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ORIGINAL RESEARCH

Ten-Year Trends in Coronary Bifurcation Percutaneous Coronary Intervention: Prognostic Effects of Patient and Lesion Characteristics, Devices, and Techniques

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BACKGROUND: Despite advances in devices and techniques, coronary bifurcation lesion remains a challenging lesion subset in the field of percutaneous coronary intervention (PCI). We evaluate 10-year trends in bifurcation PCI and their effects on patient outcomes.

METHODS AND RESULTS: We analyzed 10-year trends in patient/lesion characteristics, devices, PCI strategy, stent optimization techniques, and clinical outcomes using data from 5498 patients who underwent bifurcation PCI from 2004 to 2015. Clinical outcomes 2 years after the index procedure were evaluated in terms of target vessel failure (a composite of cardiac death, myocardial infarction, and target vessel revascularization) and a patient-oriented composite outcome (a composite of all-cause death, myocardial infarction, and any revascularization). During the 10-year study period, patient and lesion complexity, such as multivessel disease, diabetes mellitus, chronic kidney disease, and left main bifurcation, increased continuously (all P<0.001). The risk of target vessel failure or patient-oriented composite outcome decreased continuously from 2004 to 2015 (target vessel failure: from 12.3% to 6.9%, log-rank P<0.001; patient-oriented composite outcome: from 13.6% to 9.3%, log-rank P<0.001). The use of a second-generation drug-eluting stent and decreased target vessel failure risk in true bifurcation lesions were the major contributors to improved patient prognosis (interaction P values were <0.001 and 0.013, respectively).

CONCLUSIONS: During the past decade of bifurcation PCI, patient and lesion characteristics, devices, PCI techniques, and patient prognosis have all significantly changed. Despite increased patient and lesion complexity, clinical outcomes after bifurcation PCI have improved, mainly because of better devices and more widespread adoption of procedural optimization techniques and appropriate treatment strategies.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifiers: NCT01642992 and NCT03068494.

Key Words: clinical outcome ■ coronary bifurcation lesion ■ drug-eluting stent ■ percutaneous coronary intervention

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CLINICAL PERSPECTIVE

What Is New?

- The current study evaluated the 10-year trends and prognostic implications of bifurcation percutaneous coronary intervention (PCI).
- Despite increased patient and lesion complexity, clinical outcomes after bifurcation PCI have improved.
- The main contributing factors in improved patient prognosis after bifurcation PCI were enhanced devices, better patient and lesion selection, simplification of procedures, and advanced procedural optimization techniques.

What Are the Clinical Implications?

- Because the procedural success and clinical outcomes of bifurcation PCI are determined by multiple factors, including patient and lesion characteristics, device choice, and bifurcation PCI and stent optimization techniques, comprehensive insights into how those factors have changed and affected patient prognosis will improve daily practice and guide future research.
- The current results from 10 years of experience support the contemporary consensus statement about bifurcation PCI and imply that practice patterns are heading in the right direction to enhance patient outcomes.

Nonstandard Abbreviations and Acronyms

COBIS	Korean Coronary Bifurcation Stenting
DES	drug-eluting stent
FKB	final kissing balloon
MV	main vessel
NCDR	National Cardiovascular Data Registry
NIS	National Inpatient Sample
POT	proximal optimization technique
SB	small branch
TVF	target vessel failure
TIMI	Thrombolysis in Myocardial Infarction

Coronary bifurcation lesion is a challenging lesion subset whose treatment requires more complex procedures and carries a higher risk of adverse clinical events than nonbifurcation lesions.[1,2] In daily practice, ≈20% of percutaneous coronary interventions (PCIs) are performed for bifurcation lesions,[3] and continuous efforts have been made to establish a standardized approach to improve patient prognosis after bifurcation PCI.[4–6] During the past decade, the devices, strategies, and techniques of bifurcation PCI have significantly changed. Efforts continue to refine the drug-eluting stent (DES),[7] find appropriate treatment strategies for various bifurcation lesions,[8–15] and support the clinical usefulness of optimization techniques such as intravascular ultrasound (IVUS) guidance[16,17] and proximal optimization technique (POT) for bifurcation PCI.[5]

Although previous studies have evaluated the efficacy of emerging techniques or devices, few data are available on temporal trends in the procedures and clinical outcomes of bifurcation PCI. Because the procedural success and clinical outcomes of bifurcation PCI are determined by multiple factors, comprehensive insights into how those factors have changed and affected patient prognosis will improve daily practice and guide future research. Therefore, we here evaluate 10-year trends in bifurcation PCI and their prognostic effects in a large nationwide cohort that reflects real-world practice of bifurcation PCI.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

The study population was derived from the COBIS (Korean Coronary Bifurcation Stenting) II (Clinicaltrials.gov, NCT01642992) and COBIS III (Clinicaltrials.gov, NCT03068494) registries, which are multicenter registries of consecutive patients who underwent bifurcation PCI with DES. The protocol and details of those studies have been previously described.[18,19] Briefly, both registries had the same inclusion criteria, and the key inclusion criteria were as follows: (1) any type of coronary bifurcation lesion in a major epicardial artery; (2) main vessel (MV) diameter ≥2.5 mm and side branch (SB) ≥2.3 mm confirmed by a core laboratory quantitative coronary angiography analysis; and (3) treated with DES. In the COBIS II registry, patients with (1) cardiogenic shock; (2) experience of cardiopulmonary resuscitation; or (3) protected left main disease were excluded. In the COBIS III registry, patients with severe left ventricular systolic dysfunction (ejection fraction <30%) were additionally excluded in addition to the above exclusion criteria.

This patient-level, pooled analysis included 2897 patients in the COBIS II registry from January 2003 to December 2009 and 2648 patients in the COBIS III registry from January 2010 to December 2014. Because the COBIS III registry excluded patients with severe left ventricular systolic dysfunction, 45 patients with that condition were excluded from the COBIS II registry for the current analysis. As a result, the final study population was composed of 5498 patients. The study protocols of both registries were approved by the institutional review board at each study center and the requirement for written informed consent was waived because of the retrospective nature of the study. This study was conducted according to the principles of the Declaration of Helsinki.

