Predicting Midterm Coronary Artery Bypass Graft Failure by Intraoperative Transit Time Flow Measurement

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Background. Transit time flow measurement has been accepted as a valuable tool to predict early coronary artery bypass graft failure immediately after surgery. However, if the graft is patent in the early postoperative period, the ability of transit time flow measurement to predict midterm graft failure is unknown.

Methods. Midterm postoperative angiography was performed between 1 and 4 years after surgery for 104 grafts, which were evaluated by intraoperative transit time flow measurement and confirmed to be fully patent in early postoperative angiography.

Results. Of the 104 grafts, 21 grafts were found to have a new, midterm occlusion or worsening of stenosis. Univariate analysis revealed that a lower mean flow (odds ratio 0.96 per flow unit, mL/min, \( p < 0.001 \)) and a higher percentage of backward flow (odds ratio 1.08 per percentage point, \( p < 0.05 \)) measured by transit time flow measurement was a risk factor for predicting midterm graft failure. An increasing interval between the surgery and the midterm angiography was also a predictive risk factor (odds ratio 1.06 per month, \( p < 0.05 \)). In the multivariate stepwise logistic regression analysis, a lower mean flow was found to be the independent risk factor for midterm graft failure (\( p < 0.01 \)). A venous graft and an increasing interval between surgery and midterm angiography were also found to be possible risk factors.

Conclusions. Transit time flow measurement provides a good prognostic index, not only for the immediate term but also for the midterm follow-up. A graft with intraoperative lower mean flow, and especially with a higher percentage of backward flow, should be carefully monitored, even if it was initially anatomically patent.


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Graft patency can influence, either early or late, the outcome of coronary artery bypass graft surgery (CABG) [1, 2]. Transit time flow measurement (TTFM) is reported to be a suitable method for quick and reproducible intraoperative assessment of coronary artery bypass graft function, independent of graft size [3–6]. Although postoperative angiography still represents the gold standard for anatomical evaluation, it is widely accepted that intraoperative TTFM is very valuable in predicting early coronary artery bypass graft failure immediately after surgery. However, there is little information available on the role of intraoperative TTFM in predicting midterm graft failure [3–7]. We aimed to evaluate the usefulness of TTFM in predicting midterm graft failure.

Patients and Methods

Approval for the study was obtained on March 15, 2007, from the Ethical Committee of the departments of cardiovascular surgery and cardiology of Gifu Prefectural Tajimi Hospital. The Committee waived individual consent for the study. We retrospectively reviewed the surgical databases, hospital records, and angiographies of all patients in our hospital who, between 2002 and 2006, underwent CABG with intraoperative TTFM, early postoperative angiography within 10 weeks of surgery, and midterm postoperative angiography in the period between 1 year and 4 years after surgery.

Of the 142 patients who underwent intraoperative TTFM, 123 patients underwent early postoperative angiography immediately after surgery. In the early postoperative angiography group, 36 of 261 grafts (5.4%) were found to be occluded or stenotic. Subsequently, 51 patients underwent follow-up angiography between 1 and 4 years after surgery. As we aimed to evaluate potential predictors of midterm graft failure, the statistical analysis was performed per conduit and not per patient. Also, since we specifically focused on predicting midterm graft failure, we only analyzed the grafts confirmed to be fully patent, without significant stenosis, in early angiography immediately after surgery. Therefore, we excluded grafts that were occluded or exhibited significant stenosis immediately after the operation. Accordingly, we also excluded grafts that failed after the initial angiography and before 1 year after surgery. The sequential anastomoses...
and their distal anastomoses were excluded, as the interpretation of flow measurements was difficult and complicated. The final tally of grafts that satisfied all these criteria and were included in the study were 104 coronary artery grafts (31 venous grafts and 73 arterial) from 51 patients. Bypass grafting was performed in the standard manner, either with (n = 36) or without (n = 15) cardiopulmonary bypass. Left or right internal thoracic artery (n = 54), saphenous vein graft (n = 31), radial artery (n = 11), and gastroepiploic artery (n = 8) were used as the conduits.

