OBJECTIVES

We used myocardial fractional flow reserve (FFR\textsubscript{myo}) and coronary flow reserve (CFR) to estimate cut-off values for assessment of the functional severity of coronary stenosis and myocardial ischemia, and we tested the usefulness of coronary blood hemodynamic measurements before and after plain old balloon angioplasty (POBA) and coronary artery bypass graft surgery (CABG).

BACKGROUND

Fractional flow reserve and CFR are useful for assessing the functional severity of coronary artery stenosis, coronary microvascular dysfunction, and myocardial ischemia during cardiac catheterization in adults. However, there have been no reports on the use of these measurements in children with Kawasaki disease (KD).

METHODS

The study group included 128 patients with 314 coronary branches. The subjects were classified into three groups: normal coronary group, with 206 branches; abnormal coronary artery without ischemia group, with 58 branches; and ischemia group, with 50 branches.

RESULTS

In each branch, CFR and FFR\textsubscript{myo} were significantly lower in the ischemia group than in the other groups. Cut-off values for assessing the functional severity of coronary stenosis and CFR were approximately equal to those obtained for adults (CFR: <2.0; FFR\textsubscript{myo}: <0.75). We obtained very high sensitivity and specificity for estimating myocardial ischemia using CFR and FFR\textsubscript{myo} (CFR: 94.0% and 98.5%, respectively; FFR\textsubscript{myo}: 95.7% and 99.1%, respectively). Both CFR and FFR\textsubscript{myo} were reliable indicators of coronary hemodynamics before and after POBA and CABG.

CONCLUSIONS

Together, CFR and FFR\textsubscript{myo} provide a useful index for assessing the functional severity of coronary artery stenosis and myocardial ischemia and estimating the effectiveness of POBA and CABG in children with KD, the same as they do for adults. (J Am Coll Cardiol 2004; 43:653–61) © 2004 by the American College of Cardiology Foundation

Serious complications of Kawasaki disease (KD), including myocardial ischemia and myocardial infarction, affect the prognosis of children with coronary artery stenosis caused by KD (1,2). Therefore, early diagnosis of these complications is very important. However, it is difficult to detect myocardial ischemia and infarction in infants and young children by using standard methods.

Recently, catheter intervention, such as plain old balloon angioplasty (POBA), has been used to treat KD patients with severe coronary artery stenosis, and the general consensus is that catheter intervention effectively dilates coronary artery stenosis (3,4). Also, coronary artery bypass graft surgery (CABG) has been used to treat KD patients with severe coronary stenosis and myocardial ischemia, and long-term follow-up studies of CABG have found a high bypass graft patency and growth of the bypass graft in length and diameter (5,6). The best approach is prevention, i.e., intervening before and thereby preventing myocardial infarction. The success of such interventional treatments and CABG is primarily dependent on detection of the affected coronary artery, the localization of this artery, and the severity of the stenosis causing myocardial ischemia. Coronary angiography (CAG) is the method most commonly used to estimate localization and severity of coronary artery stenosis. However, there are some disadvantages when using CAG to assess the physiologic significance of certain dilated or stenotic lesions in the coronary circulation (7,8). Also, in infants and young children, coronary collateral arteries are often found in ischemic myocardium after KD (9,10).

Myocardial fractional flow reserve (FFR\textsubscript{myo}) and coronary flow reserve (CFR) are functional indexes of stenosis severity that can be derived from values of intra-coronary pressure and flow velocity obtained during maximal hyperemia (8,11–14). Reports indicate that they are very useful not only for assessment of functional severity of coronary artery stenosis but also for estimation of coronary hemodynamics after coronary interventions in adults (11,15,16). Other than our own reports, there have been no previous articles describing estimation of the functional severity of coronary artery stenosis and myocardial ischemia in children by using FFR\textsubscript{myo} and CFR (17,18).

