Pulsus Alternans in Aortic Stenosis

Hemodynamic Observations in 50 Patients Studied by Left Heart Catheterization

By Theodore Cooper, M.D., Ph.D., Eugene Braunwald, M.D., and Andrew G. Morrow, M.D., F.A.C.S.

Although it has been recognized for many years that pulsus alternans may occur in patients with aortic stenosis, the fact that these 2 conditions are frequently associated has not been documented. The presence of a stenotic aortic valve reduces the central aortic pressure, the central aortic pulse pressure, and also the magnitude of any alternation present in the aortic pressure pulse. Thus, in patients with aortic stenosis, the clinical detection of pulsus alternans in the peripheral pulse is difficult.

Left heart catheterization has made possible the direct measurement of left ventricular pressures in man and, therefore, even minimal alternations in the left ventricular pressure pulse are readily detectable. Furthermore, the technic of left heart catheterization facilitates the quantification of alternation and permits direct measurement of the duration of the events in the cardiac cycle. The purpose of this communication is to characterize the relationship between pulsus alternans and aortic stenosis in 50 patients in whom the presence of aortic stenosis was confirmed by the demonstration of a significant pressure gradient between the left ventricle and aorta at the time of left heart catheterization.

Material

Acquired Aortic Stenosis. The 28 patients with acquired rheumatic aortic stenosis ranged in age from 30 to 55 years and the average age was 41 years. There were 19 males and 9 females. In 4 patients aortic stenosis was considered to be the sole valvular lesion on the basis of both hemodynamic and clinical evaluation. In 11 patients, aortic stenosis was considered to be predominant although minimal aortic regurgitation or a mitral lesion was demonstrated or suspected. In the remaining 13 patients, aortic stenosis was present, but was not considered to be the most important lesion hemodynamically; the majority of this group presented aortic regurgitation as the principal abnormality. In the entire group with acquired stenosis, the left ventricular-aortic pressure gradients ranged from 20 to 161 mm. Hg and averaged 74 mm. Hg.

Congenital Aortic Stenosis. The 22 patients in this group ranged in age from 6 to 36 years, and the average age was 16 years. Fourteen were male and 8 were female. The clinical features in these patients have been described elsewhere in detail. Of these patients, 5 had aortic diastolic murmurs suggesting associated aortic regurgitation. In none, however, was this lesion considered hemodynamically significant. Three patients exhibited, in addition to aortic stenosis, relatively mild degrees of pulmonic stenosis. In the 22 patients with congenital stenosis the left ventricular-aortic pressure gradients ranged from 15 to 172 mm. Hg and averaged 83 mm. Hg.

Methods

In 46 patients left heart catheterization was performed by the transbronchial route. This technic has been described previously in detail. In 4 patients with congenital aortic stenosis, left ventricular pressures were measured by percutaneous puncture of this chamber through the anterior chest wall. Arterial pressure measurements were made either in the central aorta by means of retrograde arterial catheterization or by percutaneous puncture of the femoral or brachial artery. Left ventricular pressure, arterial pressure, and
lead II of the electrocardiogram were recorded simultaneously on a multichannel cathode-ray photographic oscillograph. Paper speeds of 25 and 75 mm. per second were employed. The left ventricular-aortic pressure gradient was measured as the difference between the peak systolic left ventricular pressure and the peak systolic aortic pressure. It is realized that in those patients in whom the femoral arterial pressure was used, the gradient was underestimated, since femoral artery systolic pressure may exceed that in the central aorta.7,8 In 3 patients with pulsat alternans in whom simultaneous left ventricular and central aortic pressures were recorded, the duration of left ventricular isometric contraction was measured from the onset of the left ventricular pressure ascent to the onset of the central aortic pressure ascent. The duration of total left ventricular systole was measured from the onset of the left ventricular pressure ascent to the incisura of the central aortic pressure pulse.

