Five-year clinical outcomes of first-generation versus second-generation drug-eluting stents following coronary chronic total occlusion intervention

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Abstract

Background There are limited data comparing long-term clinical outcomes between first-generation (1G) and second-generation (2G) drug-eluting stents (DESs) in patients who underwent successful percutaneous coronary intervention (PCI) for coronary chronic total occlusion (CTO) lesion. Methods A total of 840 consecutive patients who underwent PCI with DESs for CTO lesion from January 2004 to November 2015 were enrolled. Finally, a total of 324 eligible CTO patients received 1G-DES (Paclitaxel-eluting stent or Sirolimus-eluting stent, n = 157) or 2G-DES (Zotarolimus-eluting stent or Everolimus-eluting stent, n = 167) were enrolled. The clinical endpoint was the occurrence of major adverse cardiac events (MACE) defined as all-cause death, recurrent myocardial infarction (re-MI), total repeat revascularization [target lesion revascularization (TLR), target vessel revascularization (TVR), and non-TVR]. We investigated the 5-year major clinical outcomes between 1G-DES and 2G-DES in patient who underwent successful CTO PCI. Results After propensity score matched (PSM) analysis, two well-balanced groups (111 pairs, n = 222, C-statistic = 0.718) were generated. Up to the 5-year follow-up period, the cumulative incidence of all-cause death, re-MI, TLR, TVR and non-TVR were not significantly different between the two groups. Finally, MACE was also similar between the two groups (HR = 1.557, 95% CI: 0.820–2.959, P = 0.176) after PSM. Conclusions In this study, 2G-DES was not associated with reduced long-term MACE compared with 1G-DES following successful CTO revascularization up to five years.

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1 Introduction

Coronary chronic total occlusion (CTO) is found about 15%–30% of patients undergoing diagnostic coronary angiography.[1,2] Compared to non-CTO lesion, the success rates of CTO lesion is much lower (> 98% vs. 50%–88%).[3] Several factors may be attributable to this relatively low success rates, including technical complexity such as inability for guidewire crossing, high risks of serious complications during and after the procedure and requirement of skilled operators.[4] However, successful CTO percutaneous coronary intervention (PCI) can improve quality of life and left ventricular systolic function, and reduce ischemia.[5,6] Several studies[7,8] had showed acceptable mid-term to long-term survival outcomes after successful CTO PCI.

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Compared to plain old balloon angioplasty (POBA), bare-metal stents (BMS) implantation showed better outcomes.\[^9\] The first-generation (1G) drug-eluting stents (DES) such as Sirolimus-eluting stents (SES) or Paclitaxel-eluting stents (PES) were also associated with reductions in angiographic target vessel revascularization (TVR) and major adverse cardiac events (MACE) compared with BMS.\[^10,11\] Therefore, in present “real world” practice, BMS was replaced by DES because its anti-proliferative and anti-inflammatory characteristics.\[^12\] Many data suggested that DES can enhance long-term patency rates and freedom from restenosis and repeated revascularization compared with BMS in patients with CTO.\[^9\] Recently several studies showed clinical outcomes comparison between 1G-DES and second-generation (2G)-DES [Zotarolimus-eluting stent (ZES) or Everolimus-eluting stent (EES)]\[^13–15\] But these studies showed relatively short-term or mid-term outcomes (three years)\[^16\] compared with our study. Thus, we investigated the 5-year long-term major clinical outcomes between 1G-DES and 2G-DES in patient with CTO lesions underwent successful CTO PCI.

2 Methods

This study is a single-center, prospective, all-comer registry designed to reflect the “real world” practice from January 2004 to November 2015. Data were obtained from CTO registry of Korea University Guro Hospital (KUGH), Seoul, South Korea and collected by trained study-coordinators with a standardized case report form. The study protocol was approved by Medical Device Institutional Review Board of KUGH according to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study prior to enrollment.