In the present study, using FFR\textsubscript{myo} and CFR values, we estimated cut-off values for detection of myocardial isch-
Patients. The study population consisted of 128 patients (98 males and 30 females; mean age 6.6 ± 2.8 years [range 1 to 15]). All subjects had at least one coronary lesion with dilatation and/or an aneurysm during the acute to convalescence stages (estimated by two-dimensional echocardiography) in at least one of three coronary branches, and all had a history of KD. The time from onset of KD to the present examination ranged from 2 to 158 months. None of the patients had experienced acute myocardial infarction or congestive heart failure. All patients were receiving anticoagulant therapy consisting of 5 mg/kg per day aspirin and/or warfarin (Table 1).

After the study and treatment were fully explained, written informed consent was obtained from all patients or their parents.

Intravascular ultrasonography (IVUS). An ultrasound 2.9F imaging catheter with a 20-MHz transducer and a frame rate of 10/s (JOMED) was advanced down the coronary artery over a 0.014-inch (0.035-cm) guide wire. The IVUS images were recorded on compact disk and were used to determine the diameter and character of the coronary arteries.

Rest and dobutamine stress technetium-99m tetrofosmin myocardial scintigraphy. Single-photon emission computed tomography was performed with technetium-99m tetrofosmin in the patient at rest and after dobutamine infusion (maximum dose: 30 μg/kg/min). Regions of myocardial ischemia were defined by perfusion defects at rest and/or extension of defects during dobutamine stress.

Grouping of coronary artery branches. We divided the 314 coronary branches into three groups (normal coronary group [N], abnormal coronary artery without ischemia group [D], and ischemia group [IS]), based on the findings of CAG, IVUS, and dobutamine stress myocardial scintigraphy, as in a previous study of ours (4). Myocardial ischemia was detected by rest and dobutamine stress myocardial scintigraphy. The N group had normal-appearing coronary branches (n = 128 patients with 206 branches: 78 in the left anterior descending artery [LAD], 34 in the left circumflex artery [LCx], and 94 in the right coronary artery [RCA]). The D group had lesions with coronary stenosis <75% without myocardial ischemia (n = 36 patients with 58 branches: 24 in the LAD; 8 in the LCx; and 26 in the RCA). The IS group had lesions with coronary stenosis ≥75% and myocardial ischemia (n = 34 patients with 50 branches: 23 in the LAD, 6 in the LCx, and 21 in the RCA).

Measurement of coronary flow velocity and calculation of CFR. To measure coronary flow velocity, we used a 0.014-inch-diameter flexible angioplasty guide wire with a 15-MHz piezoelectric ultrasound transducer mounted in its tip (FloWire XT, Cardiometrics Inc., Mountain View, California). The Doppler guide wire was advanced into the coronary artery and positioned at the distal portion of the stenotic lesion. Digitized spectral waveforms from five cardiac cycles were averaged to compute several parameters of intra-coronary flow velocity, including instantaneous spectral peak velocity and time-averaged spectral peak velocity (8,19,20).

Averaged peak velocity (APV) was measured at rest and after papaverine hydrochloride infusion through the guiding catheter. The infusion dose of papaverine hydrochloride was calculated from the adult dose, as reported by De Bruyne et al. (21) (LCA, 0.3 mg/kg, with a maximum dose of 12 mg; RCA, 0.2 mg/kg, with a maximum dose of 8 mg). The CFR was calculated according to the following equation: CFR = APV after stress/APV at rest (Fig. 1).

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Onset (months)</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>N group</td>
</tr>
<tr>
<td>D group</td>
</tr>
<tr>
<td>IS group</td>
</tr>
</tbody>
</table>

Data are expressed as the mean value ± SD.

