Comparisons of Baseline Demographics, Clinical Presentation, and Long-Term Outcome Among Patients With Early, Late, and Very Late Stent Thrombosis of Sirolimus-Eluting Stents

Observations From the Registry of Stent Thrombosis for Review and Reevaluation (RESTART)

Takeshi Kimura, MD; Takeshi Morimoto, MD; Ken Kozuma, MD; Yasuhiro Honda, MD; Teruyoshi Kume, MD; Tadanori Aizawa, MD; Kazuaki Mitsudo, MD; Shunichi Miyazaki, MD; Tetsu Yamaguchi, MD; Emi Hiyoshi; Eizo Nishimura; Takaaki Isshiki, MD; for the RESTART Investigators

Background—Stent thrombosis (ST) after sirolimus-eluting stent implantation has not yet been adequately characterized, mainly because of its low incidence.

Methods and Results—The Registry of Stent Thrombosis for Review and Reevaluation (RESTART) is a Japanese nationwide registry of sirolimus-eluting stent–associated ST comprising 611 patients with definite ST (early [within 30 days; EST], 322 patients; late [between 31 and 365 days; LST], 105 patients; and very late [>1 year; VLST], 184 patients). Baseline demographics, clinical presentation, and long-term outcome of sirolimus-eluting stent–associated ST were compared among patients with EST, LST, and VLST. Baseline demographics were significantly different according to the timing of ST. Characteristic demographic factors for LST/VLST versus EST identified by multivariable model were hemodialysis, end-stage renal disease not on hemodialysis, absence of circumflex target, target of chronic total occlusion, prior percutaneous coronary intervention, and age <65 years. For LST versus VLST, they were hemodialysis, heart failure, insulin-dependent diabetes mellitus, and low body mass index. Patients with LST had a significantly higher rate of Thrombolysis in Myocardial Infarction grade 2/3 flow (36%) at the time of ST than those with EST (13%) (P<0.0001) and VLST (17%; P<0.0001). Mortality rate at 1 year after ST was significantly lower in patients with VLST (10.5%) compared with those with EST (22.4%; P=0.003) or LST (23.5%; P=0.009).

Conclusion—ST timing—dependent differences in baseline demographic features, Thrombolysis in Myocardial Infarction flow grade, and mortality rate suggest possible differences in the predominant pathophysiological mechanisms of ST according to timing after sirolimus-eluting stent implantation. (Circulation. 2010;122:52-61.)

Key Words: coronary artery disease ■ stents ■ thrombosis

Although stent thrombosis (ST) is a dreaded complication of percutaneous coronary intervention (PCI) with drug-eluting stents (DES), ST occurring late after DES implantation has not yet been adequately characterized, mainly because of its low incidence. Previous studies reporting risk factors of ST were hampered by the small number of events analyzed.1–4 Furthermore, although the incidence and timing of ST occurring between 30 days and 1 year (late ST [LST]) were reported to be similar after both bare metal stent (BMS) and DES implantation, ST beyond 1 year after stent implantation (very LST [VLST]) was reported to occur more frequently after DES implantation than after BMS implantation.4 The underlying mechanisms might be different between LST and VLST. How-

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From the Department of Cardiovascular of Medicine (T. Kimura) and Center for Medical Education and Clinical Epidemiology Unit (T.M.), Graduate School of Medicine, Kyoto University, Kyoto, Japan; Division of Cardiology, Teikyo University Hospital, Teikyo, Japan (K.K., T.I.); Division of Cardiovascular Medicine, Stanford University Medical Center, Stanford, Calif (Y.H., T. Kume); Division of Cardiology, Cardiovascular Institute Hospital, Tokyo, Japan (T.A.); Division of Cardiology, Kurashiki Central Hospital, Kurashiki, Japan (K.M.); Division of Cardiology, Department of Internal Medicine, Kinki University School of Medicine, Higashi-Osaka City, Japan (S.M.); Division of Cardiology, Cardiovascular Center, Toranomon Hospital, Tokyo, Japan (T.Y.); and Cordis Cardiology Japan, Johnson and Johnson, Tokyo, Japan (E.H., E.N.).

The online-only Data Supplement is available with this article at http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.109.903955/DC1. Correspondence to Takeshi Kimura, Department of Cardiovascular of Medicine, Graduate School of Medicine, Kyoto University, 54 Shogoin Kawahara-cho, Sakyu-ku, Kyoto 606-8507 Japan. E-mail taketaka@kuhp.kyoto-u.ac.jp

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ever, no previous study has evaluated the differences between LST and VLST in terms of baseline characteristics, clinical presentation, and long-term outcome. The present study was undertaken to further characterize ST according to the timing of ST in a large number of patients with ST after sirolimus-eluting stent (SES) implantation in real-world clinical practice in Japan.

Clinical Perspective on p 61

Methods

Study Design

The Registry of Stent Thrombosis for Review and Reevaluation (RESTART) is a Japanese nationwide registry of patients with ST after SES implantation. After the approval of SES in Japan in May 2004, the Japanese Ministry of Health, Labor, and Welfare mandated the SES manufacturing company (Cordis Cardiology Japan, Johnson and Johnson, Tokyo, Japan) to undertake a comprehensive surveillance of ST after SES implantation. The company contacted all PCI centers in Japan every 2 weeks and collected information on the patients with ST after SES implantation. RESTART, as an investigator-initiated study, was designed to adjudicate whether those patients who were reported to have ST after SES implantation did in fact experience definite ST after SES implantation and to collect additional information on those patients. The participating centers were also encouraged to enroll in the RESTART study those patients who had ST but who thus far had not been reported to the company. Adjudication of ST, which was conducted by a physician (T. Kimura) and clinical research coordinators (Hitomi Sasae and Naoko Okamoto) in the data management center (Kyoto University Hospital, Department of Cardiology, Kyoto, Japan), was based on the angiographic findings and signs and symptoms of acute coronary syndrome reported by the site investigators. Logical inconsistencies were resolved by inquiries to the site investigators.

Angiographic and intravascular ultrasound (IVUS) substudies were also conducted, and for patients enrolled in the substudies, coronary angiograms and/or IVUS images both at baseline and at the time of ST were analyzed by the angiographic (Cardiocore, Tokyo, Japan) and IVUS (Cardiovascular Core Analysis Laboratory, Stanford University, Stanford, Calif) core laboratories. The study protocol was approved by the ethics committees of the 2 centers with which the 2 principal investigators are affiliated (Kyoto University Hospital and Teikyo University Hospital). Because this study was conducted retrospectively, written informed consent was waived according to the guidelines for epidemiological studies issued by the Ministry of Health, Labor, and Welfare of Japan.

Definitions

ST was defined according to the Academic Research Consortium (ARC) definition.6 Only patients with ARC-definite ST were enrolled in RESTART. ST was judged by the site investigators to have occurred if Thrombolysis in Myocardial Infarction (TIMI) flow was graded 0, 1 with occlusion persisting in the peri-stent region, 2, or 3 in the presence of angiographic evidence of thrombus associated with signs and symptoms of acute coronary syndrome. ST was categorized according to the timing of occurrence of ST as early ST (within 30 days [EST]), LST (between 31 and 365 days), and VLST (>1 year). Myocardial infarction was adjudicated according to the definition in the Arterial Revascularization Therapy Study.7

Site investigators evaluated status of antiplatelet therapy (APT) at the time of ST by asking the patients and/or their relatives about their compliance with APT. If the patient had discontinued aspirin and/or thienopyridine, the date of discontinuation was recorded in the case report form. If a patient had restarted APT after temporary discontinuation, the patient was included in the group of patients without discontinuation of APT at the time of ST.

ST related to surgical procedures included not only ST occurring after surgical procedures but also ST that occurred while the patient stopped APT before the scheduled surgical procedures. Surgical procedures were defined as any procedure requiring general or local anesthesia except for percutaneous endovascular procedures. Endoscopic therapeutic procedures were included as surgical procedures.

Statistical Analysis

Categorical variables were compared by use of the y2 test. Continuous variables were expressed as mean±SD unless otherwise indicated. Continuous variables were compared by use of the Student t test or Wilcoxon rank-sum test on the basis of the distribution.

Baseline demographics, clinical presentation of ST and APT at the time of ST, and treatment and outcome of ST were compared according to the timing of ST. Multivariable logistic regression models were constructed using those baseline demographic variables that were significantly different by univariate analysis in the comparison of LST/VLST versus EST and LST versus VLST, respectively. The nonparsimonious multivariable models were refitted so that they retained only those variables that had nominally significant results. The selected models were confirmed by forward and backward procedures. Characteristic demographic factors in each comparison were expressed as odds ratios and their 95% confidence intervals.

Cumulative incidences of recurrent ST and death after the index ST events were estimated by the Kaplan-Meier method, and differences were assessed with the log-rank test. In the comparison of mortality after ST according to the timing of ST, differences in baseline characteristics at the time of the index SES implantation were adjusted by use of a Cox proportional-hazard model.

All analyses were conducted by a physician (T. Kimura) and an independent statistician (T.M.) using SAS software version 9.1 (SAS Institute, Inc, Cary, NC), and all reported P values are 2-sided. Values of P<0.05 were regarded as statistically significant.

Results

Study Population

Among the 1335 Japanese PCI centers invited, 543 centers agreed to participate in RESTART (see the Appendix in the online-only Data Supplement). From May 2004 to June 2008, 491 128 PCI procedures, including 294 212 procedures with SES, were performed in the participating centers. The study patient flow is shown in Figure 1. The study population for the present analysis consisted of 611 patients with ARC-definite ST reported until June 30, 2008. Except for 1 patient with pathological confirmation only, 610 patients had angiographic confirmation of ST.

There were 322 patients with EST (52 acute ST within 24 hours and 270 subacute ST between 1 and 30 days), 105 patients with LST, and 184 patients with VLST. ST events occurred most commonly during the first 4 weeks, particularly during the first week after SES implantation (Figure 2). During hospitalization for SES implantation, aspirin and thienopyridine were administered in 97% and 97% (ticlopidine, 89%; clopidogrel, 8%) of patients, respectively.

Baseline Demographics

Baseline demographic features were significantly different between the 2 groups of patients with EST and LST/VLST (Table 1). Characteristic demographic factors for LST/VLST compared with EST identified by multivariable logistic model were hemodialysis, end-stage renal disease not on hemodialysis, absence of left circumflex coronary artery target lesion, target lesion of chronic total occlusion, any previously performed PCI, and age.
Among 315 patients enrolled in the angiographic substudy, residual dissection was seen significantly more frequently in patients with EST (n=169) compared with those with LST/VLST (n=144) (17% versus 4.2%; \(P=0.0002\); see Table I in the online-only Data Supplement).

