showed that once cardiovascular variables stabilized following the initial response to SIN-1, variables did not change for at least another 20 min. The fall in MABP was primarily attributed to vasodilatation (29 ± 7% decrease in SVR; $P < 0.05$). In CH rats, SIN-1 (i.c.v.) did not alter PVR, but it did decrease MPAP by 21 ± 3% ($P < 0.01$) owing to a 22 ± 5% decrease in CO ($P < 0.05$). Syndnonimine-1 provoked a larger decrease in CO in CH rats (22 ± 5% decrease; $P < 0.05$), so that the fall in MABP was also greater in CH rats (46 ± 3% decrease), because the decline in SVR was similar for N rats and CH rats (27 ± 7 and 29% decrease in SVR, respectively).

In N rats, the CO response to acute hypoxia was depressed by SIN-1 so that, even though the MPAP response appeared to be unchanged (Fig. 2a), the PVR response to hypoxia was accentuated by SIN-1 (64 ± 24 and 127 ± 26% increase, respectively; Fig. 2b). Syndnonimine-1 reduced the magnitude of the MABP and SVR responses to hypoxia, although the absolute MABP (and SVR) values during hypoxia before and after SIN-1 were similar. In addition, SIN-1 abolished the small hypoxia-induced decline in HR observed prior to SIN-1 administration.

In CH rats, SIN-1 restored the pulmonary vasoconstriction in response to acute hypoxia. This was evident by a 33 ± 5% increase in MPAP (cf. a 3% increase for control) and a 90 ± 11% increase in PVR (cf. a 20% increase for control). The effect of SIN-1 on the MABP, SVR, CO and HR responses to acute hypoxia were similar for N and CH rats (Fig. 2a,b).

DISCUSSION

To date, this is the first study to investigate the central role of NO in: (i) modulating MPAP in the normal and hypertensive state; and (ii) acute HPV. The primary findings of the present study show that, in both N and CH rats, the acute central inhibition of NOS does not appear to modulate baseline MPAP or pulmonary vascular

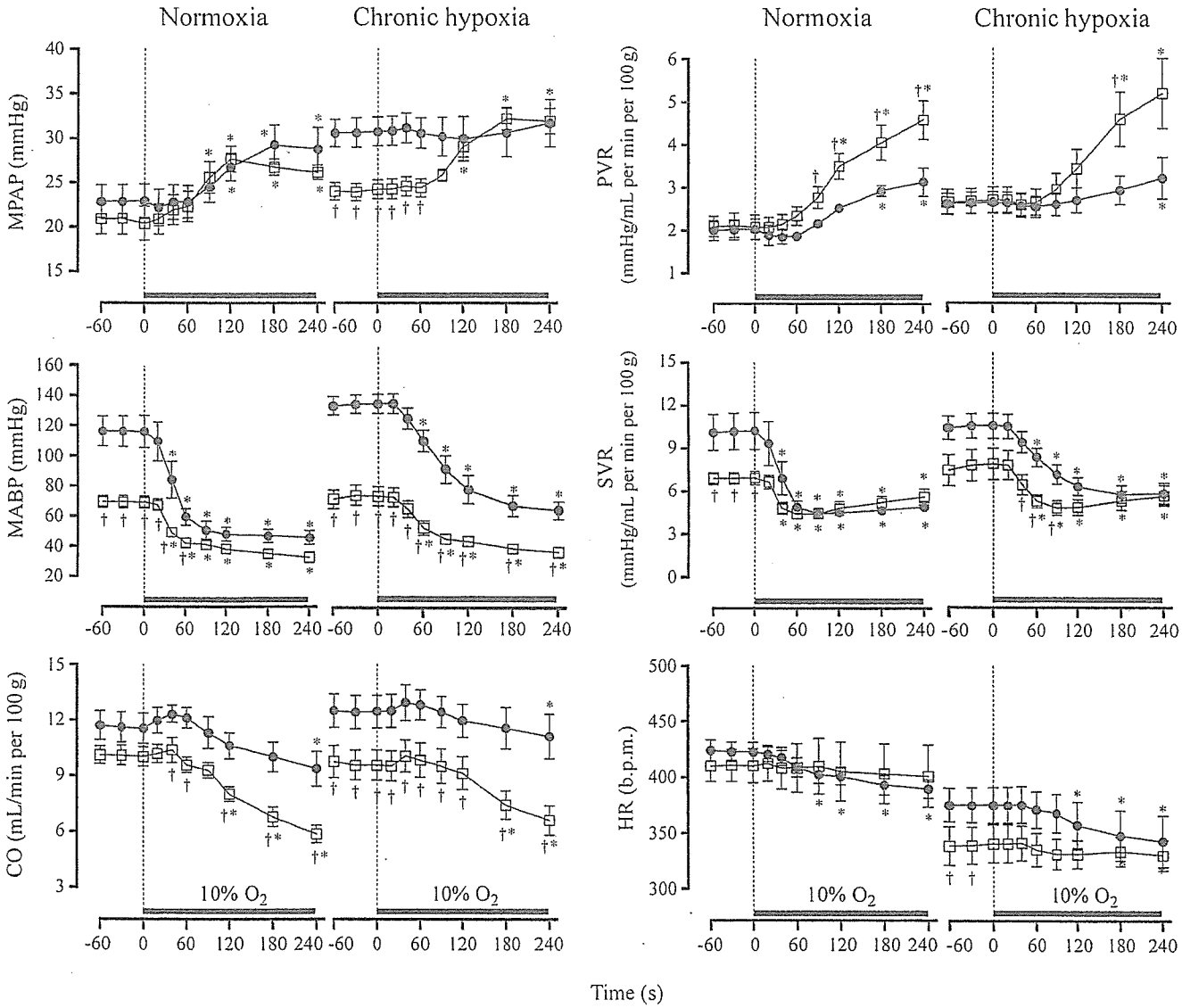

Fig. 2 Effect of i.c.v. syndnonimine-1 (SIN-1) on mean pulmonary arterial pressure (MPAP), mean arterial blood pressure (MABP), cardiac output (CO), pulmonary vascular resistance (PVR), systemic vascular resistance (SVR) and heart rate (HR) responses to acute hypoxia (10% O_2 for 4 min) in normoxic (N) rats ($n = 5$) and chronic hypoxic (CH) rats ($n = 6$). (●), control (artificial cerebrospinal fluid); (□), SIN-1 (100 μg in 10 μL). *$P < 0.05$ compared with pre-acute hypoxia values; †$P < 0.05$ compared with SIN-1-values.

Table 3 Steady state responses to intracerebroventricular syndnonimine-1 (100 μg in 10 μL) in normoxic rats (n = 5) and chronic-hypoxic rats (n = 6)

	Normoxia		Chronic hypoxia	
	Control	SIN-1	SIN-1	Control
MPAP (mmHg)	22.9 ± 1.7	20.8 ± 1.8	30.6 ± 1.6	24.1 ± 1.0*
MABP (mmHg)	116 ± 10	69 ± 4*	122 ± 6	67 ± 6**
CO (mL/min per 100 g)	11.64 ± 0.81	10.08 ± 0.51	12.46 ± 0.89	9.63 ± 0.81*
HR (b.p.m.)	423 ± 9	410 ± 15	375 ± 16	339 ± 17**
SVR (mmHg/mL per min per 100 g)	10.20 ± 1.28	6.93 ± 0.42*	10.07 ± 0.82	7.36 ± 1.06*
PVR (mmHg/mL per min per 100 g)	2.02 ± 0.23	2.10 ± 0.27	2.54 ± 0.24	2.58 ± 0.28

Data are the mean±SEM. *$P < 0.05$, **$P < 0.01$ compared with control values.

SIN-1, syndnonimine-1; MPAP, mean pulmonary arterial pressure; MABP, mean arterial blood pressure; CO, cardiac output; HR, heart rate; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance.

reactivity to acute hypoxia. However, exogenous NO reduces baseline MPAP in CH rats, primarily by reducing CO, and enhances the HPV.

We demonstrated that exposure to 12% O_2 for 2 weeks induced pulmonary arterial hypertension, which concurs with numerous reports in the literature regarding the effects of CH on the pulmonary vasculature.[6,29,30] Compared with the pulmonary vasculature, the systemic vasculature seems to be less affected by CH. We did not observe any difference in MABP between N and CH rats, which is similar to some reports.[30,31] In contrast, Huang *et al.*[6] did note an increase in MABP after 2 weeks of CH, although they described the increase in MABP as mild compared with the increase in MPAP.

The mechanisms responsible for the development of pulmonary hypertension remain poorly understood. Although a reduction in the local release of NO from the pulmonary endothelium has been implicated,[5,8,32] Hampl *et al.*[30] reported that chronic inhibition of NOS did not increase MPAP, indicating that factors other than, or in addition to, a decrease in pulmonary NOS activity were responsible for the development of pulmonary hypertension. Furthermore, Weissmann *et al.*[27] investigated the role of pulmonary NO in the acute HPV response and concluded that attenuation of the acute HPV by chronic hypoxia preceded the development of pulmonary hypertension and was independent of the pulmonary endothelial NO system. Therefore, we hypothesized that disruption of the central NO pathways may contribute, at least in part, to the pathogenesis of pulmonary hypertension during chronic hypoxia.