Percutaneous Coronary Intervention

Coronary interventions were performed in accordance with relevant standard guidelines at the time of each procedure.[20] All procedural decisions, including stent type, technique (1 stent or 2 stents), access site, intravascular imaging, and stent optimization were left to the operators' discretion. Both first- and second-generation DES were used in the COBIS II registry, but only the second-generation DES was used in the COBIS III registry. During bifurcation PCI, the POT was defined in 1 of 2 ways, as follows: (1) immediately after MV stenting with a nominal pressure, the stent balloon was pulled back to postdilate the proximal MV just proximal to the carina with a high pressure targeting 0.25 to 0.5 mm overexpansion above the nominal balloon diameter; or (2) after MV stenting, the MV stent was postdilated immediately proximal to the carina using a short, noncompliant balloon sized for the proximal MV reference diameter.[21]

Data Collection, Follow-Up, and Quantitative Coronary Angiography

Baseline clinical, angiographic, procedural, and follow-up data were recorded using a web-based system. Since the current study was retrospective, demographic data, cardiovascular risk factors, comorbidities, and follow-up data were collected using medical records. If medical records were unavailable for follow-up data, telephone contacts were performed.

All quantitative coronary angiography analyses were performed at an independent core laboratory (Heart Vascular Stroke Institute, Samsung Medical Center, Seoul, Republic of Korea) using validated software (Centricity CA 1000, GE). Standardized definitions for each segment of a bifurcation lesion (proximal MV, distal MV, and SB ostium) were used as previously described.[22] Medina classification types 1.1.1, 1.0.1, and 0.1.1 lesions were defined as true bifurcation lesions. The bifurcation angle, minimum lumen diameter, reference vessel diameter, and lesion length for each vessel were measured, and the percent diameter stenosis for each vessel was calculated. Procedural success was defined as angiographic residual stenosis <30% with TIMI (Thrombolysis in Myocardial Infarction) 3 flow for the MV and angiographic residual stenosis <50% with TIMI 3 flow for the SB.

Definitions and Outcome Measurements

The primary outcome was target vessel failure (TVF), a composite of cardiac death, spontaneous myocardial infarction (MI), and target vessel revascularization, 2 years after the index procedure. The secondary outcome was the patient-oriented composite outcome, a composite of all-cause death, spontaneous MI, and any revascularization. All deaths were considered cardiac unless a definite noncardiac cause could be established. Spontaneous MI was defined as an elevation of the creatine kinase–myocardial band or a troponin level greater than the upper limit of normal with concomitant ischemic symptoms or ECG findings indicative of ischemia unrelated to the index procedure. Periprocedural MI was not counted as a clinical event. Target lesion revascularization was defined as repeated revascularization of lesions within 5 mm of the previous stenting site. Definite stent thrombosis was defined using the Academic Research Consortium definition.[23] Clinical outcomes were adjudicated by an independent event adjudicating committee.

Statistical Analysis

Categorical data are summarized as numbers and relative frequencies and were compared using chi-square test. Continuous variables are presented as the mean±SD and were compared using unpaired *t* or Mann–Whitney rank sum tests, depending on their distribution. When we compared >2 groups, we analyzed continuous variables using Mantel–Haenszel statistic or ANOVA, depending on their distribution. The survival analysis was performed using Kaplan–Meier method, and comparisons were made with log-rank or Breslow tests. Cumulative incidences of clinical events are presented at 2 years after the index procedure. Patients were censored at 2 years (730 days) or when events occurred. Proportional hazards assumptions were graphically inspected in the log-minus-log plot and were also tested using Schoenfeld residuals. Hazard ratios (HRs) with 95% CIs were calculated. Interaction terms between time (year of index procedure) and covariables were calculated to evaluate whether the covariables affected the temporal changes of a trend in outcomes. Multivariable Cox proportional hazards regressions were performed to evaluate the prognostic effects of bifurcation PCI optimization techniques. The adjusted covariables were age, sex, acute coronary syndrome, diabetes mellitus, chronic kidney disease, current smoking, previous PCI, previous cerebrovascular accident, left main bifurcation, multivessel disease, type of stent, true bifurcation lesion, left ventricular ejection fraction, and stenosis severity of the MV and SB. All analyses were 2-tailed, and statistical significance was defined as a *P* value <0.05. All statistical analyses were conducted using SPSS Statistics version 22.0 (IBM) and R version 3.6.0 (R Foundation for Statistical Computing).

Table 1. Baseline Clinical and Lesion Characteristics According to Treatment Period

	2004–2007 (N=1580)	2008–2011 (N=2075)	2012–2015 (N=1843)	*P* Value
Demographics				
Age, y	62.0±10.2	62.6±10.7	63.9±10.9	<0.001
Men	1129 (71.5)	1508 (72.7)	1424 (77.3)	0.001
Cardiovascular risk factors				
Hypertension	913 (57.8)	1209 (58.3)	1037 (56.3)	0.429
Diabetes mellitus	435 (27.5)	662 (31.9)	631 (34.2)	<0.001
Chronic kidney disease	45 (2.8)	58 (2.8)	75 (4.1)	0.047
Hyperlipidemia	521 (33.0)	703 (33.9)	682 (37.0)	0.030
Current smoking	388 (24.6)	567 (27.3)	564 (30.6)	<0.001
Previous PCI	255 (16.1)	244 (11.8)	231 (12.5)	<0.001
Previous myocardial infarction	117 (7.4)	81 (3.9)	81 (4.4)	<0.001
Previous CVA	99 (6.3)	133 (6.4)	129 (7.0)	0.644
Initial presentation				
Clinical presentation				0.366
Stable coronary disease	594 (37.6)	829 (40.0)	689 (37.4)	
Unstable angina or NSTEMI	813 (51.5)	1008 (48.6)	946 (51.3)	
STEMI	173 (10.9)	238 (11.5)	208 (11.3)	
LVEF, %	59.1±9.7	58.8±8.9	58.8±9.5	0.514
Medication at discharge				
Aspirin	1574 (99.6)	2055 (99.0)	1814 (98.4)	0.002
P2Y12 inhibitors	1557 (98.5)	2056 (99.1)	1819 (98.7)	0.294
Clopidogrel	1557 (98.5)	2054 (99.0)	1644 (89.2)	<0.001
Prasugrel	0 (0.0)	0 (0.0)	79 (4.3)	<0.001
Ticagrelor	0 (0.0)	2 (0.1)	98 (5.3)	<0.001
Cilostazol	413 (26.1)	456 (22.0)	183 (9.9)	<0.001
Lesion characteristics				
Multivessel disease	780 (49.4)	1143 (55.1)	1141 (61.9)	<0.001
Bifurcation location				<0.001
Left main	406 (25.7)	704 (33.9)	661 (35.9)	
LAD/diagonal	883 (55.9)	1013 (48.8)	843 (45.7)	
LCX/OM	207 (13.1)	253 (12.2)	230 (12.5)	
RCA (PL/PDA)	84 (5.3)	105 (5.1)	109 (5.9)	
Medina classification				0.011
1.1.1	514 (32.5)	654 (31.5)	587 (31.9)	
1.0.1	121 (7.7)	143 (6.9)	114 (6.2)	
1.0.0	191 (12.1)	243 (11.7)	206 (11.2)	
0.1.1	192 (12.2)	232 (11.2)	170 (9.2)	
1.1.0	238 (15.1)	320 (15.4)	287 (15.6)	
0.1.0	270 (17.1)	394 (19.0)	413 (22.4)	
0.0.1	54 (3.4)	89 (4.3)	66 (3.6)	
True bifurcation	827 (52.3)	1029 (49.6)	871 (47.3)	0.011

