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The Natural History of Adults With Asymptomatic, Hemodynamically Significant Aortic Stenosis

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The natural history of asymptomatic, hemodynamically significant, valvular aortic stenosis in adults was documented. Of 471 patients with aortic stenosis identified by Doppler echocardiography (peak systolic flow velocity ≥4 m/s) from January 1984 through August 1987, 143 were asymptomatic and had isolated valvular aortic stenosis. Thirty patients underwent aortic valve intervention within 3 months (group 1); the remaining 113 patients did not have an intervention within 3 months (group 2). Follow-up information was available for all patients; the mean duration of follow-up study was 20 months (range 6 to 48).

Three cardiac events occurred in the 30 group 1 patients after operation (two deaths, one reoperation). Among the 113 group 2 patients, three had cardiac death presumed to be a result of the aortic stenosis; all three developed symptoms at least 3 months before death. The actuarial probability of remaining free of symptoms of angina, dyspnea or syncope for group 2 was 86% at 1 year and 62% at 2 years. For this group, the 1 and 2 year probabilities of remaining free of cardiac events, including aortic valve intervention or cardiac death, were 93% and 74%, respectively. Of all clinical and echocardiographic variables (group 2), only Doppler flow velocity ($p = 0.004$) and ejection fraction ($p = 0.01$) were independent predictors of subsequent cardiac events. Among the 44 patients (groups 1 and 2) with a flow velocity ≥4.5 m/s, the relative risk of sustaining a cardiac event (by Cox regression analysis) was 4.9 ($p = 0.004$).

Patients with asymptomatic, hemodynamically significant aortic stenosis are at significant risk for cardiac events within 2 years. However, during the time they remain asymptomatic, the risk of sudden death is low. The asymptomatic patient may be treated medically but requires careful follow-up evaluation for the development of symptoms.

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Although the natural history of adults with symptomatic, severe, valvular aortic stenosis has been well documented (1,2), much less is known about the prognosis of those with asymptomatic severe aortic stenosis. It has been estimated that 3% to 5% of deaths in persons with acquired aortic stenosis occur suddenly, unpreceded by symptoms (3). However, this estimate is derived largely from retrospective clinical and postmortem studies (4–6) done before 1955, in which hemodynamic information was not available. More recently, several studies (7,8) involving small numbers of asymptomatic patients with hemodynamically severe aortic stenosis have suggested that these patients are at low risk and that surgical treatment can be postponed until symptoms appear without a significant risk of sudden death.

With the advent of Doppler echocardiography, more asymptomatic patients with severe aortic stenosis are being identified. These patients pose a therapeutic dilemma because the risk of medical management must be balanced against the risk of surgical intervention and the impact of a prosthetic aortic valve on future morbidity and mortality. In this study, the outcome in 143 adults with asymptomatic, isolated, hemodynamically significant, valvular aortic stenosis identified by Doppler echocardiography (peak systolic velocity ≥4 m/s) is described.

Methods

Study patients. The study group was derived from 471 patients ≥40 years old with valvular aortic stenosis and a peak systolic flow velocity ≥4 m/s (identified by Doppler echocardiography) who were evaluated at the Mayo Clinic

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from January 1984 through August 1987. All patients were evaluated by a cardiologist or an internist in consultation with a cardiologist. Eighty-five patients were excluded from this study for the following reasons: 1) multivalvular involvement, 2) moderate to severe aortic regurgitation, 3) documented myocardial infarction, 4) prior coronary artery bypass grafting, 5) prior percutaneous aortic balloon valvuloplasty, or 6) prior valve replacement. Among the remaining 386 patients, 243 (63%) were excluded from further study because of cardiac symptoms present at the time of the initial clinical and echocardiographic evaluation. Patients with mild fatigue or mild dyspnea occurring with maximal exertion were not excluded because of the nonspecificity of these symptoms.

The 143 patients who met the entrance criteria formed the study group. Their ages ranged from 40 to 94 years (mean 72); 89 of the patients were men. The peak aortic flow velocity ranged from 4.0 to 6.4 m/s (mean 4.4), the aortic valve mean gradient by Doppler study averaged 51 mm Hg and the mean ejection fraction was 64%. Of the 143 patients, 30 (group 1), although remaining asymptomatic, underwent operation or valvuloplasty within 3 months at the discretion of the cardiologist, and 113 patients (group 2) did not have an intervention within 3 months, either at the discretion of the cardiologist or because of the reluctance of the patient to undergo operation. These patients were advised to return for reevaluation at 6 months or 1 year and to return promptly at the onset of symptoms.