Baseline demographic features were also significantly different between the 2 groups of patients with LST and VLST (Table 3). Characteristic demographic factors for LST compared with VLST were hemodialysis, history of heart failure, insulin-dependent diabetes mellitus, and low body mass index (Table 4). The prevalence of hemodialysis in patients with LST was as high as 29%. An angiographic substudy demonstrated that calcification was significantly less prevalent in patients with VLST (n=59) compared with those with LST (n=85) (22% versus 42%; \(P=0.01\); Table II in the online-only Data Supplement).
Table 1. Baseline Demographics and Procedural Characteristics in Patients With EST Compared With LST or VLST

<table>
<thead>
<tr>
<th>Patient data</th>
<th>EST</th>
<th>LST/VLST</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>322</td>
<td>289</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>67 ± 10.7</td>
<td>62.8 ± 12.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Age ≥65 y, %</td>
<td>61</td>
<td>53</td>
<td>0.049</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>81</td>
<td>83</td>
<td>0.59</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.8 ± 3.4</td>
<td>23.5 ± 3.5</td>
<td>0.31</td>
</tr>
<tr>
<td>Body mass index &lt;25.0 kg/m², %</td>
<td>67</td>
<td>70</td>
<td>0.48</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>32</td>
<td>36</td>
<td>0.33</td>
</tr>
<tr>
<td>Prior PCI, %</td>
<td>42</td>
<td>52</td>
<td>0.009</td>
</tr>
<tr>
<td>Prior coronary artery bypass grafting surgery, %</td>
<td>6.0</td>
<td>7.3</td>
<td>0.51</td>
</tr>
<tr>
<td>Heart failure, %</td>
<td>19</td>
<td>21</td>
<td>0.59</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>43</td>
<td>40</td>
<td>0.56</td>
</tr>
<tr>
<td>Insulin dependent, %</td>
<td>11</td>
<td>11</td>
<td>0.79</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>72</td>
<td>75</td>
<td>0.47</td>
</tr>
<tr>
<td>Stroke, %</td>
<td>9.7</td>
<td>9.2</td>
<td>0.83</td>
</tr>
<tr>
<td>Peripheral artery disease, %</td>
<td>12</td>
<td>11</td>
<td>0.69</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>31</td>
<td>37</td>
<td>0.15</td>
</tr>
<tr>
<td>eGFR, mL·min⁻¹·1.73 m⁻²</td>
<td>62.0 ± 24.0</td>
<td>56.9 ± 30.1</td>
<td>0.02</td>
</tr>
<tr>
<td>eGFR &lt;30 mL·min⁻¹·1.73 m⁻², %</td>
<td>6.8</td>
<td>9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Nonhemodialysis, %</td>
<td>2.3</td>
<td>6.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemodialysis, %</td>
<td>4.4</td>
<td>14</td>
<td>0.0001</td>
</tr>
<tr>
<td>Acute myocardial infarction, %</td>
<td>30</td>
<td>22</td>
<td>0.03</td>
</tr>
<tr>
<td>Unstable angina, %</td>
<td>21</td>
<td>25</td>
<td>0.19</td>
</tr>
<tr>
<td>Emergency procedure, %</td>
<td>37</td>
<td>28</td>
<td>0.03</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>56.5 ± 13.8</td>
<td>55.6 ± 13.4</td>
<td>0.53</td>
</tr>
<tr>
<td>Single-vessel disease, %</td>
<td>37</td>
<td>41</td>
<td>0.07</td>
</tr>
<tr>
<td>Lesions treated, n</td>
<td>1.42 ± 0.73</td>
<td>1.49 ± 0.85</td>
<td>0.22</td>
</tr>
<tr>
<td>Stents/patient, n</td>
<td>2.05 ± 1.22</td>
<td>2.23 ± 1.54</td>
<td>0.12</td>
</tr>
<tr>
<td>Total stent length/patient, mm</td>
<td>45.4 ± 28.4</td>
<td>49.0 ± 36.2</td>
<td>0.18</td>
</tr>
<tr>
<td>Statin use, %</td>
<td>46</td>
<td>52</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Lesion data

| n | 336 | 296 |
| Stents/lesion, n | 1.51 ± 0.76 | 1.55 ± 0.83 | 0.48 |
| Stent length/lesion, mm | 33.6 ± 18.6 | 34.1 ± 20.6 | 0.75 |
| Average stent diameter, mm | 2.88 ± 0.36 | 2.93 ± 0.35 | 0.07 |
| Maximum inflation pressure, atm | 16.8 ± 3.5 | 17.1 ± 3.3 | 0.11 |
| IVUS use, % | 56 | 56 | 0.98 |
| ST vessel, % | 3.3 | 3.0 | 0.25 |
| Left main coronary artery | 56 | 56 | 0.98 |
| Left anterior descending coronary artery | 18 | 13 | 0.03 |
| Left circumflex coronary artery | 22 | 26 | 0.21 |
| Right coronary artery | 0.9 | 2.0 |
| Lesion type, % | 87 | 85 | 0.89 |
| De novo | 19 | 13 | 0.04 |
| Culprit of ST-elevation myocardial infarction | 7.3 | 12 | 0.03 |
| Chronic total occlusion | 29 | 25 | 0.21 |
| Bifurcation | 8.4 | 5.8 | 0.2 |

Table 2. Univariate and Multivariable Analyses of the Characteristic Demographic Factors in Patients With LST or VLST Compared With EST

<table>
<thead>
<tr>
<th>Variables</th>
<th>EST</th>
<th>LST/VLST</th>
<th>P</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis</td>
<td>4.4</td>
<td>14</td>
<td>0.0001</td>
<td>3.42</td>
<td>1.79–6.52</td>
<td>0.0002</td>
</tr>
<tr>
<td>ESRD not on hemodialysis</td>
<td>2.3</td>
<td>6.3</td>
<td>0.01</td>
<td>3.77</td>
<td>1.51–9.43</td>
<td>0.005</td>
</tr>
<tr>
<td>Target lesion of LCx</td>
<td>27</td>
<td>19</td>
<td>0.03</td>
<td>0.59</td>
<td>0.39–0.88</td>
<td>0.01</td>
</tr>
<tr>
<td>Target lesion of CTO</td>
<td>7.8</td>
<td>14</td>
<td>0.01</td>
<td>2.06</td>
<td>1.19–3.57</td>
<td>0.01</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>42</td>
<td>52</td>
<td>0.009</td>
<td>1.54</td>
<td>1.1–2.16</td>
<td>0.01</td>
</tr>
<tr>
<td>Age ≥65 y</td>
<td>61</td>
<td>53</td>
<td>0.049</td>
<td>0.71</td>
<td>0.5–0.99</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Clinical Presentation of ST

Overall, clinical presentation of ST was ST-segment elevation acute coronary syndrome in 69%, non-ST-segment elevation acute coronary syndrome in 23%, and cardiac arrest or ventricular fibrillation in 8% of patients, a proportions pattern that did not significantly differ with the timing of ST (Table 5). Multivessel ST was present in 3.4% of patients, which accounted for 17.4% of the 121 ST patients who underwent multivessel stenting. Initial TIMI flow grades at the time of ST were significantly different according to the timing of ST. Patients with LST had a markedly higher rate of TIMI grade 2 or 3 flow compared with patients in both the EST and VLST groups.

Surgical Procedure and Status of APT Before ST

Overall, ST was related to surgical procedures in 4.6% of patients (Figure 3). APT before surgical procedures included none in 68%, aspirin alone in 14%, dual APT in 14%, and thienopyridine alone in 4% of patients (Table 5). Among 20 patients with ST after surgical procedures, dual APT was not stopped before surgery in 4 patients, and no other patients restarted dual APT before ST events.

The status of APT at the time of ST was significantly different according to the timing of ST (Table 5). In patients with EST, 76% of patients were on dual APT at the time of ST. Although the proportion of patients on dual APT decreased with time, 52% of patients with LST and 21% of patients with VLST had ST while they were taking both aspirin and thienopyridine.

Discontinuation of APT before ST events was reported in 216 patients (36%; discontinuation of both thienopyridine and aspirin, 77 patients; discontinuation of thienopyridine only, 133 patients; and discontinuation of aspirin only, 6 patients), with a median interval between discontinuation and ST of 121 days (interquartile range, 14 to 513 days). The median interval from discontinuation of APT to the onset of ST was significantly shorter after discontinuation of both

eGFR indicates estimated glomerular filtration rate.
aspirin and thienopyridine than after discontinuation of thienopyridine only (13 days [interquartile range, 6 to 61 days] versus 314 days [interquartile range, 79 to 711 days]; \( P < 0.0001\)). However, among patients with ST after discontinuation of both thienopyridine and aspirin, 62 patients (81%) had ST beyond 5 days after discontinuation (Figure 4).

Treatments and Outcomes of ST
Treatments of ST were generally similar according to the timing of ST (Table 6). PCI was performed in 97% of patients with frequent use of thrombus aspiration. Additional stent