Our results indicate that, using L-NAME, central NO has a minimal role, if any, in modulating tonic pulmonary vascular tone in the normal and hypertensive state. However, we cannot rule out the possibility that the dose of L-NAME selected in the present study did not completely inhibit NOS within the cardiovascular control centres. Preliminary experiments indicated that when L-NAME is injected i.v., doses above 150 μg had small direct systemic effects (similar preliminary experiments were conducted to determine the dose of SIN-1 with which to inject i.c.v. that did not directly alter pulmonary vasculature when injected i.v.). Therefore, because L-NAME can cross the blood–brain barrier,[33] we avoided higher doses of L-NAME that could have potentially directly modulated pulmonary vascular tone. Furthermore, a study by Nurminen *et al.*[34] reported that 30 μg L-NAME, i.c.v., provoked a significant increase in ABP that lasted for 10 min. Therefore, we were confident that a dose of 150 μg L-NAME would induce sufficient central NOS inhibition.

Although we found that L-NAME did not alter the acute HPV, we cannot exclude the possibility that the central actions of L-NAME had fully subsided before testing acute hypoxia. However, preliminary experiments (data not shown) indicated that, even when L-NAME was administered immediately before the acute hypoxic test, the cardiovascular responses to acute hypoxia were not different to the responses prior to L-NAME. Alternatively, acute hypoxia is known to be a powerful activator of sympathetic nerve activity.[35] Because it has been well documented that the central administration of L-NAME increases sympathetic activity,[36,37] it may be possible that, in the present study, L-NAME did not alter the HVR because sympathetic activity was already elevated by the acute hypoxic stimulus.

Although central L-NAME did not alter pulmonary vasculature tone, the intravenous administration of L-NAME did cause a small increase in PVR in N rats, which was accentuated after chronic hypoxia. Furthermore, the acute HVR was accentuated by L-NAME (i.v.) in both N and CH rats. Several studies have indicated that local endothelial NO has a limited role, if any, in the tonic modulation of MPAP,[6,38] although Huang *et al.*[6] indicated that local NO: (i) was more important in modulating pulmonary vasculature after chronic hypoxia; and (ii) was essential for maintaining low pulmonary resistance during acute hypoxia.

In comparison, the magnitude of the systemic vasoconstrictive response to L-NAME (i.v.) was substantially larger than that of the pulmonary vasculature. In agreement, several studies have indicated that local inhibition of NOS has an insignificant effect on tonic modulation of the pulmonary vasculature, but it is critical in modulating the systemic vasculature.[6,30,38]

It has been well documented that central inhibition of NO increases MABP[34,39,40] by increasing sympathetic nerve activity.[36,37] We also reported that i.c.v. L-NAME provoked a significant increase in MABP, although one of the limitations of the present study is that we did not measure sympathetic activity. However, we found that the provoked increase in MABP by i.c.v. L-NAME in the normoxic rat was not accompanied by a baroreflex decrease in HR, which occurs when L-NAME is injected intravenously. Nurminen *et al.*[34] also reported that i.c.v. L-NAME caused a paradoxical increase in HR and, thus, concluded that the increase in HR was indirect evidence that L-NAME provoked an increase in sympathetic activity.

With regards to the pulmonary vasculature, an increase in sympathetic activity can cause either vasoconstriction (α-adrenoreceptor mediated) or vasodilation (β-adrenoreceptor mediated), depending on the initial pulmonary vascular tone.[41,42] Therefore, assuming that i.c.v. L-NAME did increase pulmonary sympathetic activity, it is possible that we were unable to detect any change

in MPAP because of the potential opposing effects of α- and β-adrenoceptor activation within the pulmonary vasculature.

In the present study, as well as in other studies, the central administration of NO donors has been shown to reduce MABP.[25,43] Nurminen and Vapaatalo[44] also showed that certain NO-releasing substances, such as nitroprusside, reduced MABP, although they also mentioned that the central administration of SIN-1 (approximately 600 μg/kg) increased MABP.

At high doses, SIN-1 can cogenerate NO and superoxide anions.[45,46] Furthermore, an increase in the central generation of superoxide anions has been reported to increase sympathetic activity and, consequently, ABP.[47] Therefore, the increase in MABP in the study of Nurminen and Vapaatalo[44] may be attributed to the formation of superoxide anions. At low doses, the superoxide-associated effects of SIN-1 are significantly outweighed by the actions of NO.[45] Therefore, because the present study used a comparatively low dose of SIN-1 (100 μg), we interpret the decrease in MABP to indicate that, at this dose, SIN-1 was acting solely as an NO donor.

The decrease in MABP following the central administration of exogenous NO has been attributed to a decrease in sympathetic activity.[40,48] To date, the present study is the first to investigate the effects of a central NO donor on MPAP. The important finding of the present study is that exogenous NO did not directly alter baseline pulmonary vascular tone (i.e. PVR was not altered), but it did enhance (in N rats) or restore (in CH rats) the acute HPV response. These results support the idea that central NO has little influence on the tonic modulation of pulmonary vascular tone, although it enhances the acute HPV.

Although we cannot confirm the underlying mechanisms responsible for these observations, it is possible that SIN-1 did reduce sympathetic activity in the rats in the present study, subsequently enhancing the HPV. Shirai *et al.*[49] demonstrated that β-adrenoceptor blockade had only a minor effect on baseline pulmonary vascular tone in normoxia, but it significantly accentuated the acute HPV (α-adrenoceptor blockade had no effect on the magnitude of the HPV). This observation may explain the reason as to why central SIN-1 did not affect baseline PVR but accentuated the HPV in the present study. Although PVR was not affected, central SIN-1 did reduce MPAP in the present study (significantly in CH rats), solely due to a reduction in CO. This, too, may be due to a reduction in β-adrenoceptor activity, because β-adrenoceptor attenuation has been reported to significantly reduce CO.[50,51]

The mechanism(s) responsible for the attenuation of the HPV after chronic hypoxia remain poorly understood. However, it is possible to speculate that β-adrenoceptor upregulation may be one contributing factor because previous studies have shown that chronic hypoxia significantly increases β-adrenoceptor numbers within the lung.[52,53] Changes in β-adrenoceptor availability during chronic hypoxia could potentially limit the development of pulmonary hypertension and, therefore, be physiologically beneficial; an important area that warrants further research.

In summary, we have shown that central NO has a limited role in modulating tonic MPAP in the normal and hypertensive states. However, exogenous NO enhanced the acute HPV, although central NO inhibition had no effect on the acute HPV. Whether central NO acts to inhibit β-adrenoceptor-mediated vasodilation of the acute HPV is another area that warrants further investigation. The present study used an anaesthetized preparation to investigate the modulation of MPAP in normoxia and after chronic hypoxia. We did not, however, address any potential changes in the control of MPAP during the development of pulmonary hypertension. Hampl and Herget[38] indicated that, during the development of pulmonary hypertension, NO was essential in preventing pulmonary hypertension in the early stages, but became insignificant in the latter stages owing to endothelial dysfunction. Therefore, we will subsequently develop a conscious, chronically cannulated rat model to monitor the development of pulmonary hypertension during the chronic central inhibition/infusion of NO.

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Assessment of Quality of Life With 5 Different Scales in Patients Participating in Comprehensive Cardiac Rehabilitation After Acute Myocardial Infarction

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Background Measures assessing quality of life (QOL) in patients participating in comprehensive cardiac rehabilitation (CCR) have not been established in Japan.

Methods and Results To compare different types of QOL scales and to determine the impact of CCR on QOL in Japanese cardiac patients, 5 different types of questionnaires were assessed in 44 patients participating in CCR after acute myocardial infarction (AMI). After 3-month CCR, peak oxygen uptake ($P\dot{V}O_2$, $p<0.01$), Sickness Impact Profile (SIP) total score ($p<0.05$) and physical function-related QOL scores (Specific Activity Scale (SAS), $p<0.01$; SIP physical score, $p<0.01$) significantly improved, whereas psychosocial/mental aspect-related QOL scores (Ministry of Health and Welfare (MHW)-QOL score, SIP psychosocial score, State-Trait Anxiety Inventory, Self-rating Depression Scale) did not change on the average. However, patients with low $P\dot{V}O_2$ ($<21.7\,ml\cdot min^{-1}\cdot kg^{-1}$) showed significant improvements in all scores after CCR, whereas patients with preserved exercise capacity showed improvements only in physical function-related scores (SAS and physical SIP). Furthermore, patients with anxiety and depression showed significant improvements in these respective measures after CCR.

Conclusion In patients with AMI, physical function-related QOL scores improve after a 3-month CCR program, but psychosocial/mental aspect-related QOL scores improve only in those with impaired exercise tolerance or anxiety/depression. Thus, changes in QOL after CCR depend on type of QOL scale used and the baseline status of the patient. In addition, in Japanese cardiac patients MHW-QOL mainly reflects psychosocial/mental aspect-related QOL, as well as overall QOL. (*Circ J* 2005; **69:** 1527–1534)

Key Words: Acute myocardial infarction; Cardiac rehabilitation; Depression; Psychological wellbeing; Quality of life

Comprehensive cardiac rehabilitation (CCR) improves psychological well-being or quality of life (QOL) in patients after acute myocardial infarction (AMI)[1–4] but because the various QOL scales assess the physical and psychological aspects of QOL differently, it is not fully understood which aspect of QOL is improved by CCR. In addition, it remains unclear which patient group benefits most from CCR in terms of QOL. Furthermore, because most QOL instruments, except for the QOL score of the Ministry of Health and Welfare in Japan (MHW-QOL)[5,6] were devised in Western countries, their features have not been comparably determined in Japanese cardiac patients. In fact, conflicting results have been reported on the effect of CCR on the MHW-QOL score in Japanese patients after AMI; Yoshida et al reported a significant improvement in the MHW-QOL score[6] whereas Fujiwara et al reported no significant change[7]

The effect of CCR on the different aspects of QOL in Japanese patients after AMI using multiple QOL instruments has not been intensively assessed. Accordingly, the purpose of the present study was to use multiple QOL instruments to assess Japanese patients after AMI, to determine the comparative features of the various QOL scales, including the MHW-QOL score, and to clarify the characteristics of the patients who are likely to benefit most from CCR in terms of QOL.