Data are presented as mean±SD or number (percentage). CVA indicates cerebrovascular accident; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; NSTEMI, non–ST-segment–elevation myocardial infarction; OM, obtuse marginal artery; PCI, percutaneous coronary intervention; PDA, posterior descending artery; PL, posterolateral artery; RCA, right coronary artery; and STEMI, ST-segment–elevation myocardial infarction.

RESULTS

Temporal Changes in Clinical and Lesion Characteristics and Procedures

Table 1 and Figure 1 summarize the temporal changes in patient and lesion characteristics during the 10-year study period. The target population for bifurcation PCI showed increased age and worsened comorbidities over time, with an increased prevalence of diabetes mellitus, hyperlipidemia, chronic kidney disease, and current smoking. In terms of lesion complexity, the proportion of multivessel disease and left main bifurcation significantly increased. Table 2 summarizes temporal changes in the procedural characteristics. During the study period, 1-stent crossover without SB ballooning was a predominant strategy whose use continuously increased (Figure 2). At the same time, the transradial approach became the most preferred access, and the second-generation DES replaced the first-generation DES in 2008 to 2009 (Figure S1). Among the stent optimization techniques, the use of IVUS and POT significantly increased (Table 2). The angiographic procedural success rate continuously increased for the MV, but it decreased for the SB, mainly because of residual stenosis (Table 2).

Ten-Year Trends in Clinical Outcomes and Factors Contributing to Changes

Table 3 and Figure 3 present the annual trends in 2-year TVF and 2-year patient-oriented composite outcome. During the 10-year period, the risks

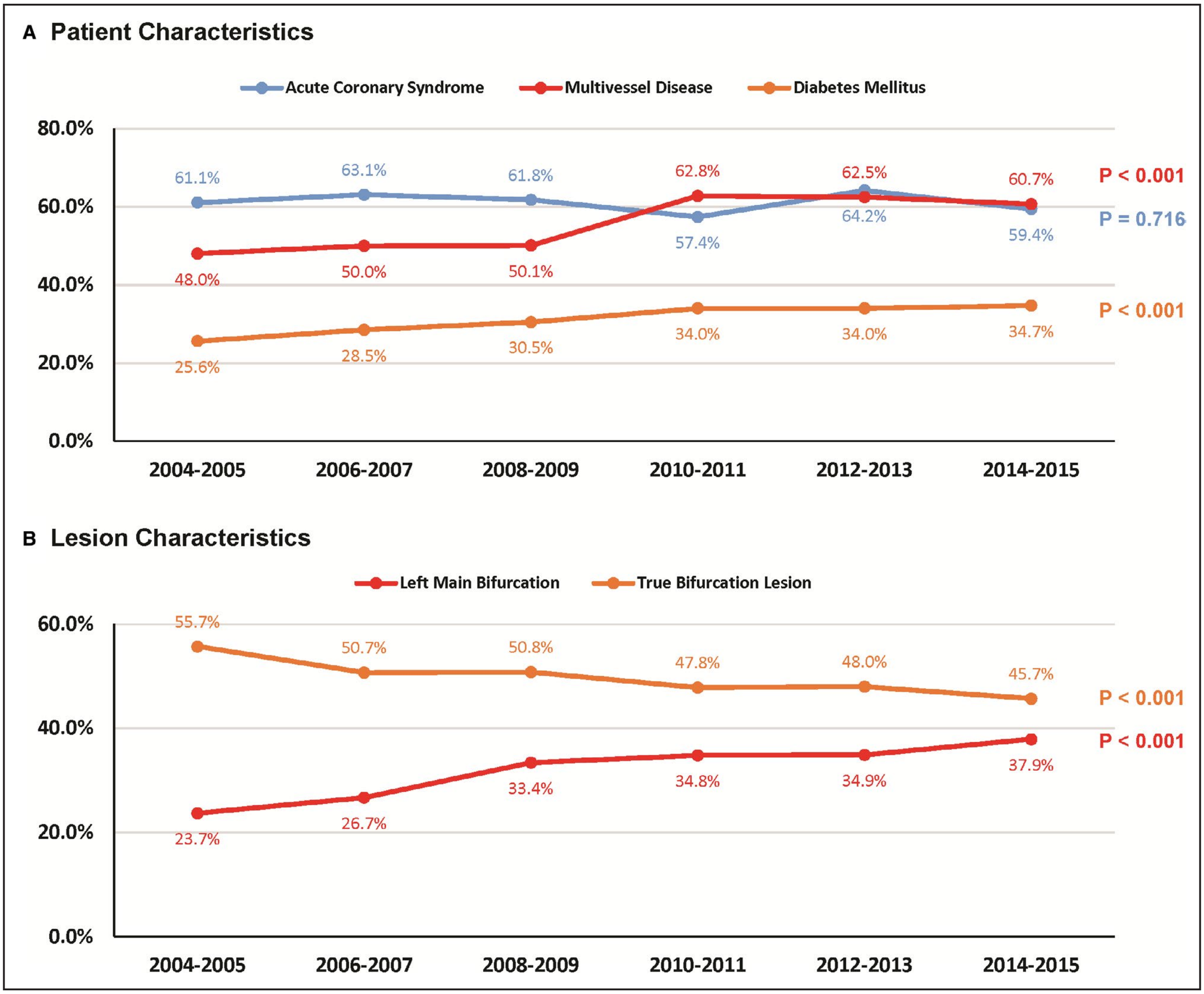

Figure 1. Changes in patient and lesion characteristics.
Temporal changes in (**A**) patient and (**B**) lesion complexity in the target population for bifurcation percutaneous coronary intervention are summarized. The percentage of patients with diabetes mellitus, multivessel disease, and left main bifurcation increased, but the incidence of true bifurcation lesions decreased. The incidence of acute coronary syndrome did not significantly change.