| Table 3. Baseline Demographics and Procedural Characteristics in Patients With LST Compared With VLST |
|---------------------------------------------------------------|----------|-----|
|                                | LST      | VLST | \( P \) |
| Patient data                  |          |      |        |
| n                              | 105      | 184  |        |
| Age, y 68.0 ± 10.8             | 62.9 ± 12.3 | 0.0003 |
| Age ≥ 65 y, %                  | 63       | 48   | 0.02  |
| Male gender, %                 | 77       | 86   | 0.047 |
| Body mass index, kg/m²         | 22.3 ± 3.4 | 24.2 ± 3.4 | 0.0001 |
| Body mass index < 25.0 kg/m², % | 80       | 63   | 0.002 |
| Prior myocardial infarction, % | 36       | 36   | 0.95  |
| Prior PCI, %                   | 50       | 54   | 0.48  |
| Prior coronary artery bypass   | 11       | 4.9  | 0.045 |
| surgery, %                     |          |      |       |
| Heart failure, %               | 33       | 13   | 0.0001|
| Diabetes mellitus, %           | 54       | 32   | 0.0002|
| Insulin-dependent diabetes      | 22       | 5.1  | 0.0001|
| mellitus, %                    |          |      |       |
| Hypertension, %                | 84       | 69   | 0.006 |
| Stroke, %                      | 11       | 8.4  | 0.54  |
| Peripheral artery disease, %   | 12       | 11   | 0.73  |
| Current smoker, %              | 27       | 42   | 0.0007|
| eGFR, mL·min\(^{-1}\)·1.73\(^{-m-2}\) 48.7 ± 38.7 | 61.6 ± 22.6 | 0.002 |
| eGFR < 30 mL·min\(^{-1}\)·1.73\(^{-m-2}\), % | 34       | 9.9  | 0.0001|
| Nonhemodialysis, %             | 7.6      | 5.5  | 0.48  |
| Hemodialysis, %                | 29       | 4.9  | 0.0001|
| Acute myocardial infarction, % | 24       | 22   | 0.69  |
| Unstable angina, %             | 24       | 26   | 0.74  |
| Emergency procedure, %         | 32       | 26   | 0.26  |
| Ejection fraction              | 53.6 ± 14.6 | 56.7 ± 12.7 | 0.13  |
| Single-lesion disease, %       | 33       | 45   | 0.06  |
| Lesions treated, n             | 1.46 ± 0.78 | 1.52 ± 0.88 | 0.56  |
| Stents/patient, n              | 2.2 ± 1.44 | 2.24 ± 1.69 | 0.8   |
| Total stent length/patient, mm | 47.8 ± 30.7 | 49.7 ± 39.0 | 0.64  |
| Statin use, %                  | 43       | 57   | 0.03  |
| Lesion data                    |          |      |       |
| n                              | 106      | 190  |        |
| Stents/lesion, n               | 1.56 ± 0.69 | 1.55 ± 0.91 | 0.97  |
| Stent length/lesion, mm        | 33.3 ± 17.1 | 34.5 ± 22.3 | 0.61  |
| Average stent diameter, mm     | 2.88 ± 0.34 | 2.96 ± 0.35 | 0.06  |
| Maximum inflation pressure, atm| 17.0 ± 3.3 | 17.2 ± 3.4 | 0.69  |
| IVUS use, %                    | 54       | 57   | 0.58  |
| ST vessel, %                   |          |      | 0.91  |
| Left main coronary artery      | 2.8      | 3.2  |      |
| Left anterior descending      | 54       | 58   |      |
| coronary artery                |          |      |      |
| Left circumflex coronary artery| 14       | 12   |      |
| Right coronary artery          | 26       | 25   |      |
| Graft                          | 2.8      | 1.6  |      |
| Lesion type, %                 |          |      |      |
| De novo                        | 89       | 83   | 0.17  |
| Culprit of ST-segment elevation| 11       | 14   | 0.44  |
| myocardial infarction          |          |      |      |
| Chronic total occlusion        | 9.6      | 14   | 0.26  |
| Bifurcation                    | 28       | 23   | 0.33  |
| Side-branch stenting           | 6.6      | 5.3  | 0.65  |
| eGFR indicates estimated      |          |      |      |
| glomerular filtration rate.    |          |      |      |

<table>
<thead>
<tr>
<th>Table 4. Univariate and Multivariable Analyses of the Characteristic Demographic Factors in Patients With LST Compared With VLST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate Analysis</strong></td>
</tr>
<tr>
<td><strong>Prevalence of Variables, %</strong></td>
</tr>
<tr>
<td><strong>Odds Ratio</strong></td>
</tr>
<tr>
<td><strong>95% CI</strong></td>
</tr>
<tr>
<td><strong>Late ST</strong></td>
</tr>
<tr>
<td><strong>Very Late ST</strong></td>
</tr>
<tr>
<td><strong>P</strong></td>
</tr>
<tr>
<td>Hemodialysis                                                                                       29</td>
</tr>
<tr>
<td>History of heart failure                                                                            33</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus                                                                     22</td>
</tr>
<tr>
<td>Body mass index &lt; 25 kg/m²                                                                              80</td>
</tr>
<tr>
<td>CI indicates confidence interval.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5. Clinical Presentation of ST and Status of APT According to Timing of ST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EST</strong> (n = 322), %</td>
</tr>
<tr>
<td><strong>LST</strong> (n = 105), %</td>
</tr>
<tr>
<td><strong>VLST</strong> (n = 184), %</td>
</tr>
<tr>
<td><strong>P</strong></td>
</tr>
<tr>
<td>Clinical presentation</td>
</tr>
<tr>
<td>ST-segment elevation acute coronary syndrome</td>
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<tr>
<td>Non-ST-segment elevation acute coronary syndrome</td>
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<tr>
<td>Cardiac arrest</td>
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<tr>
<td>Initial TIMI flow grade</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>Multivessel ST</td>
</tr>
<tr>
<td>ST related to surgery</td>
</tr>
<tr>
<td>ST within 30 d after surgery</td>
</tr>
<tr>
<td>Status of APT at time of ST</td>
</tr>
<tr>
<td>Dual</td>
</tr>
<tr>
<td>Aspirin alone</td>
</tr>
<tr>
<td>Thienopyridine alone</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

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placement was performed in 36% of patients. Final TIMI grade 3 flow after PCI was achieved in 84% of patients. Emergency coronary artery bypass graft surgery was performed in only 1.2% of patients.

Myocardial infarction was the most common clinical sequel of ST, occurring in 89% of patients. During follow-up, cumulative incidence of recurrent ST at 1 year after the index ST was 4.6% (Figure 5A). Cumulative incidence of death
Table 6. Treatment and Outcome of ST

<table>
<thead>
<tr>
<th>Treatment of ST</th>
<th>EST (n=322)</th>
<th>LST (n=105)</th>
<th>VLST (n=184)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td>97%</td>
<td>96%</td>
<td>98%</td>
<td>0.73</td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>78%</td>
<td>69%</td>
<td>81%</td>
<td>0.07</td>
</tr>
<tr>
<td>Balloon dilation</td>
<td>94%</td>
<td>92%</td>
<td>92%</td>
<td>0.49</td>
</tr>
<tr>
<td>Additional stent placement</td>
<td>32%</td>
<td>35%</td>
<td>43%</td>
<td>0.06</td>
</tr>
<tr>
<td>DES</td>
<td>18%</td>
<td>12%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>BMS</td>
<td>14%</td>
<td>23%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Intraaortic balloon pumping</td>
<td>41%</td>
<td>30%</td>
<td>27%</td>
<td>0.003</td>
</tr>
<tr>
<td>Percutaneous cardiopulmonary support</td>
<td>8.3%</td>
<td>5.0%</td>
<td>4.5%</td>
<td>0.21</td>
</tr>
<tr>
<td>Emergency coronary artery bypass grafting surgery</td>
<td>1.6%</td>
<td>0.0%</td>
<td>1.1%</td>
<td>0.25</td>
</tr>
<tr>
<td>Final TIMI flow grade</td>
<td></td>
<td></td>
<td></td>
<td>0.7</td>
</tr>
<tr>
<td>0</td>
<td>6.2%</td>
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<td>3.5%</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.3%</td>
<td>4.0%</td>
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</tr>
<tr>
<td>2</td>
<td>7.5%</td>
<td>6.1%</td>
<td>8.8%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>84%</td>
<td>84%</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Final diagnosis of myocardial infarction</td>
<td>90%</td>
<td>85%</td>
<td>90%</td>
<td>0.32</td>
</tr>
<tr>
<td>Q-wave myocardial infarction</td>
<td>65%</td>
<td>57%</td>
<td>71%</td>
<td>0.07</td>
</tr>
<tr>
<td>Non-Q-wave myocardial infarction</td>
<td>24%</td>
<td>28%</td>
<td>20%</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Discussion

The main finding of the present study analyzing the largest number of patients with SES-associated ST ever reported was that baseline characteristics, TIMI flow grade at the time of ST, and mortality rate after ST were markedly different according to the timing of ST after SES implantation.

Early ST within 30 days has been relatively well characterized compared with ST occurring beyond 30 days. Risk factors reported for EST included acute coronary syndrome, suboptimal APT, and procedural factors such as residual dissection and underexpansion of stents, which were mostly consistent across studies. Several recent studies assessed risk factors for late ST beyond 30 days. In the Estudio Español Sobre Trombosis De Stents Farmacoactivos (ESTROFA) registry, ST-elevation myocardial infarction, stenting of the left anterior descending coronary artery, and long stents were identified as risk factors for late ST beyond 30 days, whereas in the Dutch ST registry, undersizing, malignancy, proximal lesion, peripheral artery disease, diabetes mellitus, bifurcation, long stents, and younger age were reported to be risk factors for late ST. The apparent inconsistency for the reported risk factors across studies might partly be explained by the fact that no previous study discriminated between LST and VLST. In the present study, we demonstrated marked differences in the baseline characteristics between the patients with LST and VLST, suggesting that the predominant mechanisms also might be different between LST and VLST. From these findings, distinguishing between LST and VLST in future investigations of ST seems to be crucial.

In the earlier pathological studies of BMS, nearly complete endothelialization was reported to be present by 3 to 4 months after BMS implantation. A postmortem human pathological study reported that in all 14 patients with late ST, including VLST of DES, delayed arterial healing was found to be a cardinal risk factor and was the only pathological risk factor in 3 patients (21%). However, if the predominant mechanisms of LST were to be related only to delayed arterial healing, it would be difficult to explain why the rate of ST at 1 year was similar between SES- and BMS-treated lesions despite the fact that the latter were reported to heal better pathologically. It is noteworthy that hemodialysis and insulin-dependent diabetes mellitus were highly prevalent in patients with LST. Although restenosis was dramatically reduced by SES, restenosis is most commonly seen during the first year of SES implantation. Hemodialysis and insulin-dependent diabetes mellitus were reported to be very strong risk factors for restenosis of SES. In addition, patients with LST had a markedly higher rate of TIMI grade 2 or 3 flow at the time of ST compared with those in both the EST and VLST groups, and it is possible that patients with a very aggressive restenosis process were judged as having ST. Alternatively, there might be some causal relationship between neo-intimal hyperplasia and ST within the first year. Significant neo-intimal proliferation might be prone to ultimate thrombus formation. In a postmortem human pathological study, 2 cases of DES LST and 2 cases of BMS LST were reported to be causally related to in-stent restenosis with superimposed thrombus. The hypothesis of a causal relationship between neo-intimal hyperplasia and ST could partially explain why the rate of ST at 1 year was not lower after BMS implantation than after SES implantation.

The mechanisms of VLST are currently very poorly understood. Delayed arterial healing had also been incriminated as the predominant cause of VLST. However, in a serial analysis using optical coherence tomography, additional neo-intimal coverage was observed between 6 and 12 months after SES implantation. In addition, a case report of human pathological evaluation of an SES-treated lesion showed complete endothelialization at 11 months after implantation. Despite these observations suggesting improved healing with time after DES implantation, the slopes of the cumulative incidence curve of VLST were constant (0.3% to 0.6%) up to 3 years. Therefore, some mechanisms other than delayed arterial healing must be operative in the pathogenesis of VLST. Cook et al compared the IVUS findings in 13 patients who had VLST with those findings in 144 patients.
undergoing routine IVUS examination at 8 months after DES implantation. Incomplete stent apposition was reported to be more frequent (77% versus 12%) with a larger incomplete stent apposition area in patients with VLST compared with control subjects. Stented segments in patients with VLST revealed more marked positive remodeling compared with control subjects. The same group of investigators extended the observation to another 10 patients with VLST by both IVUS and histological examination of the thrombi aspirated, demonstrating that VLST was associated with histopathological signs of inflammation and IVUS evidence of vessel remodeling. They also demonstrated that eosinophilic infiltrates were more common in thrombi harvested from patients with VLST compared with other causes of myocardial infarction. These observations were consistent with chronic inflammation (hypersensitivity) reported in several autopsy cases after DES implantation, suggesting profound chronic inflammation as one of the most dominant mechanisms of VLST.

