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CLINICAL STUDIES

Echocardiographic Assessment of Patients With Infectious Endocarditis: Prediction of Risk for Complications

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To enhance the echocardiographic identification of high risk lesions in patients with infectious endocarditis, the medical records and two-dimensional echocardiograms of 204 patients with this condition were analyzed. The occurrence of specific clinical complications was recorded and vegetations were assessed with respect to predetermined morphologic characteristics.

The overall complication rates were roughly equivalent for patients with mitral (53%), aortic (62%), tricuspid (77%) and prosthetic valve (61%) vegetations, as well as for those with nonspecific valvular changes but no discrete vegetations (57%), although the distribution of specific complications varied considerably among these groups. There were significantly fewer complications in patients without discernible valvular abnormalities (27%).

In native left-sided valve endocarditis, vegetation size, extent, mobility and consistency were all found to be significant univariate predictors of complications. In multivariate analysis, vegetation size, extent and mobility emerged as optimal predictors and an echocardiographic score based on these factors predicted the occurrence of complications with 70% sensitivity and 92% specificity in mitral valve endocarditis and with 76% sensitivity and 62% specificity in aortic valve endocarditis.

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In roughly 80% of patients with a clinical syndrome compatible with the diagnosis of infectious endocarditis, a distinct mass adherent to valvular structures can be identified by two-dimensional echocardiography (1–8). Such masses have been shown in surgical and pathologic studies to represent valvular vegetations (9,10), and many investigations (2,4,6, 11–14) have established that patients with vegetations are at higher risk for the development of complications than are patients who have similar clinical findings without vegetations.

Clearly, there is limited specificity in any method that identifies 80% of an affected population as being at higher risk when the incidence of complications is known to be far less. Methods of further refining the echocardiographic features in such patients would therefore aid considerably in their clinical management.

The purpose of this study was to utilize two-dimensional echocardiography to identify and define the physical characteristics of infectious vegetations in patients with valvular endocarditis. By relating these characteristics to the occurrence of important clinical events, we hoped to develop a method for more precisely estimating risk in individual patients.

Methods

Patient selection. A computerized search of the medical records of the Massachusetts General Hospital for the 6 calendar years 1982 through 1987 was carried out. Adult patients with the primary discharge diagnosis of infectious endocarditis were sought and 292 patients were identified. The names of these patients were then cross-referenced with the computer data base of the echocardiography laboratory to identify those patients who underwent a two-dimensional echocardiographic study within 5 days of the admission in which infectious endocarditis was diagnosed. This search yielded 219 patients, consisting of 132 men and 87 women with a mean age (± SD) of 54.5 ± 18.6 years. Both the medical records and videotaped echocardiographic examinations of the 219 study patients were reviewed.

Records before 1982 were not searched because two-dimensional imaging was not generally available before that year and the computerized data base was not in place.

Medical record review. The medical record of the admission during which endocarditis was diagnosed was reviewed by one of us. The following documentation was required to

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Table 1. Complications in 204 Patients by Location of Vegetation or Valve Abnormality

Echocardiographic Finding	No.	Any Cx (%)	FTR	CHF	SEmb	PEmb	CEmb	Surg	Mort
Mitral veg.	51	27 (52.9)	7	10	5	0	14	11	6
Aortic veg.	34	21 (61.8)	0	10	6	0	5	12	4
Tricuspid veg.	13	10 (76.9)	3	1	0	9	1	1	1
PVE	56	34 (60.7)	2	10	4	0	10	19	5
NST	14	8 (57.1)	1	5	1	0	3	2	4
AVD	4	3 (75.0)	1	1	0	0	1	1	1
MVD	3	2 (66.7)	1	1	0	0	1	1	0
MVP	3	1 (33.3)	0	1	0	0	0	0	0
No abnormality	26	7 (26.9)	0	0	4	0	4	0	2
Totals									
No.	204	113	15	38	20	9	39	47	23
%	100	55.4	7.4	18.6	9.8	4.4	19.1	23.0	11.3
(Exclusions: 15)									

Any Cx = development of any complication; AVD = aortic valve disease; CEmb = central nervous system embolism; CHF = congestive heart failure; FTR = failure to respond to antibiotic treatment; Mort = mortality; MVD = mitral valve disease; MVP = mitral valve prolapse; NST = non-specific thickening; PEmb = pulmonary embolism; PVE = prosthetic valve endocarditis; SEmb = systemic embolism; Surg = surgical valve replacement; veg. = vegetation.

establish the diagnosis: 1) a persistent *febrile illness*; 2) *bacteremia*, as established by multiple blood cultures; 3) the presence of one of the following *clinical findings* compatible with the diagnosis of endocarditis: evidence of preexisting structural cardiac abnormalities, documented evidence of embolic complications and surgical or pathologic confirmation.

