**The Role of Myocarditis and Myocardial
Fibrosis in Dilated Cardiomyopathy
Analysis of 28 Necropsy Cases**

Nobuteru MAHASHI, M.D., Yoshiyuki YOKOTA, M.D.,
Akira TAKARADA, M.D.,** Seiichiro USUKI, M.D.,
Sakan MAEDA, M.D.,* Hiroshi YOSHIDA, M.D.,**
Taketoshi SUGIYAMA, M.D.,* and Hisashi FUKUZAKI, M.D.

SUMMARY

The hearts of 28 necropsy cases with DCM and 10 control cases were analysed to elucidate the role of myocarditis and fibrosis in dilated cardiomyopathy (DCM). The extent of fibrosis and myocyte diameter were measured in the transverse sections of the left ventricle. The degree and pattern of fibrosis varied widely from case to case. The DCM cases were then classified into 3 groups: 1) Group Ia, 8 cases with mild diffuse fibrosis; 2) Group Ib, 9 cases with severe diffuse fibrosis and 3) Group II, 11 cases with segmental fibrosis.

Myocardial fibrosis and hypertrophy were significantly more prominent in Groups Ib and II than in the control group ($p < 0.01$), but no differences were observed between Group Ia and the control group. Thus, it is reasonable to attribute the chronic CHF and LV dilatation in Groups Ib and II to the extensive myocardial fibrosis. In contrast, it is not reasonable to attribute the chronic CHF and LV dilatation in Group Ia to myocardial fibrosis.

Focal lymphoid cell infiltration was graded to assess inflammatory changes. Group II showed more prominent inflammatory changes than the other 2 groups ($p < 0.05$). Thus, it is possible that myocarditis is an etiologic factor for DCM with a segmental pattern of fibrosis.

Additional Indexing Words:

Dilated cardiomyopathy Myocarditis Myocardial fibrosis

ENDOMYOCARDIAL biopsy has now been widely used to evaluate a variety of cardiac diseases. However, this method requires further evaluation for the diagnosis of dilated cardiomyopathy (DCM). Some have concluded that analyses of biopsy specimens from DCM patients do not correlate

From the First Department of Internal Medicine and the Second Department of Pathology,* Kobe University School of Medicine, Kobe and Himeji Cardiovascular Center,** Himeji, Japan.

Mailing address: Yoshiyuki Yokota, M.D., First Department of Internal Medicine, Kobe University School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650, Japan.

Received for publication October 20, 1989.

Accepted June 13, 1990.

with clinical findings or prognosis.^{1),2)} However, DCM is considered to be a heterogeneous disorder. Thus, it is unreasonable to evaluate myocardial lesions on a single basis. Although there have been many reports concerning the pathological aspects of DCM,^{3),4)} few reports have quantitatively evaluated the variability of myocardial lesions in DCM.

Endomyocardial biopsy is used to detect myocarditis. Myocarditis has been reported to occur in 9–63% of unselected cases of biopsy.⁵⁾ However the identification of inflammatory cells in small biopsy samples is often difficult, and the mere presence of inflammatory cells does not indicate myocarditis,⁶⁾ because inflammatory cells such as lymphocytes appear in numerous other processes that affect the myocardium.

We have observed considerable variations in the pattern and extent of fibrosis and in the severity of inflammatory cell infiltration in autopsied hearts from DCM patients. In this study, we clinically and pathologically examined the autopsied cases of DCM to elucidate the pathogenesis of DCM and its relationship to myocarditis.

METHODS

Patients: Autopsy cases of DCM at Kobe University Hospital and Himeji Cardiovascular Center were reviewed pathologically. The DCM cases fulfilled the following criteria: (1) a clinical history of congestive heart failure (CHF), (2) cardiac death, (3) no clinical history of acute myocarditis, (4) marked left ventricular (LV) dilatation, (5) absence of valvular lesions, (6) absence of significant stenosis (50% or more) of the extramural coronary arteries, (7) absence of extensive myocardial disarray, suggesting a dilated form of hypertrophic cardiomyopathy,⁷⁾ and (8) absence of systemic disorders causing secondary cardiomyopathies, such as amyloidosis and neuromuscular disorders. A few cases involving alcoholism or pregnancy at the onset of cardiac symptoms were included because their causal relationship to CHF remains ambiguous. We also included cases of lymphoid cell infiltration when they fulfilled other criteria of DCM, because one of the main purposes of the present studies was to analyze the role of myocarditis in DCM. Of the 10 control patients, 9 died accidentally and 1 died of an acute onset of diabetes mellitus after her delivery. They showed no evidence of heart disease.