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Methods

Subjects

We studied 44 patients who had experienced an AMI (mean age: 58±9 years, range 45–78, male/female: 37/7) and who participated in CCR with exercise training program. All patients gave written informed consent.

The diagnosis of AMI was confirmed by electrocardiographic changes and serum creatine kinase (CK) elevation. Peak serum CK was 3,255±2,588 U/L. Seven patients (16%) had had a prior myocardial infarction and 2 patients (5%) had congestive heart failure (Killip's class ≥2) on admission. All patients underwent cardiac catheterization: 38 patients (86%) had successful percutaneous coronary intervention (PCI), 2 patients (5%) underwent coronary artery bypass grafting (CABG) and 5 patients (11%) with residual myocardial ischemia were medically controlled. Mean left ventricular ejection fraction (LVEF) was 45±8%

by left ventriculography 3–4 weeks after the onset of AMI.

Cardiac Rehabilitation Program

The CCR program consisted of exercise training of moderate intensity and education for 3 months, as previously described[8–10] Patients who did not have angina or ischemic changes on ECG at a low level of exercise (200–500 m walking test) were enrolled in the exercise training approximately 10–15 days after AMI. Patients with uncontrolled heart failure and/or angina, multiple organ disorders such as serum creatinine ≥2.0 mg/ml, serum transaminase ≥40 IU/ml, inflammatory disease or embolic disorders were excluded. The exercise program consisted of walking, bicycling on an ergometer, and aerobic dance sessions of 50–80 min, 3–5 times each week for 3 months. Exercise intensity was determined individually at 50–60% of heart rate reserve (Karvonen's equation, k=0.5–0.6)[11,12] obtained by maximal symptom-limited cardiopulmonary exercise testing (CPX) or at level 13 ("a little hard") of the 6–20 scale perceived rating of exercise (original Borg's score)[13] The exercise program started with supervised sessions for 2 weeks, followed by home exercise combined with once or twice weekly supervised sessions for the remaining 10 weeks. Home exercise consisted mainly of brisk walking at a prescribed heart rate for 30–60 min 3–5 times per week. There were no adverse cardiac events such as death, AMI, unplanned PCI or CABG, or worsening of heart failure during the 3-month CCR.

Patients were encouraged to attend the education classes, which were held 3 times each week with lectures on coronary artery disease, secondary prevention, diet, smoking cessation, medication, and home exercise given by physicians, nurses, dieticians, pharmacists and exercise instructors. In addition, all patients received individual counseling on exercise prescription, secondary prevention, and daily life activities by a physician and a CCR nurse at the time of hospital discharge and at the end of the CCR program.

CPX

A symptom-limited CPX was performed at the beginning and end of the 3-month CCR[14] After a 2 min rest on the bicycle ergometer (Examiner, Lode B.V. Groningen-Holland), patients started pedaling at an intensity of 0 W for 1 min (warm-up), then performed an incremental exercise test with a ramp protocol (15 W/min) until exhaustion. During exercise testing, breathed gas was continuously collected to measure oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) with a gas analyzer AE280 (Minato Medical Electronics, Osaka, Japan). Blood pressure was measured every minute and a 12-lead ECG was continuously monitored during exercise. Patients who showed angina or ischemic ECG changes at the initial exercise test were excluded.

Peak oxygen uptake ($P\dot{V}O_2$) was defined as the highest $\dot{V}O_2$ value achieved at peak exercise after reaching the respiratory compensation point. The $\dot{V}O_2$ value at the anaerobic threshold (AT) or ventilatory threshold was determined as the point at which $\dot{V}CO_2$ increased in a nonlinear fashion relative to the rate of $\dot{V}O_2$, according to the time trend of the ratio of minute ventilation ($\dot{V}E$) and $\dot{V}O_2$ ($\dot{V}E/\dot{V}O_2$), an abrupt increase in the respiratory exchange ratio, or the V-slope method[15,16]

QOL Questionnaires

At the beginning and end of the 3-month CCR program, all patients answered the 5 types of questionnaires assessing QOL: Specific Activity Scale (SAS), Sickness Impact Profile (SIP), MHW-QOL, State-Trait Anxiety Inventory (STAI) and Self-rating Depression Scale (SDS). SAS is a scale of functional capacity related to daily activities expressed by metabolic equivalents[17,18] and SIP comprises 136 items including 12 domains to assess patient behaviors, such as physical disorders (ambulation, mobility, body care and movement), psychosocial disorders (social interaction, alertness behavior, emotional behavior, communication) and other disorders (sleep and rest, eating, work, home management, recreation and pastimes), expressed by the percentage of acquired scores[19,20] It has been successfully used in the field of CCR[20–22] MHW-QOL has both generic and disease-related scales and mainly assesses the psychosocial and mental aspects of QOL[5–7] It comprises 39 items, including 3 domains (2 generic domains and 1 disease-specific domain) for subjective evaluation of health (8 items), social attitude and subjective wellbeing (21 items), and disease-specific conditions (10 items). In the present study we used a total score for the 39 items (so-called "broad sense score") as the MHW-QOL score. STAI is a scale of anxiety and comprises 2 domains of state-anxiety and trait-anxiety, the former representing an anxiety state that a patient faces and the latter mainly representing an anxious personality. Each domain comprises 20 items with 4-point scales[23] SDS evaluates depression by 20 items with 4-point scales[24] A state of anxiety and/or depression was judged when the percent score of STAI and/or SDS was above 50%. Higher scores indicate a more favorable QOL trait in SAS and MHW-QOL, whereas lower scores indicate a more favorable QOL trait in SIP, STAI and SDS.

Data Analysis

Data were analyzed in 3 steps. First, data for exercise capacity and QOL were compared between the 2 time points (ie, before and after the 3-month CCR) in the whole group of patients. Second, to assess the influence of baseline exercise capacity on the improvement in QOL scores after CCR, QOL data were compared between the 2 time points in the subgroups of preserved and impaired exercise capacity. Because the average $P\dot{V}O_2$ measured by CPX at the beginning of the CCR was 21.7±1.7 ml·min^{-1}·kg^{-1}, patients were divided into 2 groups according to their initial $P\dot{V}O_2$ value: Low $P\dot{V}O_2$ group ($P\dot{V}O_2$ <21.7 ml·min^{-1}·kg^{-1}, n=22) and Preserved $P\dot{V}O_2$ group ($P\dot{V}O_2$ ≥21.7 ml·min^{-1}·kg^{-1}, n=22). Finally, QOL data were compared between the 2 time points in the subgroups with and without initial anxiety (STAI score ≥50% or <50%, respectively) and with and without initial depression (SDS score ≥50% or <50%, respectively).

Statistical Analysis

All values are expressed as mean±SD. The paired t-test was used to compare paired variables before and after CCR within a group. Comparisons between groups were made by unpaired t-test. Statistical analysis was performed using StatView software (Abacus, Cupertino, CA, USA). A p-value less than 0.05 was considered statistically significant.

Results

Changes in Exercise Capacity and QOL Scores in the Whole Group

As shown in Table 1, which summarizes the baseline

Table 1 Characteristics of 44 Patients After Acute Myocardial Infarction

	Total (n=44)	Preserved $P\dot{V}O_2$ group (n=22)	Low $P\dot{V}O_2$ group (n=22)	p value
Age (years)	58±10	57±11	59±9	NS
Sex (M/F)	37/7	20/2	17/5	NS
Hypertension	21 (48%)	12 (55%)	9 (41%)	NS
Hyperlipidemia	18 (41%)	10 (45%)	8 (36%)	NS
Diabetes mellitus	12 (27%)	6 (27%)	6 (27%)	NS
Obesity (BMI ≥26 kg/m^2)	10 (23%)	4 (18%)	6 (27%)	NS
Smoking	23 (52%)	14 (64%)	9 (41%)	NS
Family history	9 (20%)	4 (18%)	5 (23%)	NS
Killip class ≥2 (numbers)	2	0	2	NS
PCI/CABG/none	38/2/5	18/1/3	20/1/2	NS
peak CK (IU/ml)	3,255±2,588	3,009±1,986	3,384±2,796	NS
LVEF (%)	44.5±8.2	45.9±6.6	42.9±9.6	<0.05
$P\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	21.7±4.9	24.7±3.6	18.1±3.8	<0.001

Values are mean±SD. P values for comparisons between Preserved $P\dot{V}O_2$ and Low $P\dot{V}O_2$ groups.
$P\dot{V}O_2$, peak oxygen uptake; Preserved $P\dot{V}O_2$ group, patients whose baseline $P\dot{V}O_2$ values were equal to or above average ($P\dot{V}O_2$ ≥21.7 $ml \cdot kg^{-1} \cdot min^{-1}$); Low $P\dot{V}O_2$ group, patients whose baseline $P\dot{V}O_2$ value were below average ($P\dot{V}O_2$ <21.7 $ml \cdot kg^{-1} \cdot min^{-1}$); BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CK, serum concentration of creatine kinase; LVEF, left ventricular ejection fraction.