After review of the medical records, 10 patients were excluded because of persistently normal blood cultures (4 patients) or lack of compatible clinical findings (6 patients). An additional five patients were subsequently excluded because of echocardiograms of insufficient quality for adequate assessment of all valves. The remaining 204 patients formed the study group. Twelve patients who had been taking antibiotic agents before admission had normal blood cultures but fulfilled all other criteria and were therefore included in the study.

Documentation of the following clinical events was recorded for each admission: 1) *failure to respond*: persistence of the febrile illness despite an appropriate course of antibiotic agents requiring a change in therapy; 2) *congestive heart failure*: occurring on or after admission and documented by compatible clinical or hemodynamic findings, or both; 3) *peripheral embolization*: objective evidence of pulmonary or systemic events, excluding central nervous system emboli; 4) *central nervous system embolization*: a compatible clinical syndrome, as well as diagnostic imaging evidence of cerebral infarction or a confirmatory neurologic consultation; 5) requirement for *surgery*: defined as the need for valve replacement during the index admission; 6) *mortality*: during the index admission and as a result of complications directly attributable to endocarditis.

Review of echocardiograms. All echocardiograms were reviewed by three of us (A.J.S., M.H.P., R.D.) without knowledge of the clinical events. A valvular vegetation was defined as a *discrete* mass of echogenic material *adherent* at some point to a leaflet surface and *distinct* in character from the remainder of the leaflet. An echocardiogram displaying diffuse irregularities of one or more valves was categorized as showing *nonspecific thickening* and was not considered compatible with the diagnosis of a valvular vegetation. Similarly, studies were entered into the analysis as *aortic valve disease*, *mitral valve disease* or *mitral valve prolapse* if they showed findings compatible with these conditions but no evidence of vegetations. The presence of a mechanical prosthesis or a bioprosthesis in any position was also noted and patients with a prosthesis were analyzed separately regardless of morphologic findings. The breakdown of the study group on the basis of this review is shown in Table 1.

Characterization of Vegetations

Once identified, valvular vegetations were further characterized on the basis of four physical properties, as assessed echocardiographically.

Vegetation size. Two orthogonal dimensions of the identified vegetations were assessed (Fig. 1). One measurement was made perpendicular to the leaflet surface (D1) and a second parallel to the leaflet (D2). Each was made at the point of maximal thickness. For both mitral and aortic valves, the vegetation was measured in the parasternal long-axis view during diastole. This convention was adopted because it was found to yield the clearest imaging of the boundaries of the vegetations.

Vegetation mobility. The mobility of the identified vegetations was assessed by real time imaging on the basis of a four-point scale (Fig. 2) as follows.

Grade 1: a *fixed* vegetation with no detectable independent motion.

Grade 2: a vegetation with a *fixed base* but with a mobile free edge and larger in its parallel dimension (D2) than its perpendicular dimension (D1).

Grade 3: a *pedunculated* vegetation, defined as a lesion that has a stalk and a perpendicular dimension (D1) greater

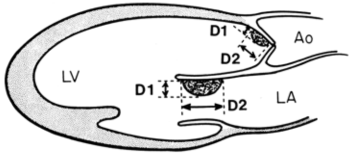


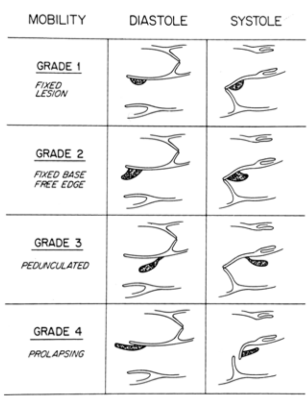
Figure 1. Vegetation size was measured as illustrated in this diagram. The perpendicular dimension (D1) was the distance from the leaflet surface to the external surface of the vegetation at its maximum. The parallel dimension (D2) was the maximal extent of the vegetation parallel to the leaflet surface. Measurements were made in diastole for both aortic and mitral valve vegetations using the parasternal long-axis imaging plane whenever possible. AO = aorta; LA = left atrium; LV = left ventricle.

than the parallel dimension (D2) but that remains within the same chamber throughout the cardiac cycle.