Activity level was graded on a scale of 1 to 4 (1 = wheelchair bound; 2 = ambulatory, nursing home; 3 = living independently; 4 = engaging in regular physical exercise). Other clinical factors included hypertension, diabetes mellitus, cigarette smoking, digoxin therapy, diuretic drug use and ventricular ectopic activity on the electrocardiogram (ECG) or Holter ECG monitor (when such information was available). The ECG was analyzed for left ventricular hypertrophy according to the criteria of Romhilt and Estes (9) and for a classic strain pattern (10).

Echocardiographic and Doppler measurements. All patients underwent a comprehensive two-dimensional and Doppler echocardiographic examination by an experienced echocardiographer. Left ventricular ejection fraction was calculated by measuring the left ventricular minor axis at end-diastole and end-systole with a modification of the method of Quinones et al. (11). Measurements of left ventricular end-diastolic wall thickness at the high papillary muscle level were obtained by M-mode echocardiography. Left ventricular hypertrophy was identified when the ventricular septum or posterior wall thickness exceeded the 95% prediction intervals for normal subjects as assessed using correction factors for age and body surface area (12). Continuous wave Doppler examinations were performed with a 2 MHz nonimaging transducer and multiple windows to obtain the maximal jet velocity. The maximal instantaneous and mean pressure gradients across the aortic valve were calculated with the modified Bernoulli equation (13,14). In patients with atrial fibrillation, velocities from 10 consecutive beats were analyzed to obtain an average value.

Cardiac catheterization. Cardiac catheterization was performed in 60 of the 143 patients within 6 months of echocardiography. The mean aortic valve gradient measured was compared with the Doppler-derived transvalvular mean systolic pressure gradient. Coronary angiography was performed in 56 patients.

Follow-up. Follow-up clinical information was obtained from interviews with the patients. Data recorded at the Mayo Clinic include subsequent histories and physical examinations, follow-up letters (sent to all patients who had not been seen within 6 weeks of the time follow-up study was completed) and telephone conversations with the patients, their physicians and relatives. Information regarding the development of cardiac symptoms, subsequent aortic valve operation and mortality was obtained. Death certificates were obtained for all patients who had died. Deaths were classified as cardiac deaths directly related to aortic stenosis, other cardiac deaths and noncardiac deaths. Cardiac deaths directly related to aortic stenosis included sudden death and death from congestive heart failure. The end point of the follow-up evaluation was death or the termination of this study in March 1988.

Statistical methods. Baseline differences between the two groups of patients were studied with a two sample *t* test or a chi-square test for equality of proportions. The probability of developing symptoms or the probability of cardiac death or death from all causes among the patients who did not undergo intervention (group 2) was analyzed with the Kaplan-Meier method. The effect of the clinical, ECG and echocardiographic variables on subsequent cardiac events, including aortic valve operation and cardiac death, was studied with Cox regression analysis. The Doppler-derived aortic valve gradient was correlated with the catheterization-derived gradient by linear regression analysis.

Results

Patients receiving early intervention (group 1). This group of 30 patients included 13 men and 17 women; their mean age was 73 years (range 47 to 87). The Doppler-derived variables included a mean peak aortic velocity of 4.6 m/s (range 4 to 6.4), an average maximal instantaneous gradient of 85 mm Hg (range 64 to 164) and an average aortic valve mean gradient of 63 mm Hg (range 35 to 110). The mean echocardiographic ejection fraction was 66% (range 49% to 80%). In these 30 patients, aortic valve intervention was performed for the following reasons: in 18, the cardiologist believed that the severity of stenosis warranted intervention; 8 were scheduled for a major noncardiac operation and the aortic stenosis was treated first to reduce operative risks; in 2, a

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stroke or transient ischemic attack was suspected to be related to the aortic stenosis; in 1, a decrease in left ventricular function was noted on serial echocardiography; and in 1, the intention was to decrease bleeding from angiodysplasia. Aortic valve intervention included aortic valve replacement in 23 patients, percutaneous balloon valvuloplasty in 5 and surgical decalcification in 2.