Table 2 Exercise Capacity and QOL Scores Before and After Comprehensive Cardiac Rehabilitation in All Patients

	Before CCR	After CCR	p value
Peak R	1.26±0.12	1.24±1.0	NS
$P\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	21.7±1.7	24.7±2.6	<0.01
$\dot{V}O_2$ at AT ($ml \cdot kg^{-1} \cdot min^{-1}$)	11.8±2.3	13.1±2.5	<0.01
SAS (METs)	4.5±1.7	5.3±0.7	<0.05
SIP (% scores)			
Total	7.9±5.6	5.5±4.9	<0.05
Physical disorders	7.2±3.1	1.5±1.6	<0.01
Psychosocial disorders	6.0±4.4	5.8±7.4	NS
Other disorders	11.5±7.5	10.6±8.4	NS
MHW-QOL (scores)	57.4±12.7	58.6±20.5	NS
STAI (% scores)			
Total	49.3±10.9	46.9±13.2	NS
State-anxiety	48.2±11.7	45.3±12.2	NS
Trait-anxiety	49.7±12.0	47.1±12.3	NS
SDS (% scores)	45.3±9.5	43.4±7.9	NS

Values are mean±SD.
QOL, quality of life; CCR, comprehensive cardiac rehabilitation; Peak R, respiratory exchange ratio at peak exercise; $P\dot{V}O_2$, peak oxygen uptake; AT, anaerobic threshold (or ventilatory threshold); SAS, specific activity scale; METs, metabolic equivalents; SIP, sickness impact profile; MHW-QOL, QOL score of the Ministry of Health and Welfare in Japan; STAI, state-trait anxiety inventory; SDS, self-rating depression scale.

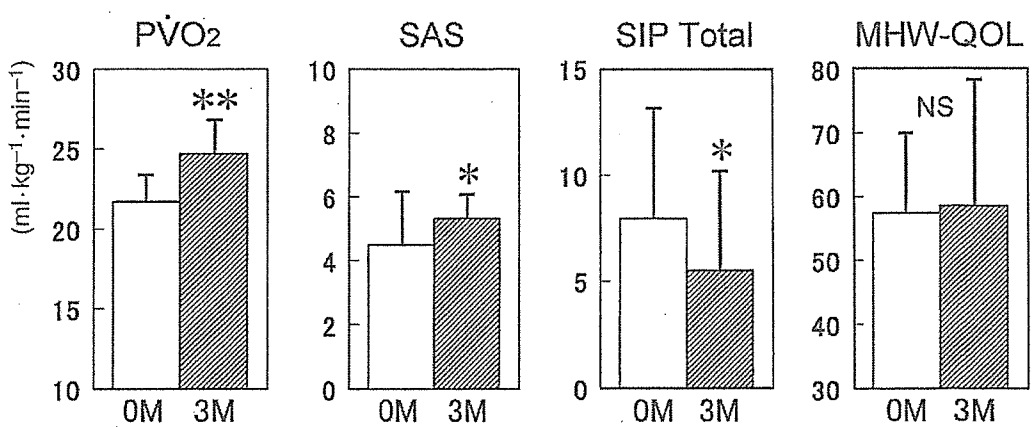

Fig 1. Comparisons of exercise capacity and quality of life (QOL) scores before and after 3-month comprehensive cardiac rehabilitation (CCR) in all 44 patients. $P\dot{V}O_2$, peak oxygen uptake; SAS, Specific Activity Scale; SIP total, Sickness Impact Profile total score; MHW-QOL, Ministry of Health and Welfare QOL broad sense score: 0M, baseline values (before CCR); 3M, values after 3-month CCR program. *p<0.05 and **p<0.01 compared with baseline values.

Table 3 Exercise Tolerance and QOL Related Scores Change in Subgroups

	Preserved $P\dot{V}O_2$ group (n=22)			Low $P\dot{V}O_2$ group (n=22)		
	Before CCR	After CCR	p value#	Before CCR	After CCR	p value#
$P\dot{V}O_2$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	24.7±3.6	27.5±5.0	<0.01	18.1±3.8**	21.3±5.4**	<0.01
$\dot{V}O_2$ at AT ($ml \cdot kg^{-1} \cdot min^{-1}$)	13.2±1.8	14.5±2.3	0.05	10.2±1.7	11.6±1.8	<0.05
SAS (METs)	5.0±1.7	5.6±1.9	<0.05	3.9±1.5*	4.9±1.3	<0.05
SIP (% scores)						
Total	7.7±5.8	6.0±4.8	<0.05	8.1±5.6	4.1±5.2	<0.05
Physical disorders	6.9±7.9	0.8±1.7	<0.01	6.8±5.8	2.1±3.4	<0.01
Psychosocial disorders	6.2±6.9	6.6±7.6	NS	4.8±5.5	2.7±5.6	<0.05
Other disorders	10.5±6.2	10.6±8.1	NS	12.7±8.8	8.6±7.9	<0.05
MHW-QOL (scores)	61.0±8.1	60.3±10.8	NS	53.1±10.0**	56.6±9.3	<0.05
STAI (% scores)						
Total	47.7±10.1	47.9±15.3	NS	51.2±11.8	45.7±10.3	<0.05
State-anxiety	47.9±10.3	47.6±17.0	NS	49.6±13.2	44.4±10.3	<0.05
Trait-anxiety	47.6±11.1	48.3±14.7	NS	52.7±12.6	46.9±11.2	<0.05
SDS (% scores)	42.3±7.0	43.6±10.7	NS	49.2±10.5*	44.4±6.7	<0.05

Values are mean±SD.
#Comparisons were made by paired t-test before and after CCR within the group; *p<0.05, **p<0.01 compared with corresponding values in the Preserved $P\dot{V}O_2$ group.
Abbreviations as in Table 2.

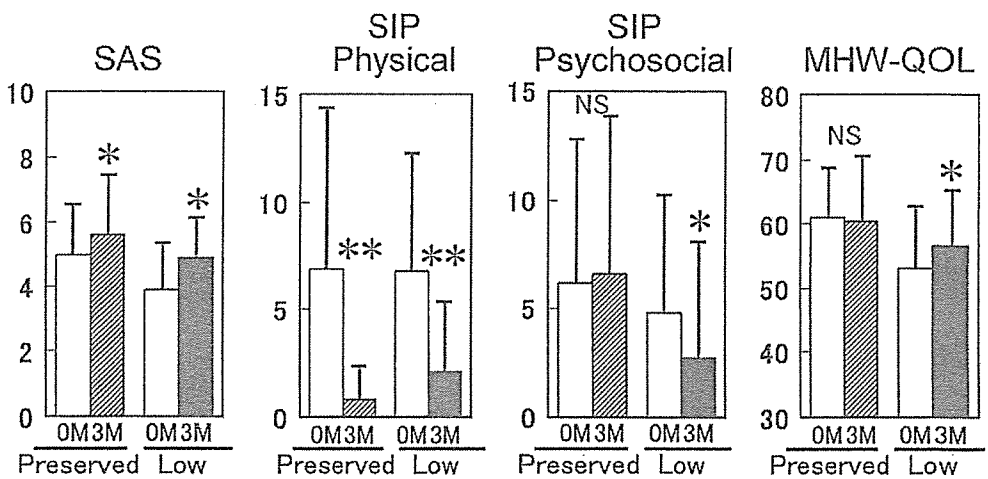

Fig 2. Changes in representative quality of life (QOL) scores before and after 3-month comprehensive cardiac rehabilitation program in patients with preserved and impaired exercise capacity. Patients with preserved exercise capacity showed improvements in Specific Activity Scale (SAS) and Sickness Impact Profile (SIP) physical score, but not in SIP psychosocial and Ministry of Health and Welfare (MHW)-QOL scores, whereas patients with impaired exercise capacity showed improvements in all 4 scores. SIP physical, SIP physical disorder score; SIP psychosocial, SIP psychosocial disorder score; Preserved, preserved exercise capacity group (peak $\dot{V}O_2$ ≥21.7 $ml \cdot min^{-1} \cdot kg^{-1}$); Low, impaired exercise capacity group (peak $\dot{V}O_2$ <21.7 $ml \cdot min^{-1} \cdot kg^{-1}$). *p<0.05 and **p<0.01 compared with baseline values.

clinical characteristics of the 2 groups with preserved and impaired exercise capacity, there were no significant differences except for LVEF and $P\dot{V}O_2$. Table 2 and Fig 1 summarize the data for exercise capacity and QOL scores before and after the 3-month CCR. The respiratory exchange ratio at peak exercise was sufficiently high both before and after CCR, suggesting that the measured $P\dot{V}O_2$ values are reliable. After 3 months of CCR, $P\dot{V}O_2$ (+13.8%, p<0.01), $\dot{V}O_2$ at AT (+11.0%, p<0.01) and SIP total score (–30.4%, p<0.05) improved significantly, as did the SAS (+17.8%, p<0.05) and SIP physical disorder score (–79.2%, p<0.01), both representing QOL related to physical function. However, other QOL scores such as the SIP score for psychosocial disorders and other disorders, MHW-QOL, STAI and SDS, all representing QOL related to psychosocial or mental function, did not change after 3 months of CCR.