Furthermore, the de novo atherosclerosis, defined as lipid-laden foamy macrophage infiltrates within the neointima above the stent that did not communicate with the underlying atherosclerotic plaque, was reported to be seen earlier and more frequently in lesions treated with DES compared with those treated with BMS. Those de novo atherosclerotic plaques might be susceptible to VLST.

It is intriguing that diabetic and elderly patients were less common in the group of patients with VLST, a finding consistent with reports from the Bern/Rotterdam cohort and the ESTROFA registry. Together with the finding that angiographic calcification was significantly less common in lesions with VLST, this indicates that very advanced atherosclerosis such as that often seen in diabetic and elderly patients might be less susceptible to the inflammatory reactions suspected as the dominant mechanism of VLST. Alternatively, fibrotic maturation of the relatively thick neointima after DES implantation in diabetic patients might protect the thrombogenic constituents of the plaque from being exposed to the bloodstream in a fashion similar to the plaque-sealing effect of BMS.

Relative to the status of APT at the time of ST, one third of the patients had ST after discontinuation of APT. Although the proportion of patients on aspirin monotherapy increased with time after SES implantation, long intervals between discontinuation of thienopyridine only and ST cast doubt on the causal link between discontinuation and ST, particularly in cases of VLST. Relatively short intervals between discontinuation of both thienopyridine and aspirin and ST suggest a causal relationship between discontinuation and ST. These observations are consistent with our prior report suggesting an increased risk of ST in patients stopping both aspirin and thienopyridine but not in patients stopping thienopyridine only.
Finally, it is noteworthy that multivessel ST was reported in 3.4% of patients, which accounted for 17.4% of the 121 ST patients undergoing multivessel stenting. This observation suggests that the pathological processes prone to ST may not be limited to 1 site in patients undergoing multivessel stenting. In addition, ST in 1 lesion might be the trigger of ST in another lesion through several mechanisms, including activation of platelets and the sympathetic nervous system. Considering the dismal prognosis of multivessel ST and the potential involvement of platelet activation in this situation, stringent compliance and adherence to APT seem to be particularly important in patients undergoing multivessel stenting.

The present study has several important limitations. First, although this study included the largest number of patients with SES-associated ST ever reported, we did not have data on control patients without ST. Therefore, we could not evaluate the risk factors of ST according to the timing after SES implantation. Second, we did not use angiographic core laboratory evaluation for the presence of thrombus and TIMI flow at the time of ST. Therefore, adjudication of patients with TIMI grade 2 or 3 flow as having ST was dependent on the interpretation of the site investigators. However, among 313 patients included in the angiographic substudy, 301 patients (96%) were confirmed by the angiographic core laboratory as having ARC-definite ST with angiographic evidence of thrombus. In addition, TIMI flow grade reported by the site investigators was confirmed to be concordant with the evaluation by the angiographic core laboratory in 91% of cases. Third, considering that 224 patients were reported spontaneously by the referring centers to RESTART, the accuracy of the system monitoring ST by the government and the SES manufacturing company seemed to be far from complete. In addition, we should admit that we could not guarantee consecutive enrollment of ST patients by all the participating centers. ST events in patients who had lost contact with the referring hospital were likely not to be reported. Furthermore, the mean number of ST cases per center was only 1.24. Among 543 participating centers, 279 centers did not report any ST cases. Therefore, it is possible that ST cases might have been underreported by some participating centers. Finally, although we used the ARC definition to classify the timing of ST, we are not sure whether the ARC classification of ST is the best way to account for the different pathophysiological mechanisms that may be operative at various times after stent implantation.

Conclusion

ST timing–dependent differences in baseline demographic features, TIMI flow grade, and mortality rate suggest possible differences in the predominant pathophysiological mechanisms of ST according to timing after SES implantation.

Acknowledgments

We appreciate the efforts of the investigators in the 543 participating centers and of the clinical research coordinators supporting the study. We also appreciate the secretarial support by Hiromi Yoshida, Megumi Hirose, and Mai Fujino.

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Disclosures

Dr Kimura is an advisory board member for, speaker for, and recipient of research grants from Cordis Cardiology Japan, Johnson and Johnson. Dr Kozuma is a recipient of honoraria from Cordis Cardiology Japan, Johnson and Johnson. Drs Aizawa and Ishihara are advisory board members for and recipients of honoraria from Cordis Cardiology Japan, Johnson and Johnson. Drs Miyazaki and Yamaguchi are advisory board members for Cordis Cardiology Japan, Johnson and Johnson. E. Hiyoshi and E. Nishimura are full-time employees of Cordis Cardiology Japan, Johnson and Johnson. The other authors report no conflicts.

References

CLINICAL PERSPECTIVE

Stent thrombosis (ST) after sirolimus-eluting stent implantation has not yet been adequately characterized, mainly because of its low incidence. The Registry of Stent Thrombosis for Review and Reevaluation (RESTART) is a Japanese nationwide registry of sirolimus-eluting stent–associated ST comprising 611 patients with definite ST (early [within 30 days; EST], 322 patients; late [between 31 and 365 days; LST], 105 patients; and very late [>1 year; VLST], 184 patients). Baseline demographics, clinical presentation, and long-term outcome of sirolimus-eluting stent–associated ST were compared among patients with EST, LST, and VLST. Baseline demographics were significantly different according to the timing of ST. Characteristic demographic factors for LST/VLST versus EST identified by multivariable model were renal failure, absence of circumflex target, target of chronic total occlusion, prior percutaneous coronary intervention, and age <65 years. For LST versus VLST, they were hemodialysis, heart failure, insulin-dependent diabetes mellitus, and low body mass index. Patients with LST had a significantly higher rate of Thrombolysis in Myocardial Infarction grade 2/3 flow (36%) at the time of ST than those with EST (13%; P<0.0001) and VLST (17%; P<0.0001). Mortality rate at 1 year after ST was significantly lower in patients with VLST (10.5%) compared with those with EST (22.4%; P=0.003) or LST (23.5%; P=0.009). From these findings, distinguishing between LST and VLST in future investigations of ST seems to be crucial. ST timing–dependent differences in baseline demographic features, Thrombolysis in Myocardial Infarction flow grade, and mortality rate suggest possible differences in the predominant pathophysiological mechanisms of ST according to timing after sirolimus-eluting stent implantation.
Comparisons of Baseline Demographics, Clinical Presentation, and Long-Term Outcome Among Patients With Early, Late, and Very Late Stent Thrombosis of Sirolimus-Eluting Stents: Observations From the Registry of Stent Thrombosis for Review and Reevaluation (RESTART)

Takeshi Kimura, Takeshi Morimoto, Ken Kozuma, Yasuhiro Honda, Teruyoshi Kume, Tadanori Aizawa, Kazuaki Mitsudo, Shunichi Miyazaki, Tetsu Yamaguchi, Emi Hiyoshi, Eizo Nishimura and Takaaki Isshiki

for the RESTART Investigators

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Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2010/06/17/CIRCULATIONAHA.109.903955.DC1

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## SUPPLEMENTAL MATERIAL

Supplemental Table 1. Baseline angiographic findings in the angiographic sub-study: EST vs. LST/VLST

<table>
<thead>
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<th>Variables</th>
<th>EST</th>
<th>LST/VLST</th>
<th>P value</th>
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<tr>
<td>N=169</td>
<td>N=144</td>
<td></td>
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</tr>
<tr>
<td><strong>Lesion location</strong></td>
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<td></td>
<td>0.52</td>
</tr>
<tr>
<td>LMCA</td>
<td>3 (1.8%)</td>
<td>2 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>97 (57%)</td>
<td>74 (52%)</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>21 (12%)</td>
<td>26 (18%)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>48 (28%)</td>
<td>42 (29%)</td>
<td></td>
</tr>
<tr>
<td><strong>Pre TIMI flow</strong></td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>TIMI 0</td>
<td>32 (19%)</td>
<td>30 (21%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 1</td>
<td>12 (7.1%)</td>
<td>10 (6.9%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 2</td>
<td>21 (12%)</td>
<td>24 (17%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 3</td>
<td>104 (62%)</td>
<td>80 (56%)</td>
<td></td>
</tr>
<tr>
<td><strong>AHA/ACC lesion type</strong></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>A</td>
<td>2 (1.2%)</td>
<td>1 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>6 (3.6%)</td>
<td>9 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>63 (37%)</td>
<td>60 (42%)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>98 (58%)</td>
<td>74 (51%)</td>
<td></td>
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<tr>
<td><strong>Lesion type</strong></td>
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<td>0.56</td>
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<tr>
<td>Discrete</td>
<td>22 (13%)</td>
<td>16 (11%)</td>
<td></td>
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<tr>
<td>Tubular</td>
<td>56 (33%)</td>
<td>56 (39%)</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>91 (54%)</td>
<td>72 (50%)</td>
<td></td>
</tr>
<tr>
<td>Thrombus</td>
<td>36 (21%)</td>
<td>29 (30%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Calcification (moderate / severe)</td>
<td>64 (38%)</td>
<td>44 (31%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>87 (51%)</td>
<td>71 (49%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Chronic total occlusion</td>
<td>12 (7.1%)</td>
<td>23 (16%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Residual dissection</td>
<td>28 (17%)</td>
<td>6 (4.2%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Overlapping stent</td>
<td>68 (40%)</td>
<td>65 (45%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>22.0±14.1</td>
<td>19.0±10.3</td>
<td>0.046</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>-------</td>
</tr>
<tr>
<td>Reference diameter pre-procedure (mm)</td>
<td>2.5±0.57</td>
<td>2.57±0.59</td>
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<tr>
<td>Minimal luminal diameter (mm)</td>
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</tr>
<tr>
<td>Pre-procedure</td>
<td>0.56±0.45</td>
<td>0.56±0.44</td>
<td>0.96</td>
</tr>
<tr>
<td>Post-procedure in segment</td>
<td>1.88±0.44</td>
<td>1.9±0.47</td>
<td>0.73</td>
</tr>
<tr>
<td>Post-procedure in stent</td>
<td>2.22±0.4</td>
<td>2.32±0.41</td>
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</tr>
<tr>
<td>Percent diameter stenosis (%)</td>
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<tr>
<td>Pre-procedure</td>
<td>77.2±17.2</td>
<td>78.4±17.7</td>
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<tr>
<td>Post-procedure in segment</td>
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<td>26.5±11.2</td>
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<tr>
<td>Post-procedure in stent</td>
<td>15.6±8.7</td>
<td>14.1±8.9</td>
<td>0.15</td>
</tr>
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</table>