**Results**

Acquired Aortic Stenosis. In 15 of the 28 patients with acquired aortic stenosis persistent pulsat alternans was present in the left ventricular pressure pulse tracing. Four of the 13 patients without persistent alternans displayed the abnormality in several pulses following the occurrence of ventricular premature contractions. The magnitude of left ventricular alternation, i.e., the pressure difference between the large and small pulses, ranged between 2 and 43 mm. Hg and averaged 15 mm. Hg. Careful scrutiny of the arterial pressure tracings revealed that when left ventricular alternation was present, pulsat alternans could consistently be detected in the arterial pressure pulse tracing. However, the magnitude of the alternation was strikingly reduced in the arterial pressure pulse. In several patients the arterial pressure tracings exhibited alternation of diastolic pressure (fig. 1). Concordant alternation of the left ventricular end-diastolic pressure was noted in 2 of the 15 patients, while no distinct alternation of left ventricular end-diastolic or left atrial "z" point pressure could be detected in any of the other 13 patients. Electrical alternans was not noted in any of the electrocardiographic records.

In 3 patients with pulsat alternans in whom simultaneous left ventricular and central aortic pressure pulses were recorded, it was observed that left ventricular isometric contraction showed no evidence of alternation. In 1 of these patients, who had relatively severe left ventricular alternans (24 mm. Hg), there was concordant alternation in the duration of ventricular ejection and, therefore, also in the duration of total mechanical systole. In the other 2 patients, who had relatively mild left ventricular alternans (4 mm. Hg and 6 mm. Hg), there was no detectable alternation in the durations of ventricular ejection, or total systole. These findings are at variance with the observations of Katz and Feil9 and of von Wallenstern.10

Right heart catheterization was performed in 24 of the 28 patients with acquired aortic stenosis. Right ventricular or pulmonary arterial alternans could not be detected in any of the patients who did not exhibit left ventricular alternans. However, 2 of the 13 patients with left ventricular alternans, in whom right heart catheterizations were performed, exhibited right ventricular alternans.11 It should be noted that the right and left heart catheterizations were per-
formed several days apart and the conditions under which the measurements were obtained were not necessarily comparable.

There appeared to be little correlation between the age of the patient, the duration of symptoms, or the presence and severity of fatigue or syncope with the presence of persistent pulsus alternans. There was a distinct tendency for those patients who had exhibited severe congestive heart failure, angina pectoris, and marked cardiomegaly to have pulsus alternans; however, this was
PULSUS ALTERNANS IN AORTIC STENOSIS

Fig. 3. Products of left ventricular systolic pressure and heart rate in patients with and without persistent pulsus alternans, and acquired aortic stenosis. Symbols same as in figure 2.

not a consistent relationship. Eleven of the 15 patients with persistent pulsus alternans had pure or predominant aortic stenosis. Of the 13 patients without alternans only 4 had pure or predominant aortic stenosis.

The presence of persistent pulsus alternans was related to a variety of hemodynamic parameters. No statistically significant separation was observed (fig. 2A and B) although the averages of the heart rates and of left ventricular end-diastolic pressures in the group with pulsus alternans were somewhat higher than in the group without alternans. The patients with pulsus alternans, however, had significantly higher left ventricular systolic pressures \( p < .01 \) as well as significantly higher aortic valve gradients \( p < .01 \) (fig. 2C and D). The hemodynamic parameter that afforded the best separation of the patients with pulsus alternans from those without pulsus alternans was the product of the left ventricular systolic pressure and the heart rate (fig. 3). This relationship was statistically highly significant \( p < .001 \).

Two patients with pulsus alternans were studied before and after aortic valvulotomy. In one patient it was observed that pulsus alternans was abolished following partial relief of the aortic obstruction and the concomitant lowering of the product of left ventricular systolic pressure and heart rate. This index fell from \( 233 \times 10^2 \) to \( 174 \times 10^2 \) (fig. 4). However, the other patient exhibited alternans both before and after operation. The product of left ventricular systolic pressure and heart rate showed little change \( (188 \times 10^2 \) to \( 193 \times 10^2 \)).