Follow-up information was available for all 30 patients in group 1; the mean duration of follow-up study was 21 months (range 6 to 48). Two patients died during this period. One patient who had undergone successful valvuloplasty before planned exploratory laparotomy for presumed ovarian cancer died suddenly on the 13th day after valvuloplasty. The other patient experienced a thrombotic occlusion of the left main coronary artery during aortic valve replacement; the thrombus was removed and her condition stabilized, but she died suddenly on the fifth postoperative day. No autopsy was performed on either patient. One patient required reoperation because of severe aortic regurgitation that developed after placement of an aortic valve homograft. Thus, three cardiac events occurred within the first 6 months of follow-up in this group of patients. The actuarial probability of remaining free of cardiac events was 90 ± 5% at 6 months, 1 year and 2 years. Among these 30 patients, no noncardiac deaths occurred during the follow-up study.

Patients not receiving early intervention (group 2). This group of 113 patients included 76 men and 37 women; their mean age was 70 years (range 40 to 94). The mean Doppler-derived peak aortic velocity was 4.3 m/s (range 4 to 6). The average maximal instantaneous Doppler gradient was 74 mm Hg (range 64 to 145), and the average aortic valve mean gradient was 47 mm Hg (range 35 to 90). The mean echocardiographic ejection fraction was 63% (range 37% to 78%).

Follow-up information was available for all 113 patients in group 2; the mean duration of follow-up study was 20 months (range 6 to 48). During this period, 37 patients (33%) developed symptoms. Only one patient became symptomatic within 3 months of the initial evaluation; this patient underwent aortic valve replacement. The probability of remaining free of cardiac symptoms was 94 ± 2% at 6 months, 86 ± 3% at 1 year and 62 ± 6% at 2 years. The survival free of developing any symptom is plotted in Figure 1.

During the follow-up study, 20 patients (18%) required aortic valve intervention. The indications for intervention were the development of symptoms in 13 (12%) and stroke presumed to be a result of the aortic stenosis in 1 (1%). In six (5%) of the patients, operation was performed because of evidence of progression of the aortic stenosis on Doppler study or cardiac catheterization, although the patient remained asymptomatic.

Among the group 2 patients, there were 14 deaths. Three cardiac deaths were presumed to be a result of the aortic stenosis and included sudden death in two patients and

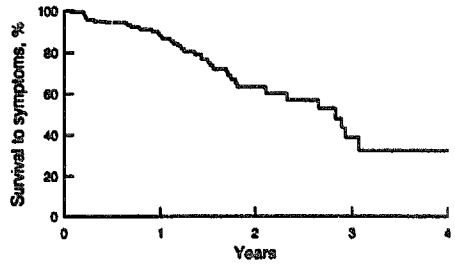
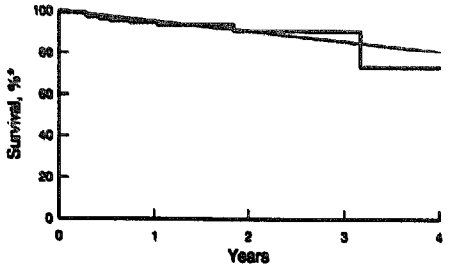


Figure 1. Survival free of development of symptoms for 113 patients with asymptomatic aortic stenosis who did not receive early intervention (group 2).

congestive heart failure in one. Eight noncardiac deaths involved metastatic cancer in four patients, stroke in two, sepsis in one and renal failure in one. Three other cardiac deaths involved two patients who died during cardiac catheterization and one patient who died of aortic root dissection with tamponade (confirmed at autopsy); these deaths were classified as cardiac deaths not related to aortic stenosis. Among this group of 113 patients, the actuarial probability of survival was 96 ± 2% at 6 months, 94 ± 2% at 1 year and 90 ± 4% at 2 years. The survival did not differ from that predicted for age- and gender-matched control subjects (Fig. 2).

The actuarial probability of remaining free of cardiac events related to aortic stenosis, including cardiac death or aortic valve operation, was 95 ± 2% at 6 months, 93 ± 2% at 1 year and 74 ± 6% at 2 years (Fig. 3). By Cox regression analysis, peak aortic velocity by Doppler study ($p = 0.004$) and ejection fraction ($p = 0.013$) were independent predictors of subsequent cardiac events. Age, gender, hypertension, diabetes mellitus, left ventricular hypertrophy by echocardiography, left ventricular hypertrophy by ECG, ECG "strain" pattern, ventricular ectopic activity on the ECG, activity level, cigarette smoking, use of digoxin or a diuretic drug and the presence of coronary artery stenosis ≥70% on angiography were not predictors of subsequent events related to aortic stenosis by univariate or multivariate analysis.