Table 2. Procedural Characteristics and Quantitative Coronary Angiography Data According to Treatment Period

	2004–2007 (N=1580)	2008–2011 (N=2075)	2012–2015 (N=1843)	*P* Value
Procedural characteristics				
Treatment strategy				<0.001
One-stent technique	1144 (72.4)	1626 (78.4)	1520 (82.5)	
Two-stent technique	436 (27.6)	449 (21.6)	323 (17.5)	
Provisional	137/436 (31.4)	110/449 (24.5)	54/323 (16.7)	
Elective	299/436 (68.6)	339/449 (75.5)	269/323 (83.3)	
Specific techniques				
Crush	207/436 (47.5)	223/449 (49.7)	175/323 (54.2)	
T stenting or TAP	154/436 (35.3)	153/449 (34.1)	89/323 (27.6)	
Culottes	7/439 (1.6)	24/449 (5.3)	21/323 (6.5)	
Kissing or V stenting	65/436 (14.9)	43/449 (9.6)	27/323 (8.4)	
Others	3/436 (0.7)	6/449 (1.3)	11/323 (3.4)	
No. of stents used	1.9±1.0	1.9±1.0	1.8±0.9	<0.001
Stent type				<0.001
First-generation DES	1579 (99.9)	857 (41.3)	0 (0.0)	
Second-generation DES	1 (0.1)	1218 (58.7)	1843 (100.0)	
Transradial intervention	326 (20.6)	727 (35.0)	1133 (61.5)	<0.001
Use of intravascular ultrasound	525 (33.2)	886 (42.7)	763 (41.4)	<0.001
FKB	775 (49.1)	779 (37.5)	565 (30.7)	<0.001
POT	303 (19.2)	514 (24.8)	510 (27.7)	<0.001
Procedural success				
Main vessel	1559 (98.7)	2055 (99.0)	1832 (99.4)	0.027
SB	1201 (76.0)	1497 (72.1)	1301 (70.6)	0.001
Quantitative coronary angiography				
Bifurcation angle	64.1±25.2	67.2±24.3	71.5±21.5	<0.001
Before procedure				
MV RD, mm	3.1±0.5	3.1±0.5	3.3±0.5	<0.001
SB RD, mm	2.5±0.4	2.6±0.4	2.6±0.4	<0.001
MV percent diameter stenosis, %	68.4±14.9	69.2±16.6	74.0±14.5	<0.001
SB percent diameter stenosis, %	46.0±23.5	45.2±24.8	43.8±27.5	0.033
MV lesion length, mm	19.2±12.4	18.5±11.9	18.0±10.1	0.014
SB lesion length, mm	5.4±7.7	5.4±7.1	5.2±6.8	0.445
After procedure				
MV RD, mm	3.1±0.5	3.2±0.5	3.3±0.5	<0.001
SB RD, mm	2.5±0.4	2.6±0.4	2.6±0.4	<0.001
MV residual percent diameter stenosis, %	14.8±11.7	14.5±11.1	16.0±9.8	<0.001
SB residual percent diameter stenosis, %	31.8±24.3	34.2±25.3	35.6±26.2	<0.001

Data are presented as mean±SD or number (percentage). DES indicates drug-eluting stent; FKB, final kissing balloon; MLD, minimum lumen diameter; MV, main vessel; POT, proximal optimization technique; RD, reference diameter; SB, side branch; and TAP, T and small protrusion.

of both TVF (from 12.3% in 2004–2005 to 6.9% in 2014–2015; log-rank *P*<0.001) and patient-oriented composite outcome (from 13.6% in 2004–2005 to 9.3% in 2014–2015; log-rank *P*<0.001) significantly decreased, mainly because of a decreased risk of repeated revascularization. Those decreased risks were similarly observed with both the 1-stent and 2-stent strategies, with more prominent changes seen in patients treated with the 2-stent strategy. Among the major changes in patient, lesion, and procedural characteristics, the use of a second-generation DES and decreased TVF risk after true bifurcation lesion PCI were significantly associated with the overall decrease in TVF risk (interaction *P* values were <0.001 and 0.013, respectively) (Table S1 and Figure 4).