2.1 Study population

A total of 4909 consecutive patients were diagnosed with significant coronary artery disease (≥ 70% of coronary stenosis) by coronary angiogram. Among these patients, 840 patients (17.1%) had CTO on the coronary main vessels. Exclusion criteria were optimal medical treatments (n = 410), previous coronary artery bypass graft (n = 12), history of cardiogenic shock or cardiopulmonary resuscitation (n = 7), failed PCI (n = 40), POBA (n = 13), other kinds of stents implantation except for SES, PES, ZES, and EES (n = 47), stent size required to treat lesion > 3.5 mm (maximum diameter of SES, n = 14), and not participate or follow-up loss (n = 15). Finally, a total of 324 eligible CTO patients who underwent PCI with 1G-DES (SES: n = 54 or PES: n = 103, total n = 157) or 2G-DES (ZES: n = 126 or EES: n = 41, total n = 167) were enrolled. After propensity score-matching (PSM) analysis, two PSM groups (222 pairs, n = 111) were generated (Figure 1).

Figure 1. Flow chart. *Other kinds of stents except for sirolimus-eluting stent, paclitaxel-eluting stent, zotarolimus-eluting stent or everolimus-eluting stent. CABG: coronary artery bypass graft; CPR: cardiopulmonary resuscitation; CTO: chronic total occlusion; OMT: optimal medical treatment; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty; SES: sirolimus-eluting stent; 1G-DES: first-generation drug-eluting stents; 2G-DES: second-generation drug-eluting stents.
2G-DES group, 80% of the vessels were treated with ZES \((n = 88)\) and 20% of the vessels treated with EES \((n = 23)\).

2.2 PCI procedure and medical treatment

A diagnostic coronary angiography and PCI were done through either the femoral or radial artery after an administration of unfractionated heparin \((70–100 \text{ IU/kg})\). Patient’s activated clotting time was maintained above 250 seconds during the procedure. All patients received a loading dose of 200 to 300 mg aspirin and 300 to 600 mg of clopidogrel as the dual antiplatelet regimen and maintained with 100 mg of aspirin and 75 mg of clopidogrel. After stent implantation, dual antiplatelet therapy \((100 \text{ mg daily aspirin and } 75 \text{ mg daily clopidogrel})\) was prescribed for at least 12 months. During hospitalization period, all the enrolled patients had taken cardiovascular beneficial medications, including beta-blockers, angiotensin converting enzyme inhibitors, or angiotensin receptor blockers, calcium channel blockers, and lipid lowering agents. After discharge, the patients were encouraged to stay on the same medications they received during hospitalization.

2.3 Study definitions and clinical follow-up

CTO is defined as a complete obstruction of the coronary vessel with thrombolysis in myocardial infarction (TIMI) flow grade 0 for at least three months.\(^{[1]}\) A successful PCI was defined as the achievement of an angiographic residual stenosis than 30\% and final TIMI blood flow grade 3 on CTO vessel. The coronary main vessels was defined as stenosis than 30\% and final TIMI blood flow grade 3 on CTO vessel. The recording of cardiovascular risk factors and past medical histories were based on patients’ self-report. All participants were required to visit the outpatient department of cardiology at the end of the first month and then every three to six months after the index CTO PCI procedure and we could follow up on the clinical data of all enrolled patients through face-to-face interviews at regular outpatient clinic, medical chart reviews, and telephone contacts.