Macroscopic measurements: Formalin-fixed hearts were sliced transversely from the apex to the base. The slices from the middle third of the ventricles were used for the analysis. The thickness of the LV wall was measured at five different sites: the anterior, lateral and posterior free walls, and the anterior and posterior interventricular septa, and the mean wall thickness was

Fig. 1-a.

Fig. 1-b.

Fig. 1. Photomicrographs showing a "focus" of lymphoid cell infiltration. a: The region where a few lymphoid cells were infiltrated sparsely without focal aggregation was not considered a "focus". b: The region where many lymphoid cells aggregated was considered a "focus". Hematoxylin-eosin stain; original magnification $\times 25$.

calculated. Papillary muscles and epicardial fat tissue were excluded from the measurement.

The cavity perimeter of the LV measured was used to assess the diameter of the LV because the ventricular diameter can be distorted by fixation. The endocardia of the transverse sections of the LV were projected onto a screen and traced on paper. The perimeter (P) was measured from the tracing with an IBAS-II image analyzer (Karl Zeiss, West Germany), and the cavity diameter (D) was obtained by $D=P/\pi$.

Microscopic measurements: The transverse histologic sections were stained with hematoxylin-eosin for routine analysis and Mallory Azan staining for

Fig. 2-a.

Fig. 2-b.

Fig. 2. A typical case of diffuse and mild fibrosis (Case 3, Group Ia). A 27-year-old man who died of progressive refractory heart failure 1 year after onset. a: A cardiac transverse section showing wall thinning and cavity dilation of both ventricles. There is no grossly visible infarct. b: Histology. Myofibrils are wavy and elongated but not degenerative. Interstitial fibrosis is minimal and no lymphoid cell infiltration is found. Some erythrocytes fill capillaries. Hematoxylin-eosin stain; original magnification $\times 25$.

fibrosis. The LV wall was divided into five sections: the anterior, lateral and posterior walls, and the anterior and posterior interventricular septa. The degree of fibrosis was measured in each section by the point-counting method⁸⁾: A grid with 121 intersecting points was placed onto a 10-power ocular lens and heart muscles were studied histologically for the *fibrosis rate* which was calculated by the following formula:

$$\text{Fibrosis rate (\%)} = \frac{\text{Number of points falling on fibrous tissue}}{\text{Number of points on heart muscle and fibrous tissue}} \times 100$$

Fig. 3-a.

Fig. 3-b.

Fig. 3. A typical case of diffuse and severe fibrosis (Case 16, Group Ib). A 42-year-old man who died of CHF 2 years after the onset. a: A cardiac transverse section showing wall thinning and dilation of both ventricles. The gross appearance is almost the same as that of Case 3 (Fig. 2), although fine fibrosis is spread mainly in the outer half of the LV free wall (arrows). b: Histology shows myocyte hypertrophy and diffuse interstitial fibrosis accompanied by myocytolysis (arrow). There is no lymphoid cell infiltration. Hematoxylin-eosin stain; original magnification $\times 25$.

The points falling on empty spaces such as vascular lumen and tissue space were not counted. Papillary muscles, trabeculae and epicardial fat were excluded from the measurement. The whole LV was scanned in a transverse section using a 4-power objective lens. The available number of points in each section averaged 700, though it depended on the size of sections. The fibrosis rate in a given case was obtained by averaging the rates of five sections.

The diameter of myocytes was determined by measuring the width of

Fig. 4-a.

Fig. 4-b.

Fig. 4. A typical case of focal fibrosis (Case 23, Group 11). A 23-year-old man who first noted exertional dyspnea at the age of 20 and died suddenly while sitting on a train. a: A transverse section showing localized transmural fibrosis (arrows) in the anterior two thirds of the interventricular septum and subendocardial fibrosis in the anterior and lateral free LV wall (arrowheads). The posterior wall is spared and the wall thickness is preserved. b: A histologic section with infiltration of numerous lymphoid cells in a boundary region between unaffected and fibrotic areas. Hematoxylin-eosin stain; original magnification $\times 25$.

cells in a longitudinal section in the middle layer of the ventricular wall. Fifty myocytes were randomly selected from the anterior, posterior, and septal walls to calculate the average diameter. Myocytes showing degenerative changes were not included in the measurements.