Intraoperative Flow Measurement

Intraoperative flow measurement for all grafts was performed just before sternal closure using a transit time flowmeter (BF1001; Medi-Stim AS, Oslo, Norway) on the distal portion of the graft body. Mean blood pressure was maintained between 70 and 90 mm Hg during the flow measurement, and a properly fitted probe was used with acceptable contact between the probe and the graft (acoustic coupling index ≥ 50%). The following measurements were obtained by TTFM analysis: mean flow calculated across five cardiac cycles (Qmean); pulsatility index (PI) as the ratio of the difference between the maximum flow (Qmax) and the minimum flow (Qmin) and the value of mean flow ([Qmax − Qmin]/Qmean); and the percentage of backward flow (%BF) as the percentage of the flow through the graft directed backward across the anastomotic site (area below zero) compared with the total forward flow (area above zero) of the same cardiac cycle (Fig 1) [3–7].

Postoperative Angiography

Visual assessments of the angiographies of the bypass grafts were made by two or more cardiologists and the results were classified according to the following system: (1) normal widely patent, less than 50% stenosis at any location in the graft, proximal anastomosis, distal anastomosis, or immediate 1 cm of target vessel, and normal Thrombolysis In Myocardial Infarction (TIMI) III flow characteristics; (2) abnormal patent, with greater than 50% stenosis at any location in the graft, proximal or distal anastomosis, or immediate 1 cm of target vessel, or poor flow characteristics (non–TIMI III flow); or (3) occluded [3].

As described previously, we only included grafts that were fully patent and normal in early angiography performed within 10 weeks of surgery. Based on the reevaluation by the midterm postoperative angiography performed between 1 year and 4 years, the total 104 grafts were divided into two groups: group A (21 grafts), in which grafts became abnormal or occluded; and group B (83 grafts), in which grafts remained normal. Thus, group A indicated grafts with a new occlusion, or newly developed stenosis, and group B indicated patent grafts without worsening stenosis.

In Japan, it is common practice to perform postoperative angiography to check graft patency and the status of native coronary arteries, including previous angioplasty sites. This type of follow-up evaluation is performed even if no signs of ischemia—such as recurrent angina or detection of electrocardiographic or scintigraphic markers—are detected. Thus, the patients who underwent midterm angiography in our study included those with (n = 18) and without (n = 33) obvious ischemic signs. We analyzed operative and postoperative angiographies performed as per the usual clinical practice of the hospital; no angiography was undertaken specifically for the purposes of this observational study.

Statistical Analysis

The two groups were compared using the unpaired Student’s t test or Welch’s test for continuous variables. For categorical variables, comparisons were performed using the χ² test or Fisher’s exact test. Logistic regression was used to assess risk factors for midterm graft failure. The TTFM variables were entered as exploratory vari-
Table 1. Comparison of Variables Between Group A and Group B and Odds Ratios (OR) of Midterm Graft Failure

