remarkably from 0.6% to 4.4%. These changes may be mostly due to prolonged survival of HD patients. It cannot be ignored that the number of HD patients with diabetic nephropathy has remarkably increased in the recent years (17.0% of 10,832 new patients on HD treatment in 1984) (Odaka, 1986).

CONCLUSION

Although HD has been made more than 10 years survival of CRF patients possible, substitution of renal function by this artificial device has produced new serious clinical features, which were not experienced in the pre-HD period, such as severe renal osteodystrophy, severe arterosclerosis and abnormal lipid metabolism probably relating with coronary or cerebral vascular problems, aluminium intoxication causing dialysis encephalopathy or osteomalacia, and recently discovered HD-related amyloidosis. On the other hand, there are still important problems in the pre-dialysis treatment including those of dietary management, secondary hyperparathyroidism, anemia, and, if possible, prevention of irreversible progression of renal dysfunction, the mostly expected future dream.

2. Pathophysiology and Metabolic Abnormalities

(1) Cardiac Function

Myocardial Lesions, Cardiac Function and Arrhythmias in Patients on Maintenance Hemodialysis

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Cardiac complications, such as heart failure and ventricular arrhythmias, are the major causes of death in uremic patients on chronic hemodialysis, although the wide-spread application of hemodialysis has improved the prognosis of uremic patients. This paper demonstrated cardiac structures, cardiac function, and ventricular arrhythmias in hemodialysis patients.

METHOD

Three hundred and forty-six uemic patients on maintenance hemodialysis and 60 autopsied cases were studied. Left ventricular (LV) manifestations were evaluated by macroscopic examination, and myocardial structure by microscopic technique in the autopsied cases. LV function was determined using M-mode echocardiography and LV cine-angiogram with catheter-tip manometer. LV volume were calculated by radial hemi-axis method using an Oscon angioanalyzer. Moreover, LV diastolic function was studied at rest and during weight-sustaining isometric exercise (WSID). Repeated 24-hour Holter ECG recordings were performed in 368 patients in order to evaluate the frequency of ventricular premature beats (VPBs), and the relationship between sudden deaths and VPBs was studied. Additionally, ventricular electric instability was examined by programmed electric ventricular stimulation in 19 hemodialysis patients.

RESULTS

1) Morphological findings of left ventricle

At necropsy, the hearts weighed 435 ± 90 g (mean ± SD) in male, and 364 ± 80 g in female. Increased heart weight was observed in 88% of male, and in 77% of female. Left ventricular hypertrophy (LVH) was noted in 47 of 60 autopsied cases (88%). Asymmetric septal hypertrophy (ASH) was observed in 10 cases (17%). LV pos-
terior wall hypertrophy associated with thickened ventricular septum was noticed in 18 cases (30%). LV posterior wall hypertrophy alone was recognized in 15 cases (25%), and ventricular septal hypertrophy unsatisfied the criteria of ASH was seen in 4 cases (6%). Macroscopic myocardial findings were characterized by hypertrophy and fibrosis with interspersed bleeding. The concentric hypertrophy was observed in 79% of the autopsied cases, although the eccentric hypertrophy was seen in only 21%. Fibrosis was noted in 68% of the cases, bleeding in 56%, and myocardial infarction in 11%. Histologically, disarray and fragmentation of myocardial fibers were usually present with interstitial or intramuscular fibrosis.

2) Left ventricular dysfunction

LV enddiastolic dimension was $47.7 \pm 6.8$ mm (mean ± SD), although it was normal in 72% of the patients on chronic hemodialysis. Ejection fraction (EF) was $65.5 \pm 11.3$%, whereas decreased EF was observed in only 3% of the patients. Fractional shortening (FS) was $37.7 \pm 8.4$%, and showed the reduction in 8% of the cases. Mean velocity of circumferential fiber shortening (mVCF) was $1.12 \pm 0.31$ circ/sec, and it was normal except in 19% of the patients.

LV in 5 uremic patients was compared with that in 3 control subjects. LV diastolic wall motion was reduced in the uremic patients, although EF was normal in both groups. Diastolic compliance ($\Delta V/\Delta P$) was decreased in the uremic patients (11.5 ml/mmHg), compared with that (22.0 ml/mmHg) in the control subjects. Additionally, LV filling volume in the first half of the diastolic period was 36% of the diastolic filling volume in the uremic patients, whereas it was 67% in the control subjects. The time spent in the first half of LV filling volume was 65% of the diastolic phase in the hemodialysis patients, although it was 38% in the normal subjects.