ACC = American College of Cardiology, AHA = American Heart Association, EST = early stent thrombosis, LAD = left anterior descending coronary artery, LCX = left circumflex coronary artery, LMCA = left main coronary artery, LST = late stent thrombosis, RCA = right coronary artery, TIMI = thrombolysis in myocardial infarction, VLST = very late stent thrombosis.
Supplemental Table 2. Baseline angiographic findings in the angiographic sub-study: LST vs. VLST

<table>
<thead>
<tr>
<th>Variables</th>
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<th>VLST N=85</th>
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<td>Lesion location</td>
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<tr>
<td>LAD</td>
<td>32 (54%)</td>
<td>42 (49%)</td>
<td></td>
</tr>
<tr>
<td>LCX</td>
<td>12 (20%)</td>
<td>14 (16%)</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>14 (24%)</td>
<td>28 (33%)</td>
<td></td>
</tr>
<tr>
<td>Pre TIMI flow</td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>TIMI 0</td>
<td>9 (15%)</td>
<td>21 (25%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 1</td>
<td>7 (12%)</td>
<td>3 (3.5%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 2</td>
<td>10 (17%)</td>
<td>14 (16%)</td>
<td></td>
</tr>
<tr>
<td>TIMI 3</td>
<td>33 (56%)</td>
<td>47 (55%)</td>
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<td>AHA/ACC lesion type</td>
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<td>0.62</td>
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<tr>
<td>A</td>
<td>0 (0%)</td>
<td>1 (1.2%)</td>
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<tr>
<td>B1</td>
<td>3 (5.1%)</td>
<td>6 (7.1%)</td>
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<td>B2</td>
<td>27 (46%)</td>
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<td>C</td>
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<td>Tubular</td>
<td>22 (37%)</td>
<td>34 (40%)</td>
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</tr>
<tr>
<td>Diffuse</td>
<td>28 (47%)</td>
<td>44 (52%)</td>
<td></td>
</tr>
<tr>
<td>Thrombus</td>
<td>13 (22%)</td>
<td>16 (19%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Calcification (moderate / severe)</td>
<td>25 (42%)</td>
<td>19 (22%)</td>
<td>0.01</td>
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<tr>
<td>Bifurcation</td>
<td>28 (47%)</td>
<td>43 (51%)</td>
<td>0.71</td>
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<tr>
<td>Chronic total occlusion</td>
<td>7 (12%)</td>
<td>16 (19%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Residual dissection</td>
<td>3 (5.1%)</td>
<td>3 (3.5%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Overlapping stent</td>
<td>31 (53%)</td>
<td>34 (40%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>18.4±10.5</td>
<td>19.4±10.2</td>
<td>0.63</td>
</tr>
<tr>
<td>Reference diameter pre-procedure (mm)</td>
<td>2.5±0.62</td>
<td>2.62±0.57</td>
<td>0.22</td>
</tr>
<tr>
<td>Minimal luminal diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-procedure</td>
<td>Post-procedure in segment</td>
<td>Post-procedure in stent</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------</td>
<td>---------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Percent diameter stenosis (%)</td>
<td>0.53±0.4</td>
<td>1.83±0.53</td>
<td>2.25±0.43</td>
</tr>
<tr>
<td></td>
<td>0.58±0.46</td>
<td>1.95±0.43</td>
<td>2.36±0.39</td>
</tr>
<tr>
<td></td>
<td>0.51</td>
<td>0.17</td>
<td>0.11</td>
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</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>Pre-procedure</th>
<th>Post-procedure in segment</th>
<th>Post-procedure in stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent diameter stenosis (%)</td>
<td>78.9±17.6</td>
<td>28.8±12.2</td>
<td>15.9±8.6</td>
</tr>
<tr>
<td></td>
<td>78.0±17.9</td>
<td>24.8±10.2</td>
<td>12.9±8.9</td>
</tr>
<tr>
<td></td>
<td>0.76</td>
<td>0.04</td>
<td>0.04</td>
</tr>
</tbody>
</table>

ACC = American College of Cardiology, AHA = American Heart Association, EST = early stent thrombosis, LAD = left anterior descending coronary artery, LCX = left circumflex coronary artery, LMCA = left main coronary artery, LST = late stent thrombosis, RCA = right coronary artery, TIMI = thrombolysis in myocardial infarction, VLST = very late stent thrombosis.
Supplemental Appendix:

List of the participating centers and the investigators

Aichi Cardiovascular and Respiratory Center: Syuuiji Harada, Toru Asai
Aichi Medical University Hospital: Takayuki Ito, Hiroaki Takashima
Aidunishi Hospital: Naoto Ohara
Aizawa Hospital: Syunpei Sakurai, Tomohiro Suzuki
Akashi Medical Center: Masahito Kawata,
Akita University Hospital: Hiroshi Ito, Kenji Iino
Amakusa Chuo General Hospital: Tomio Wakita
Amakusa Medical Center: Naritsugu Sakaino
Anjo Kosei Hospital: Kenji Takemoto
Aomori Prefectural Central Hospital: Fuminobu Yoshimachi, Dai Miura
Aozora Hospital: Yoshihiro Hirose, Ito Hirotaka
Asahi Rosai Hospital: Tomomitsu Tani
Asahikawa City Hospital: Yoshinao Ishii
Asahikawa Medical College Hospital: Naoyuki Hasebe, Toshiharu Takeuchi
Atsugi Municipal Hospital: Kenichi Maie, Shinichiro Takizawa
Ayabe City Hospital: Kouji Shiga
Ayase Heart Hospital: Imun Tei, Hidenari Hozawa
Bellland General Hospital: Iku Toda, Nobuya Matsushita
Cardio-vascular Center Hokkaido Ohno Hospital: Takehiro Yamashita, Toshiya Satoh
Caress Sappro Hokko Memorial Hospital: Masayuki Sakurai, Yoichi Nozaki
Chiba Aoba Municipal Hospital: Nobuaki Shikama
Chiba Kaihin Municipal Hospital: Mizuo Nameki
Chiba Rosai Hospital: Yasuro Ishikawa
Chiba Tokusyuukai Hospital: Osamu Ueda
Chiba University Hospital: Yoshio Kobayashi, Naoki Ishio
Chibaniishi-General Hospital: Kazuo Misumi
Chikamori Hospital: Kazuya Kawai, Syuuiichi Seki
Chitose City Hospital: Takefumi Ozaki
Chukyo Hospital: Naoya Tsuboi, Kenji Kada
Cibune General Hospital: Shigeki Ito, Kozo Ninomiya
City Hospital Iizuka: Yutaka Kagiyama
Comfort Hospital: Junichi Hirose
Cyno Kousei Hospital: Tutomu Tanaka, Masahiko Koda
Daido Hospital: Shinichi Kamide
Daini Okamoto General Hospital: Takafumi Yagi
Disaster Medical Center: Yasuhiro Sato
Dokkyo Medical University: Shigeo Horinaka, Shichiro Abe, Hiroshi Yagi
East Medical Center Higashi Municipal Hospital City of Nagoya: Shigenori Ito
Ehime Prefectural Central Hospital: Makoto Suzuki, Hirokazu Habara
Ehime Prefectural Imabari Hospital: Hiroshi Matsuoka, Hideo Kawakami
Ehime Prefectural Minamiuwa Hospital: Yukio Kazatani
Ehime Prefectural Niihama Hospital: Shozo Sueda, Tomoki Sakaue
Ehime Rosai Hospital: Shunsuke Mikami
Ehime University Hospital: Hideki Okayama, Jun Aono
Fuchu Hospital: Shiro Yanagi
Fuji City General Hospital: Hiroshi Sakamoto, Satoshi Arase
Fujimoto Hayasuzu Hospital: Kouichi Kihara, Masanori tsurugida
Fujinomiya City General Hospital: Nobuyuki Wakahara
Fujisawa Shounandai Hospital: Takahiro Takei
Fujita Health University Hospital: Yukio Ozaki, Hiroyuki Naruse
Fukaya Red Cross Hospital: Masao Yamazaki, Makoto Sekiguchi
Fukuchiyama City Hospital: Manabu Nishio
Fukui General Hospital: Kazuo Satake, Haruhisa Sirasaki
Fukui Prefectural Hospital: Takahiko Aoyama, Susumu Fujino
Fukuiken Saiseikai Hospital: Kouji Maeno
Fukuoka City Hospital: Kiyoshi Hironaga
Fukuoka City Medical Association Hospital: Yosuke Katsuda, Hiroshi Saito
Fukuoka Kinen Hospital: Hideki Fujiwara
Fukuoka Shin Mizumaki Hospital: Tadao Kuruma
Fukuoka Tokushukai Medical Center: Hideki Shimomura, Yuji Ogura
Fukuoka University Hospital: Kenjiro Saku, Akira Kawamura
Fukuoka Wajiro Hospital: Taro Saito, Keita Nakamura
Fukushima Medical University Hospital: Yasuchika Takeishi, Hiroyuki Kunii
Fukuyama Cardiovascular Hospital: Seiichi Haruta, Hideo Takebayashi
Fukuyama City Hospital: Makoto Nakahama, Katsushi Hashimoto
Fukuyama Medical Center: Yutaka Kajikawa
Funabashi Municipal Medical Center: Shigeru Fukuzawa
Gakkentoshi Clinic: Hiroaki Yamamoto, Akira Ito
Gakkentoshi Hospital: Ryuta Sakai
General Ota Hospital: Nobuyuki Kobayashi
Gifu Prefectural General Medical Center: Toshiyuki Noda, Makoto Iwama
Gifu Prefectural Tajimi Hospital: Takeshi Hibino
Gifu University Hospital: Kazuhiko Nishigaki
Hachinohe City Hospital: Yoichi Inokubo
Hadano Red Cross Hospital: Reimin Sawada
Hagiwarayuou Hospital: Jun Segawa
Haibara General Hospital: Masaki Matsunaga
Hakodate General Central Hospital: Hiroshi Asajima, Naotaka Saito
Hakujikai Memorial Hospital: Kunio Tanaka
Hamamatsu Medical Center: Masakazu Kobayashi
Hamamatsu City Hospital: Makoto Usui
Handa City Hospital: Kiyokazu Shimizu, Tetsu Nakajima
Harasanshin General Hospital: Yasuo Hayashi, Yasuo Hayashi
Hashimoto Municipal Hospital: Katsuhiko Yamamoto, Hironobu Hoshiya
Hayama Heart Center: Hiroshi Amemiya, Masakazu Goto
Heart Center Iwata: Okazaki Katsuo
Heartmind Kokura-dai Heart Clinic: Yasuhiko Ooshiro, Atsushi Miyagi
Higashi Kani Hospital: Tomoyasu Shin
Higashi Takarazuka Satoh Hospital: Satoru Otsuji, Masashi Ikushima
Higashihiroshima Medical Center: Kaoru Yanagihara, Yuiro Ono
Higashiosaka City General Hospital: Yoshiyuki Kijima, Megumi Kunishige
Hikone Municipal Hospital: Yoshihiro Himura, Tsuyoshi Miyazawa
Hiraka General Hospital: Nobuyo Sekiguchi
Hirakata Kohsai Hospital: Shoji Kitaguchi, Eiji Tada, Yoshisumi Haruna
Hiratsuka City Hospital: Takashi Matsubara, Masaru Shibata
Hiratsuka Kyosai Hospital: Shigeo Umezawa, Yuko Onishi
Hirosaki University Hospital: Ken Okumura, Takumi Higuma
Hiroshima City Hospital: Ichiro Inoue
Hiroshima General Hospital: Takashi Fujii, Shuji Tsujiyama
Hiroshima Kyoeritu Hospital: Hirohiko Murata, Sunao Takaya
Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital: Syunichi
Kaseda