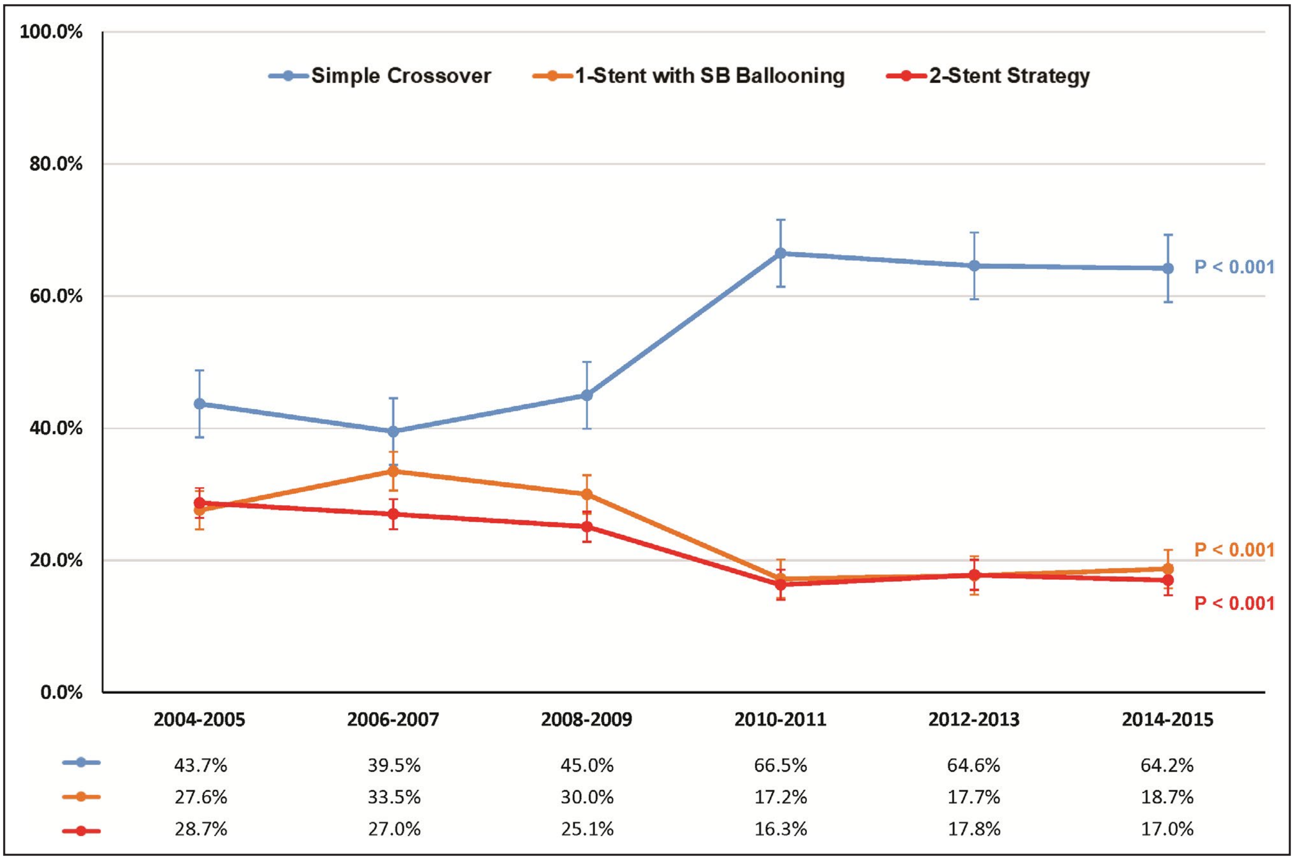

Figure 2. Changes in treatment strategy trends from 2004 to 2015.
During the past decade, use of the simple crossover (1-stent without side branch [SB] ballooning) strategy has continuously increased. Conversely, use of the 1-stent with SB ballooning and 2-stent strategy significantly decreased. The circle represents the mean proportion, and the vertical whiskers represent 95% CIs.

Clinical Relevance of Bifurcation PCI Optimization Techniques

Figure 5 presents the annual trends in the use of optimization techniques and their prognostic effects according to the treatment strategies. With both the 1- and 2-stent strategies, the use of the transradial approach, IVUS-guided optimization, and POT significantly increased. The use of a final kissing balloon (FKB) significantly decreased after 1-stent procedures, but it was performed in most cases using the 2-stent

Table 3. Clinical Outcomes 2 Years After Index Procedure According to Treatment Period

	2004–2007 (N=1580)	2008–2011 (N=2075)	2012–2015 (N=1843)	*P* Value
All-cause death	2.6	2.9	2.7	0.916
Cardiac death	1.3	1.2	1.6	0.378
MI	1.6	1.1	1.5	0.214
Target vessel MI	1.0	0.9	0.9	0.893
Any revascularization	10.7	8.9	6.6	<0.001
Target lesion revascularization	7.3	5.2	2.8	<0.001
Target vessel revascularization	10.4	7.5	4.5	<0.001
Definite stent thrombosis	0.6	0.3	0.6	0.283
TVF*	12.0	8.8	6.7	<0.001
Patient-oriented composite outcome†	13.5	11.6	9.7	<0.001

Values are cumulative incidences of events as Kaplan-Meier estimates (percentages) at 2 years. *P* values were used for the log-rank or Breslow test in the survival analysis.
*Target vessel failure (TVF) is defined as a composite of cardiac death, target vessel myocardial infarction (MI), and target vessel revascularization.
†Patient-oriented composite outcome is defined as the composite of all-cause death, MI, and any revascularization.

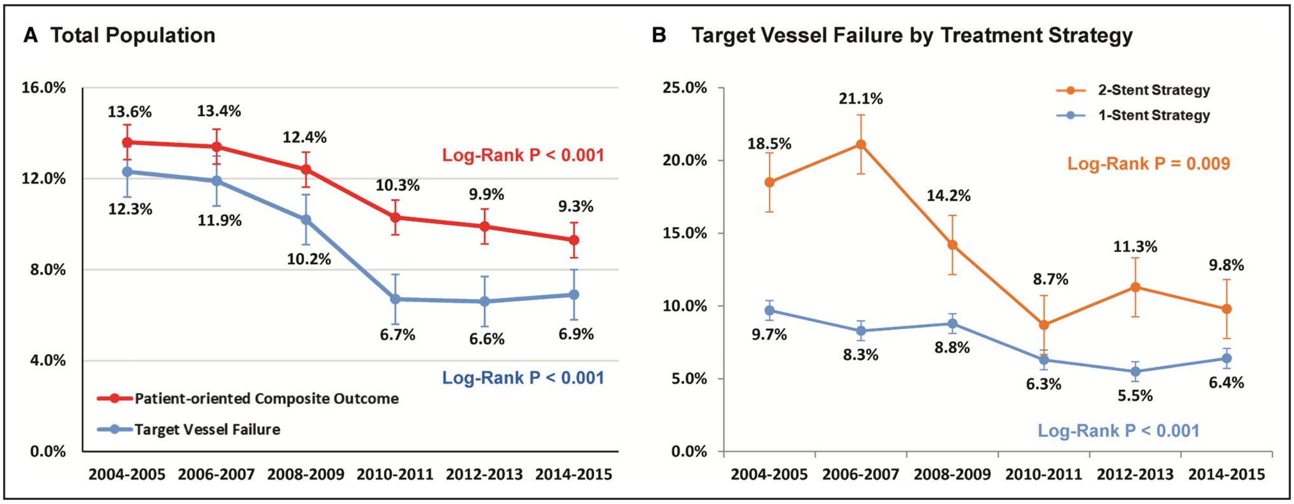

Figure 3. Changes in clinical outcomes 2 years after the index procedure.
A, Cumulative incidence of patient-oriented composite outcome (red line) and target vessel failure (TVF; blue line) 2 years after the index procedure is presented. Patient-oriented composite outcome a composite of all-cause death, spontaneous myocardial infarction (MI), and any revascularization. TVF is a composite of cardiac death, spontaneous MI, and target vessel revascularization. **B**, Temporal changes in the cumulative incidence of TVF are presented according to the treatment strategy for bifurcation percutaneous coronary intervention. Cumulative incidence was estimated using Kaplan-Meier estimates (percentages). Whiskers represent 95% CIs.

strategy. IVUS-guided PCI (adjusted HR, 0.73; 95% CI, 0.55–0.97), FKB (adjusted HR, 0.57; 95% CI, 0.40–0.82), and POT (adjusted HR, 0.64; 95% CI, 0.43–0.95) all effectively reduced the risk of TVF when used with the 2-stent strategy but not with the 1-stent strategy (Figure 5).