Inflammation was graded by the degree of focal lymphoid infiltration; 0: no infiltration; 1+: 1–2 foci; 2+: 3–9 foci; and 3+: more than 10 foci. A “focus” was defined as an aggregation of 20 or more lymphocytes (Fig. 1).

The continuously distributed data were all expressed by $\text{mean} \pm \text{SD}$.

Table I. Clinical Findings from 28 DCM and 10 Control Subjects

Group	Case	Age (yr)	Sex	Duration of CHF (yr)	Type of death	Chest discomfort	Cold-like onset	Other factors
Ia (N=8)	1	52	M	3	CHF	0	0	0
	2	16	F	2	CHF	0	0	0
	3	27	M	1	CHF	+	0	0
	4	44	M	11	CHF	0	0	Alcohol
	5	28	M	5mo	CHF	0	0	0
	6	66	F	3	CHF	+	0	0
	7	28	M	5	CHF	0	0	0
	8	42	F	16	CHF	0	0	0
	Mean±SD	38±16	5/3*	5±5				
Ib (N=9)	9	59	F	1	CHF	0	0	0
	10	54	M	16	Sudden	0	0	0
	11	25	F	2	CHF	0	0	Peripartum
	12	49	M	6	CHF	0	0	0
	13	48	M	4	CHF	+	0	0
	14	21	M	1	CHF	0	+	0
	15	48	M	3	CHF	0	+	0
	16	42	M	2	CHF	+	0	0
	17	50	M	10	CHF	0	0	0
	Mean±SD	44±13	7/2*	5±5				
II (N=11)	18	34	M	4mo	CHF	0	0	0
	19	26	F	3	CHF	+	0	Peripartum
	20	71	M	1	CHF	0	0	0
	21	36	F	2mo	CHF	0	0	Peripartum
	22	57	M	12	CHF	+	0	0
	23	23	M	3	Sudden	0	0	0
	24	52	M	5	CHF	0	0	0
	25	26	M	5	CHF	0	+	0
	26	22	F	3	CHF	0	0	Familial
	27	63	F	1	CHF	+	0	0
	28	49	F	12	CHF	0	0	0
Combined (N=28)	Mean±SD	42±17	6/5*	5±6				
	Mean±SD	41±15	18/10*	5±6				
Control (N=10)	Mean±SD	39±8	7/3*					

* = male/female; + = present; 0 = absent.

CHF = congestive heart failure; F = female; M = male; SD = standard deviation.