2.4 Statistical analysis

For continuous variables, differences between the two groups were evaluated with the unpaired \(t\)-test or Mann-Whitney rank test. Data were expressed as mean ± SD. For discrete variables, differences were expressed as counts and percentages and analyzed with \(\chi^2\) or Fisher’s exact test between the groups as appropriate. To adjust for any potential confounders, PSM analysis was performed using the logistic regression model. We tested all available variables that could be of potential relevance: gender \((\text{men})\), age, systolic blood pressure, left ventricular ejection fraction, ST-segment elevation myocardial infarction (STEMI), non-STEMI, cardiovascular diseases risk factors \((\text{hypertension, diabetes, dyslipidemia, chronic kidney disease, cerebrovascular accident, peripheral vascular disease, previous history of MI, previous history of PCI, current smoker})\), laboratory findings \((\text{i.e., creatine kinase myocardial band, troponin T, high-sensitivity C-reactive protein, lipid profiles and serum creatinine})\), angiographic and procedural characteristics. The PSM analysis was estimated with the use of C-statistic for the logistic regression model \((\text{C-statistics } = 0.718)\). Patients in the 1G-DES group were then one-to-one matched to those in the 2G-DES group according to propensity scores with the nearest available pair matching method. Subjects were matched with a caliper width equal to 0.01. Between the two groups were compared with the log-rank test. Proportional hazard models were used to assess the hazard ratio of the 1G-DES group compared with the 2G-DES group adjusted propensity score. For all analyses, a two-sided \(P\)-value of < 0.05 was considered statistically significant. All data were processed with SPSS \((\text{version 20.0, SPSS-PC, Inc. Chicago, Illinois})\).
3 Results

Table 1 shows baseline, angiographic and procedural characteristics of the study population. Before PSM adjustment, the mean age of the 1G-DES group was 60.2 ± 10.6 years and 2G-DES was 62.0 ± 10.5 years (P = 0.123). Gender distribution (men) was also similar between the two groups (74.5% vs. 78.4%, P = 0.405). The numbers of dyslipidemia (33.8% vs. 22.8%, P = 0.028) and current smokers (51.6% vs. 29.3%, P < 0.001) were significantly higher in the 1G-DES group. The numbers of Rentrop collateral grade I patients were higher in the 1G-DES (27.4% vs. 13.8%, P = 0.002) but Rentrop collateral grade II patients were higher in the 2G-DES (52.7% vs. 31.8%, P = 0.003). Table 2 shows clinical outcomes such as, MACE, all-cause death, cardiac death, non-fatal MI, total repeat revascularization [TLR-CTO vessel, TVR-CTO vessel, non-TV R (non-CTO vessel)] by Cox-proportional hazards ratio analysis and Kaplan-Meir curved analysis up to five years. Before and after PSM, the cumulative incidences of MACE, all-cause death, MI, total repeat revascularization, TLR-CTO vessel, TVR-CTO vessel, and non-TV R-CTO vessel were similar between the two groups. Figure 2 shows Kaplan-Meir curved analysis of MACE, TLR-CTO vessel, TVR-CTO vessel up to 5-year.

Table 1. Baseline and angiographic characteristics.