N group = normal-appearing coronary branch group; D group = lesions with coronary stenosis ≥75% without myocardial ischemia group; IS group = lesions with coronary stenosis >75% and myocardial ischemia group; PT/INR = prothrombin time international ratio.
Measurement of intra-coronary pressure and calculation of FFR\textsubscript{myo}. Measurements of intra-coronary pressure and coronary flow were performed simultaneously. We were able to measure intra-coronary pressure in 128 patients and 272 branches, which were divided into three groups (N, D, and IS group) according to the criteria described earlier: the N group comprised 128 patients and 174 branches (LAD, 68; LCx, 19; RCA, 87); the D group comprised 36 patients and 51 branches (LAD, 23; LCx, 6; RCA, 22); and the IS group comprised 34 patients and 47 branches (LAD, 21; LCx, 6; RCA, 20).

Measurement of intra-coronary pressure and calculation of FFR\textsubscript{myo} were performed according to the same method of Pijls et al. (11). A 5F or 6F balloon catheter was placed into the right atrium for measurement of right atrial pressure (P\textsubscript{a}). A 5F or 6F guiding catheter was advanced into the ostium of the coronary artery, and pressure was then measured (P\textsubscript{d}). To measure P\textsubscript{d}, we used a 0.014-inch pressure monitoring wire (PressureWire, Radi Medical Systems, Uppsala, Sweden). The wire was advanced into the coronary artery, positioned across the stenotic lesion, and used to measure intra-coronary pressure (P\textsubscript{d}). After these pressure measurements had stabilized, maximum coronary hyperemia was induced by intravenous infusion of papaverine hydrochloride. We calculated FFR\textsubscript{myo} from simultaneously recorded values of P\textsubscript{a}, P\textsubscript{d}, and P\textsubscript{v} at steady-state maximum hyperemia, using the following formula (11):

\[
\text{FFR}\textsubscript{myo} = \frac{P\textsubscript{d}}{P\textsubscript{v}}/\left(\frac{P\textsubscript{a}}{P\textsubscript{v}}\right)
\]

POBA and CABG. Plain old balloon angioplasty was performed in seven patients (age range 1 to 12 years) who had coronary aneurysm, severe coronary stenosis, and myocardial ischemia. Before and immediately after POBA, FFR\textsubscript{myo} and CFR were calculated using the methods described earlier. About six months after POBA, we again estimated FFR\textsubscript{myo} and CFR.

Coronary artery bypass graft surgery, using intra-thoracic graft arteries to the LAD, was performed in 13 patients (age range 3 to 15 years) who had a giant coronary aneurysm, severe stenosis in the proximal and distal portions of the aneurysm, and/or thrombosis in the aneurysm and myocardial ischemia. In addition to the standard measurement sites, coronary arterial pressure was measured at the orifice of each intra-
thoracic artery used as a bypass graft and at the distal portion of anastomosis between each bypass graft and coronary artery.

Statistics. All results are shown as the mean value ± SD. The APV, CFR, and FFR\textsubscript{myo} values were compared among 9 branches by one-way analysis of variance (Scheffé method). The CFR and FFR\textsubscript{myo} values before and after POBA or CABG were compared by the paired \textit{t} test.

The sensitivity and specificity of detection of myocardial ischemia were compared between CFR and FFR\textsubscript{myo} values by using the chi-square test for independence method. A value of \( p < 0.05 \) was considered to indicate statistical significance.

RESULTS

Patient reports. These procedures were performed safely in all subjects. Also, none of the patients who underwent these tests had clinical complaints, complications, or side effects from dobutamine and papaverine hydrochloride. The time during pressure and flow wire tests was from 10 to 15 min. In eight patients (10 of 206 branches), the stenosis could not be crossed.

Averaged peak velocity and CFR. Averaged peak velocity at rest and after papaverine stress. The APV values were significantly lower in the IS group than in the other groups. Within each group, there were no significant differences in APV among the three coronary branches. After papaverine stress, APV values in the IS group were significantly lower than in the other groups (Table 2).