Table II. Pathological Findings from 28 Patients and 10 Control Subjects

Group	Case	Heart weight (g)	LVWT (mm)	LVD (mm)	LVD/LVWT	Fibrosis rate (%)	SDFR (%)	Myocyte diameter (μ m)	Grade of inflammation
Ia (N=8)	1	710	11	71	6.5	5.2	2.3	13.6	0
	2	600	10	57	5.7	8.2	2.7	15.5	1
	3	505	8	59	7.4	9.5	4.1	13.7	0
	4	590	10	62	6.2	9.7	2.0	15.5	1
	5	580	10	57	5.7	11.7	5.5	20.5	0
	6	540	10	63	6.3	12.0	4.8	14.0	1
	7	650	9	59	6.6	13.9	1.8	15.8	2
	8	500	11	61	5.6	14.3	7.0	19.0	1
	Mean $\pm$ SD	584 $\pm$ 72 ⁺	10 $\pm$ 1	61 $\pm$ 5 ⁺	6.2 $\pm$ 0.6 ⁺	10.6 $\pm$ 3.0	3.8 $\pm$ 1.9	15.9 $\pm$ 2.5	
Ib (N=9)	9	380	7	50	7.1	16.9	6.7	21.4	2
	10	700	13	59	4.5	19.4	4.3	18.8	0
	11	360	8	68	8.5	25.0	5.3	20.9	1
	12	480	12	65	5.4	25.1	9.6	18.0	2
	13	620	9	66	7.3	25.5	5.8	14.0	1
	14	670	11	62	5.6	27.1	3.4	20.7	0
	15	410	7	53	7.6	28.1	2.5	19.2	2
	16	500	7	65	9.3	28.2	9.9	17.0	0
	17	850	14	62	4.4	37.7	7.3	27.5	0
	Mean $\pm$ SD	552 $\pm$ 167 ⁺	10 $\pm$ 3 [*]	61 $\pm$ 6 ⁺	6.7 $\pm$ 1.7 ⁺	25.9 $\pm$ 5.9 ⁺	6.1 $\pm$ 2.6	19.7 $\pm$ 3.7 ⁺	
II (N=11)	18	460	8	57	7.1	16.8	11.2	14.0	3
	19	415	10	57	5.7	20.8	15.5	16.9	3
	20	490	7	65	9.3	21.2	8.8	18.7	3
	21	540	13	57	4.5	27.0	14.8	15.8	2
	22	780	10	75	7.5	28.4	5.4	18.9	1
	23	330	8	45	5.6	31.6	21.2	19.6	3
	24	440	6	66	11.0	36.7	9.8	18.3	3
	25	700	9	62	6.9	36.7	10.2	23.8	1
	26	760	13	64	4.9	41.6	14.9	18.4	2
	27	500	9	67	7.4	47.2	16.8	16.6	2
	28	300	7	51	7.3	57.1	32.8	17.3	3
Combined (N=28)	Mean $\pm$ SD	520 $\pm$ 163 ⁺	9 $\pm$ 2 ⁺	61 $\pm$ 8 ⁺	7.0 $\pm$ 1.9 ⁺	33.2 $\pm$ 12.2 ⁺	14.7 $\pm$ 7.4 ⁺	18.0 $\pm$ 2.5 ⁺	
	Mean $\pm$ SD	549 $\pm$ 142	10 $\pm$ 2 ⁺	61 $\pm$ 7 ⁺	6.7 $\pm$ 1.6 ⁺	24.4 $\pm$ 12.5 ⁺	8.8 $\pm$ 6.9 ⁺	18.0 $\pm$ 3.2 ⁺	
Control (N=10)	Mean $\pm$ SD	292 $\pm$ 37	13 $\pm$ 2	33 $\pm$ 6	2.7 $\pm$ 0.7	5.5 $\pm$ 1.0	1.7 $\pm$ 0.7	13.5 $\pm$ 1.5	

*= $p < 0.05$; += $p < 0.01$, compared to control.

F=female; LVD=left ventricular dimension; LVWT=left ventricular wall thickness; M= male; SD=standard deviation; SDFR=standard deviation of fibrosis rate among 5 sections.

The differences among groups were subjected to a one-way analysis of variance and to a modified t-test (Bonferroni's).⁹⁾ The differences in lymphoid infiltration were assessed with a chi-square test. A probability value of less than 0.05 was considered significant.

RESULTS

Pattern of fibrosis: Patterns of fibrosis varied widely from case to case. Some cases showed diffuse fibrosis, whereas in others it was localized and looked like a scar of a myocardial infarction. Therefore, DCM cases were first classified into 2 groups: Group I: 17 cases with diffuse fibrosis; and Group II: 11 cases with segmental fibrosis. The former was further divided into 2 subgroups on the basis of the severity of fibrosis: Group Ia: 8 cases of mild fibrosis; and Group Ib: 9 cases with severe fibrosis. Cases of segmental fibrosis were defined as those with transmural scars extending more than half way across the LV wall. Typical cases from each group are shown in Figs. 2-4.

Clinical data: Table I shows typical clinical features of each group. There were no differences in age, sex, and total length of the clinical courses among the 3 DCM subgroups. One patient in Group Ib and 1 in Group II died suddenly. Others died of CHF and CHF-related ventricular arrhythmia. Seven patients (2 in Group Ia, 2 in Group Ib, and 3 in Group II) complained of pain or vague discomfort in the chest. Two cases in Group Ib and 1 in Group II revealed CHF after common-cold-like symptoms, but other clinical evidence of acute myocarditis, such as electrocardiographic changes or serum enzyme changes, were not observed. One patient in Group Ia was a habitual alcoholic. One in Group Ib and 2 in Group II were pregnant when cardiac symptoms started. One patient in Group II, whose 5 relatives died suddenly, was considered to have familial cardiomyopathy.

Macroscopic findings: Table II shows pathological features of each group. The heart was larger in the DCM groups than in the control group (549 ± 142 g vs 292 ± 37 g). However, in 2 cases from Group II with focal fibrosis, the loss of myofibrils was so prominent that the heart weight was indistinguishable from controls (Fig. 5). The enlarged LV cavity (61 ± 7 mm; control: 33 ± 6 mm) and decreased LV wall thickness (10 ± 2 mm; control: 13 ± 2 mm) in DCM cases produced a degree of dilatation (LV cavity size/LV wall thickness) that was about 3 times higher than that of the control group (6.7 ± 1.6 vs 2.7 ± 0.7). However, the degree of dilatation was identical in the DCM subgroups. In Group II, the LV wall was segmentally scarred and thinned, but the wall thickness was preserved in segments grossly free of fibrosis.