DISCUSSION

In this study, we evaluated the 10-year trends in bifurcation PCI in terms of patient/lesion characteristics, devices, PCI strategy, stent optimization techniques, and clinical outcomes. Our major findings are as follows. First, during the past decade, patient and lesion complexity have increased, and procedural patterns also significantly changed, including a significant increase in the use of the 1-stent strategy and bifurcation PCI optimization techniques. Second, clinical outcomes after bifurcation PCI have significantly improved, mainly through the use of second-generation DES and significantly improved clinical outcomes after true bifurcation lesion PCI. Third, bifurcation PCI optimization techniques (IVUS-guided optimization, FKB, and POT) were significantly associated with a lower risk of TVF in patients treated with the 2-stent strategy but not in patients treated with the 1-stent strategy (Figure 6).

Changes in the Target Population and Lesions for Bifurcation PCI

During the past decade, the clinical characteristics of patients with bifurcation PCI changed. In our study population, patient age and the prevalence of diabetes mellitus and chronic kidney disease increased. A similar increase in the overall risk profile of the PCI population was reported in data from the NCDR (National Cardiovascular Data Registry) and NIS (National Inpatient Sample) database.[24,25] Along with the increased comorbidities of patients, lesion complexity, such as multivessel disease and left main bifurcation, also increased. These trends could have multiple causes, including an increased prevalence of underlying comorbidities,[26] enhanced patient accessibility to treatment,[24] expanded indications for PCI based on the improved safety and efficacy of second-generation DES,[27–29] and an accumulation of clinical experience and improved techniques.[25]

Conversely, the prevalence of true bifurcation lesion PCI decreased during the study period. True bifurcation lesion PCI is associated with a higher risk of procedural complications and worse clinical outcomes than nontrue bifurcation lesion PCI.[30] It should be noted that the decrease in the prevalence of true bifurcation lesion PCI was seen more prominently in left main bifurcation (40.9% in 2004–2007, 40.5% in 2008–2011, and 34.8% in 2012–2015; P=0.029) than in nonleft main bifurcation (56.3% in 2004–2007, 54.3% in 2008–2011, and 54.2% in 2012–2015; P=0.313) in our study population. Those trends imply better patient selection for left main bifurcation PCI based on previous results, which showed that PCI for complex left main disease with a true bifurcation lesion had worse clinical outcomes than coronary artery bypass grafting.[31–33]