| Variables                        | Entire patients | Propensity score-matched patients |
|-----------------------------------|-----------------|----------------------------------|
|                                   | 1G-DES (n = 157) | 2G-DES (n = 167) | P-value | 1G-DES (n = 111) | 2G-DES (n = 111) | P-value |
| Gender, men                       | 117 (74.5%)     | 131 (78.4%)     | 0.405 | 86 (77.5%)     | 83 (74.8%)     | 0.637   |
| Age, yrs                          | 60.2 ± 10.6     | 62.0 ± 10.5     | 0.123 | 61.1 ± 10.0    | 61.6 ± 10.9    | 0.749   |
| Systolic blood pressure, mmHg     | 144.0 ± 26.6    | 141.1 ± 21.3    | 0.285 | 140.4 ± 24.6   | 141.8 ± 20.0   | 0.455   |
| LVEF                              | 50.1% ± 10.6%   | 51.5% ± 12.7%   | 0.294 | 50.9% ± 10.0%  | 51.6% ± 12.8%  | 0.698   |
| ST segment elevation MI           | 19 (12.1%)      | 11 (6.6%)      | 0.087 | 6 (5.4%)       | 7 (6.3%)       | 0.775   |
| Non-ST segment elevation MI       | 24 (15.3%)      | 19 (11.4%)     | 0.300 | 14 (12.6%)     | 15 (13.5%)     | 0.842   |
| Hypertension                      | 97 (61.8%)      | 107 (64.1%)    | 0.670 | 71 (64.0%)     | 59 (62.2%)     | 0.781   |
| Diabetes mellitus                 | 56 (35.7%)      | 66 (39.5%)     | 0.474 | 41 (36.9%)     | 40 (36.0%)     | 0.889   |
| Dyslipidemia                      | 53 (33.8%)      | 38 (22.8%)     | 0.028 | 27 (24.3%)     | 30 (27.0%)     | 0.645   |
| Chronic kidney disease            | 10 (6.4%)       | 14 (8.4%)      | 0.489 | 5 (4.5%)       | 9 (8.1%)       | 0.269   |
| Cerebrovascular accident          | 9 (5.7%)        | 15 (9.0%)      | 0.264 | 9 (8.1%)       | 10 (9.0%)      | 0.810   |
| Ischemic stroke                   | 6 (3.8%)        | 11 (6.7%)      | 0.087 | 6 (5.4%)       | 9 (9.9%)       | 0.226   |
| Hemorrhagic stroke                | 3 (1.9%)        | 4 (3.1%)       | 0.503 | 3 (2.7%)       | 1 (1.1%)       | 0.416   |
| Peripheral vessel disease         | 8 (5.1%)        | 15 (9.0%)      | 0.173 | 7 (6.3%)       | 4 (3.6%)       | 0.354   |
| Previous MI                       | 26 (16.6%)      | 27 (16.2%)     | 0.924 | 19 (17.1%)     | 11 (9.9%)      | 0.116   |
| Previous PCI                      | 38 (24.2%)      | 36 (21.6%)     | 0.571 | 25 (22.5%)     | 17 (15.3%)     | 0.170   |
| Current smoker                    | 81 (51.6%)      | 49 (29.3%)     | < 0.001 | 50 (45.0%) | 40 (36.0%) | 0.172 |
| CK-MB, mg/dL                      | 12.2 ± 32.4     | 9.8 ± 24.5     | 0.462 | 11.2 ± 29.7    | 11.6 ± 28.4    | 0.919   |
| Troponin T, mg/dL                 | 0.24 ± 0.81     | 0.13 ± 0.28      | 0.254 | 0.11 ± 0.43    | 0.18 ± 0.66    | 0.410   |
| High sensitivity CRP, mg/dL       | 1.8 ± 5.0       | 2.2 ± 8.0      | 0.628 | 1.5 ± 5.1      | 2.7 ± 9.0      | 0.300   |
| Total cholesterol, mg/L           | 164.9 ± 39.0    | 168.1 ± 41.4    | 0.508 | 163.9 ± 40.1   | 168.5 ± 35.2   | 0.401   |
| Triglyceride, mg/L                | 146.6 ± 78.4    | 143.0 ± 97.0    | 0.737 | 146.5 ± 77.2   | 145.4 ± 102    | 0.936   |
| HDL cholesterol, mg/L             | 44.5 ± 32.5     | 42.2 ± 11.4     | 0.436 | 45.3 ± 38.9    | 43.4 ± 11.5    | 0.650   |
| LDL cholesterol, mg/L             | 110.1 ± 36.7    | 105.6 ± 38.3    | 0.344 | 108.8 ± 35.4   | 105.6 ± 35.9   | 0.560   |
| Serum creatinine, mg/L            | 1.28 ± 1.54     | 1.23 ± 1.25     | 0.762 | 1.16 ± 0.65    | 1.18 ± 1.23    | 0.885   |
| Angiographic and Procedural characteristics | | | | | | |
| Multivessel disease               | 72 (45.9%)      | 104 (62.3%)    | 0.003 | 56 (50.5%)     | 54 (48.6%)     | 0.788   |
| Number of CTO vessels             | 1.10 ± 0.30     | 1.09 ± 0.31     | 0.954 | 1.07 ± 0.26    | 1.05 ± 0.25    | 0.429   |
| CTO lesion artery                 | | | | | | |
| Left anterior descending          | 66 (42.0%)      | 68 (40.7%)     | 0.810 | 41 (36.9%)     | 49 (44.1%)     | 0.274   |
| Left circumflex                   | 43 (27.4%)      | 45 (26.9%)     | 0.929 | 35 (31.5%)     | 27 (24.3%)     | 0.231   |
| Right coronary artery             | 63 (40.1%)      | 69 (41.3%)     | 0.828 | 44 (39.6%)     | 42 (37.8%)     | 0.783   |
| Ramus                             | 0 (0.0%)        | 1 (0.6%)       | 0.331 | 0 (0.0%)       | 0 (0.0%)       | -       |
| No of multivessel CTO (≥ 2 vessels) | 15 (9.6%)      | 14 (8.4%)     | 0.536 | 12 (10.8%)     | 5 (4.5%)       | 0.077   |
Table 1. Cont.

