). On the other hand,
subject to error because of our inability to control for these factors.

We determined the origin of VPCs, whether left- or right-sided, and the degree of their prematurity from the routine scalar ECG. There was, however, no discernible correlation between pulsus alternans and either the origin or prematurity of the extra beats.

Three typical cases are presented in figures 3, 5 and 6 to illustrate observations noted above.

**Retrospective Study**

The clinical and echophonocardiographic findings are summarized in tables 2 and 3.

All echocardiographic measurements revealed severe left ventricular dysfunction: elevated PEP/ET, dilatation of the left ventricle, decreased systolic thickening of the ventricular wall, decreased velocity of circumferential fiber shortening. These findings were uniformly present in view of the criteria used for inclusion in this study. However, these studies did not show any significant differences among the three groups (fig. 7).

Eleven patients had VPCs and a length of ECG tracing adequate to assess the presence or absence of pulsus alternans. Seven of them (group B) demonstrated alternation and four did not. The PEP/ET in the control beats in these four cases was in the range of 0.51-0.62 (average 0.58), which was not statistically different from that in the subjects with alternans.

The ratio of PEP/ET displayed an alternating magnitude in pulsus alternans whether persistent or induced by VPCs. The opening of the aortic valve was also larger with the stronger beats. Similarly, alternation in the amplitude of vibrations of the first heart sound (S1) was seen in three cases with persistent and in two cases with VPC-induced alternans. Intensity was greater with the stronger beats with both mitral and tricuspid components of S1, where both elements could be identified (fig. 1), the second heart sound was also found to vary in intensity in similar fashion in three cases. Gallop sounds also alternated in three cases (fig. 2), but with no consistent pattern. The inci-

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**Figure 4.** Comparison of pre-ejection period/ejection time (PEP/ET) determined by dual echocardiography between groups with (+) and without (−) pulsus alternans (PA). There is no significant difference between PEP/left ventricular ET in patients with left-sided PA (0.62 ± 0.13, mean ± SD) and those without (0.55 ± 0.15). However, the PEP/right ventricular ET was higher in those with right-sided PA than those without (+) 0.50 ± 0.07 vs 0.40 ± 0.09, respectively (p < 0.05). The dotted line shows upper limit of normal for PEP/ET: 0.56, 0.58.

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**Figure 5.** Dual echocardiogram from a 59-year-old man with mitral and tricuspid valve replacement (patient 4 in table 1). It illustrates asymmetric effect of a ventricular premature beat (VPB) on ejection time (ET) with resulting unilateral pulsus alternans. A VPB (beat 2) has a shorter ET on the left side (aortic valve echo [AVE]), but no effect on right-sided ET (pulmonic valve echo [PVE]). Beats 3–5 show left-sided alternans while right-sided systolic time intervals are constant.
dence of regurgitation of atrioventricular valves and dicrotism was not different among the three groups of patients.

Discussion

Most studies of pulsus alternans have relied on invasive techniques that have precluded observations under physiologic conditions. However, measurements of systolic time intervals by means of carotid pulse tracings with phonocardiograms, or by M-mode echocardiography have made it possible to investigate pulsus alternans extensively. Observations by these techniques have been limited to left-sided events. Dual echocardiography is ideally suited for overcoming this problem, since time intervals from both ventricles can be measured continuously and simultaneously by means of observations of semilunar valve echograms. Studies can be repeated as necessary with no risk of discomfort to the patient.

The principal disadvantage of the method is that a satisfactory pulmonary valve echo cannot always be obtained. Even when the pulmonary valve can be visualized, it is not always possible to record the aortic valve simultaneously because of the small acoustic window, which may be inadequate to accommodate both ultrasonic transducers. For our purposes, the types of patients in whom pulsus alternans might be expected to occur invariably have dilated cardiac chambers, which facilitates the registration of echoes from all the heart valves.

The Genesis of Pulsus Alternans

The principal theories for the genesis of pulsus alternans are alternation of end-diastolic volume due to the Frank-Starling mechanism and alternating contractility of the ventricle. Either of these hypotheses may be valid, but the exact mechanism of pulsus alternans cannot be determined from our present study. The methods used, however, permit a precise measurement by noninvasive means of diastolic time intervals, which may be important. These intervals include the isovolumic relaxation time (IRT), which is shorter after the strong beat and longer after the weak beat (fig. 8). The dual echocardiographic method provides very accurate markers

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** Dual echocardiogram from a 67-year-old man with coronary artery disease illustrating bilateral pulsus alternans (patient 9 in table 1). This recording was made during expiratory apnea of Cheyne-Stokes respiration. A ventricular premature beat (beat 2) results in a short ejection time (ET) on both sides of the circulation. Subsequent beats 3–6 demonstrate bilateral, symmetrical pulsus alternans.