Grade 4: a *prolapsing* vegetation, that is, one that crosses the coaptation plane of the leaflets at some point during the cardiac cycle.

Vegetation extent. The maximal extension of each vegetation was assessed in multiple echocardiographic views. This variable was graded as follows: *Grade 1*: a single vegetation; *Grade 2*: multiple vegetations limited to a single valve leaflet; *Grade 3*: involvement of multiple valve leaflets; *Grade 4*: a vegetation that extended to *extravalvular* structures.

Figure 2. Assessment of vegetation mobility. See text for further details.



Vegetation consistency. The consistency or texture of each vegetation was assessed by using the appearance of the myocardial echoes as a reference. Calcification was assessed on the basis of characteristic bright reflections: *Grade 1*: a completely calcified vegetation; *Grade 2*: a partially calcified vegetation; *Grade 3*: consistency denser than myocardial echoes but without calcification; *Grade 4*: consistency equal to that of myocardial echoes.

Statistical analysis. The occurrence of clinical events in various subgroups was compared by using chi-square testing, with significance determined as a probability < 0.05. For analysis of multiple potentially important variables, logistic regression analysis was carried out. A probability < 0.01 was required for inclusion of any independent variable into the regression models.

Results

Analysis of Clinical Complications

Incidence. At least one of the previously described complications occurred in 55% of the patients studied. This incidence was statistically equivalent for mitral (53%) and aortic (62%) native valves, prosthetic valves (61%) and for endocarditis diagnosed in patients with nonspecific valvular thickening (57%). However, significantly more complications occurred in tricuspid valve endocarditis (77%, $p < 0.001$) and significantly fewer when no vegetation or valvular abnormality was identified (27%, $p < 0.005$).

Distribution of complications according to site of infection (Table 1). Among patients with native mitral or aortic valve endocarditis the most frequently encountered complications were the need for valve replacement (23 of 85; 27%), congestive heart failure (20 of 85; 23.5%) and central nervous system embolization (19 of 85; 22%). Pulmonary embolism was the most common complication in patients with tricuspid valve endocarditis, occurring in 69% of patients. The major complication of prosthetic valve endocarditis was the need for valve replacement, which occurred in a third of patients. Among those patients with nonspecific valvular abnormalities, heart failure (5 of 14; 36%) was the most common clinical complication and 4 (29%) of these patients died. The small number of complications occurring in patients with no detectable vegetations were evenly distributed among peripheral and central nervous system emboli (4 of 26; 15%).

Specific complications. Endocarditis resulted in patient *death* in 11% of cases overall, with no significant difference in its occurrence among the various subgroups (Table 2). The requirement for *surgical valve replacement* was highest among patients with aortic (35%) and prosthetic valve endocarditis (34%) and uncommon in tricuspid valve disease (8%) or when endocarditis resulted in nonspecific valve changes (14%). In no case was surgery required when no significant valvular abnormalities were detected echocardiographically. The overall incidence of *central nervous system*

Table 2. Findings in 23 Cases Ending in Mortality

Pt	Age (yr)/ Gender	Valve Involved*	Autopsy Performed	Cause of Death
1	51/F	Mitral	Yes	Multiple per. emboli, CHF
2	27/M	Mitral	Yes	CNS embolus, per. emboli
3	90/M	Mitral	Yes	Septic shock, ARDS
4	77/F	Mitral	No	CNS embolus, CHF
5	86/F	Mitral	No	Acute MR, CHF
6	25/F	Mitral	No	CNS embolus; per. emboli
7	45/M	Aortic	Yes	Acute MI (cor art embolus)
8	46/F	Aortic	Yes	Sepsis
9	28/M	Aortic	Yes	Acute AR
10	69/M	Aortic	No	Sepsis, CHF
11	29/M	Tricuspid	No	Sepsis, pulmonary emboli
12	67/M	PV	No	CNS embolus and hemorrhage
13	73/M	PV	No	Sepsis, CNS embolus
14	69/F	PV	Yes	CNS emboli, per. emboli
15	58/F	PV	Yes	CNS embolus
16	57/F	PV	No	Regurgitation, CHF
17	85/M	NST	Yes	Acute MI, pulmonary edema
18	55/M	NST	No	Acute AR, CHF
19	57/M	NST	Yes	CNS and per. emboli
20	90/F	NST	No	Sepsis, ARDS
21	85/M	AVD	No	CHF
22	72/F	None	No	CNS embolus with hemorrhage
23	73/F	None	No	Sepsis, ARDS