The hemodialysis patients were classified into two groups (LVH: 14 patients, non-LVH: 14 patients). Diastolic phase was divided into three periods of rapid filling, slow filling, and atrial contraction. In the rapid filling phase, the increment of LV dimension ($\Delta D$) was $7.8 \pm 0.2$ mm in group of LVH, $6.9 \pm 0.9$ mm in group of non-LVH, and $10.0 \pm 0.5$ mm in the control group. In the same phase the relaxation velocity of LV dimension ($\Delta D/\Delta T$) was $65 \pm 5$ mm/sec in group of LVH, $89 \pm 10$ mm/sec in group of non-LVH, and $91 \pm 8$ mm/sec in the control group. Both $\Delta D$ and $\Delta D/\Delta T$ in group of LVH were larger than those in the other two. In the slow filling period, $\Delta D$ was $9.1 \pm 0.3$ mm in group of LVH, $8.3 \pm 0.5$ mm in group of non-LVH, and $5.1 \pm 0.5$ mm in the control subjects. $\Delta D/\Delta T$ was $33 \pm 4$ mm/sec in group of LVH, $25 \pm 4$ mm/sec in group of non-LVH, and $18 \pm 4$ mm/sec in the normal subjects.
RESPONSE OF LV DIASTOLIC FUNCTION TO WSIE IN SLOW FILLING PERIOD

Fig. 2. In slow filling period: \( \Delta T/T \) and \( \Delta D/\Delta T \) remain unchanged in hemodialysis patients with LVH during WSIE, although they are decreased in hemodialysis patients without LVH and control subjects during WSIE.

(Fig. 1). In the control group and uremic non-LVH group, \( \Delta D/\Delta T \) was significantly increased during WSIE in the slow filling phase, whereas it remained unchanged in group of LVH (Fig. 2).

3) Ventricular arrhythmia

Of 368 patients who underwent 24-hour Holter ECG monitoring, ventricular premature beats (VPBs) were observed in 63%. According to Lown's grades, there were 100 cases with grade I, 21 with grade II, 50 with grade III, 24 with grade IV, and 35 with grade V arrhythmias. The incidence of high grade arrhythmias was 30%, and frequency of VPBs was divided into three grades (F1: VPBs 100, F2: 100 < VPBs < 1000, F3: VPBs > 1000). There were 280 cases (76%) with (F1, 50 cases (14%) with F2, 38 cases (10%) with F3. Additionally, in 76% of the uremic patients BPBs were noted during hemodialysis and/or within 6 hours after hemodialysis. Sudden death occurred in 7 (2%) of 368 patients. Of these patients there were 2 cases (1.5%) with grade 0, 2 (1.7%) with grade I and II, and 3 (2.7%) with grade III-V.

Electrophysiologic studies (EPS) were performed in 19 hemodialysis patients, in 20 patients with acute myocardial infarction (AMI), and in 20 control subjects. Ventricular tachycardia (VT) was induced in 10 (53%) uremic patients (Fig. 3). This result (sustained VT: 16%, non-sustained VT: 37%) was nearly equal to the induction rate of VT (50%) in patients with AMI, whereas no VT was induced in the control subjects (Table 1).

4) Treatments

Calcium (Ca) antagonists and \( \beta \) blockers were administered in 12 uremic patients with LVH for one year, and the effect of these drugs was compared with that of other drugs. The tendency of reduced LV wall thickness was noted in the patients treated with Ca antagonists and \( \beta \) blockers.

<table>
<thead>
<tr>
<th>Table 1. Electrophysiologic Study</th>
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<tr>
<td><strong>VT DURABILITY</strong></td>
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<tr>
<td><strong>SUSTAINED VT</strong></td>
</tr>
<tr>
<td>HD (%) 3/16 (19) AMI (%) 6/20 (30) C (%) 0/20 (0)</td>
</tr>
<tr>
<td><strong>NON-SUSTAINED VT</strong></td>
</tr>
<tr>
<td>HD (%) 7/19 (37) AMI (%) 4/20 (20) C (%) 0/20 (0)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
</tr>
<tr>
<td>HD (%) 10/19 (53) AMI (%) 10/20 (50) C (%) 0/20 (0)</td>
</tr>
</tbody>
</table>

HD: hemodialysis, AMI: acute myocardial infarction, VT: ventricular tachycardia, C: control subjects. Programmed electric ventricular stimulation (three premature stimuli).
In addition, the role of potassium added dialysate (4.0 mEq/L) in the management of VPBs disopyramide was studied in 16 patients.