Figure 2. Survival for 113 patients with asymptomatic, severe aortic stenosis (thick line) who did not receive early intervention (group 2) compared with survival for age- and gender-matched control subjects (thin line). *Censored at symptoms, aortic valve replacement or valvuloplasty.



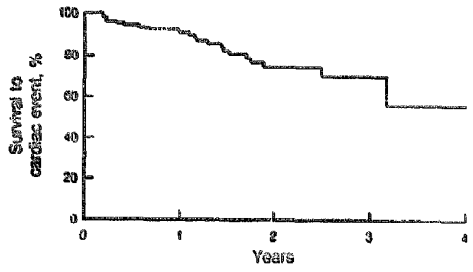


Figure 3. Survival free of aortic stenosis-related cardiac events in group 2.

Each of the three patients who had a cardiac death secondary to aortic stenosis developed symptoms at least 3 months before death. One patient, aged 88 years, with a peak Doppler aortic velocity of 4.5 m/s and an ejection fraction of 37% developed congestive heart failure 5.5 months before sudden death. A 75 year old man with a peak velocity of 4 m/s and normal left ventricular function experienced syncope 4 months before sudden death. An 85 year old woman with a peak aortic velocity of 5 m/s and an ejection fraction of 63% developed Canadian Heart Association class 3 angina followed by progressive (class 3 to 4) dyspnea 3 months before death from congestive heart failure.

Comparison of groups 1 and 2. Group 1 (early intervention) and group 2 (no early intervention) did not differ significantly with regard to most of the variables analyzed (Table 1), but the peak aortic flow velocity in group 1 (4.6 m/s) was significantly higher than that in group 2 (4.3 m/s) ($p = 0.004$). The peak velocity was ≥4.5 m/s in 15 (50%) of the 30 patients in group 1 but in only 29 (26%) of the 113 in group 2. Group 1 included a larger percent of women (57% versus 33%, $p = 0.01$). Group 2 included 10 patients who were very sedentary (activity level ≤2), whereas all patients in group 1 were living independently or were physically active ($p = 0.1$).

Survival free of cardiac events related to aortic stenosis did not differ significantly between groups 1 and 2. However, because there were no noncardiac deaths among the patients in group 1, the total mortality for this group was less, although the difference did not achieve statistical significance.

Relation of peak aortic velocity and ejection fraction with outcome. Among the 143 patients, 44 had a peak velocity ≥4.5 m/s. When they were compared with those who had a peak velocity <4.5 m/s, the relative risk of developing symptoms (by Cox regression analysis) was 2.04 (95% confidence interval 0.846 to 4.94; $p = 0.10$) and the relative risk of sustaining a cardiac event, including aortic valve intervention or cardiac death, was 4.9 (95% confidence interval 1.64 to 14.6; $p = 0.004$). Six patients had an ejection fraction <50%. Compared with those who had an ejection fraction ≥50%, the relative risk of developing symptoms was 2.93 (95% confidence interval 0.839 to 10.2; $p = 0.09$) and the relative risk of sustaining a cardiac event was 5.6 (95% confidence interval 1.46 to 21.3; $p = 0.01$).

Results of cardiac catheterization. Among the 60 patients who underwent cardiac catheterization, the average aortic valve mean gradient was 62 mm Hg; this was directly related to the mean Doppler-derived systolic pressure gradient in the 21 patients whose mean gradient had been determined by both methods ($r = 0.76$). Hemodynamically significant coronary artery disease (>70% stenosis of a coronary artery or >50% stenosis of the left main coronary artery) was present in 14 patients.

Table 1. Comparison of Groups Receiving (group 1) and Not Receiving (group 2) Early Intervention Among 143 Patients With Asymptomatic Aortic Stenosis

Variable	Group 1 (n = 30)	Group 2 (n = 113)	p Value
Mean age (yr)	73	72	NS
Mean peak aortic velocity (m/s)	4.6	4.3	0.004
Average aortic valve mean gradient (mm Hg)			
By Doppler study	63	47	0.04
By cardiac catheterization	65	56	NS
Mean ejection fraction (%)	66	63	NS
Mean age first diagnosis of severe AS (yr)	72	69	NS
Female (%)	57	33	0.01
Activity level ≤2 (no. of patients)	0	10	NS
LVH by ECG (%)	53	40	NS
LVH by echocardiography (%)	93	83	NS
Hypertension (%)	43	41	NS
Abnormal rhythm (A Fib, VPC, other) (%)	17	15	NS

A Fib = atrial fibrillation; AS = aortic stenosis; ECG = electrocardiography; LVH = left ventricular hypertrophy; VPC = ventricular premature complexes.