Hiroshima University Hospital: Yasuki Kihara, Futoshi Tadehara
Hiroshima-Nishi Medical Center: Hitoshi Fujiwara, Takashi Umemura
Hitachiomiya Saiseikai Hospital: Yukiyo Ogata
Hitoyoshi General Hospital: Hideki Oka, Yuri Iwasaki
Hokkaido Cancer Center: Takashi Takenaka
Hokkaido Chuo Rosai Hospital: Hideyuki Takano, Hiroto Sakai
Hokkaido Social Insurance Hospital: Keiichi Igarashi, Jungo Furuya
Hokuriku Hospital: Hisanori Oiwake, Yuuji Itou
Hokusei Hospital: Satoshi Tanazawa
Hokusho Central Hospital: Jun Fukui, Akiyo Ninomiya
Hokuto Hospital: Ichiro Yoshida
Horikawa Hospital: Haruki Endo
Hoshi General Hospital: Mikihiro Kijima, Yuichi Ujiie
Houju Memorial Hospital: Kiyoo Mori
Hyogo Brain and Heart Center: Takatoshi Hayashi, Sachiyoh Iwata
Hyogo College of Medicine: Toru Arii
Hyogo Prefectural Amagasaki Hospital: Yoshiaki Takatsu, Ryoji Taniguchi
Hyogo Prefectural Nishinomiya Hospital: Yoshihiro Chimori, Tetsuro Matsuoka
Ibaraki Prefectural Nishinomiya Hospital: Noriyuki Takeyasu, Daisuke Abe
Ibaraki Seinan Medical Center Hospital: Hiroshi Maeda
Ibi Kousei Hospital: Hironobu Kawasaki
Iida Municipal Hospital: Kazuya Yamamoto
Ikegami General Hospital: Yoshihito Sakata, Yasufumi Hayama
Imazato Heart Clinic: Shinji Negoro
Imizu City Hospital: Hisanari Ishise, Hiroshi Ueno
International Goodwill Hospital: Makoto Shimizu
Isehara Kyodo Hospital: Shunsuke Takagi
Iseikai Hospital: Takashi Yamada
Ishikawa Prefectural Central Hospital: Hounin Kanaya, Takao Matsubara
IUHW Atami Hospital: Shigemasa Tomohiko, Syunichi Kobayashi
Iwaki Kyouritsu Hospital: Masafumi Sugi
Iwakuni Clinical Center: Kunihisa Kohno
Iwate Medical University Hospital: Tomonori Itoh
Iwate Prefectural Central Hospital: Akihiro Nakamura
Iwatsuki-minami Hospital: Yutaka Koyama
Izumi Municipal Hospital: Yoshio Kawase
Izumiotsu Municipal Hospital: Motoaki Kitagawa
JA Kochi Hospital: Hiroyuki Ikefuji
JA Shizuoka Kohseiren Enshu Hospital: Hiroyuki Takase
Japan Red Cross Musashino Hospital: Toru Oabayashi, Takamichi Miyamoto
Japan Self Defence Central Hospital: Akemi Uehata, Akira Hamabe
Japanese Red Cross Fukuoka Hospital: Hiroshi Menu
Japanese Red Cross Hamamatsu Hospital: Kei Tawarahara
Japanese Red Cross Kochi Hospital: Takashi Furuno, Keisuke Morimoto
Japanese Red Cross Kumamoto Hospital: Yasuhiro Ogata, Ryusuke Tsunoda, Jun Hokamaki
Japanese Red Cross Society Himeji Hospital: Naoki Mukohara
Japanese Red Cross Society Wakayama Medical Center: Hiroki Sakamoto, Hiroshi Ueda
Japanese Red Cross Takayama Hospital: Eisyun Horibe
Japanese Redcross Nagoya First Hospital: Haruo Kamiya
Jichi Medical University Hospital: Takaaki Katsuki, Tomokazu Ikemoto
Joetsu General Hospital: Tatsuya Saigusa
Jouban Hospital: Tadami Maeyama
JR Tokyo General Hospital: Shinichi Usui
Juntendo University Hospital: Hiroyuki Daida, Katsumi Miyauchi
Juntendo University Shizuoka Hospital: Satoru Suwa
Kagawa Inoshita Hospital: Kentaro Matsumura
Kagawa Prefectural Shiratori Hospital: Shigenobu Bando, Akiyoshi Nishikado
Kagoshima Medical Center: Kazuhiko Nakamura, Masahiro Sonoda, Hitoshi Nakajima Katsuro Kashima,
Kainan Hospital: Shinichi Sakai, Takashi Yamada
Kakegawa City General Hospital: Hirohide Uchiyama, Hirohumi Okazaki
Kameda Medical Center: Akihiko Matsumura, Masakazu Ohno
Kanagawa Cardiovascular and Respiratory Center: Kazuki Fukui
Kanazawa Arimatsu Hospital: Masaaki Hirono
Kanazawa University Hospital: Masakazu Yamagishi, Hidekazu Ino
Kanoya Heart Center: Hidekazu Arai
Kansai Medical University Hirakata Hospital: Hiroshi Kamihata, Kenichi Manabe
Kansai Medical University Takii Hospital: Yoshihiro Yamamoto
Kansai Rosai Hospital: Shinsuke Nanto, Masaki Awata
Kanto Central Hospital of the Mutual Aid Association of Public School Teachers:
Hiroshi Ikenouchi, Yasuyuki Sugishita
Kanto Medical Center NTT EC: Satoshi Ohnishi, Masao Yamasaki
Kanto Rosai Hospital: Atsu Namiki
Kariwa General Hospital: Toru Ida
Kasugai Municipal Hospital: Akihiro Terasawa, Yuzo Hayashi
Kasukabe Chuo General Hospital: Minoru Shimizu, Satoru Tohara
Kasukabe Municipal Hospital: Ken Arima
Kawachi General Hospital: Young-Jae Lim, Shigeo Kawano
Kawakita General Hospital: Yoichi Sugimura, Akio Oshima
Kawasaki Medical School Hospital: Hiroyuki Okura, Takahiro Kawamoto
Kawasaki Municipal Kawasaki Hospital: Kenya Nishizawa
Kawasaki Saiwai Hospital: Nobuhiro Omura
Kawashima Hospital: Takeshi Nishiuchi, Shunji Hashidume
Kensei Hospital: Toshinori Iida
Kinki University Hospital: Shunichi Miyazaki, Akio Kimura
Kirishima Medical Center: Toshihiko Terashi
Kishiwada City Hospital: Mitsuo Matsuda, Takashi Uegaito
Kitaibaraki Municipal Hospital: Keichou Miyamoto
Kitakyushu City Yahata Hospital: Takashi Harada
Kitano Hospital: Ryuji Nohara, Moriaki Inoko
KKR Sapporo Medical Center: Shunichi Saito
KKR Takamatsu Hospital: Yuichiro Takagi
Kobe City Medical Center General Hospital: Yutaka Furukawa, Natuhiko Ehara
Kobe Red Cross Hospital: Yuichi Kuroda
Kobe Rosai Hospital: Kazuo Ohnishi, Toru Ozawa
Kobe University Hospital: Junya Shite
Kochi Medical School Hospital: Yoshinori Doi, Hiroaki Kitaoka
Kochi National Hospital: Takashi Yamasaki
Kofu Kyoritsu Hospital: Yoko Kurumatani
Kofu Municipal Hospital: Takao Sawano
Kohka Public Hospital: Tomoyuki Takayama, Hiroshi Sakai
Kokura Memorial Hospital: Masashi Iwabuchi, Shinichi Shirai
Komaki City Hospital: Katsuhiro Kawaguchi
Komatsu Hospital: Hisahito Nakamori
Konan Kose Hospital: Fumio Saito
Kosei General Hospital: Shozo Hirai
Koseikai Takeda Hospital: Noriyuki Kinoshita
Koto Hospital: Eiji Tamiya
Koto Memorial Hospital: Tomoyuki Murakami, Hiroshi Mabuchi, Teruki Takeda
Kotoni Royal Hospital: Masaaki Tanehata
Koudoukai Moriguchi Ikuno Memorial Hospital: Yoshiki Kobayashi
Kouseikai Hospital: Yoshihiro Iwasaki
Kouseikai Takai Hospital: Yasunori Nishida, Shoichi Shinohara
Koyo Newtown Hospital: Hironobu Tateishi
Kumamoto Chuo Hospital: Katsuo Noda
Kumamoto Medical Center: Kazuteru Fujimoto
Kumamoto University Hospital: Hisao Ogawa, Hitoshi Sumida
Kurashiki Central Hospital: Kazuaki Mitsudo, Masao Imai
Kurume University Hospital: Takafumi Ueno
Kurume University Medical Center: Hisao Ikeda, Atsushi Kato
Kusatsu Heart Center: Hideo Tamai, Takafumi Tsuji
Kyorin University Hospital: Hideaki Yoshino
Kyoritsu General Hospital: Junichi Konishi, Hideki Mori
Kyoto City Hospital: Kinya Matsubara, Tomoko Sakamoto
Kyoto Hakuaikei Tomita Hospital: Tetsuya Tomita, Akiyoshi Kawashima
Kyoto Katsura Hospital: Shigeru Nakamura, Tomoko Kobayashi, Noriko Fujita
Kyoto Keishinkai Kizugawa Hospital: Hajime Miyanaga
Kyoto University Hospital: Takeshi Kimura, Toshihiro Tamura
Kyushu Kousei Nenkin Hospital: Masahiro Mohri
Kyushu University Hospital: Masao Takamoto
Machida Municipal Hospital: Toshiro Kurosawa
Makiminato Chuo Hospital: Koichi Higa, Youichi Uechi
Masuda Red Cross Hospital: Tadahiko Minoji, Toshihiko Uchida
Matsue Red Cross Hospital: Nobuo Shiode, Fumiyo Tunoda
Matsue Seikyo Hospital: Takayuki Maki
Matsumoto Kyoritsu Hospital: Hidetoshi Abe
Matsusaka Chuo General Hospital: Takashi Tanigawa
Matsushita Memorial Hospital: Hiroki Sugihara, Tadaaki Kamitani
Matsuyama Shimin Hospital: Tomoaki Yoshino, Kohei Ochi
Mazda Hospital: Kotaro Sumii, Yuichi Orita
Meijo Hospital: Yoshio Iwama, Akira Kimura