Changes in QOL Scores in the Subgroups With Preserved and Impaired Exercise Capacity (Table 3, Fig 2)

In the Preserved $P\dot{V}O_2$ group, $P\dot{V}O_2$ (+11.3%, p<0.01), $\dot{V}O_2$ at AT (+9.8%, p=0.05), SIP total score (–22.1%, p< 0.05), and physical function-related QOL scores (ie, SAS (+12.0%, p<0.05) and SIP physical disorder score (–88.4%, p<0.01), significantly improved after CCR, but there was no significant change in the psychosocial and mental aspect-related QOL scores (ie, SIP psychosocial disorder score, SIP other disorder score, MHW-QOL, STAI, and SDS). In contrast, the Low $P\dot{V}O_2$ group showed significant improvements in $P\dot{V}O_2$ (+17.7%, p<0.01), $\dot{V}O_2$ at AT (+13.7%, p< 0.05), SIP total score (–49.4%, p<0.05), and both physical function-related QOL (SAS +25.6%, p<0.05; SIP physical disorder score –69.1%, p<0.01) and psychosocial/mental aspect-related QOL scores after CCR (SIP psychosocial disorder score –43.8%, p<0.05; MHW-QOL +6.7%, p<0.05;

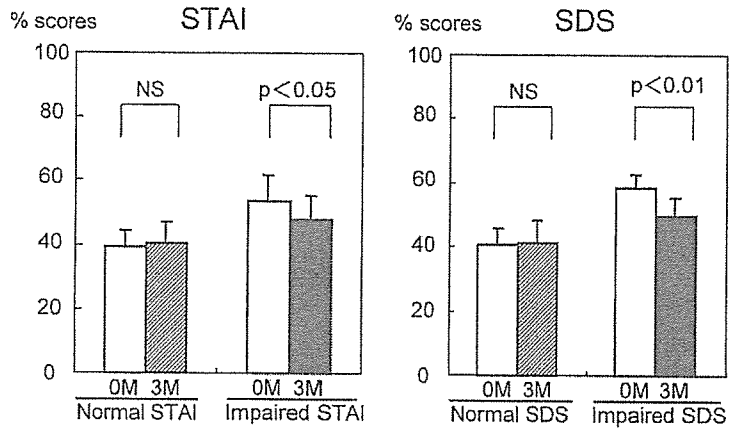

Fig 3. Changes in anxiety (STAI) and depression (SDS) scores before and after 3-month comprehensive cardiac rehabilitation (CCR) program in patients with normal and impaired mental function. Anxiety scores (STAI: State-Trait Anxiety Inventory) and depression scores (SDS: Self-rating Depression Scale) improved after CCR only in patients with impaired STAI score and impaired SDS score at baseline. 0M, baseline values (before CCR); 3M, values after 3-month CCR. *p<0.05 and **p<0.01 compared with baseline values.

Table 4 Correlation Matrix of Different Types of QOL Scores

	PV̇O2	*V̇O2 at AT*	*SAS*	*SIP total*	*SIP physical*	*SIP psychosocial*	*STAI*	*SDS*
MHW-QOL	*0.14*	*0.21*	*0.49****	*0.36****	*0.27**	*0.38****	*0.77****	*0.69****
PV̇O2		*0.74****	*0.29***	*0.01*	*0.08*	*0.09*	*0.07*	*0.09*
V̇O2 at AT			*0.32***	*0.14*	*0.20*	*0.01*	*0.04*	*0.18*
SAS				*0.35***	*0.32***	*0.30***	*0.37****	*0.43****
SIP total					*0.74****	*0.81****	*0.31***	*0.25**
SIP physical						*0.40****	*0.12*	*0.18*
SIP psychosocial							*0.37****	*0.28***
STAI								*0.73****

Correlation coefficients and their statistical significance are presented.
Data both before and after 3-month comprehensive cardiac rehabilitation for all 44 patients were included for regression analysis.
*Abbreviations as in Table 2. *p<0.05, **p<0.01, ***p<0.001.*

STAI −10.7%, p<0.05; SDS −9.8%, p<0.05).

Changes in Anxiety and Depression (Fig 3)

When the patients were divided into 2 groups according to the initial STAI score ≥ or <50%, 22 patients (50.0%) with STAI score ≥50% (ie, anxiety state) showed a significant improvement after CCR (58.2±6.1 to 53.0±9.3, p< 0.05), but the remaining 22 patients with initial STAI score <50% (ie, normal) showed no significant change. When the patients were divided into 2 groups according to the initial SDS score ≥ or <50%, 12 patients (27.3%) with SDS score ≥50% (ie, depressive state) showed a significant improvement in SDS score after CCR (58.2±4.4 to 49.7±6.4, p< 0.01), butthe remaining 32 patients with initial SDS score <50% (ie, normal) showed no significant change.

Correlations Between MHW-QOL and Other QOL Scores (Table 4)

The MHW-QOL score significantly correlated with SAS (r=0.49, p<0.001) and SIP total score (r=0.36, p<0.001), indicating that MHW-QOL represents the overall QOL of cardiac patients. Intriguingly, the MHW-QOL score correlated very tightly with the SIP psychosocial disorder score (r=0.38, p<0.001), STAI (r=0.77, p<0.001) and SDS (r=0.69, p<0.001), but less tightly with the SIP physical disorder score (r=0.27, p<0.05) and not significantly with $PV\dot{O}_2$ (r=0.14, NS) or $V\dot{O}_2$ at AT (r=0.21, NS). These findings suggest that in cardiac patients MHW-QOL mainly reflects the psychosocial and mental aspects of QOL rather than physical aspects.

Discussion

The major findings of the present study are that (1) exercise capacity and physical function-related QOL scores (ie, SAS and SIP physical disorder score) significantly improved, whereas psychosocial and mental aspect-related QOL scores (SIP psychosocial disorder score, MHW-QOL, STAI, and SDS) did not change in the whole patient group participating in the 3-month CCR program after AMI, (2) patients with impaired exercise capacity at baseline showed significant improvements in all QOL scores including both physical function-related scores and psychosocial and mental aspect-related scores, whereas patients with preserved exercise capacity showed improvements only in physical function-related QOL scores, (3) patients with anxiety or depression at baseline showed an improvement in each score after CCR, whereas those without anxiety or depression showed no change, and finally, (4) the MHW-QOL score correlated more tightly with psychosocial/mental function-related QOL scores rather than with physical function-related aspects.

Previous Studies

Many previous studies have demonstrated the benefits of CCR for QOL in patients after AMI,[1–4,6,7,20–22] but most have used only 1 or 2 QOL instruments and assessed changes in QOL scores after CCR in the whole group. In other words, few studies have investigated which aspect of QOL (physical, psychosocial or mental aspects) is most improved by CCR, which QOL instruments are most sensitive to changes occurring during CCR, and what type of patients obtain the

greatest benefit from CCR after AMI. In fact, Jolliffe et al noted in their meta-analysis that it was not possible to combine the data from studies reporting health-related QOL as an outcome, because 18 different instruments were used in the 11 randomized studies reporting it as an outcome[25] Shephard et al also noted that there were few direct comparisons between different types of QOL instruments!

One direct comparisons was made by Taylor et al, who utilized 3 generic QOL instruments, including SIP, to assess changes in QOL over time in 88 patients after AMI, and found that all 3 QOL instruments had modest sensitivity[26] Smith et al[27] compared 4 QOL instruments, including the Medical Outcome Study 36-item Short Form Survey (SF-36),[28] in 22 cardiac patients before and after CCR, and found that only 1 of the SF-36 subscales, vitality, significantly improved over time, from which they concluded that all 4 QOL measures lacked sensitivity to change. In Japan, where most QOL questionnaires invented in Western countries and written in English cannot be directly applied to Japanese patients, comparative assessments of the different QOL instruments during CCR has not been done so far. Yoshida et al studied the MHW-QOL, STAI and SDS in patients with AMI participating in 2-week hospitalized CCR, but did not analyze correlations among the measures[6] Seki et al also investigated SF-36, STAI and SDS in elderly patients with coronary artery disease participating in phase III CCR, but did not analyze correlations among the measures[29] Thus, the optimal QOL test instrument or the best method of interpreting the resultant scores there has not been established!

Present Study

In the present study, we compared 5 different QOL instruments in Japanese patients participating in a 3-month CCR program with supervised exercise training and education after AMI. This enabled us to analyze which aspect of QOL improves after CCR and what type of patients gain the greatest improvement in QOL from CCR after AMI. In addition, we were able to determine the nature of the Japan-invented MHW-QOL by assessing the correlations between MHW-QOL and other established QOL scales.

Improvement in QOL After CCR

The present study has shown that $P\dot{V}O_2$, SAS, SIP total score and SIP physical disorder score significantly improved, whereas the SIP psychosocial disorder score, MHW-QOL, STAI, and SDS did not change in the whole patient group after CCR, which indicates that overall the physical function-related QOL scores improved, but the psychosocial and mental aspect-related QOL scores did not. Therefore, not all aspects of QOL (or all types of QOL scores) necessarily improve after CCR in patients with AMI.

Many previous studies have demonstrated an improvement in physical function-related QOL after CCR,[4,20,30–32] but the improvement in mental/psychosocial aspect-related QOL has been inconsistent; some studies have reported a significant improvement,[20,30–33] and others have not.[34–36] For example, Sledge et al[30] and Tyni-Lenne et al[31] reported significant improvements in all areas of QOL (overall, physical, and psychosocial scores) in an 8-week CR program in cardiac patients, whereas Worcester et al[35] and Daumer et al[36] reported no significant difference in the psychosocial and mental aspects of QOL between an exercise training group and a control group. Recently, Izawa et al,[37] using SF-36,[28] reported significant improvements in the physical function-related SF-36 subscales (ie, physical functioning, role-physical, general health) but not in the mental function-related subscales (ie, social functioning, role-emotional, mental health) after CCR in patients with AMI. Thus, whether or not QOL improves after CCR in cardiac patients appears to depend on the aspect of QOL and the type of QOL instrument.