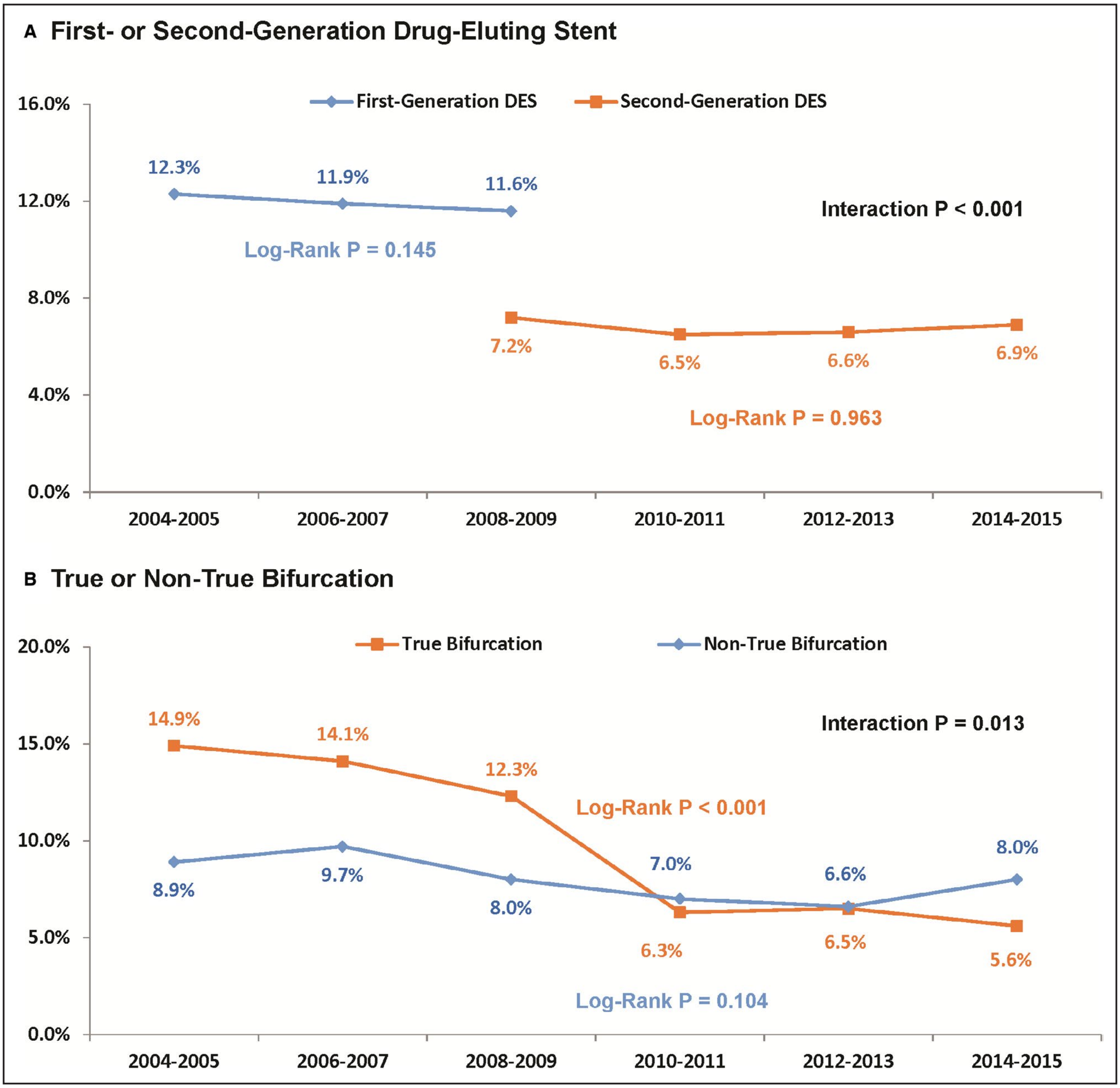

Figure 4. Changes in target vessel failure (TVF) according to stent type and lesion characteristics.
Annual changes in 2-year TVF are presented according to (**A**) the use of first- or second-generation drug-eluting stent (DES) and (**B**) the occurrence of true or nontrue bifurcation lesion percutaneous coronary intervention (PCI). Differential prognosis was observed between first- and second-generation DES and between true and nontrue bifurcation lesion PCI, and those effects showed a significant interaction with changes in the risk of TVF.

Changes in Bifurcation PCI Strategy

One of the most prominent changes during the past decade was a substantial increase in the use of the 1-stent strategy without SB treatment. The use of both the 1-stent with SB ballooning and 2-stent strategies significantly decreased. Previous randomized controlled trials that compared the 1-stent and 2-stent strategies showed worse clinical outcomes after the 2-stent strategy when using a first-generation DES.[8–13] Although studies with second-generation DES show comparable prognosis between the 1-stent and 2-stent strategies,[19,34,35] the current consensus is that "simple is better than complex, if possible."[4,5] During the past 10 years, this concept has been implemented in real-world practice, and our results show that the 1-stent strategy has become the main technique used for bifurcation PCI.

Nevertheless, it should be noted that ≈17% of bifurcation PCI cases still need the 2-stent strategy. Considering that even bifurcation lesions with the same

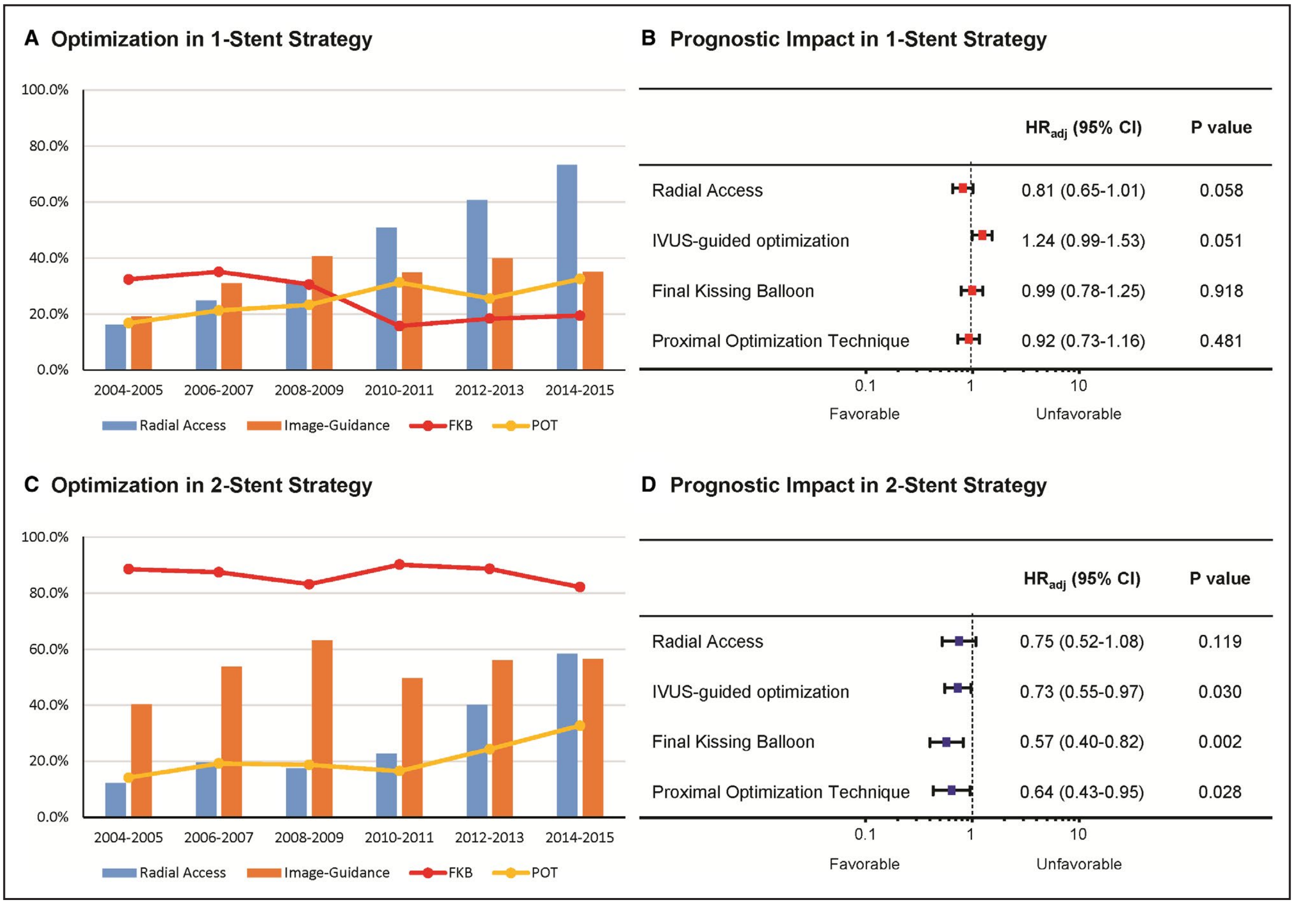

Figure 5. Prognostic implications of procedural factors in 1-stent and 2-stent strategies.
Annual changes in the implementation of radial access and optimization techniques and their prognostic implications for the risk of 2-year target vessel failure (TVF) are presented. With both the 1- and 2-stent strategies, the use of radial access, intravascular ultrasound (IVUS)–guided optimization, and proximal optimization technique (POT) significantly increased. **A**, With the 1-stent strategy (n=4290), the use of final kissing balloon (FKB) significantly decreased. **B**, No variables significantly affected the risk of 2-year TVF with the 1-stent strategy. **C**, With the 2-stent strategy (n=1208), most procedures were accompanied by FKB. **D**, Optimization techniques in bifurcation percutaneous coronary intervention (PCI; image-guided PCI, FKB, and POT) effectively reduced the risk of TVF only in patients treated with the 2-stent strategy. The multivariable analyses were complete case analysis. HR_{adj} indicates adjusted hazard ratio.