Discussion

With the longer survival of the population in general, calcific aortic stenosis in the elderly has become one of the principal cardiac problems. Although the need for treatment of symptomatic severe aortic stenosis is well recognized, no reliable information has been available concerning prophylactic operation for severe aortic stenosis in asymptomatic patients. Also, the incidence of sudden death in these patients was unknown (15). In this study, we retrospectively identified a group of asymptomatic patients with Doppler echocardiographic evidence of significant aortic stenosis and prospectively obtained follow-up information regarding the development of symptoms, subsequent need for aortic valve operation and mortality.

Patients not receiving early intervention: outcome. Survival free of sudden death in these patients was analyzed.

During the follow-up study, sudden death occurred in 3 (3%) of the 113 patients who, on the basis of their initial evaluation, did not undergo aortic valve operation within 3 months. In one case, death was confirmed by autopsy to have been the result of aortic root dissection. In the remaining two cases, the development of cardiac symptoms preceded sudden death by 3 and 5.5 months, respectively. Thus, no case of sudden unexpected death was related directly to aortic stenosis in the absence of symptoms.

During the follow-up period (average duration 20 months), most patients remained symptom-free and did not undergo aortic valve operation. By 1 year, the actuarial probability of having developed symptoms was 14%, and the probability of having sustained a cardiac event (including cardiac operation or cardiac death directly related to aortic stenosis) was 7%. The actuarial probability of survival was 94% at 1 year, which was not significantly different from that of life-table survival estimates of age- and gender-matched patients. Among the variables studied, both increased peak aortic velocity by Doppler examination and decreased ejection fraction were independent predictors of subsequent cardiac events; velocity was related primarily to operation.

Patients receiving early intervention: comparison and outcome. With regard to many of the variables examined, including age and ejection fraction, the 30 patients who underwent aortic valve intervention within 3 months, despite remaining asymptomatic, did not differ significantly from the 113 patients who did not have intervention. The different course of management of the patients who had intervention, who constituted 27% of those with asymptomatic severe aortic stenosis, reflects the differing opinions of the 60 cardiologists at our institution regarding the optimal management of this clinical problem. However, the group who had an intervention included a larger percent of women with a higher peak aortic velocity (range 4 to 6 versus 4 to 6.4 m/s), although there was much overlap between the two groups. There were two deaths in this group, both of which were sudden. The absence of noncardiac deaths in this group suggests that cardiologists favored patients without serious underlying diseases as candidates for aortic valve operation.

Each of the three cardiac events in the group receiving early intervention may have been complications of the intervention. Events included aortic valve reoperation for aortic regurgitation in one patient and sudden death that occurred within 2 weeks of intervention in two patients. Thus, cardiac events in this group may not have happened if the intervention had not been undertaken.

Limitations. This study has several limitations. First, the selection of patients was based on two-dimensional echocardiographic evidence of valvular aortic stenosis along with the Doppler criterion of peak aortic velocity ≥4 m/s. Previous studies (16–18) of patients with aortic stenosis have demonstrated an excellent correlation between pressure gradients determined by Doppler study and by cardiac catheterization. Doppler velocimetry alone has been demonstrated as a specific means of identifying severe aortic stenosis (19), and in the absence of severe aortic regurgitation, a peak velocity ≥4 m/s has been proposed as an indicator of severe aortic stenosis (20). If the true peak velocity is not identified with Doppler study, the peak gradient and severity of stenosis would be underestimated rather than overestimated. However, in cases in which left ventricular outflow tract velocity is abnormally accelerated, the gradient across the aortic valve may be less than assumed. In 1984, it was not the practice of our echocardiographic laboratory to record left ventricular outflow tract velocities and mean aortic valve gradients for all patients. Therefore, some patients included in this study may have had less severe degrees of stenosis. Conversely, patients with a peak aortic velocity <4 m/s but reduced cardiac output and decreased left ventricular outflow tract velocity were not included in this study, although some may have had severe valvular aortic stenosis.

A second limitation of the study is that 46 patients with mild exertional dyspnea and fatigue were included. These patients were included because of the nonspecificity of these complaints. However, these symptoms may be secondary to aortic stenosis.

Another limitation is the inclusion of 10 patients who were sedentary. Many of these patients may have been symptomatic had they been more physically active. Although inclusion of both of these groups of patients tends to bias the results of the study toward a worse outcome for patients with aortic stenosis, the outcome of our patients was generally good.