Patient Characteristics Predicting Improved QOL After CCR

In the present study, patients with impaired exercise capacity at baseline showed significant improvements in all QOL scores, including both physical function-related QOL scores and psychosocial and mental aspect-related QOL scores, whereas patients with preserved exercise capacity showed improvements only in physical function-related QOL scores. A potential explanation for this new finding is that there might be a "ceiling effect" (ie, patients with lower initial values have a greater improvement)! because the low exercise capacity group in the present study tended to have worse QOL scores at the beginning of CCR (Table 3). In support of this, Lavie et al reported that elderly patients with coronary artery disease had a lower baseline $P\dot{V}O_2$ value, but a greater improvement in QOL score (SF-36), after CCR than younger patients,[38] although Oldridge et al reported that higher exercise tolerance at baseline predicts a greater improvement in the quality of well-being in patients with AMI participating in CCR.[39] The reason for this discrepancy is unclear, and further studies are necessary to address this issue.

The present study also demonstrated that patients with anxiety or depression at baseline showed a significant improvement in each score after CCR, whereas those without showed no change. This finding is in accordance with Oldridge et al[39] who stated that a poor baseline health-related QOL was the predominant predictor of improved generic and specific health-related QOL after CCR. Likewise, Milani et al showed that depressed patients exhibited a greater improvement in psychosocial/mental aspect-related QOL than did normal patients.[40] Again, this finding may well be explained by the ceiling effect! Taken together, the findings suggest that an improvement in QOL after CCR depends not only on the type of QOL instrument but also on the patient characteristics at baseline, and that patients with impaired QOL, anxiety, or depression at baseline should be strongly recommended to participate in CCR with an expectation of greater improvements than patients without these problems.

QOL Instruments for Japanese Cardiac Patients

Although MHW-QOL was originally invented in Japan, no study to date has systematically compared it with other established QOL instruments in patients with AMI participating in CCR. The present study has demonstrated that MHW-QOL reflects overall QOL, as indicated by a significant correlation with SIP total score, but that it mainly represents psychosocial/mental aspect-related QOL rather than physical aspect-related QOL, as indicated by the tight correlations with SIP psychosocial score, STAI and SDS (Table 4).

Recently, SF-36 (Japanese version) has become used more frequently in the field of CCR.[29,37] In fact, a recent review of generic health-related QOL instruments[41] suggests that the SF-36 health survey is the most commonly

used of the generic QOL instruments reviewed.[42] However, some studies have raised a concern that SF-36 may not be sufficiently sensitive to measure the changes in QOL following CCR in cardiac patients.[27,43] Because a perfect QOL instrument for cardiac patients has not been established in Japan, further studies are needed to comparatively assess multiple QOL instruments and to invent a more appropriate QOL instrument for Japanese cardiac patients.

Study Limitations

First, because the present study did not have a control group not participating in CCR, it is unclear whether the improvement in QOL observed is attributable to the favorable effect of CCR or the natural course after AMI. However, the purpose of the present study was to compare different types of QOL instruments rather than to examine the efficacy of CCR on QOL in patients with AMI. To determine whether CCR improves QOL in Japanese patients after AMI, a prospective randomized study will be needed.

Second, the present study did not employ SF-36;[25] however, as mentioned before, it remains unclear whether SF-36 is the most appropriate instrument to assess QOL in Japanese patients participating in CCR after AMI. Further studies are needed to directly compare the usefulness and validity of various QOL instruments, such as MHW-QOL, SIP, and SF-36, in Japanese patients participating in CCR.

Third, the present study assessed changes in QOL in a relatively short-term (ie, 3 months) CCR program. Assessment of the effects of a longer term CCR on QOL in patients with AMI may also be necessary. Finally, because the present study included only a small number of elderly (6 patients (14%) >70 years of age) and female patients (7 (16%) female patients), the present results cannot be directly applied to such specific populations.

Conclusion

In patients with AMI, physical function-related QOL scores improve after 3-month CCR, whereas psychosocial and mental aspect-related QOL scores improve only in those with impaired exercise tolerance or impaired mental function at baseline. Thus, changes in QOL after CCR depend on the type of QOL scales and the patient's baseline status of physical and mental function. In addition, the present study demonstrated for the first time that MHW-QOL mainly reflects psychosocial/mental aspect-related QOL, as well as overall QOL, in Japanese cardiac patients.

Acknowledgment

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Pediatric Cardiology

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Improvement of Left Ventricular Function After Changing the Pacing Site in a Child with Isolated Congenital Complete Atrioventricular Block and Dilated Cardiomyopathy

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Abstract We report a case of isolated congenital complete atrioventricular block with left ventricular dysfunction after pacemaker implantation that improved after the pacing site was changed. During the neonatal period, a pacemaker wire was implanted on the right ventricular epicardium and pacing was initiated. Decreased ejection fraction and a perfusion defect around the septum on myocardial scintigraphy were observed during follow-up. Induced left bundle branch block was thought to be causing interventricular asynchrony, and the pacing site was change to the left ventricular epicardium. Ejection fraction improved and the perfusion defect resolved. Lead relocation may be useful for left ventricular dysfunction that develops during right ventricular pacing.

Keywords Congenital complete atrioventricular block - Pacemaker implantation - Dilated cardiomyopathy - Myocardial scintigraphy - Interventricular aynchrony - Left bundle branch block

Most patients with isolated congenital complete atrioventricular block (CCAVB) eventually require pacemaker implantation (PMI) and the prognosis has been considered relatively benign. Recent evidence suggests that a subset of patients with isolated CCAVB develop dilated cardiomyopathy (DCM) despite early pacemaker implantation [4, 11]. We describe a 5-year-old girl with isolated CCAVB who developed left ventricular dysfunction resembling DCM 5 years after pacemaker implantation. Her left ventricular function improved after the pacing site was changed.

Case Report

The patient was diagnosed as having complete atrioventricular block at 38 weeks of gestation because of fetal bradycardia. Her mother had no past history of

autoimmune disease and her serum antinuclear antibody, anti-Ro/SSA antibody, and anti-La/SSB antibody were all negative. The patient was born at 38 weeks and 3 days of gestation by normal vaginal delivery with a birth weight of 2620 g. Her Apgar score was 7 at 1 minute and 8 at 5 minutes.

Because her heart rate was 50 beats per minute (bpm) and did not increase even with crying, a pacemaker wire was implanted on the right ventricular epicardium and VVI (120 ppm) pacing was started. Although she was doing well without pacing failure and had normal growth during follow-up, echocardiographic parameters of left ventricular function gradually deteriorated. At 5years of age, she was admitted to our hospital because of suspected DCM and impending pacemaker battery failure. On admission,there were no remarkable physical findings except the operative scar of PMI. Serum HANP (Human Atrial Natriuretic Peptide) and BNP (Brain Natriuretic Peptide) were within the normal range. Her cardiothoracic ratio on chest roentgenogram was 55%, and an electrocardiogram showed complete atrioventricular block with constant pacing rhythm and complete left bundle branch block (LBBB) with a QRS duration of 140 msec. Echocardiogram showed that the interventricular septal wall motion was depressed, with a left ventricular end diastolic dimension of 39.5 mm (117% of normal) and an ejection fraction of 53%. She underwent ^{99m}Tc myocardial scintigraphy to assess myocardial perfusion and quantitative gated single photon emission computed tomography (QGS) to determine left ventricular function. Perfusion defects on ^{99m}Tc myocardial scintigraphy were revealed from the septum to the inferior segment, and the ejection fraction on QGS was 39% with hypokinesis in the same segments (Fig. 1). A myocardial biopsy of the right ventricle showed moderate degenerative and fibrous changes compatible with DCM. During cardiac catheterization, we compared the cardiac index on VVI pacing with that on DDD pacing, but there was no significant difference. We thought that artificial LBBB with induced interventricular asynchrony had contributed to her left ventricular dysfunction, and that a DDD pacing mode would be more physiological than VVI. She underwent a generator exchange with pacemaker lead implantation on the left ventricular epicardium, and left ventricular DDD mode pacing was initiated. Biventricular pacing systems are not available in Japan, so we chose to change the pacing site to the left ventricle. Two weeks after the operation, her electrocardiogram had changed from LBBB to complete right bundle branch block with a QRS duration of 140 msec, and an echocardiogram showed improved septal wall motion with an ejection fraction of 76%. One month after the operation, the perfusion defects on ^{99m}Tc myocardial scintigraphy had resolved and her ejection fraction on QGS improved to 53% without hypokinesis (Fig. 2).

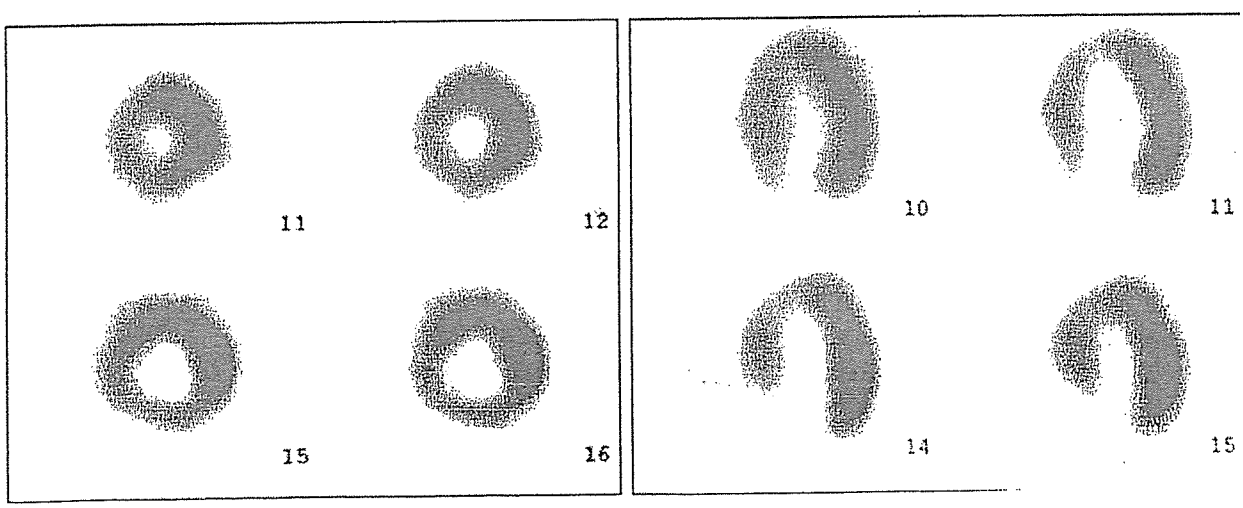

Figure 1 At admission, perfusion defects on ^{99m}Tc myocardial scintigraphy were revealed around the septum. (**Left**) Vertical long-axis images. (**Right**) Short-axis images.