*Valve involved as assessed by echocardiography. AR = aortic regurgitation; ARDS = adult respiratory distress syndrome; AVD = aortic valve disease found but no discrete vegetation; CHF = congestive heart failure; CNS = central nervous system; cor art = coronary artery; F = female; M = male; MI = myocardial infarction; MR = mitral regurgitation; NST = nonspecific thickening (no discrete vegetation detected); per. = peripheral; Pt = patient; PV = prosthetic valve.

embolization was 19%. There was a lower incidence of this complication among patients with tricuspid valve involvement but no statistically significant differences occurred among any of the other groups.

Pulmonary embolism occurred exclusively in patients with tricuspid valve endocarditis. The incidence of nonpulmonary *systemic embolism* did not vary significantly among the other groups.

The overall incidence of congestive heart failure was 19%, with no significant differences in incidence among patients with mitral (20%), aortic (29%) or prosthetic valve (18%) endocarditis or in the presence of nonspecific valvular changes (36%). However, the incidence was significantly lower in patients with tricuspid valve endocarditis (8%). Heart failure did not occur in any patients with endocarditis who had no valvular abnormalities.

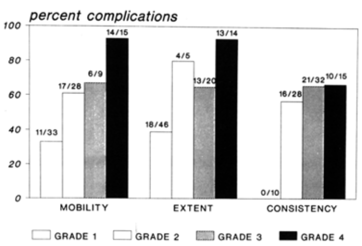
Failure to respond to antibiotic treatment was most common in patients with tricuspid valve (23%) and mitral valve (14%) endocarditis and did not occur in either those with aortic valve involvement or those with no valvular abnormalities.

Echocardiographic Analysis

The significance of the echocardiographic findings was analyzed only in patients with native left-sided endocarditis because the wide morphologic differences among prosthetic valves make direct comparisons impractical and there were too few patients with native right-sided valve endocarditis to permit meaningful conclusions to be drawn.

Grading of vegetation characteristics. The incidence of clinical complications in the 85 patients with native left-sided

Figure 3. Incidence of complications relative to the degree of morphologic abnormality is illustrated here for vegetation mobility, extent and consistency. The numbers above the bars refer to the absolute number of patients with complications relative to the total in the subgroup.



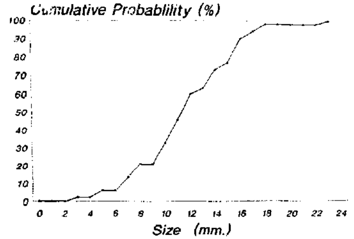


Figure 4. Graph of the cumulative occurrence of complications relative to increasing vegetation size.

Table 4. Results of Multiple Stepwise Logistic Regression Analysis

Term Entered	Improvement Chi-Square	Improvement p Value	Coeff*	Coeff/SE
Mobility	17.2	<0.001	0.95	2.79
Extent	9.6	0.002	0.65	2.53
Max size	4.6	0.032	0.27	2.75
Site	8.0	0.005	0.98	2.60

*Refers to the coefficient (Coeff) assigned to each independent variable in the logistic regression model to calculate the probability of the event of interest, that is, complications of infectious endocarditis. In the model a constant term of −5.51 was also incorporated into the regression equation and the categoric variable "site" was assigned a numeric value of −1 for mitral vegetations and +1 for aortic vegetations. Max = maximal.

valve endocarditis, subdivided on the basis of vegetation mobility, extent and consistency, is illustrated in Figure 3. In this analysis, a case was considered to have been associated with a clinical complication if any of the previously listed events occurred during the index hospitalization. Increasing grades in *mobility* were associated with increasing frequency of clinical complications. Grading of vegetation *extent* was also associated with incremental increases in the rates of complications, although grades 2 and 3 did not differ significantly possibly because of the small numbers of grade 2 lesions. In the case of vegetation *consistency*, no complications occurred in patients with a grade 1 lesion. However, grades 2 to 4 were all associated with similar complication rates.