Fig. 5.

Fig. 5. Heart weight in the 3 DCM subgroups and the control.

Fig. 6.

Fig. 6. Fibrosis rate in the 3 DCM subgroups and the control.

Histological findings: The mean fibrosis rate in DCM cases was higher than that in the controls ($24.4 \pm 12.5\%$ vs $5.5 \pm 1.0\%$) (Fig. 6). According to the classification based on fibrosis, the mean fibrosis rate in Group Ib ($25.9 \pm 5.9\%$) and Group II ($33.2 \pm 12.2\%$) was higher than that in Group Ia ($10.6 \pm 3.0\%$) and the control group ($5.5 \pm 1.0\%$). However, the rate in Group Ia did not differ significantly from the control level. The standard deviation of the fibrosis rate among the five segments of the LV was considerably higher in Group II than in the other groups. Fibrosis was distributed diffusely throughout the transverse sections in Groups Ia and Ib and the control group. Group II showed a non-uniform pattern of fibrosis but did not show a predilection for specific segments.

The mean myocyte diameter in Group Ib ($19.7 \pm 3.7 \mu\text{m}$) and Group II ($18.0 \pm 2.5 \mu\text{m}$) was significantly larger than in the control group ($13.5 \pm 1.5 \mu\text{m}$). The myocyte diameter in Group Ia ($15.9 \pm 2.5 \mu\text{m}$) did not differ significantly from controls (Fig. 7).

Of the 28 DCM patients, 21 (75%) had foci of inflammatory cells within the myocardium: 1+ in 8, 2+ in 7, and 3+ in 6 (Fig. 8). Five cases of Group Ia (59%) and 5 cases of Group Ib (63%) showed 1+ or 2+. In

Fig. 7. Myocyte diameter in the 3 DCM subgroups and the control.

Fig. 8. Degree of lymphoid cell infiltration in the 3 DCM subgroups.

Group II, lymphoid cell infiltration was observed in all 11 cases, of which 2 showed 1+, 3 showed 2+, and 6 showed 3+. The chi-square test revealed a significant difference between Group II and the 2 other DCM subgroups ($p < 0.05$). The inflammatory cells contained mainly small lymphocytes, plasma cells and macrophages.

DISCUSSION

There are few quantitative studies of myocardial fibrosis in DCM. Rose and Beck reported that the mean fibrosis rate in 54 cases of DCM was 8%, a value which did not differ from controls.¹⁰⁾ Unverferth et al studied 9 DCM hearts¹¹⁾; the fibrosis rate was 20%, which was constantly higher than in the controls, without significant intergroup differences. In contrast, the fibrosis

rate in the present studies varied from 5.2 to 57.1%, and the pattern of fibrosis also differed markedly among cases: fibrosis was diffuse in some cases and segmental in others. One possible reason for the discrepancy between these studies may be different criteria for the diagnosis of DCM. For example, cases of transmural scars grossly resembling old myocardial infarction were included in our studies, unless they had clinical and pathological evidence of acute myocardial infarction and coronary stenoses. We considered them as variants of DCM, whereas other authors frequently excluded them as cases of myocardial infarction.

There is disagreement concerning the usefulness of endomyocardial biopsy in the diagnosis of DCM. Baandrup et al found no correlation between morphological and clinical findings and concluded that sampling errors were too great to permit a reliable evaluation of myocardial diseases.²⁾ Our results suggest that the absence of such correlations are mainly due to the great variation of pathological findings in DCM cases.

Although the extent of fibrosis was variable, the degree of CHF and LV dilatation was similar among the 3 DCM subgroups. Extensive fibrosis results from severe myocardial damage. Thus, it is reasonable to attribute the chronic CHF and LV dilatation in patients with severe fibrosis (Groups Ib and II) to extensive myocardial loss. By contrast, it is not reasonable to attribute the chronic CHF and LV dilatation in patients with mild fibrosis (Group Ia) to the loss of myocardium.