![Figure 7](http://circ.ahajournals.org/)

**Figure 7.** Comparison of preejection period/ejection time (PEP/ET) among three groups: (1) no pulsus alternans (PA), (2) PA induced by ventricular premature beats (VPBs) and (3) persistent PA with congestive cardiomyopathy. There was no statistical differences of PEP/ET among three groups (0.69 ± 0.14, 0.68 ± 0.14, 0.71 ± 0.12, respectively). Systolic time intervals were measured in group 2 in the control beat, before the VPB. In persistent PA, the strong beat was used. The weaker beats had a more abnormal PEP/ET ratio (0.89 ± 0.22).


for the beginning of IRT (aortic valve closure) and its termination — (the onset of mitral valve opening). The hemodynamic and myocardial factors that determine the duration of IRT (aortic diastolic and left atrial pressures and \(-\text{dP/dt}\)) are, however, not delineated by this method. In three cases in which we measured IRT in pulsus alternans, the relationship of its duration to strength and weakness of the preceding contraction was consistent and reproducible (fig. 8), but was at variance with the observations of Spodick et al.,

\[\text{Abbreviations: HR = heart rate; PEP = preejection period; ET = ejection time; Dd = left ventricular end-diastolic dimension; Ds = left ventricular end-systolic dimension; } \%	ext{AD} = \text{percent shortening of dimension; } \text{Vcf} = \text{velocity of circumferential fiber shortening; IVS} = \text{interventricular septum; PW} = \text{left ventricular posterior wall; } \%	ext{APW} = \text{percent change of septum and posterior wall thickness during systole; VPC} = \text{ventricular premature complex; } s = \text{strong beat; w = weak beat.}\]
Figure 8. Dual echocardiogram of aortic valve (AVE) and mitral valve (MVE) from same patient as in figure 6 illustrates effects of pulsus alternans on isovolumic contraction time (ICT) and isovolumic relaxation time (IRT). After a ventricular premature complex (beat 1) with a very short IRT, there is pulsus alternans. ICT and IRT alternate in reverse relationship to left ventricular ejection time.

Prevalence of Pulsus Alternans

Pulsus alternans is thought to be a common finding in advanced heart disease of a variety of etiologic types. It has been described frequently in aortic stenosis or insufficiency, hypertension, coronary artery disease and cardiomyopathy. Pulmonary alternans is thought to be less common but has been reported in isolated cases of atrial septal defect, mitral valve disease, pulmonary embolism, and primary pulmonary hypertension.

There have been few studies of the frequency of pulsus alternans in any of the above-mentioned conditions for pulmonary alternans. White found alternation of the radial pulse in 71 of 300 cardiac and cardiorenal cases examined prospectively. Lopez-Sendon et al. observed persistent alternation of the pulmonary artery pressure in eight of 100 patients with acute myocardial infarction. In a review of catheterization studies in aortic stenosis, Cohen et al. found left-sided alternans in 29 of 96 cases, although in only two of these was the alternation persistent; Cooper et al. observed this sign in 15 of 28 cases with acquired aortic stenosis. Our retrospective study of patients with congestive cardiomyopathy indicates an incidence of only 10% persistent alternans and an additional 7% with postextrasystolic alternans. Despite the generally grave prognosis attributed to the sign of pulsus alternans, we found no measurable differences in the measurements of left ventricular dysfunction among the patients with cardiomyopathy who did or did not have pulsus alternans.

Pulsus alternans appeared and disappeared even during the relatively brief period in which the patient was in the laboratory, or during an interval of a few days between repeat studies.

The frequency with which pulmonary alternans may have occurred in the 100 cases of congestive cardiomyopathy studied retrospectively cannot be stated because details of opening and closing movements of the valve were not consistently recorded.

PVCs in the Precipitation of Pulsus Alternans

The appearance of pulsus alternans after PVCs has long been recognized. Although among our cases there was no relationship between the prematureity of the VPC and the appearance of pulsus alternans, we noted that a VPC may result in a ventricular contraction that may have a normal or an abbreviated ejection time and the abbreviation may be bilateral or unilateral (figs. 3, 5 and 6). VPCs do not uniformly initiate pulsus alternans, but when a VPC does initiate pulsus alternans, the VPC itself is associated with an abbreviated ejection time. This phenomenon may be asymmetric, with a normal ET on the right side with the PVC and a shorter ET on the left side with the same beat followed by unilateral, left-sided pulsus alternans (fig. 5). Not all cases with PVCs demonstrate alternans. Four of 11 cases in our retrospective study and three of 17 cases in the prospective study with VPCs did not show alternation. The mechanism by which PVCs lead to pulsus alternans remains unknown.

Unilateral and Bilateral Alternans

Independent behavior of both ventricles in pulsus alternans was first described by Ferrer et al. Of the 21 cases with alternans, six showed alternation in the lesser circulation, six in the greater circulation, and nine had bilateral alternans. The high incidence of pul-
monary alternans (three-fourths of total) in this series probably reflects the choice of patients, including many with cor pulmonale and left-sided heart disease, which had led to pulmonary hypertension.

This study and other investigations of pulsat alternans on both sides of the circulation have been done by invasive methods. Dual echocardiography has allowed us to observe the performance of both ventricles noninvasively, and is an ideal for determining the presence of unilateral or bilateral alternans under physiological conditions. In our prospective series studied by dual echocardiography, seven of 14 patients with pulsus alternans demonstrated pulmonary alternans. This proportion, although less than that reported by Ferrer et al., illustrates the frequency of involvement of the lesser circulation. Patients in our series with right-sided pulsus alternans had a PEP/RVET that was distinctly higher than that of the patients without right-sided pulsus alternans. This may reflect either pulmonary hypertension or a depression of right-sided 

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Circulation. 1982;65:617-626
doi: 10.1161/01.CIR.65.3.617
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1982 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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