CFR and its cut-off value. In all branches, the CFR values were significantly lower in the IS group than in the other groups. Within each group, there were no significant differences in CFR values among the three coronary branches (Table 2, Fig. 3). Based on these results, 2.0 (less than from the mean value of group N 2.61 ± 0.29 by more than 2 SD) was defined as the cut-off value for detection of abnormal CFR in children.

Four patients in group D were positive for myocardial ischemia when 2.0 was used as the cut-off CFR value; they had been diagnosed as negative for myocardial ischemia by exercise...
myocardial scintigraphy. Three of these four patients were shown, by two-dimensional echocardiography and CAG, to have hypokinesia in the left ventricular wall and/or intraventricular septal wall, suggesting myocardial ischemia.

**Myocardial FFR and its cut-off value.** In group N, the FFRmyo values were as follows: LAD, 0.91 ± 0.07; LCx, 0.92 ± 0.08; and RCA, 0.92 ± 0.08. In group D, the FFRmyo values were as follows: LAD, 0.91 ± 0.08; LCx, 0.92 ± 0.08; and RCA, 0.92 ± 0.07. In group IS, the FFRmyo values were as follows: LAD, 0.63 ± 0.07; LCx, 0.61 ± 0.08; and RCA, 0.60 ± 0.04. The FFRmyo values were significantly lower in the IS group than in the other groups. Within each group, there were no significant differences among the branches (Fig. 4).

On the basis of these results, 0.75 (less than the mean value of group N 0.92 ± 0.08 by more than 2 SD) was defined as the cut-off value for abnormal FFRmyo in children.

There were two false-positive cases in group D when the cut-off FFRmyo value of <0.75 was used; they were diagnosed as negative by exercise myocardial scintigraphy. These two patients were the same patients who had false-positive findings when a cut-off CFR value of <2.0 was used.

**Sensitivity and specificity of detection of myocardial ischemia by CFR or FFRmyo.** We estimated the sensitivity and specificity of detection of myocardial ischemia by using CFR or FFRmyo. With a cut-off value of 2.0 for CFR and 0.75 for FFRmyo, sensitivity was 94.0% and 95.7% and specificity was 98.5% and 99.1%. These values of sensitivity and specificity are very high, and those of FFRmyo are particularly high. Thus, FFRmyo and CFR proved to be very reliable for detection of myocardial ischemia.

**Myocardial FFR and CFR before and after POBA or CABG.** **PLAIN OLD BALLOON ANGIOPLASTY.** We measured CFR and FFRmyo before and after POBA. Pressure and flow wires mounted with sensors were easily steered in the coronary artery through the stenotic portions before and after POBA. Before POBA, coronary stenosis was >90% (by CAG), and POBA was performed using a balloon catheter. Values of CFR and FFRmyo ranged from 1.0 to 1.23 and 0.58 to 0.65, respectively. Immediately after POBA, coronary stenosis was <50% in all patients, and CFR and FFRmyo had recovered from 1.09 ± 0.21 and 0.62 ± 0.04 to 2.41 ± 0.24 and 0.91 ± 0.08, respectively. None of the patients who underwent POBA had clinical complaints, and there was no evidence of myocardial ischemia. About six months after POBA, cardiac catheterization was performed, and CFR and FFRmyo were still approximately equal to the levels measured immediately after POBA (Fig. 5).

**CABG.** Preoperative CFR and FFRmyo were 1.12 ± 0.22 and 0.59 ± 0.06, respectively; CFR and FFRmyo were abnormal in all cases. After CABG, patients had no complaints, and there were no findings of myocardial ischemia. All FFRmyo values had recovered to a normal range (0.92 ± 0.19) at cardiac catheterization, which was performed about six months after CABG (Fig. 6).