The effect of vegetation size is plotted in Figure 4 where maximal size (the larger of D1 and D2) is plotted against cumulative complications for the 85 patients with left-sided valve endocarditis. The 10th, 50th and 90th percentiles occurred at maximal dimensions of approximately 6, 11 and 16 mm, respectively.

Logistic regression analysis. To determine which factors are important predictors of complications, stepwise multiple logistic regression analysis was performed in the 85 cases of native left-sided valve endocarditis. In addition to the four morphologic vegetation characteristics noted previously, patient age, gender, vegetation site (that is, mitral or aortic) and the underlying organism as identified by blood culture were entered as independent variables. Both the perpendicular and parallel vegetation dimensions, as well as maximal vegetation dimension, were entered. The occurrence of any of the noted clinical complications was used as the dependent variable. Results of the univariate analysis (step 0 of the logistic regression analysis) are listed in Table 3. It is apparent that vegetation mobility, extent, consistency and all three measures of size were significant univariate predictors of outcome. Patient age, gender, vegetation site and the particular underlying organism did not demonstrate significant influence in this analysis. The final results of stepwise logistic regression analysis (step 4 of the analysis) are listed in Table 4. In this multivariate analysis, vegetation site emerged as an important independent predictor of complications in addition to mobility, extent and maximal dimension. These variables continued to show independent significance when only central nervous system embolization, congestive heart failure, requirement for surgery and mortality were used as the dependent variables. The only

Table 3. Univariate Associations With Complications in 85 Patients

Factor	Patients Without Complications (n = 37)	Patients With Complications (n = 48)	p Value
Age (yr)	57.8 ± 17.2	50.9 ± 18.5	0.085
Gender (% M)	65	65	0.979
Veg site	Categoric variable		0.428
Organism	Categoric variable		0.162
D1 (mm)	6.5 ± 3.0	8.7 ± 3.7	0.004
D2 (mm)	8.9 ± 3.7	11.8 ± 4.4	0.003
Dmax (mm)	9.1 ± 3.7	12.2 ± 4.0	0.0007
Mobility*	1.5 ± 0.8	2.5 ± 1.1	<0.0001
Extent*	1.5 ± 0.9	2.4 ± 1.3	0.0002
Consistency*	2.3 ± 1.0	2.8 ± 0.8	0.010

*Values given are scores as described in text. All values given ± standard deviation. D1 = perpendicular dimension; D2 = parallel dimension, Dmax = maximal dimension; M = male; Veg = vegetation.

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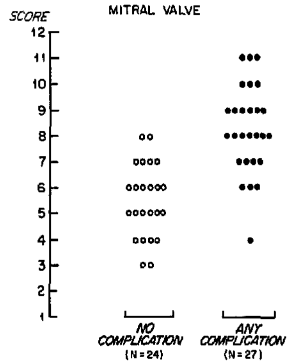
important predictor of peripheral embolization was patient age and only the nature of the underlying infecting organism predicted a failure to respond to antibiotic agents.

Derivation of an echocardiographic score. To improve the echocardiographic prediction of complications, a score was devised based on the assessment of the variables shown in multivariate analysis to carry independent significance. Because vegetation mobility, extent and size were of approximately equal influence in the multiple logistic regression analysis, they were each graded on a scale of 1 to 4, as described under Methods, thus yielding a total possible score of 12. Vegetation mobility and extent were graded as described earlier. The grading of size was based on the observed distribution of size versus incidence of complications. Thus, a score of 1, 2, 3 or 4, respectively, was assigned to a maximal vegetation dimension of ≤6, 7 to 10, 11 to 15 or >15 mm.

Logistic regression analysis was then repeated with this derived score added to the same variables included in the first analysis. Because vegetation site had also been shown to influence the incidence of complications significantly, logistic regression analysis was repeated separately for the mitral and aortic valves. In each case the derived echocardiographic score emerged as the sole independent predictor of complications with $p < 0.0001$ for the mitral valve and $p < 0.002$ for the aortic valve.