Congenital Aortic Stenosis. Of the 22 patients with congenital aortic stenosis, none exhibited persistent pulsus alternans. Three patients, however, had transient periods of alternans following the occurrence of ventricular premature contractions. In the entire group of patients with congenital aortic stenosis the product of the systolic pressure and heart rate ranged from \( 83 \times 10^2 \)
to $361 \times 10^2$ and averaged $202 \times 10^2$. Two additional patients with congenital aortic stenosis exhibited persistent left ventricular alternans. They have not been included in this report because the left ventricular pressures were measured only at the time of surgical closure of an associated large patent ductus arteriosus.

**Surgical Correlations.** Of 11 patients with pulsus alternans who have been operated upon for acquired aortic stenosis 6 have survived operation and have shown various degrees of improvement. Five died during operation or in the immediate postoperative period. Of the 4 patients with acquired aortic stenosis without pulsus alternans who were operated upon, 3 survived operation and have shown various degrees of improvement and 1 died. Of the 12 patients with congenital aortic stenosis who were operated upon, all survived the operation.

**DISCUSSION**

The fundamental mechanisms underlying pulsus alternans have not been completely elucidated. The present observations, when viewed in the light of previously reported data, suggest that a disparity between the oxygen requirement of the heart and the oxygen available to it may so alter myocardial contractility as to result in pulsus alternans. In this connection the observations by Kleinfeld, Stein, and Magin are of considerable interest. When the oxygen requirement of a single muscle fiber was increased by the administration of triiodothyronine or when oxygen availability was limited by anoxia, electrical alternans occurred. Similarly, Green observed the appearance of pulsus alternans following experimental coronary artery ligation. The relative frequency of pulsus alternans in patients with hypertensive heart disease, in whom total myocardial oxygen requirements are elevated, and in patients with arteriosclerotic heart disease, in whom the oxygen delivery is impaired, is well recognized.

It has recently been demonstrated that the oxygen consumption of the heart is not determined by the external work performed by the heart, but rather by the tension-time index; this is represented by the total area beneath the systolic portion of the ventricular pressure curve per minute. The very close correlation between the product of peak systolic ventricular pressure and heart rate and the tension-time index makes an estimation of the relative myocardial oxygen requirements in clinical conditions readily available (fig. 5). It was therefore of considerable interest to observe that this index of myocardial oxygen requirement (left ventricular systolic pressure times heart rate) correlated so well with the presence or absence of pulsus alternans (fig. 3). Furthermore, it should be noted that in the presence of aortic stenosis, the delivery of oxygen to the myocardium is limited by relatively low coronary perfusion pressure and the prolongation of ventricular systole.

Review of the data reported by Friedman and associates lends further support to the contention that pulsus alternans is related to changes in myocardial oxygenation. These investigators demonstrated in 3 patients without aortic stenosis that pulsus alternans could be regularly induced by a variety of maneuvers that decreased the venous return, and could be abolished by other maneuvers.
PULSUS ALTERNANS IN AORTIC STENOSIS

that increased venous return. Calculations from their published data indicate that in each instance the development of pulsus alternans was associated with an elevation of the product of arterial pressure and heart rate. This index declined whenever pulsus alternans was abolished.

Although the product of left ventricular systolic pressure and heart rate was high, i.e., exceeded 180 \times 10^2, in 13 of the patients with congenital aortic stenosis, persistent pulsus alternans was never present. This would suggest that in addition to the myocardial oxygen requirement another factor may play a role in the genesis of alternans. The presence of more advanced coronary arteriosclerosis or rheumatic myocardial involvement in the patients with acquired aortic stenosis could explain the observed difference.