Meitetsu Hospital: Yoshihiro Futamura, Hiroki Sugiura, Makoto Akabosi
Mie Heart Center: Hideo Nishikawa, Hiroyuki Suzuki
Mie Prefectural General Medical Center: Katsutoshi Makino
Miki City Hospital: Kojiro Awano, Yoshitaka Ohashi
Mimuro Hospital: Naofumi Doi, Yasuhiro Takeda
Misato Central General Hospital: Osamu Hirashima
Mito General Hospital: Takayoshi Yamauchi, Yasuyuki Oyake
Mito Saiseikai General Hospital: Minoru Murata, Yoshiro Chiba
Mitsubishi Kyoto Hospital: Tetsu Mizoguchi, Takafumi Yokomatsu
Mitsui Memorial Hospital: Kazuhiro Hara, Jiro Aoki
Miyagi Cardiovascular & Respiratory Center: Yoshiaki Mibiki
Miyagi Toubu Jyunkankika: Toru Naganuma
Miyakonojo Regional Medical Center: Haruhito Kumagae
Miyazaki Hospital: Noriyuki Kose
Miyazaki Medical Association Hospital: Yoshisato Shibata, Mitsuhiro Shimomura
Miyazaki Prefectural Nobeoka Hospital: Nobuyasu Yamamoto
Miyoshi Central Hospital: Kouichi Tanaka
Moji Medical Center: Masaru Araki
Motojima General Hospital: Teiji Motojisma, Shuhei Kubota
Municipal Tsuruga Hospital: Takayuki Ikeda, Kanichi Otowa
Murakami Memorial Hospital Asahik University: Yasuo Sutani
Nagahama Red Cross Hospital: Hiroshi Hamagami, Yoshiki Ueno
Nagai Hospital: Naritatsu Saito
Nagano Red Cross Hospital: Jiro Yoshioka
Nagara Medical Center: Yoichiro Ueno, Hitoshi Nishio
Nagasaki Kawatana Medical Center: Kazuro Yoshida
Nagasaki Medical Center: Koji Oku, Saburo Kusumoto
Nagasaki Municipal Hospital: Hiroshi Nakashima
Nagasaki Municipal Medical Center: Kazuaki Yakabe
Nagasaki Prefectural Saiseikai Hospital: Koichiro Sakuragawa
Nagasaki University Hospital: Koji Maemura, Yuji Koide
Nagoya Central Hospital: Fuji Somura
Nagoya City University Hospital: Nobuyuki Oote, Shogo Suzuki
Nagoya Daini Red Cross Hospital: Haruo Hirayama, Mamoru Nanasato
Nagoya Ekisaikai Hospital: Toshikazu Sofue, Daizou Ishihara
Nagoya Tokushukai General Hospital: Teiji Asakura, Ryosuke Kametani
Nissay Hospital: Atsushi Nakagawa
Northern Okinawa Medical Center: Hiroki Uehara
Noto General Hospital: Yoshiharu Murata
Nozaki Tokushukai Hospital: Satoru Sumitsuji, Masaaki Okutsu, Kashima Ito
NTT East Corporation Sapporo Hospital: Tetsuro Kouya, Noriyuki Miyamoto
Obara Hospital: Hirotaka Miyazato
Obihiro National Hospital: Hiromi Obata
Obihiro-Kosei General Hospital: Naotoshi Sato, Toru Takahashi
Oda Hospital: Hiroaki Norita
Ogaki Municipal Hospital: Takahito Sone, Hiroaki Mukawa
Ogaki Tokushyukai Hospital: Turuta Yoshio, Ryosuke Kametani
Ogasawara Clinic: Kohichi Kawasaki, Eiichiro Imamura
Ohara Medical Center: Yukihiko Abe
Ohta Nishinouti Hospital: Nobuo Komatsu
Oita Cardiovascular Hospital: Tadafumi Akimitsu
Oita Nakamura Hospital: Toru Watanabe
Oita Oka Hospital: Yoichi Tatsukawa, Toshinobu Ishikawa
Oita Prefectural Mie Hospital: Toru Nakaishi
Oita Red Cross Hospital: Tetsu Iwao
Oji General Hospital: Katsuhisa Ishii
Okayama Chuo Hospital: Kouichirou Iwasaki
Okayama Citizens Hospital: Kiyoaki Maekawa
Okayama Medical Center: Yoshihisa Fujimoto
Okayama University Hospital: Kengo Kusano, Masato Murakami
Okazaki City Hospital: Toshikazu Tanaka, Satoshi Yanagisawa
Okinawa Kyodo Hospital: Syouki Yamauchi
Okinawa Red Cross Hospital: Yuzuru Shinzato, Yuzuru Shinzato
Ome Municipal General Hospital: Kenichiro Otomo, Shigeo Shimizu
Omihachiman Community Medical Center: Hirotaka Tatsukawa, Kan Zen, Daisuke Kanbayashi
Omori Red Cross Hospital: Yasuyuki Mochida
Omura Municipal Hospital: Yoshito Tanioka, Yoshinori Sanuki
Osaka City General Hospital: Akira Ito
Osaka City University Hospital: Tohru Kataoka, Satoshi Nishimura
Osaka Ekisaikai Hospital: Kenei Shimada, Haruyuki Taguchi
Osaka Koseinenkin Hospital: Shinji Hasegawa
Osaka Medical College Hospital: Shuji Suzuki
Osaka Red Cross Hospital: Tsukasa Inada, Fujio Hayashi
Osaka Saiseikai Noe Hospital: Shunsuke Take, Shiho Koyama
Osaka Sennin Hospital: Akio Kohama
Osaka University Hospital: Shinsuke Nanto, Junichi Kotani
Otaru Kyokai Hospital: Shigeo Kakinoki, Chika Takagi
Otaru Municipal Medical Center for Brain, Cardiovascular and Mental Disorders: Yoshitoki Takagawa
Otsubi Municipal Hospital: Nobuyuki Tanaka, Yoshikazu Shigemoto
Owase General Hospital: Takafumi Koji
PL General Hospital: Iwao Ogawa
Public Fujioka General Hospital: Masahiro Inoue
Rakuwakai Otowa Hospital: Kinzou Ueda, Masato Tanabe
Rakuyo Hospital: Eiji Shinoda
Red Cross Kyoto Daiichi Hospital: Yoshio Kohno, Masayuki Hyogo
Red CrossOkayama Hospital: Toru Ujihira, Tetsuya Satou
Red Cross Otsu Hospital: Takashi Konishi, Yoshihito Takimoto
Rokko Island Hospital: Tomofumi Doi, Shuji Mikami
Ryugasaki Saiseikai Hospital: Masahiro Toyama
Sadamoto Hospital: Toshi Honda
Saga University Hospital: Yutaka Hikichi
Sagamihara Chuo Hospital: Masayuki Abe
Saiseikai Fukuoka General Hospital: Yusuke Yamamoto, Kotaro Numaguchi, Ryo Nakamura
Saiseikai Futsukaichi Hospital: Shinichi Ando, Toshiaki Kadokami
Saiseikai Hita Hospital: Hitoshi Otsubo, Toshifumi Shimada
Saiseikai Ibaraki Hospital: Takashi Tamura, Mariko Tanaka
Saiseikai Kumamoto Hospital: Kenji Horiuchi, Shinji Tayama, Naoko Takahashi
Saiseikai Senri Hospital: Yasuji Doi, Shouji Kaibe
Saiseikai Shigakuen Hospital: Takashi Nakamura, Yoshifumi Nakahara
Saiseikai Takaoka Hospital: Tomoyuki Nakabayashi
Saiseikai Yamaguchi Hospital: Shiro Ono, Shinji Kawahara
Saiseikai Yokohama-city Eastern Hospital: Toshiya Muramatsu, Kanai Nunoya
Saiseikei Hiroshima Hospital: Koji Matsumoto
Saitama Cardiovascular And Respiratory Center: Makoto Muto, Tetsuya Ishikawa
Saitama Kinen Hospital: Muneyasu Saito, Hiroyuki Shoda
Saitama Medical Center Jichi Medical University: Norifumi Kubo, Hiroshi Funayama
Saitama Medical University Hospital: Nobuyuki Komiyama, Koichi Sano
Saitama Red Cross Hospital: Kazuyasu Takei
Sakakibara Heart Institute: Tetsuya Sumiyoshi, Ryuta Asano
Sakurabashi Waranabe Hospital: Kenishi Fujii, Atsunori Okamura
Sanokousei General Hospital: Shintarou Watanabe
Sanyudo Hospital: Hideki Abe, Osamu Kawashima
Sapporo Junkanki Hospital: Masahiro Tsuzuki, Kazuhiko Nagao
Sasebo Chuo Hospital: Yoshihisa Kizaki, Yuzo Uchida
Sassa General Hospital: Koji Nakayama
Satoh Hospital: Noboru Ishikawa, Nobuhiko Hitomi
Seikou Chuo Hospital: Takeru Kudo
Seikeikai Hospital: Toshiyuki Shibutani
Seirei Mikatahara General Hospital: Yasushi Wakabayashi, Makoto Sano
Seirei Yokohama Hospital: Eiji Uchida
Seiyu Memorial Hospital: Yoshiaki Tomobuchi, Osamu Satani
Sendai Cardiovascular Center: Masahiro Yagi, Shinya Fujii
Sendai Kosei Hospital: Naoto Inoue, Kaname Takizawa
Sendai Open Hospital: Atsushi Kato
Sendai Tokusyukai Hospital: Masahiko Ogata, Osamu Kitamukai
Seno Cardiovascular Surgery: Yoshimasa Senoo, Etsuo Mondori
Shiga Medical Center for Adults: Shigeru Ikeyama, Kunihiko Kosuga
Shiga University of Medical Science Hospital: Minoru Horie, Hiroyuki Takashima
Shimabara Hospital: Mamoru Takahashi, Yoshihiko Matoba
Shimada Municipal Hospital: Takeshi Aoyama, Michitomo Kawahito
Shimane Prefectural Hospital: Tsuyoshi Oda
Shimane University Hospital: Kazuaki Tanabe, Hidetoshi Satoh
Shin Yukuhashi Hospital: Yoshinobu Murasato, Masataka Horiuchi
Shinbeppu Hospital: Keisuke Watanabe
Shingu Municipal Medical Center: Akihiro Kawamura, Takashi Masho
Shinkatsushika Hospital: Youichi Shimizu, Masayoshi Sakakibara