Analysis of mitral valve endocarditis. The individual scores of all 51 patients are shown in Figure 5. The sensitivity, specificity and predictive value for various scores is also indicated. It is apparent that a score ≥8 maximized predictive accuracy with a sensitivity of 70% and specificity of 92%. A score >8 was invariably associated with an adverse clinical outcome. The score was also the best independent predictor of central nervous system embolism and death. Patient age and vegetation mobility were the best predictors of surgery. Vegetation extent optimally predicted the occurrence of congestive heart failure, and consistency, mobility and size combined to best predict peripheral embolization.

Analysis of aortic valve endocarditis. Figure 6 illustrates the scores of the 34 patients with aortic valve endocarditis and the corresponding levels of sensitivity, specificity and predictive accuracy. It is apparent that a score ≥5 provided a predictive accuracy of 71% with a sensitivity of 76% and specificity of 62%. Predictive accuracy was marginally increased at a score ≥4 but with a significant sacrifice in specificity. In terms of the individual complications, requirement for surgical replacement, congestive heart failure and mortality were also best predicted by the score. The occurrence of peripheral and central nervous system embolization were best related to patient age and the infecting organism, respectively.



SCORE	SENSITIVITY %	SPECIFICITY %	PREDICTIVE ACCURACY %
≥6	96	50	75
≥7	85	75	80
≥8	70	92	80
≥9	44	100	71

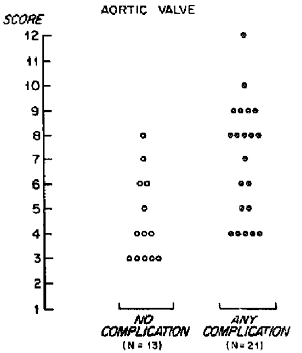
Figure 5. All patients with mitral valve endocarditis are plotted with respect to their echocardiographic score (see text) and the occurrence of complications. Sensitivity, specificity and predictive value for various scores are given below.

Discussion

The echocardiogram has become an integral part of the assessment of patients with infective endocarditis. It is used to both confirm the diagnosis and to monitor response to treatment. Central to this assessment is the identification of valvular vegetations that, as numerous studies have shown (2,4,6,11–14), identify patients at increased risk for complications. The mere presence or absence of vegetations, however, is a relatively nonspecific marker for increased risk. Because echocardiographic imaging technology has improved considerably since many of these earlier studies were undertaken, we believed it reasonable to postulate that a more complete assessment of vegetation morphology might allow better characterization of high risk lesions.

Echocardiographic Findings

In this study we have demonstrated that three easily identifiable morphologic characteristics of the vegetative mass—its mobility, extent and size—greatly enhance the identification of patients with native, left-sided valve en-



SCORE	SENSITIVITY %	SPECIFICITY %	PREDICTIVE ACCURACY %
≥4	100	39	76
≥5	76	62	71
≥6	67	69	68
≥7	57	85	68
≥8	52	92	68
≥9	29	100	56

Figure 6. Plot similar to that in Figure 6 for patients with aortic valve endocarditis. Sensitivity, specificity and predictive value for various scores are given below.

docarditis at risk for complications. Furthermore, integration of these three factors into a composite score further enhances predictive accuracy.

The prognostic value of these morphologic factors can be accounted for in two ways: 1) Infections that have not been adequately suppressed because of a failure of host defense mechanisms or because of inadequate treatment would be expected to result in detectable vegetations of larger size and with higher scores for extent and mobility. Therefore, the morphologic factors assume importance because they tend to identify infections that have not come under immediate control and are therefore a greater risk to the patient. 2) Vegetations that are larger, more extensive and more mobile are, simply by virtue of their physical nature, more likely to result in valvular obstruction, embolization and disruption of normal leaflet coaptation.

Vegetation size. The importance of vegetation size as a predictor of clinical outcome has previously been argued in echocardiographic studies. Our findings are in agreement with several studies (14–18) but conflict with others (4,6,19). Generally, size has been shown to be of prognostic importance when assessed as a continuous variable or when analyses have been limited to specific subgroups of patients with native valve endocarditis. The failure of some studies to demonstrate the importance of vegetation size may be accounted for by small sample size (4); use of a noncontinuous, qualitative assessment of size (6); or inclusion of patients with prosthetic valve endocarditis (19). In the latter patients, the assessment of vegetation morphology and size is probably considerably more difficult and complex by standard two-dimensional imaging, as other investigators have suggested (20). In such patients different prognostic markers may be required, such as valvular stability and leaflet thickening. Transesophageal imaging may prove to be particularly helpful in the morphologic assessment of this patient population.