<table>
<thead>
<tr>
<th>Transit time flow measurement variables</th>
<th>Overall n = 104</th>
<th>Group A n = 21</th>
<th>Group B n = 83</th>
<th>p Value</th>
<th>Univariate LR OR (95% CI), p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qmean (mL/min)</td>
<td>43.4 ± 29.0</td>
<td>26.5 ± 14.7</td>
<td>47.7 ± 30.2</td>
<td>&lt; 0.01</td>
<td>0.96 (0.93–0.98), &lt; 0.01</td>
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<tr>
<td>PI</td>
<td>3.00 ± 2.80</td>
<td>4.03 ± 2.50</td>
<td>2.75 ± 0.30</td>
<td>0.06</td>
<td>1.14 (0.98–1.40), 0.12</td>
</tr>
<tr>
<td>%BF</td>
<td>3.08 ± 6.32</td>
<td>6.13 ± 9.47</td>
<td>2.30 ± 5.02</td>
<td>&lt; 0.05</td>
<td>1.08 (1.01–1.17), &lt; 0.05</td>
</tr>
<tr>
<td><strong>Graft characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Venous graft</td>
<td>31</td>
<td>9</td>
<td>22</td>
<td>0.18</td>
<td>2.08 (0.76–5.61), 0.15</td>
</tr>
<tr>
<td>Proximal stenosis of target vessel (%)</td>
<td>86.6 ± 15.3</td>
<td>83.4 ± 17.7</td>
<td>87.4 ± 14.7</td>
<td>NS</td>
<td>0.98 (0.96–1.01), NS</td>
</tr>
<tr>
<td>Time to angiography (months)</td>
<td>16.5 ± 7.6</td>
<td>20.0 ± 9.6</td>
<td>15.6 ± 6.8</td>
<td>&lt; 0.05</td>
<td>1.06 (1.01–1.13), &lt; 0.05</td>
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<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>84</td>
<td>16</td>
<td>68</td>
<td>NS</td>
<td>1.41 (0.41–4.29), NS</td>
</tr>
<tr>
<td>Female</td>
<td>29</td>
<td>8</td>
<td>21</td>
<td>NS</td>
<td>1.81 (0.64–4.95), NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>61</td>
<td>14</td>
<td>47</td>
<td>NS</td>
<td>1.53 (0.57–4.40), NS</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>61</td>
<td>12</td>
<td>49</td>
<td>NS</td>
<td>0.93 (0.35–2.45), NS</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>22</td>
<td>6</td>
<td>16</td>
<td>NS</td>
<td>1.68 (0.53–4.86), NS</td>
</tr>
</tbody>
</table>

Group A included grafts with a new, midterm occlusion, or worsening of stenosis, and group B included those grafts that remained normal in the midterm period.

%BF = percentage of backward flow; CI = confidence interval; LR = logistic regression; NS = not significant; PI = pulsatility index; Qmax = maximum flow; Qmean = mean flow; Qmin = minimum flow; time to angiography = interval between the operation and the midterm postoperative angiography.

Results

In this study group, the early postoperative angiography was performed 16.5 ± 10.4 days (range, 6 to 68) after surgery. The midterm angiography was performed 16.5 ± 7.6 months (range, 12 to 45) after the operation. A comparison of TTFM values between the two groups is shown in Table 1. Group A had a lower mean flow (26.5 ± 14.7 versus 47.7 ± 30.2, p < 0.01) and a higher percentage of backward flow (6.13 ± 9.47 versus 2.30 ± 5.02, p < 0.05) than group B. The results of the univariate logistic regression analysis are also shown in Table 1. Univariate analysis revealed that both a lower mean flow (OR 0.96 per flow unit, mL/min, p < 0.01) and a higher percentage of backward flow (OR 1.08, per percentage point, p < 0.05) were risk factors for predicting midterm graft failure. An increasing interval between the CABG surgery and the midterm angiography was also a predictive risk factor (OR 1.06 per month, p < 0.05). Venous grafts (OR 2.08, p = 0.18) and mild proximal stenosis of target vessel (OR 0.98 per percent stenosis, p = 0.28) had a tendency to increase the risk of failure though they were not statistically significant. In terms of patient characteristics, both female sex (OR 1.81, p = 0.28) and diabetes mellitus (OR 1.53, p = 0.30) had a tendency to increase the risk of graft failure, although these factors were also not statistically significant.

In the multivariate stepwise regression analysis, a lower mean flow was found to be the only statistically significant independent risk factor for midterm graft failure (OR 0.95, 95% confidence interval: 0.92 to 0.98, p = 0.004). The interval between CABG surgery and midterm angiography (OR 1.05 per month, 95% confidence interval: 0.99 to 1.12, p = 0.11) and venous graft (OR 2.43, 95%...
Confidence interval: 0.78 to 7.65, \( p = 0.15 \) were also found to be possible risk factors in the multivariate analysis.

**Comment**

With an increasing emphasis being placed on quality assessment in cardiac surgery, TTFM has become a popular method for assessing graft patency during CABG operations. The combination of the three major values of intraoperative TTFM (Qmean, PI, and %BF) is reported to be a valuable predictor of early graft failure immediately after surgery [3–7]. A Qmean of around 15 or less, a PI of about 3 or higher, and a %BF of approxi-mately 3 or higher were previously proposed as the cut-off criteria to predict a higher incidence of early graft failure, for both arterial and venous conduits [4, 7, 8].