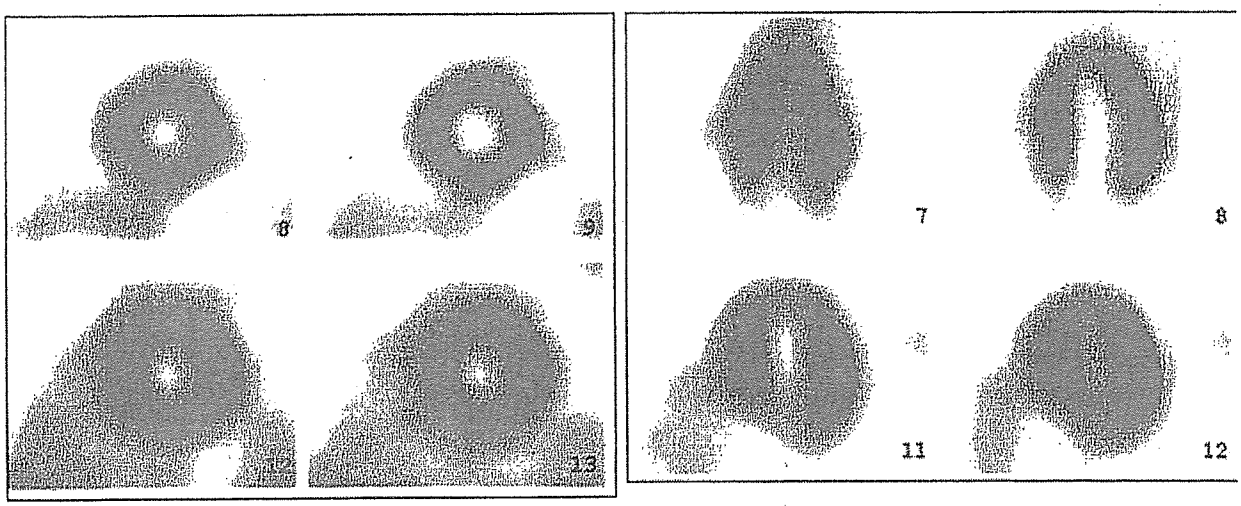

Figure 2 One month after operation, perfusion defects on ^{99m}Tc myocardial scintigraphy disappeared, (**Left**) Vertical long-axis images. (**Right**) Short-axis images.

Discussion

The prognosis for children diagnosed with CCAVB *in utero* or CCAVB associated with structural cardiac disease is generally poor. In contrast, the prognosis for children with isolated CCAVB has been considered relatively benign, with a normal life expectancy, although most patients require pacemaker implantation at some stage [4, 6, 8]. Recently, evidence has emerged that a subset of patients with isolated CCAVB develop chronic heart failure resembling DCM during follow-up, despite early pacemaker implantation [3, 11, 14]. Consequently, the long-term prognosis for isolated CCAVB is now more uncertain. One of the mechanisms of CCAVB was thought to be due to, autoimmune injury of the fetal conduction system by maternally derived IgG antibodies(anti-SSA/Ro and anti-SSB/La). Furthermore, maternal anti-SSA/Ro and anti-SSB/La antibodies react not only with the fetal conducting system but also with all fetal myocardial tissue [4]. Nevertheless, the etiology of isolated CCAVB with DCM is not fully explained [5, 8]. In our patient, maternal anti-SSA/Ro and anti-SSB/La antibodies were negative; it is difficult to believe that maternal antibody reacted with the entire fetal myocardial tissue and that isolated CCAVB with DCM developed despite pacing from the neonatal period.

Recently, it has been proposed that interventricular conduction abnormalities may impair cardiac function through ventricular asynchrony leading to cardiac failure. Therefore, biventricular or left ventricular pacing is emerging as a treatment for patients with severe heart failure or DCM with ventricular asynchrony [l, 2, 7, 12]. In patients with interventricular conduction abnormality such as LBBB, isolated LBBB caused global ventricular abnormalities manifested by shorting of diastolic filling times, changes in heart sounds, abnormal interventricular septal motion, and reduced left ventricular ejection fraction [5]. Myocardial scintigraphical studies of isolated LBBB

patients demonstrated perfusion defects in the septum without coronary artery disease. LBBB may reduce myocardial perfusion and glucose uptake in the septum because interventricular asynchrony associated with LBBB causes excess systolic thickening and augmented intramyocardial pressure in the septum [9]. In addition, in patients with right ventricular pacing, a high incidence of myocardial perfusion defects in the septum associated with pacing-induced artificial LBBB has been reported [10, 12].

In our patient, right ventricular epicardial VVI pacing from the neonatal period was associated with a gradual reduction in left ventricular function and a perfusion defect on myocardial scintigraphy in the septum to inferior segment. We thought that artificial LBBB-induced interventricular asynchrony contributed to left ventricular dysfunction, and that DDD pacing mode would be more physiological than VVI. We changed the pacing site from the right ventricular epicardium to the left ventricular epicardium and the pacing mode from VVI to DDD. The rate of 120 bpm on VVI mode is quite fast for a 5-year-old, and we cannot exclude the possibility that a tachycardia-induced cardiomyopathy may have resolved when changing to the DDD mode. However, changing the pacing site may have induced the disappearance of left ventricular asynchrony and the perfusion defects on ^{99m}Tc myocardial scintigraphy, resulting in an improved ejection fraction on QGS and echocardiography. We speculate that some patients with isolated CCAVB will develop left ventricular dysfunction caused by artificial LBBB-induced interventricular asynchrony. In patients with CCAVB and right ventricular pacing, if decreasing cardiac function or perfusion defects on myocardial scintigraphy are found, it is worthwhile to change the pacing site.

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Case Reports

Late Distortion of the Original Palmaz Stent Implanted in Postoperative Lesions Associated With Congenital Heart Disease

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The objective of this study was to report late distortion of a Palmaz stent. Late distortion of an original Palmaz stent, implanted in an extracardiac lesion, is rare. We completed a 1-year follow-up of 54 patients who had been implanted with 80 Palmaz stents in extracardiac lesions. Distortion of two stents was detected in two patients. For case 1, we implanted a P188 stent for supravalvar pulmonary stenosis complicating an arterial switch operation in a 14-year-old girl. Seven months later, we found compression of the stent. Although we implanted two P308 stents anterior to the distorted stent, distortion of both stents developed after 1 month. Two more P308 stents placed inside each stent were gradually recompressed. A CAT scan showed compression of the stent by a dilated sinus of valsalva. For case 2, we implanted a P308 stent for stenosis of the superior vena cava after Williams operation in an 11-year-old boy. A chest X-ray documented longitudinal compression of the stent 27 months after implantation and a CAT scan showed the ascending aorta was in contact with the stent. A Palmaz stent may be distorted when implanted in a lesion adjacent to a pulsating aorta.

Key words: congenital heart defects; heart catheterization; complications; child

INTRODUCTION

Late distortion of an original Palmaz stent, implanted in an intracardiac lesion, has been occasionally reported [1,2]. While compression of a stent with less radial strength in an extracardiac lesion has been reported [3–5], late distortion of an original Palmaz stent in the pulmonary artery or superior vena cava is rare [6,7], as its radial strength is sufficient to support an extracardiac lesion. We describe late fracture and distortion of Palmaz stents implanted in the pulmonary artery and superior vena cava.

CASE REPORTS

We completed a 1-year follow-up of 54 patients who had been implanted with 80 Palmaz stents (Cordis, Johnson and Johnson, Miami, FL) in extracardiac lesions specifically: pulmonary artery, 52 stents in 33 patients; aorta, 15 stents in 9 cases; superior vena cava, 9 stents in 9 patients; and pulmonary vein, 4 stents in 3 patients. Among 33 patients with pulmonary artery stenosis, 3 had undergone a previous arterial switch operation with the Lecompte maneuver. Late distortion of two stents was detected in two patients by chest X-ray or follow-up angiography.