Echocardiographic consistency of the vegetation. It was originally hypothesized that echocardiographic consistency of a vegetation would be of prognostic significance, as suggested by previous work using image processing techniques (21). For this reason, greater vegetation reflectivity was presumed to represent an older "healed" lesion and therefore assigned lower values in our grading system. In the analysis, a highly reflective lesion (grade 1) did identify a subgroup in which no complications occurred. The failure of the other grades to differentiate significantly implies either that tissue consistency has no prognostic meaning or that technical variability in technique or acquisition variables among patients prevented proper characterization of consistency. Although these results do not allow us to resolve this issue, we believe that the latter is more likely in view of the numerous sources of technical variability that could occur in a study of this design (gain settings, transducer selection or morphologic variability among patients). This is true despite our attempt to minimize such variability by using myocardial consistency as an interstudy reference standard. The strong association observed between a heavily calcified vegetation and a noncomplicated course further suggests that there is some merit to evaluating consistency, although its full assessment may not be technically feasible in routine clinical examinations.

Valve regurgitation. This study did not incorporate Doppler assessment of valve regurgitation into the analysis because many of the studies were carried out before Doppler technology was generally available. Clearly, analysis of the *effect* of valvular endocarditis, as documented by the extent of regurgitation or secondary chamber enlargement, has the potential to add further predictive power to the echocardiographic analysis of these patients. Again, as recent reports (22–24) have suggested, transesophageal imaging may allow more precise imaging and therefore more complete morphologic assessment. These are both promising approaches to the echocardiographic characterization of endocarditis that merit further investigation.

The echocardiographic score was developed to illustrate the effect of combining all significant variables. Although the score performed well in predicting complications in patients with mitral and aortic valve endocarditis, it has not been fully validated and its clinical role can only be fully assessed in ongoing prospective studies.

Clinical Findings

Rate of complications. The rate of complications in all groups of patients with endocarditis in our study is somewhat higher than that reported in previous studies. This difference probably reflects two characteristics of our study: it was conducted in a tertiary care center and many of the patients were referred from other institutions because they were identified as being at high risk or were being considered for surgery. Our results also show equivalent complication rates for prosthetic valve and native valve endocarditis, largely because of the more favorable outcome of prosthetic valve endocarditis than has been previously reported in clinical studies (25). This result may represent a changing awareness of the danger of this disease, which has resulted in earlier and more aggressive treatment. It is also likely that further characterization of the prosthetic valve cases, in a manner similar to that carried out for the native left-sided valve lesions, will uncover subgroups of patients at considerably increased risk.

Role of valvular thickening. The observed complication rates among patients with no discrete vegetations but nonspecific valvular thickening is of particular interest. These patients had complication rates roughly equivalent to those with discrete vegetations or prosthetic valves, and four of these patients died. In all cases the cause of death was clearly attributable to endocarditis (Table 2). In two of these four patients, an autopsy was performed showing multiple small friable vegetations attached to aortic valve cusps. In retrospect, it appears that these lesions were echocardiographically indistinguishable from the irregular, thickened appearance of the aortic cusps that is commonly encountered in elderly patients and interpreted as degenerative change or aortic valve sclerosis. It is important to recognize that in the setting of clinical endocarditis such patients behave more like those with clear evidence of vegetations than those with echocardiographically "clean" valves.

Role of bacteriology. Somewhat surprisingly, our multivariate analysis failed to show that the underlying bacteriologic stratum influenced outcome. This finding contrasts with common experience and the suggestion of previous clinical reports that endocarditis secondary to certain organisms, such as *Staphylococcus aureus*, carries increased risk, but it supports the findings of a recent echocardiographic analysis of vegetations (24). This apparent discrepancy may again reflect the high risk referral population involved in this study. Alternatively, any prognostic influence of the bacteriologic findings may have been strongly correlated with the morphologic characteristics of the vegetation, such as size, and therefore did not reach statistical significance in the multivariate analysis.

Conclusions. The results of this study demonstrate that valuable information can be derived from the echocardiographic evaluation of patients with infectious endocarditis, far exceeding that provided by simply noting the presence or absence of vegetations. The size, extent and mobility of vegetations each act as independent markers of a more complicated course and have additive predictive power when considered together.

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