Shinko Kakogawa Hospital: Makoto Kadotani
Shinnittetsu Muroran General Hospital: Takayuki Matsuki, Michihiro Iwata
Shinsenkaifai Daiichi Hospital: Hiroshi Fujita
Shin-Tokyo Hospital: Sunao Nakamura, Jin Yokoyama
Shirakawa Kosei General Hospital: Tomiyoshi Saito, Tsuneyoshi Saito
Shiroyama Hospital: Yoshihisa Shimada
Shizuoka City Shizuoka Hospital: Tomoya Onodera, Hirofumi Sugiyama
Shizuoka General Hospital: Osamu Doi, Satoshi Kaburagi
Shobara Red Cross Hospital: Hirosi Sugino
Shonan Tobu Comprehensive Hospital:
Showa General Hospital: Takahiro Tanaka
Showa University Fujigaoka Hospital: Yoichi Takeyama, Fuyuki Asano
Showa University Hospital: Yuji Hamazaki
Showa University Northern Yokohama Hospital: Masahiko Ochiai, Kazuhiro Ashida, Tadayuki Yakushiji
Shuto General Hospital: Masakazu Tanaka
Social Insurance Kyoto Hospital: Chihiro Yamada, Sei Tsunoda
Social Insurance Shiga Hospital: Osamu Yamaoka
Soga Clinic: Ryo Shimada, Takahiro Imaizumi
South Tokyo Heart Clinic: Hirofumi Murakami
Southern Tohoku General Hospital: Masahiro Ono, Mitsuru Muto
St. Luke's International Hospital: Yutaro Nishi
St. Marianna University School of Medicine: Haruki Musha, Masahiro Yamauchi
St.Marianna University School of Medicine Toyoko: Kazuhiko Misu, Katsuhiko Tsutiy
Sugita Genpaku Memorial Obama Municipal Hospital: Norito Honma
Sumitomo Hospital: Hisato Yotaro, Yuji Yasuga, Masami Miyawaki
Suzuka General Hospital: Takuya Mori, Tetsuya Seko
Tachikawa General Hospital: Masaaki Okabe, Minoru Takahashi
Tachikawa Sougo Hospital: Hidetoshi Tamura, Shinichiro Otuka
Taiyo-kai Social Welfare awachiiki iryo center: Humiaki Maeda
Takagi Hospital: Yasukazu Sato
Takaishi Fujii Hospital: Yasuhiko Matsuura
Takarazuka Hospital: Masato Baden, Yoshiaki Tsuka
Takasaki National Hospital: Toyoshi Sasaki
Takase Clinic: Akitsugu Oida
Takeda General Hospital: Hiroshi Seida
Takemoto Hospital: Yasuhiro Fujinaga, Syuji Takeda
Tama-Hokubu Medical Center: Satoshi Murasaki
Tanabe Central Hospital: Norikazu Takechi
Tane Hospital: Shinichiro Ohtani
Taragi Municipal Hospital: Yosuke Harukuchi
Teikyo University Hospital: Takaaki Isshiki, Shuichi Ishikawa
Teikyo University School of medicine University Hospital, Mizonokuchi: Tomoyuki Kunishima
Teine Keijinkai Hospital: Mitsugu Hirokami, Yoshikazu Asano
Tenri Hospital: Yoshihisa Nakagawa, Jiro Sakamoto
Tenyoudai Central Hospital: Yoshihiko Atsuchi, Hiroshi Yamaguchi
The Cardiovascular Institute Hospital: Tadanori Aizawa, Junji Yajima, Shunsuke Matsuno
The Jikei University Daisan Hospital: Atsushi Seo
The Jikei University Hospital: Michihiro Yoshimura, Takayuki Ogawa
The Jikei University School of Medicine Kashiwa Hospital: Mitsuyuki Shimizu, Toshio Hasuda
The Third Sonoda Hospital: Hiroshi Okumura
Toda Chuo General Hospital: Takashi Uchiyama
Toho University Ohashi Medical Center: Masato Nakamura, Hidehiko Hara
Toho University Omori Medical Center: Kenji Wagasuma, Hideo Amano
Toho University Sakura Medical Center: Hirohumi Noike, Takuo Iiduka
Tohoku Kosai Hospital: Mitsumasa Fukuchi, Akihiko Sugimura
Tohoku Kosei Nenkin Hospital: Yoshiaki Katabira, Tamon Yamanaka
Tokai University Hachioji Hospital: Takahiko Kiyooka
Tokai University Hospital: Yoshihiro Morino, Toshiharu Fujii
Tokushima Prefectural Central Hospital: Hiroyuki Fujinaga, Akihiro Saito
Tokushima Red Cross Hospital: Yoshikazu Hiasa, Koichi Kishi
Tokushima University Hospital: Masataka Sata, Tetsuo Wakatsuki
Tokuyama Central Hospital: Hiroshi Ogawa, Takahiro Iwami
Tokyo Hokubu Hospital: Shinichiro Yokoyama, Tadashi Akabane
Tokyo Kosei Nenkin Hospital: Seiji Ayabe
Tokyo Kyosai Hospital: Hiromasa Adachi
Tokyo Medical University Hachioji Medical Center: Kenji Takazawa, Hiroshi Kobayashi, Mineko Kinou
Tokyo Medical University Hospital: Nobuhiro Tanaka
Tokyo Medical University Ibaraki Medical Center: Shinji Ohkubo, Akihiro Fukuda
Tokyo Metropolitan Police Hospital: Tetsuro Sirai, Msatoshi Suzuki
Tokyo Rinkai Hospital: Motoyuki Onikura
Tokyo Teishin Hospital: Toru Fukatsu
Tokyo University Hospital: Jiro Ando
Tokyo Womans Medical University Yachiyo Medical Center: Shoji Haruta, Kinichi Kameyama
Tokyo-Kita Social Insurance Hospital: Yoshio Tsuruya, Takuji Katayama
Tomei-Atsugi Hospital: Fumihiko Usuba, Takehiko Nakamura
Tominaga Hospital: Kazuaki Kataoka
Toranomon Hospital: Tetsu Yamaguchi, Sugao Ishiwata, Hajime Fujimoto
Totsuka Kyoritsu Daini Hospital: Mikio Ishizuka
Tottori Chuou Hospital: Yasuyuki Yoshida
Tottori University Hospital: Osamu Igawa, Yosuke Furuse
Toyama City Hospital: Hiroaki Kiyokawa
Toyama Prefectural Central Hospital: Kazuo Usuda, Yoshiki Nagata
Toyama Red Cross Hospital: Yutaka Nitta, Tomio Taguchi
Toyama University Hospital: Hiroshi Inoue, Tomoki Kameyama
Toyohashi Heart Center: Takahiko Suzuki, Masashi Kimura
Toyohashii Municipal Hospital: Osamu Ohno, Kenshin Naruse
Toyota Kosei Hospital: Masanori Shinoda
Toyota Memorial Hospital: Ryoji Ishiki, Hisashi Umeda
Tsuchiura Kyodo General Hospital: Tunekazu Kakuta, Taro Iwamoto
Tsuchiya General Hospital: Yasuhiko Hayashi, Mamoru Toyofuku, Miyo Hatanari
Tsukazaki Hospital: Hidetaka Iida
Tsukuba Medical Center Hospital: Yuichi Noguchi, Hidetaka Nishina
Tsukuba University Hospital: Shigeyuki Watanabe
Tsuyama Chuou Hospital: Issei Komatsubara
Uchinomi Hospital: Fumiyoshi Kubo, Tsunetatsu Nanba
University Hospital Kyoto Prefectural University of Medicine: Takahisa Sawada, Takeshi Nakamura
University of Fukui Hospital: Jong-Dae Lee, Akira Nakano
University of the Ryukyus Hospital: Tomomasa Kamiyama, katsuhiko ooshiro
University of Occupational And Environmental Health Japan: Yutaka Otsuji, Shinjo Sonoda
Ureshino Medical Center: Shiro Hata
Ushiku Aiwa General Hospital: Masahiro Abe
Utsunomiya Shakahoken Hospital: Hideyuki Fujikawa
Wakayama Rosai Hospital: Ken Kasamatsu, Yasushi Hayashi
Yamada Red Cross Hospital: Morimichi Setsuda
Yamagata Saisei Hospital: Kozue Ikeda
Yamaguchi Rosai Hospital: Kosaburo Seki
Yamaguchi University Hospital: Masumori Matsuzaki, Jyutaro Yamada
Yamanashi Hospital of Social Insurance: Tukasa Ishihara
Yamanashi Prefectural Central Hospital: Kazunori Aizawa, Toshikuni Seto
Yamanashi Red Cross Hospital: Noburu Konno
Yamashina Hospital: Maki Katamura
Yamashiro Public Hospital: Kiichiro Tomiyasu, Satoshi Akabame
Yame General Hospital: Ken Kusaba
Yao General Hospital: Shozo Tanaka
Yashima General Hospital: Yoko Tominaga
Yawata Medical Center: Tatsuo Katsuki
Yayoigaoka Kage Hospital: Hiroyasu Kusaba
Yokkaichi Municipal Hospital: Satoshi Ichimiya, Masaaki Kanashiro
Yokkaichi Social Insurance Hospital: Hideo Morooka
Yokohama Central Hospital: Kouji Oiwa, Masashi Kobori
Yokohama City University Hospital: Kazuaki Uchino, Teruyasu Sugano
Yokohama City University Medical Center: Kazuo Kimura, Jun Okuda
Yokohama Minami Kyousai Hospital: Mitsuhiro Nishizaki, Hiroyuki Fujii
Yokohama Sakae Kyosai Hospital: Ichiro Michishita
Yokokura Hospital: Masayoshi Yo
Yokosuka General Hospital Uwamachi: Takamasa Iwasawa
Yokosuka Kyosai Hospital: Atsushi Takahashi, Hisashi Nozato
Yokosuka Municipal Hospital: Yuji Iwasawa
Yonanbaru Chuo Hospital: Naoki Ishikawa
Yonago Heart Clinic: Akira Hoshio, Masaharu Fukuki
Yuai Memorial Hospital: Toru Tooi
Zentsuji National Hospital: Hisanori Shinohara