In this study, we evaluated whether intraoperative TTFM can predict midterm failure of the graft after the graft was confirmed to be patent in the early postoperative period. The determinants of midterm or late graft failure are known to differ from the determinants of early graft failure. Midterm graft stenosis was related to fibrous intimal hyperplasia or graft atherosclerosis [9]. The process of the development of fibrous intimal hyperplasia or atherosclerosis could be simply due to patient characteristics, and it cannot be completely predicted by intraoperative measurements alone. In the present study, because the number of subjects was relatively small, we failed to show the impact of patient characteristics on graft failure. However, a recent, large-scale, randomized trial has shown that midterm graft patency was lower among patients with diabetes mellitus, but that there was not such a tendency among the patients with hypertension or hyperlipidemia [10].

In addition to such factors, however, the presence of an anatomical problem of a graft at the time of operation could also contribute to the development of fibrous intimal hyperplasia, which may result in midterm graft failure. Flow curve patterns from TTFM should reflect such anatomical factors, although the influence of intraoperative measurements could be overshadowed after a longer follow-up. The multivariate analysis in the present study was able to prove a lower Qmean to be the independent risk of midterm failure. Poor graft flow (a low Qmean) during surgery may represent many possible problems, including an anatomic issue (intimal flap, purse-string effect), a graft body problem, poor distal runoff, or competitive flow from the native vessels [3–8]. Therefore, grafts with low flow will be continuously affected by poor downward runoff, either due to high resistance of the distal vascular bed or to competitive flow. In addition, low shear stress, or changing shear stress, is known to promote endothelial proliferation and apoptosis, shape change, and secretion of substances that promote vasoconstriction [11]. Thus, a graft with low flow, even if it was initially anatomically patent, may be prone to develop intimal hyperplasia and subsequent graft failure due to the lower shear stress throughout the graft. In the univariate analysis, a higher %BF was also a predictor of midterm graft failure. The %BF represents the percentage of flow through the graft directed backward across the anastomotic site, which reflects the amount of competitive flow through the native coronary arteries [4, 7]. It has been reported that greater competition flow from the native coronary vessel observed in the angiography is strongly associated with midterm graft failure [10, 12]. A higher %BF represents greater competitive flow and lower downward runoff, which can predispose a graft to functional failure.

There were limitations in the present study. First, although multivariate analysis was performed to obtain independent risk factors, as a retrospective study, the existence of bias could not be excluded. Various types of grafts and various target vessels were mixed in one group, and the number of subjects was relatively small. The small sample size of this study (21 events of new occlusion or stenosis) limited the ability of logistic regression analysis to detect risk factors. Thus, we were unable to show the effects of previously established risk factors on midterm graft failure. In addition, not every patient underwent postoperative angiography, leaving the possibility of selection bias. Second, the measurement taken at the time of surgery may not truly reflect the capacity of the graft to carry flow because the measurement could be affected by various factors, such as the recovery of the heart, graft spasm, and the patient's blood pressure or hemodynamics. To minimize these effects, we followed the protocol to standardize the measurements, as described previously [3–8]. The final TTFM, taken just before sternal closure, was used for the analysis and blood pressure was adjusted at the time of measurement (as described in Methods).

Despite its limitations, this study demonstrates a significant correlation between abnormal TTFM values and midterm graft failure. Intraoperative TTFM provides a good prognostic index and is helpful, not only for the immediate term, but also for the midterm follow-up of the post-CABG patient. Grafts with a lower Qmean, and especially with a higher %BF, should be carefully monitored, even if they were confirmed to be patent immediately after surgery. Intraoperative TTFM may be of value in selecting patients for postoperative angiographic evaluation. In addition to the known risk factors of midterm graft failure such as diabetes mellitus, or greater competition flow from native coronary arteries in angiography, an intraoperative lower mean flow as measured by TTFM should be recognized as a new predictive factor of midterm graft failure.

**References**

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