Last, the study patients were identified retrospectively. Their asymptomatic status was determined by review of the patient records obtained at and before the time of the Doppler examination. Follow-up information and information regarding patient outcome were obtained prospectively and reviewed separately.

Conclusions. Several conclusions may be drawn from this study. First, the occurrence of sudden death unpreceded by symptoms is rare in patients with severe aortic stenosis. Second, most patients will remain asymptomatic during 2 years of follow-up. Third, the actuarial probability of having a cardiac event within 2 years, including cardiac death or aortic valve operation, is approximately 25%. Our data indicate that the asymptomatic patient with moderately severe aortic stenosis is at low risk for cardiac death until cardiac symptoms develop. These patients require careful follow-up evaluation.

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References

1. Frank S, Johnson A, Ross J Jr. Natural history of valvular aortic stenosis. Br Heart J 1973;35:41–6.
2. Chizner MA, Pearle DL, deLeon AC Jr. The natural history of aortic stenosis in adults. Am Heart J 1980;99:419–24.
3. Ross J Jr, Braunwald E. Aortic stenosis. Circulation 1968;37(suppl V):V-61–7.
4. Mitchell AM, Sackett CH, Hunzicker WJ, Levine SA. The clinical features of aortic stenosis. Am Heart J 1954;48:684–720.
5. Dry TJ, Willius FA. Calcareous disease of the aortic valve: a study of two hundred twenty-eight cases. Am Heart J 1939;17:138–57.
6. Contratto AW, Levine SA. Aortic stenosis with special reference to angina pectoris and syncope. Ann Intern Med 1937;10:1636–53.
7. Turina J, Hess O, Sepulcri F, Krayenbuehl HP. Spontaneous course of aortic valve disease. Eur Heart J 1987;8:471–83.
8. Kelly TA, Rothbart RM, Cooper CM, Kaiser DL, Smucker ML, Gibson RS. Comparison of outcome of asymptomatic to symptomatic patients older than 20 years of age with valvular aortic stenosis. Am J Cardiol 1988;61:123–30.
9. Romhilt DW, Estes EH Jr. A point-score system for the ECG diagnosis of left ventricular hypertrophy. Am Heart J 1968;75:752–8.
10. Chung EK. Electrocardiography: Practical Applications With Vectorial Principles. 3rd ed. East Norwalk, CT: Appleton-Century-Crofts, 1985:56.
11. Quinones MA, Waggoner AD, Reduto LA, et al. A new, simplified and accurate method for determining ejection fraction with two-dimensional echocardiography. Circulation 1981;64:744–53.
12. Gardin JM, Henry WL, Savage DD, Ware JH, Burn C, Borer JS. Echocardiographic measurements in normal subjects: evaluation of an adult population without clinically apparent heart disease. J Clin Ultrasound 1979;7:439–47.
13. Hatle L, Angelsen B. Doppler Ultrasound in Cardiology. Philadelphia: Lea & Febiger, 1985:8–31.
14. Currie PJ, Seward JB, Reeder GS, et al. Continuous-wave Doppler echocardiographic assessment of severity of calcific aortic stenosis: a simultaneous Doppler-catheter correlative study in 100 adult patients. Circulation 1985;71:1162–9.
15. Selzer A. Changing aspects of the natural history of valvular aortic stenosis. N Engl J Med 1987;317:91–8.
16. Zoghbi WA, Farmer KL, Soto JG, Nelson JG, Quinones MA. Accurate noninvasive quantification of stenotic aortic valve area by Doppler echocardiography. Circulation 1986;73:452–9.
17. Hegrenæs L, Hatle L. Aortic stenosis in adults: noninvasive estimation of pressure differences by continuous wave Doppler echocardiography. Br Heart J 1985;54:396–404.
18. Currie PJ, Hagler DJ, Seward JB, et al. Instantaneous pressure gradient: a simultaneous Doppler and dual catheter correlative study. J Am Coll Cardiol 1986;7:800–6.
19. Oh JK, Taliercio CP, Holmes DR Jr, et al. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: prospective Doppler-catheterization correlation in 100 patients. J Am Coll Cardiol 1988;11:1227–34.
20. Harrison MR, Gurley JC, Smith MD, Grayburn PA, DeMaria AN. A practical application of Doppler echocardiography for the assessment of severity of aortic stenosis. Am Heart J 1988;115:622–8.