| Variables                                | Entire patients | 1G-DES (n = 157) | 2G-DES (n = 167) | P-value | 1G-DES (n = 111) | 2G-DES (n = 111) | P-value |
|------------------------------------------|-----------------|------------------|------------------|---------|-----------------|-----------------|---------|
| Location of CTO lesion                   |                 |                  |                  |         |                 |                 |         |
| Proximal                                 | 70 (44.6%)      | 85 (50.9%)       | 0.256            |         | 48 (43.2%)      | 51 (45.9%)      | 0.685   |
| Mid                                      | 72 (45.9%)      | 67 (40.1%)       | 0.297            |         | 50 (45.0%)      | 50 (45.0%)      | 1.000   |
| Distal                                   | 15 (9.6%)       | 15 (9.0%)        | 0.859            |         | 13 (11.7%)      | 10 (9.0%)       | 0.508   |
| Rentrop collateral grade                 |                 |                  |                  |         |                 |                 |         |
| Grade 0                                  | 10 (6.4%)       | 11 (6.6%)        | 0.937            |         | 7 (6.3%)        | 9 (8.1%)        | 0.604   |
| Grade 1                                  | 43 (27.4%)      | 25 (15.8%)       | 0.002            |         | 20 (18.0%)      | 22 (19.8%)      | 0.732   |
| Grade 2                                  | 50 (31.8%)      | 88 (52.7%)       | < 0.001          |         | 47 (42.3%)      | 46 (41.4%)      | 0.892   |
| Grade 3                                  | 54 (34.4%)      | 45 (26.9%)       | 0.146            |         | 37 (33.3%)      | 34 (30.6%)      | 0.666   |
| Mean total stent length, mm              | 40.1 ± 19.4     | 42.3 ± 22.1      | 0.348            |         | 40.8 ± 19.6     | 39.5 ± 21.8     | 0.620   |
| Mean stent diameter, mm                  | 2.79 ± 0.4      | 2.88 ± 1.7       | 0.539            |         | 2.80 ± 0.2      | 2.81 ± 0.1      | 0.810   |
| Discharge medications                    |                 |                  |                  |         |                 |                 |         |
| Beta-blockers                            | 82 (52.2%)      | 85 (50.9%)       | 0.811            |         | 54 (48.6%)      | 59 (53.2%)      | 0.502   |
| CCB-DHP                                  | 18 (11.5%)      | 34 (20.4%)       | 0.029            |         | 15 (13.5%)      | 24 (21.6%)      | 0.112   |
| CCB-NDHP                                 | 60 (38.3%)      | 62 (37.1%)       | 0.840            |         | 51 (45.9%)      | 43 (38.7%)      | 0.277   |
| ACEI                                     | 62 (39.5%)      | 59 (35.3%)       | 0.439            |         | 34 (30.6%)      | 40 (36.0%)      | 0.393   |
| ARB                                      | 49 (31.2%)      | 48 (28.7%)       | 0.628            |         | 39 (35.1%)      | 29 (26.1%)      | 0.145   |
| Lipid lowering agents                    | 139 (88.5%)     | 154 (92.2%)      | 0.260            |         | 96 (86.5%)      | 100 (90.1%)     | 0.404   |
| Diuretics                                | 35 (22.3%)      | 37 (22.2%)       | 0.976            |         | 22 (19.8%)      | 25 (22.5%)      | 0.622   |

Data are presented as means ± SD or n (%). The P-value for continuous data from analysis of variance. The P-value for categorical data from chi-square test. ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCB-DHP: calcium channel blockers-dihydropyridine; CCB-NDHP: calcium channel blockers-non-dihydropyridine; CK-MB: creatine kinase myocardial band; CTO: chronic total occlusion; HDL: high-density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention; 1G-DES: first-generation drug-eluting stents; 2G-DES: second-generation drug-eluting stents.