**DISCUSSION**

It is very difficult to determine the indications for catheter intervention and CABG in children, based on the diagnosis and localization of the affected coronary artery, using standard methods. Recently, it has been reported that

---

**Table 2.** APV at Rest and After Stress and CFR

<table>
<thead>
<tr>
<th>Group</th>
<th>APV at Rest</th>
<th>APV After Stress</th>
<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>LAD 22.3 ± 3.8</td>
<td>58.1 ± 5.4</td>
<td>2.64 ± 0.31</td>
</tr>
<tr>
<td></td>
<td>LCx 23.8 ± 5.4</td>
<td>59.8 ± 7.3</td>
<td>2.46 ± 0.26</td>
</tr>
<tr>
<td></td>
<td>RCA 24.3 ± 4.0</td>
<td>62.1 ± 8.2</td>
<td>2.56 ± 0.29</td>
</tr>
<tr>
<td>D</td>
<td>LAD 20.3 ± 3.2</td>
<td>49.8 ± 4.6</td>
<td>2.46 ± 0.22</td>
</tr>
<tr>
<td></td>
<td>LCx 23.1 ± 6.1</td>
<td>59.2 ± 5.2</td>
<td>2.55 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>RCA 24.3 ± 4.0</td>
<td>54.9 ± 5.2</td>
<td>2.39 ± 0.31</td>
</tr>
<tr>
<td>IS</td>
<td>LAD 11.9 ± 3.2*</td>
<td>12.9 ± 3.8*</td>
<td>1.11 ± 0.28*</td>
</tr>
<tr>
<td></td>
<td>LCx 12.3 ± 4.8*</td>
<td>13.1 ± 4.4*</td>
<td>1.08 ± 0.34*</td>
</tr>
<tr>
<td></td>
<td>RCA 12.6 ± 4.5*</td>
<td>14.3 ± 4.7*</td>
<td>1.16 ± 0.25*</td>
</tr>
</tbody>
</table>

*p < 0.05 vs. each branch in N and D groups. Data are expressed as the mean value ± SD.

APV = averaged peak velocity; CFR = coronary flow reserve; other abbreviations as in Table 1.

---

**Figure 3.** The coronary flow reserve (CFR) values in different coronary arteries in each branch. The error bar shows 1 SD from the mean value. *p < 0.05 vs. other branches in the N and D groups.

**Figure 4.** The myocardial fractional flow reserve (FFRmyo) values in different coronary arteries in each branch. *p < 0.05 vs. other branches in the N and D groups. D = abnormal coronary artery without ischemia group; IS = ischemia group; LAD = left anterior descending artery; LCx = left circumflex artery; N = normal coronary group; RCA = right coronary artery.
evaluation of coronary hemodynamics using a pressure wire and Doppler flow wire is very useful in adult cases (12–16).

In the present study, we evaluated cut-off values of $\text{FFR}_{\text{myo}}$ and CFR in children and tested their usefulness for determination of the functional severity of coronary artery stenosis and myocardial ischemia during cardiac catheterization, and we also assessed their usefulness for estimation of the effectiveness of POBA and CABG. **Estimation of functional severity of coronary artery and silent myocardial ischemia by CFR and FFR_{myo}**. Coronary flow reserve is a useful index for detection of the functional severity of coronary artery stenosis, myocardial ischemia, and the no-reflow phenomenon after coronary intervention (22) in adults. The cut-off value of CFR in adults is $<2.0$ (12,15,19), but there have been no previous reports of the cut-off value of CFR in children. In the present study, CFR values were significantly lower in the IS than in the other groups. However, within each group, there were no significant differences in CFR values among the three branches.

The cut-off value of 2.0 was estimated and is less than the mean value by 2 SD in normal-appearing coronary vessels; there were no false-positive or false-negative results. Thus, a CFR value $<2.0$ (same as the adult value) was considered to be an abnormal value in children. When 2.0 was used as the cut-off CFR value, the sensitivity and specificity for detection of myocardial ischemia were very high. This shows that a cut-off CFR value of 2.0 is not only a good index of the functional severity of coronary artery stenosis but is also a good parameter for detection of myocardial ischemia in children.