Seven patients (58%) with more than 50% reduction in VPB frequency responded to K added dialysate, and the improvement of Lown’s grade was observed in 8 cases (67%). More than 50% reduction in VPB frequency was seen in 8 patients (76%) and improvement of Lown’s grade in 5 cases (42%) (Fig. 4).

**DISCUSSION**

Heart failure and arrhythmias are the major cardiac disorders in patients on long-term hemodialysis, considering clinical backgrounds. Especially, cardiac manifestations consist of myocardial hypertrophy and fibrosis, and initial abnormality of cardiac functions was decreased LV diastolic property characterized by myocardial stiffness. According to echocardiographic study, LV hypertrophy was observed in 50% of uremic patients related to hypertension. However, it is considered that additional factors such as acidosis, aging, duration of hemodialysis, anemia, electrolytes disturbance, and uremic toxin may play a role.

Angiographic and echocardiographic examinations revealed LV rapid filling disturbance including reduced ΔD and ΔD/ΔT at rest in the uremic patients with normal systolic function, although these parameters were increased in the slow filling period. Moreover, the response of slow filling parameters to WSIE was decreased in the hemodialysis patients with LVH. Several papers reported that LV diastolic filling disturbance was produced by increased LV wall stiffness secondary to myocardial degeneration and hypertrophy. Ca antagonist and β-blockers were administered to these patients; however, the effects of these drugs have not been apparent with regard to LV hypertrophy.

The incidence of VPBs in uremic patients was three times as high as in age-matched normal subjects, and the prevalence of high grade arrhythmias was thirteen times as high, compared with that in the control subjects. Moreover, the correlation between the incidence of VPBs and age was noted in the uremic patients. With regard to preventive treatments of VPBs, high potassium dialysate (K 4.0 mEq/L) was effective in patients with hypopotassemia, and disopyramide in the other patients. EPS showed a high induction of VT in the uremic patients nearly equal to that in patients with AMI. This result suggests that sudden death may be related to LV electrical instability in uremic patients.

**SUMMARY**

Three hundred and forty-six patients on chronic hemodialysis and 60 autopsy cases were studied to assess myocardial lesions, cardiac function, and ventricular arrhythmias from the epidemiological backgrounds. Cardiac manifestations were characterized by myocardial hypertrophy with interspersed fibrosis, and disarray or fragmentation of myocardial fibers. LV diastolic properties were decreased in uremic patients with LVH due to increased myocardial stiffness, and they were compensated by accelerated slow filling phase. VPBs were observed in about 50% of hemodialysis patients, and were highly related to hemodialysis
treatment. Particularly, electrical instability of LV muocardium was assessed by electrophysiological study. Renasol with KCL and dysopyramide were effective to VPBs, although the effects of Ca antagonists and β blockers were not apparent in uremic patients with LVH.

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A Study of Cardiac Function in Patients with Chronic Renal Failure. Special Reference to Hemodynamic Response to Exercise Test

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Patients with chronic renal failure (CRF) conventionally been thought to be restricted for work. Recently, exercise therapy for patients under hemodialysis (HD) has been evaluated, and studies concerning the clinical picture on physical exercise stress in patients with CRF with stable symptoms are occasionally seen.

In the present study, application of exercise test and allowance of daily activities were discussed from the viewpoint of cardiac function as the functional and metabolic approaches in the management of patients with CRF.

MATERIALS AND METHODS

This study was conducted on 88 patients with chronic nephritis (CN Group) and 45 patients with diabetic nephropathy (DM Group). The patients were divided into the endstage group under HD, the group with serum creatinine (Scr) higher than 3.0 mg/dl, the group with Scr between 1.5 mg/dl and 3.0 mg/dl and the group with Scr less than 1.5 mg/dl. After a sufficient rest, 4 grades of 3 minutes' bicycle ergometric (BE) exercise at 25, 50, 75 and 100 Watts were given on supine position, according to the Holmgren method intermittently with 3–5 minutes' rest intervals. Measurement of the body oxygen consumption (\(\bar{V}O_2\)), ECG by CM5 lead, blood pressure (BP), cardiac output (CO) by dye-dilution method and blood gas analysis (BGA) on arterialized ear lobe blood were performed during the last 1 minute of each stage. Catecholamine measurement in blood before and after exercise were carried out, along with determination of creatinine clearance (Cr) on urine samples obtained before, during and after exercise.

In addition to BE test, treadmill (TM) exercise test was carried out for the concrete exercise prescription. The protocol used was the modification of Bruce's one, with 10% slope and 1 mile/hour stage, added to the initial stage.

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