Table 2. Clinical outcomes by Kaplan–Meier curved analysis and Cox-proportional hazard ratio analysis.

| Outcomes                                | Cumulative Events at five years | HR (95% CI) | P-value |
|------------------------------------------|---------------------------------|-------------|---------|
| MACE                                     | 1G-DES (n = 157)                | 2G-DES (n = 167) | Log rank | 1.600 (0.966–2.651) | 0.068 |
| All-cause death                          | 5 (3.2%)                       | 5 (3.6%)    | 0.870   | 0.901 (0.259–3.137) | 0.870 |
| Cardiac death                            | 3 (1.9%)                       | 2 (1.2%)    | 0.663   | 1.485 (0.248–8.901) | 0.665 |
| Re-MI                                    | 4 (2.6%)                       | 1 (0.6%)    | 0.169   | 4.127 (0.461–36.96) | 0.205 |
| Total repeat revascularization           | 38 (24.5%)                     | 20 (16.1%)  | 0.048   | 1.719 (0.997–2.965) | 0.051 |
| Target lesion (TLR-CTO vessel)           | 23 (14.9%)                     | 13 (10.7%)  | 0.213   | 1.540 (0.776–3.057) | 0.217 |
| Target vessel (TVR-CTO vessel)           | 28 (18.1%)                     | 15 (12.0%)  | 0.094   | 1.703 (0.906–3.202) | 0.099 |
| Non-target vessel (Non-CTO vessel)       | 18 (11.7%)                     | 10 (8.6%)   | 0.242   | 1.584 (0.728–3.119) | 0.246 |

ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CTO: chronic total occlusion; HR: hazard ratio; MACE: major adverse cardiac event; Re-MI: recurrent myocardial infarction; TLR: target lesion revascularization; TVR: target vessel revascularization; 1G-DES: first-generation drug-eluting stents; 2G-DES: second-generation drug-eluting stents.
Figure 2. Kaplan-Meier curved analysis of MACE (A & B), TLR-CTO vessel (C & D), TVR-CTO (E & F) according to the generation of DES (1G-DES vs. 2G-DES) and the types of DES (SES vs. PES vs. ZES vs. EES) up to 5-year after PSM. CTO: chronic total occlusion; DES: drug-eluting stent; EES: everolimus-eluting stent; MACE: major adverse cardiac event; PES: paclitaxel-eluting stent; PSM: propensity-score matched analysis; SES: sirolimus-eluting stent; TLR: target lesion revascularization; TVR: target vessel revascularization; 1G-DES: first-generation drug-eluting stents; 2G-DES: second-generation drug-eluting stents.
according to the generation of DES (1G-DES vs. 2G-DES) and types of DES (SES vs. PES vs. ZES vs. EES) after PSM.

4 Discussion

The main finding of this study was that the cumulative incidence of MACE defined as the composite of all-cause death, non-fatal MI, repeat revascularization (TLR, TVR, and Non-TV) was not significantly different between the 1G-DES and the 2G-DES following successful CTO PCI up to 5-year follow-up period.

2G-DES have relatively thin stent struts and biocompatible polymers which improved stability. Lipotropism of eluting drugs lead to reduced endothelial damage and proliferations compared with 1G-DES.[15,22] In addition to previous studies which showing superiority of 2G-DES in the occurrence of MI, TLR and stent thrombosis over 1G-DES, recently a large meta-analysis also showed better efficacy and safety of 2G-DES compared to 1G-DES.[16] According this report, 2G-DES were associated with lower incidence of death (OR = 0.59, 95% CI: 0.40–0.87), and reocclusion (OR = 0.35, 95% CI: 0.17–0.71) compared to 1G-DES. By contrast, the comparative results between 1G-DES and 2G-DES in CTO lesions were also reported. Ahn, et al.[16] reported that the efficacy of 2G-DES is comparable to 1G-DES for treating CTO up to 2-year follow-up periods. The cumulative incidence of MACE (HR = 0.93, 95% CI: 0.63–1.37, P = 0.71) were not significantly different between 1G-DES (SES or PES) and 2G-DES (ZES or EES). Cho, et al.[10] also reported similar clinical outcomes between 1G-DES and 2G-DES up to 3-year follow-up periods. In that report, the composite of death, Q-wave MI, or TVR (HR = 1.42, 95% CI: 0.69–2.56, P = 0.39) were similar between the two groups.