There were four false-positive patients in group D and two false-negative patients in group IS when 2.0 was used as the cut-off CFR value. These four false-positive patients had 50% to $<75\%$ stenosis of the coronary artery, and all four of them were under three years of age. Some previous reports state that use of exercise myocardial scintigraphy for detection of myocardial ischemia in young children can produce false-negative results (23). We determined that these three patients had positive myocardial ischemia, which we detected using a cut-off CFR value of 2.0. Of these three patients, one underwent POBA and two underwent CABG. After POBA or CABG, the CAG and two-dimensional echocardiographic findings (hypokinesia in the left ventricular wall) returned to normal. However, the other patient was diagnosed as having a true false-positive case because there were no abnormal findings by another test.

---

**Figure 5.** These averaged peak velocities and coronary flow reserves are of the same patient as in Figure 1 after plain old balloon angioplasty, which was done with a 3.0-mm-diameter balloon catheter at 10 atm twice. After plain old balloon angioplasty, there was no significant stenosis on coronary angiography (A), and coronary flow reserve turned to normal (2.3) (B, C). Moreover, the flow pattern changed from a disturbed pattern to a pulsatile pattern.
This shows that myocardial ischemia occurs in patients with KD even when coronary stenosis is <75%.

In adults, previous studies have found a favorable correlation between CFR and thallium-201 myocardial scintigraphy (24) and positron emission tomography (25). The present results show that CFR determined using a Doppler flow wire is a very useful index for detection of the functional severity of coronary stenosis and myocardial ischemia, not only in adults but also in children.

Myocardial FFR is a lesion-specific index of the functional severity of coronary stenosis, calculated from pressure measurements during coronary arteriography. In adults, the cut-off value of FFR\textsubscript{myo} is <0.75 (11), but there have been no reports on FFR\textsubscript{myo} in children. The value of FFR\textsubscript{myo} was significantly lower in the IS than in the other groups. Within each group, there were no significant differences in FFR\textsubscript{myo} values among the three branches.

We estimated the cut-off value of FFR\textsubscript{myo} for children in the same way that the cut-off value of CFR was estimated. A value of FFR\textsubscript{myo} of <0.75 (same as adult value) was considered an abnormal value in children. Moreover, when <0.75 was used as the cut-off FFR\textsubscript{myo} value, the sensitivity and specificity for detection of myocardial ischemia were very high. We believe that FFR\textsubscript{myo} <0.75 is not only a good indicator of the functional severity of coronary artery stenosis but also a good index for the detection of myocardial ischemia in children. Pijls et al. (14) reported that, in identification of reversible myocardial ischemia, the sensitivity of FFR\textsubscript{myo} was 88% and specificity was 100%.

The present results show that measurement of FFR\textsubscript{myo} during cardiac catheterization is useful for estimating the functional severity of coronary artery stenosis and detecting myocardial ischemia not only in adults but also in children.

Studies have shown that both pressure- and flow-based indexes of flow reserve are functions of stenosis resistance and myocardial bed resistance (26). Thus, CFR and FFR\textsubscript{myo} indicate not only the functional severity of coronary stenosis but also myocardial bed resistance, which depends on factors such as microvascular disease. Moreover, CFR and FFR\textsubscript{myo} are less sensitive in the evaluation of the hemodynamic severity of intermediate coronary lesions (27). Kawasaki disease consists of systemic vasculitis and probably involves microvascular disease in the acute phase. It is
difficult to determine whether a patient has microvascular disease. In the present study, of the 34 patients who had abnormal values of $\text{FFR}_{\text{myo}}$ and/or CFR, 20 had received POBA or CABG. After these interventions, myocardial ischemia improved in all cases. In patients with microvascular disease who received POBA or CABG, findings of myocardial ischemia did not improve after the intervention. Moreover, almost all patients with abnormal values of CFR and $\text{FFR}_{\text{myo}}$ had severe coronary stenosis. Thus, we concluded that $\text{FFR}_{\text{myo}}$ and CFR mainly represent the functional severity of coronary artery stenosis in the present subjects.