What, then, is the cause of severe CHF in DCM cases with mild fibrosis? We previously examined wall motion abnormalities and myocardial fibrosis in 11 DCM patients and found that severe wall motion abnormalities were often associated with marked ventricular dilatation, regardless of the extent of fibrosis.¹²⁾ As Hirota et al¹³⁾ pointed out, the afterload mismatch due to dilatation without adequate hypertrophy probably aggravates cardiac dysfunction and further increases the LV dimension. In fact, the smaller myocyte diameter in Group Ia than in Groups Ib and II attests to the lack of an adequate hypertrophic process.

Afterload mismatch may be responsible for CHF at an advanced stage of DCM, but the primary disorder in DCM seems to be a depressed myocardial contractility which leads to dilatation. Ross et al studied 81 necropsy patients with severe coronary stenoses and chronic CHF, and proposed that alcoholism was a possible cause of CHF in 13 cases of small scars.¹⁴⁾ Although only one patient of Group Ia was alcoholic in our series, metabolic and other unknown factors impairing myocardial contractility may have played an important role in cases free from significant fibrosis.

Some DCM cases show localized rather than diffuse asynergy.^{15),16)} Few

reports have mentioned the pattern of fibrosis in DCM hearts.¹⁷⁾ By observing myocardial fibrosis in transverse sections, we classified DCM into 2 main groups: diffuse and segmental fibrosis. Eleven (39%) of 28 cases belonging to the latter (Group II) showed transmural scars that penetrated at least half the thickness of the LV wall. They showed a markedly non-uniform pattern of fibrosis.

Tazelaar et al observed focal infiltration (consisting of at least 5 inflammatory cells) in 87% of excised hearts from 108 DCM patients who had undergone heart transplantation, and claimed that the greater presence of inflammatory cells did not necessarily imply active myocarditis.⁶⁾ Thus, we did not exclude the cases with lymphoid cell infiltration, if they had typical clinical signs of DCM and did not have other secondary causes of DCM, such as coronary heart disease, valvular disease or sarcoidosis. There was no history of acute myocarditis in our series of cases.

Indeed, infiltration of a few lymphocytes is commonly seen in DCM. In our studies, however, extensive lymphocyte infiltration was observed only in the cases with localized fibrosis (DCM). This suggests that inflammation has some significance in these cases. Since no such cases showed a clinical history of acute myocarditis, the disease seems to have started gradually and progressed insidiously.

Three cases in the present series were pregnant when cardiac symptoms started; of these, 2 showed focal fibrosis and severe lymphoid infiltration. This result supports the findings of O'Connell et al¹⁸⁾ that the incidence of myocarditis is higher in cases of peripartum cardiomyopathy than in idiopathic DCM cases.

There was great variation in heart weight within Group II. The heart weight in DCM cases is determined by the degree of myocardial destruction and the degree of residual myocardial hypertrophy. In most DCM cases with an increased heart weight, myocardial hypertrophy might have developed conspicuously, whereas myocardial destruction might have progressed without compensatory hypertrophy in 2 cases displaying control heart weights (Cases 23, 28).

There are no previous reports concerning the relationship between the pattern of fibrosis and myocarditis in DCM cases. However, chronic myocarditis such as sarcoidosis and giant cell myocarditis is known to cause localized inflammation and fibrosis.¹⁹⁾ Some investigators have reported segmental wall motion abnormalities of the LV wall in acute myocarditis.^{20),21)} Saffitz et al²²⁾ described an autopsy case of viral myocarditis that showed localized transmural fibrosis.

Thus, myocarditis may be a causative factor of DCM with a segmental

pattern of myocardial fibrosis.