In our study, up to 5-year follow-up periods, the cumulative incidences MACE was similar between the two groups before and after PSM. The results of Kaplan-Meier analysis for MACE, TLR and TVR among SES, PES, ZES, and EES were not statistically different (Figure 2). These results were similar with previous reports.[13,16,23,24] Moreno, et al.[13] reported that in the CTO patients, EES is as effective as SES during 1-year follow-up period. The cumulative incidence of MACE rates was 15.9% versus 11.1% with SES and EES and the rate of binary restenosis was also similar (10.8% vs. 9.1%, P = 0.709) in their study. Machado, et al.[23] reported 1G-DES and 2G-DES seem to be similarly effective in patients after PCI in the setting of acute coronary syndrome. During mean follow-up 598 days, the composite primary endpoint (all-cause death, non-fatal MI, TVR) of their study was not significantly different (10.8% vs. 12.2%, P = 0.463) between 1G-DES and 2G-DES. By contrast, there were some different reports were also reported in patients with acute coronary syndrome.[26,27] These debates were also reported in patients with coronary bifurcation lesions.[28–30] Current guidelines do not recommend specific type of DES between these two groups of DES during PCI.[31] Because our study’s follow-up periods were much longer than previous studies, the results of our study may provide a meaningful message especially, in a situation where there was rare long-term clinical outcome data between the 1G-DES and the 2G-DES after successful CTO PCI.

In the entire patients, five cases of stent thrombosis (5/324, 1.5%) were occurred up to 5-year follow-up periods. But the comparative cumulative incidence of stent thrombosis was statistically insignificant (P = 0.202). Among them four cases (1 SES and 3 PES) of stent thrombosis were occurred in 1G-DES (2.5%) and one case (1 EES) was in 2G-DES (0.6%). In the 1G-DES group, one case was acute stent thrombosis (occurring between 0 and 24 hours after stent implantation) and another one case was subacute stent thrombosis (occurring between 24 hours and 30 days) and other two cases were very late stent thrombosis (occurring after one year). In the 2G-DES group, only one case of stent thrombosis was occurred and was regarded as a very late stent thrombosis. Because only one case was included in our study after PSM, we excluded stent thrombosis from our outcome parameter inevitably.

Until today, in spite of comparative advantages of 2G-DES over 1G-DES such as stent platform which have more thinner, improved deliverability and flexibility and have reduced inflammatory reaction and improved re-endothelization, the reasons for why the long-term clinical outcomes were similar between the two groups were not thoroughly illuminated. To find out more detailed causative factors that can affect these results, more large scaled long-term randomized control study might be required.

4.1 Limitations

This study has some limitations. Firstly, because of non-randomized, single center registry design of this study, several confounding factors such as under-reporting and/or missing value and selection bias may have affected the end results. Secondly, although PSM analysis was done, the proportions of the different stent types in the both groups were not evenly distributed. Thirdly, even though this study’s follow-up periods were longer than previous study, the total numbers of included patients were relatively small to compare the individual and composite clinical outcomes. Last but not least, until today, newly developed CTO guide-
wire or devices may be more frequently used in 2D-DES group compared to 1G-DES, these factors can affect the outcomes of this study.

4.2 Conclusions

In conclusion, in our single-center, all-comer registry, 2G-DES was not associated with reduced long-term MACE compared with 1G-DES following successful CTO revascularization up to five years possibility due to limited number of the study population.

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