When deciding whether a patient needs cardiac intervention and CABG, during cardiac catheterization, CFR and $\text{FFR}_{\text{myo}}$ can be very useful in determining indications for catheter intervention and CABG, diagnosing the affected coronary artery and coronary lesion, and selecting the interventional methodology.

There were no statistically significant differences in the detection of myocardial ischemia between CFR and $\text{FFR}_{\text{myo}}$. The latter appears to be slightly superior to CFR because it produced fewer false-negative and false-positive results. Moreover, CFR is sensitive to changes in hemodynamic conditions, whereas $\text{FFR}_{\text{myo}}$ is not affected by such changes. Thus, $\text{FFR}_{\text{myo}}$ due to its ease and minimal variability, is superior to CFR in providing information on the consequences of an epicardial lesion on perfusion of the underlying myocardium (28).

Estimation of hemodynamic changes before and after POBA and CABG by CFR and $\text{FFR}_{\text{myo}}$. Before POBA, all seven of these patients had abnormal values of CFR and $\text{FFR}_{\text{myo}}$. After successful POBA, these values returned to normal, with improved findings in both CAG performed immediately after POBA and exercise myocardial scintigraphy performed several months later. Many reports have stated that, in adults, CFR and $\text{FFR}_{\text{myo}}$ are useful for making clinical decisions about revascularization procedures in patients with a significantly stenosed coronary artery (11,14,19,20,29,30). The present results show that, in children, CFR and $\text{FFR}_{\text{myo}}$ are reliable indexes for determining indications for POBA and estimating the effectiveness of POBA.

Before CABG, we estimated the values of CFR and $\text{FFR}_{\text{myo}}$ to determine indications for CABG. All 13 patients who underwent CABG had abnormal CFR and $\text{FFR}_{\text{myo}}$ values before CABG. Both CAG and exercise myocardial scintigraphy (performed several months later) showed that $\text{FFR}_{\text{myo}}$ returned to normal after CABG. Because CABG changed the coronary blood flow pattern and native flow through the stenotic coronary artery to the distal portion of the bypass graft, patients who received CABG did not undergo Doppler flow velocity measurement tests. Myocardial FFR was also very useful for confirmation of improvement of coronary hemodynamics after CABG.

**Study limitations.** There are several possible limitations of measurement of intra-coronary blood flow velocity and blood pressure using a Doppler flow wire (8,19,31) and coronary pressure wire (11,21,32). In the present study, we avoided measuring blood flow velocity in dilated or tightly curved portions of a coronary artery, and we attempted to record maximal flow velocity by manipulating the wire tip. Also, to obtain reliable data for interpretation, the wire must be positioned adjacent to the stenosis. This requires placement of the guide wire sufficiently distal to the lesion to avoid turbulence from flow separation (1.0 to 2.0 cm).

Moreover, taking the problems of measurement of coronary blood pressure into consideration, we measured intra-coronary artery pressure in each coronary branch in which only one portion of the stenosis was located in or near the ostia of the coronary artery (segments 1 to 2, 5 to 7, and 5 to 11).

**Conclusions.** The cut-off values of CFR and $\text{FFR}_{\text{myo}}$ for detection of the functional severity of coronary artery stenosis and myocardial ischemia in children with KD were $<2.0$ and $<0.75$, respectively, which are the same values obtained for adults. Together, CFR and $\text{FFR}_{\text{myo}}$ provide a useful index for assessment of the functional severity of coronary artery stenosis and myocardial ischemia and estimation of the effectiveness of POBA and CABG in children with KD, the same as they do for adults.

Reprint requests and correspondence: Dr. Shunichi Ogawa, Department of Pediatrics, Nippon Medical School Hospital, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, 113-8603 Japan. E-mail: boston@nms.ac.jp.

**REFERENCES**

before and after percutaneous transluminal coronary angioplasty.