The ability to detect pulsus alternans consistently in the peripheral arterial pressure pulse recordings in patients with aortic stenosis enhances the clinical value of the observations reported. Thus, in patients with the clinical picture of aortic stenosis, the presence of pulsus alternans in the brachial arterial tracing suggests a more serious form of the disease. The detection of pulsus alternans in the peripheral pulse tracing is facilitated by the use of high sensitivity recordings at a slow paper speed.

SUMMARY

Fifty patients with aortic stenosis were studied by means of left heart catheterization. Persistent left ventricular pulsus alternans was observed in 15 of 28 patients with acquired aortic stenosis, but in none of 22 patients with congenital aortic stenosis. No consistent relationship could be established between the presence of persistent pulsus alternans in acquired aortic stenosis and age, duration of symptoms, fatigability, syncope, heart rate, or the left ventricular end-diastolic pressure. Those patients with persistent alternans, however, more frequently had severe congestive heart failure, angina pectoris, and cardiomegaly. Furthermore, the left ventricular systolic pressures and the left ventricular-aortic pressure gradients were significantly higher in these patients.

The hemodynamic parameter that afforded the best separation of those patients with acquired aortic stenosis and persistent pulsus alternans from those without alternans, was the product of the left ventricular systolic pressure and the heart rate. This product closely correlates with the tension-time index, which has recently been shown to reflect myocardial oxygen requirement.

These observations, in the light of previously reported data, suggest that a disparity between the oxygen requirement of the heart and the oxygen available to it, can so alter myocardial contractility as to result in alternation in the strength of the ventricular contractions. The absence of alternans in patients with congenital aortic stenosis of similar severity suggests that coronary arteriosclerosis and the sequelae of rheumatic myocarditis may be contributory factors in its genesis.

SUMMARIO IN INTERLINGUA

Cinquanta patientes con stenosis aortic esseva studiate per medio de catheterismo sinistro-cardiac. Persistente pulso alternante sinistro-ventricular esseva constatate in 15 ex 28 patientes con acquirete stenosis aortic sed in nulle ex 22 patientes con congenite stenosis aortic. Il non esseva possibile establir un relation systematic inter le presentia de persistente pulso alternante in casos de acquirete stenosis aortic e factores como etate, dura- tion del symptomatas, fatigabilitate, syncope, frequentia cardiac, e pression sinistro-ventricular termino-diastolic. Tamen, le patientes con persistente pulso alternante habeva plus frequentemente conditiones como grados sever de congestive disfallimento cardiac, angina de pectore, e cardiomegalia. In plus, le pression sinistro-ventricular systolic e le gradiente de pression inter ventriculo sinistre e aorta esseva significativamente plus alte in iste patientes.

Le melior criterio hemodynamic pro le separation del patientes in qui le acquirete stenosis aortic esseva associate con persistente
pulso alternante ab le pacientes sin pulso alternante esseva le producto de pression sinistro-ventricular systolic e frequentia cardiae. Iste producto es intimeemente correlacionate con le indice de tension e tempore le qual—secundo recente constatationes—reflecte le requimentos oxygenie del myocardio.

Iste observationes, vidite in le lumine de datos previelemente reportate—suggere que un disparitate inter le requimentos de oxygeno del corde e le quantitate de oxygeno disponibile al corde es capace a alterar le contractilitate myocardial in un tal manera que un alternation resulta in le forta del contractiones ventricular. Le absentia de pulso alternante in patientes con congenite stenosis aortic de grados comparable de gravitate pare indicar que arteriosclerosis coronari e le sequellas de myocarditis rheumatic es possibilemente factores contributori in le genese de pulso alternante.

REFERENCES
Pulsus Alternans in Aortic Stenosis: Hemodynamic Observations in 50 Patients Studied by Left Heart Catheterization
THEODORE COOPER, EUGÈNE BRAUNWALD and ANDREW G. MORROW

Circulation. 1958;18:64-70
doi: 10.1161/01.CIR.18.1.64

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/18/1/64

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/