REFERENCES

1. Schwarz F, Mall G, Zebe H, Schmitzer E, Manthey J, Scheurlen H, Kübler W: Determinants of survival in patients with congestive cardiomyopathy: Quantitative morphologic findings and left ventricular hemodynamics. *Circulation* **70**: 923, 1984
2. Baandrup U, Flopio RA, Rehahn M, Richardson PJ, Olsen EGJ: Critical analysis of endomyocardial biopsies from patients suspected of having cardiomyopathy II: Comparison of histology and clinical/haemodynamic information. *Br Heart J* **45**: 487, 1981
3. Roberts WC, Ferrans VJ: Pathologic anatomy of the cardiomyopathies. Idiopathic dilated and hypertrophic types, infiltrative types, and endomyocardial disease with and without eosinophilia. *Hum Pathol* **6**: 287, 1975
4. Okada R: Pathological aspects of cardiomyopathies. in *Cardiomyopathy*, ed by Sekiguchi M, Olsen EGJ, University of Tokyo Press, Tokyo, University Park Press, Baltimore, p 79, 1980
5. Mason JW: Endomyocardial biopsy: the balance of success and failure. *Circulation* **71**: 185, 1985
6. Tazelaar HD, Billingham ME: Leukocytic infiltrates in idiopathic dilated cardiomyopathy. A source of confusion with active myocarditis. *Am J Surg Pathol* **10**: 405, 1986
7. Yutani C, Imakita M, Ishibashi-Ueda H, Hatanaka K, Nagata S, Sakakibara H, Nimura Y: Three autopsy cases of progression to left ventricular dilatation in patients with hypertrophic cardiomyopathy. *Am Heart J* **109**: 545, 1985
8. Moore GW, Hutchins GM, Bulkley BH, Tseng JS, Ki PF: Constituents of the human ventricular myocardium: Connective tissue hyperplasia accompanying muscular hypertrophy. *Am Heart J* **100**: 610, 1980
9. Wallenstein S, Zucker CL, Fleiss JL: Some statistical methods useful in circulation research. *Circ Res* **47**: 1, 1980
10. Rose AG, Beck W: Dilated (congestive) cardiomyopathy: a syndrome of severe cardiac dysfunction with remarkably few morphological features of myocardial damage. *Histopathology* **9**: 367, 1985
11. Unverferth DV, Baker PB, Swift SE, Chaffee R, Feters JK, Uretsky BF, Thompson ME, Leier CV: Extent of myocardial fibrosis and cellular hypertrophy in dilated cardiomyopathy. *Am J Cardiol* **57**: 816, 1986
12. Maehashi N, Yokota Y, Takarada A, Seo T, Kubo M, Nakanishi O, Toh S, Usuki S, Fukuzaki H, Sugiyama T: Relationships between segmental left ventricular wall motion abnormalities and pathological findings in patients with dilated cardiomyopathy. *J Cardiography* **17**: 273, 1987 (in Japanese with English summary)
13. Hirota Y, Shimizu G, Kaku K, Saito T, Kino M, Kawamura K: Mechanisms of compensation and decompensation in dilated cardiomyopathy. *Am J Cardiol* **54**: 1033, 1984
14. Ross EM, Roberts WC: Severe atherosclerotic coronary artery disease, healed myocardial infarction and chronic congestive heart failure: analysis of 81 patients studied at necropsy. *Am J Cardiol* **57**: 44, 1986
15. Kreulen TH, Gorlin R, Herman MV: Ventriculographic patterns and hemodynamics in primary myocardial disease. *Circulation* **47**: 299, 1973
16. Wallis DE, O'Connell JB, Henkin RE, Costanzo-Nordin MR, Scanlon PJ: Segmental wall motion abnormalities in dilated cardiomyopathy. A common finding and good prognostic sign. *J Am Coll Cardiol* **4**: 674, 1984
17. Isner JM, Virmani R, Itscoits SB, Roberts WC: Left and right ventricular myocardial infarction in idiopathic dilated cardiomyopathy. *Am Heart J* **99**: 235, 1980
18. O'Connell JB, Costanzo-Nordin MR, Subramanian R, Robinson JA, Wallis DE, Scanlon PJ, Gunnar RM: Peripartum cardiomyopathy: Clinical, hemodynamic, histologic and prog-

- nostic characteristics. *J Am Coll Cardiol* **8**: 52, 1986
19. Roberts WC, McAllister HA, Ferrans VJ: Sarcoidosis of the heart. A clinicopathologic study of 35 necropsy patients (group I) and review of 78 previously described necropsy patients (group II). *Am J Med* **63**: 86, 1977
 20. Desaneto A, Builington JD, Builington RH, Desser KB, Benchimol A: Coxsackie B5 heart disease. Demonstration of inferolateral wall myocardial necrosis. *Am J Med* **68**: 295, 1980
 21. Pasquini JA, Gottdiener JS, Cutler DJ, Fetcher RD: Myocarditis with transient left ventricular apical dyskinesis. *Am Heart J* **109**: 371, 1985
 22. Saffitz JE, Schwartz DJ, Southworth W, Murphree S, Rodriguez ER, Ferrans VJ, Roberts WC: Coxsackie viral myocarditis causing transmural right and left ventricular infarction without coronary narrowing. *Am J Cardiol* **52**: 644, 1983