Case 1

A 14-year-old girl who underwent pulmonary artery banding at 1 month and an arterial switch operation at 1 year and 10 months developed supravalvar pulmonary artery

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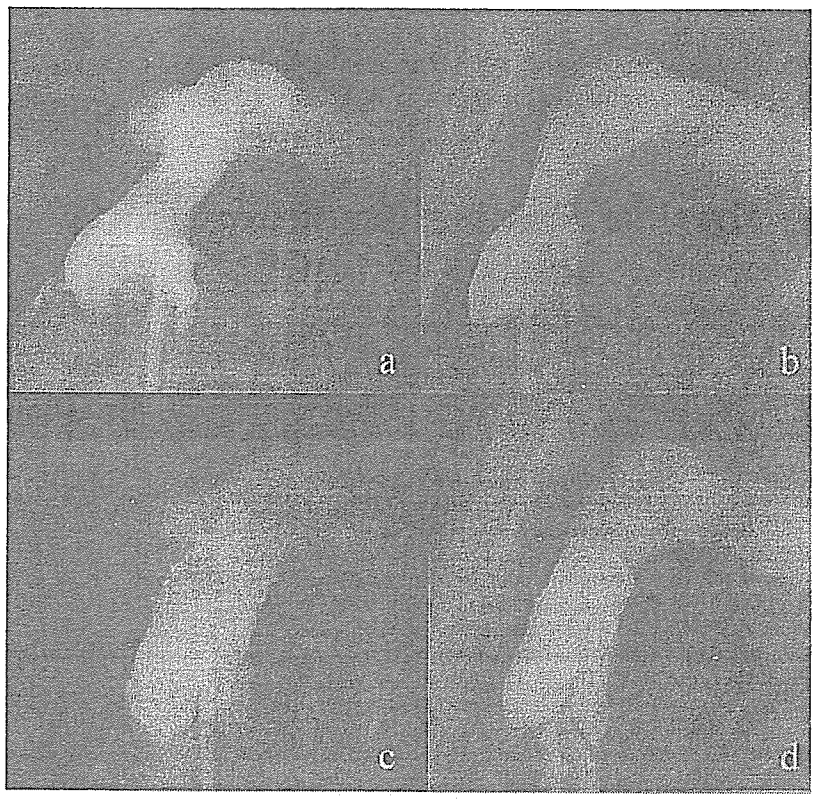

Fig. 1. Pulmonary angiogram before and after stent implantation in case 1. Anteroposterior (a) and lateral projection (b) before stent implantation. c and d: Same projection after implantation of a P188 stent.

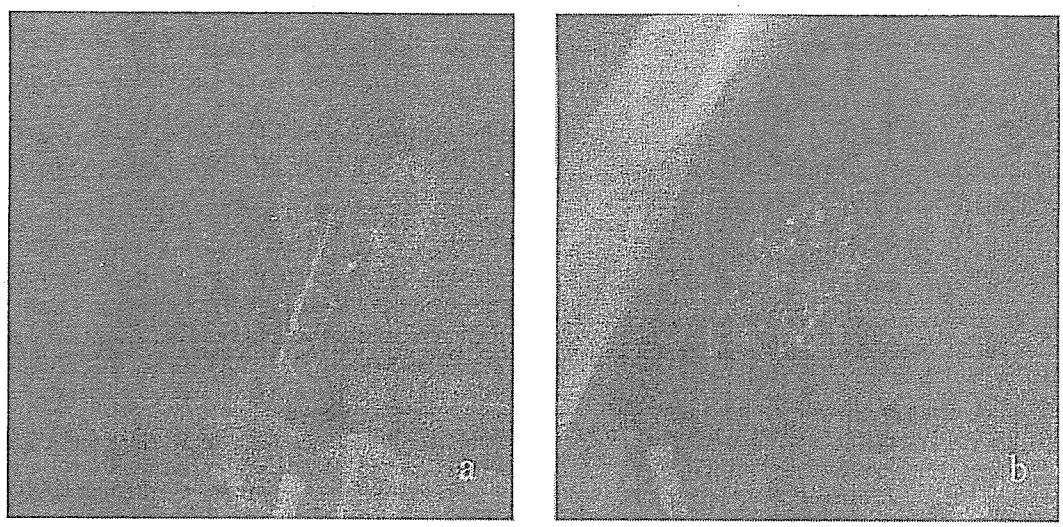

Fig. 2. Fractured stent 7 months after implantation in case 1. Anteroposterior (a) and lateral (b) view.

stenosis (PS) (Fig. 1a and b). We implanted a P188 stent on a 14 mm Z-Med balloon (NuMED, New York; Fig. 1c and d). At follow-up catheterization 7 months later, we found flattening of the stent (Fig. 2). Subsequently, we implanted two P308 stents on a 10 mm Opta 5 (Cordis) simultaneously anterior to the distorted stent (Fig. 3a), as we were concerned that a single P308 stent in the main PA might jail the bifurcation. However, compression of both stents, particularly the anterior one, developed 1 month after implantation (Fig. 3b). Although we implanted two more P308 stents on a 10 mm Opta 5 inside each distorted stent (Fig. 3c), they were gradually

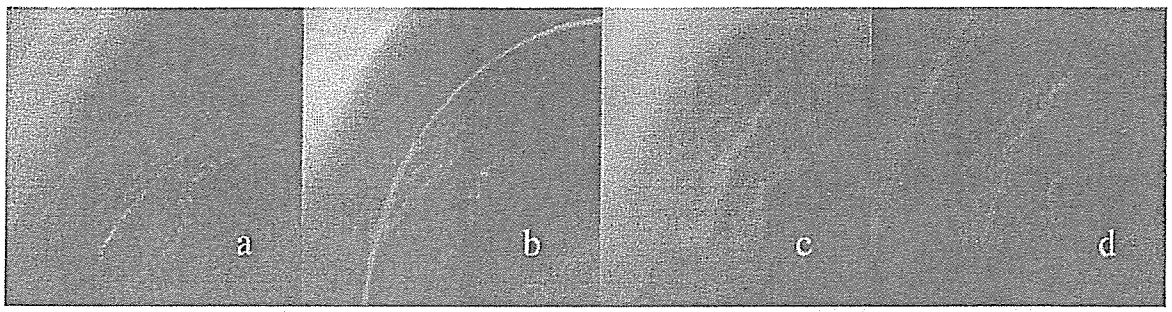

Fig. 3. Further implantation of stents in case 1. (a) Two P308 stents were implanted anterior to the collapsed one. (b) Compression of these stents. (c) Two more P308 stents inside each distorted stent. (d) Recompression of these stents.

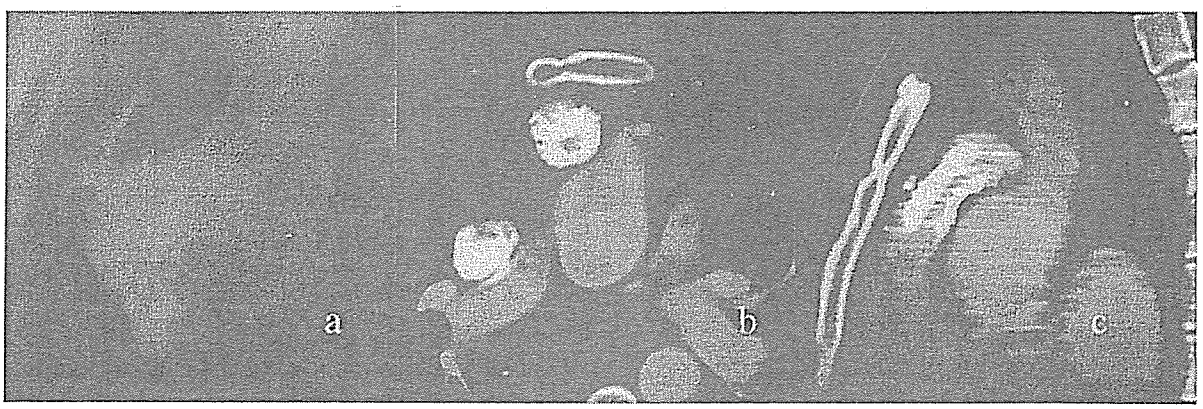

Fig. 4. Aortography (a) and CAT scan (b and c) of case 1. Stent was compressed between a markedly dilated pulsating sinus of valsalva and the sternum.

recompressed (Fig 3d). Aortography (Fig. 4a) and CAT scan (Fig. 4b and c) showed that the stent was compressed between a markedly dilated sinus of valsalva and the sternum. She is awaiting surgery.

Case 2

An 11-year-old boy developed stenosis of the superior vena cava after a Williams operation [8] for partial anomalous pulmonary venous connection (Fig. 5a), and we implanted a P308 stent on a 12 mm Ultra-thin diamond (Boston Scientific, Natick, MA) with complete elimination of the pressure gradient (Fig. 5b and c). Although follow-up angiography after 14 months showed no restenosis, a chest X-ray after 27 months documented longitudinal compression of the stent (Fig. 5d). A CAT scan showed a semicircular cross-section of the stent with flattening of the side in contact with the ascending aorta (Fig. 5e). He has been carefully observed and there has been no hemodynamic deterioration so far.

DISCUSSION

Stent placement is now a widely accepted procedure to dilate stenotic lesions associated with congenital heart disease, particularly in postoperative patients [7,9–11]. The Palmaz stent (Cordis) was originally used for such situations [9]. There are several reports of late fracture of other stents, particularly when implanted in the aorta [3–5]. However, late distortion of the Palmaz stent in extracardiac lesions is rare [6,7]. Knirsch et al. [6] reported longitudinal fracture of a stent implanted in a left pulmonary artery stenosis associated with the maneuver of Lecompte. The situation in our two patients is similar to their patient. In case 1, a markedly dilated sinus of valsalva was in close contact with the main pulmonary artery. A P188 stent dilated to 14 mm may have had insufficient radial strength in such a situation. Additionally, implantation of two stents in the narrow space between the sinus of valsalva and sternum may explain the further fracture, as collapse of the stent closer to the sternum was more marked. In case 2, although the stent has not fractured, the CAT scan clearly shows its semicircular cross-section with flattening of the side in contact with the ascending aorta. Judging from the case of Knirsch et al. [6] and ours, even the Palmaz stent may not have sufficient radial strength when implanted in lesions in close contact with the pulsating aorta. In the Lecompte maneuver, the main pulmonary artery and its