Medina classification can significantly differ inside branch ostial lesion severity, SB lesion length, angulation between MV and SB, SB size, and corresponding myocardial territory, the treatment strategy for each patient with a bifurcation lesion should be individualized.

Changes in Clinical Outcomes After Bifurcation PCI and Main Contributors

Despite the increase in patient and lesion complexity, the risk of 2-year TVF and patient-oriented composite outcome significantly improved during the past decade. Although the reduction in 2-year TVF risk was significant with both the 1-stent and 2-stent strategies, the improvement was more prominent in patients treated with the 2-stent strategy, decreasing from about 20% to 10%. The risk of TVF after true bifurcation lesion PCI also significantly decreased, although the risk after nontrue bifurcation PCI did not significantly change. It should be noted that the reduced TVF risk in patients with the 2-stent strategy or true bifurcation lesion PCI became evident beginning in 2010 to 2011, which corresponds with the period in which the second-generation DES almost completely replaced the first-generation DES. In our results, the use of a second-generation DES and differential changes in prognosis after true bifurcation lesion PCI (compared with those after nontrue bifurcation lesion PCI) showed a significant interaction with changes in the TVF risk. Our results are thus in line with recent evidence showing comparable prognosis between the 1-stent and 2-stent strategies when using a contemporary DES.[19,35]

Clinical Relevance of Optimization Techniques in Bifurcation PCI

In this study, we evaluated the prognostic role of optimization techniques in bifurcation PCI. Although

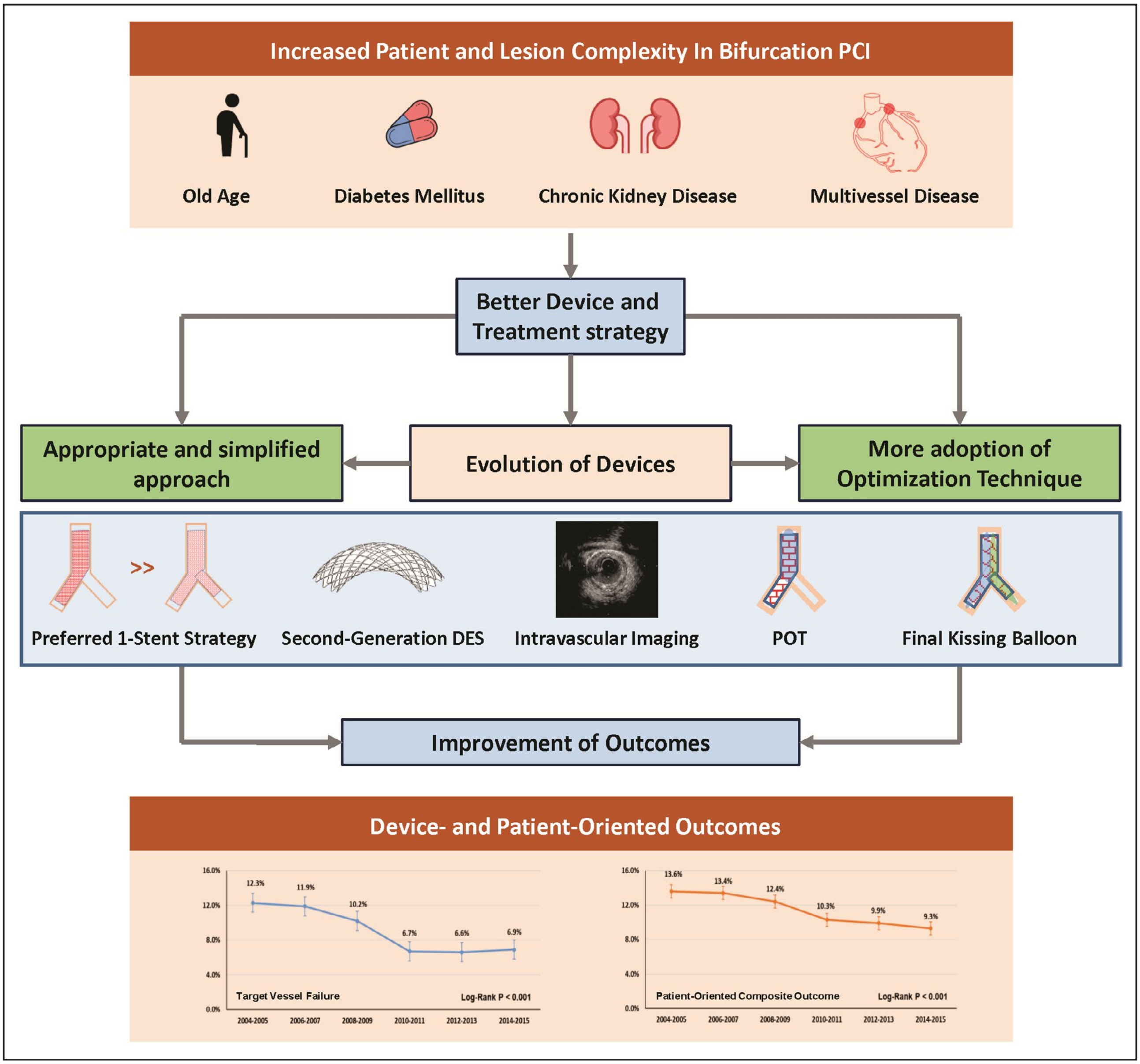

Figure 6. Ten-year trends in coronary bifurcation percutaneous coronary intervention (PCI).
This study evaluated the 10-year trends in bifurcation PCI in terms of patient/lesion characteristics, devices, bifurcation PCI and stent optimization techniques, and clinical outcomes. During the past decade, patient and lesion complexity in the target population for bifurcation PCI significantly increased. Practice patterns also significantly changed: almost all procedures are now performed using second-generation drug-eluting stents (DES); the 1-stent strategy has become the most commonly used strategy; procedural optimization techniques (intravascular ultrasound [IVUS] guidance, final kissing balloon [FKB], and proximal optimization technique [POT]) are increasingly used. Despite increased patient and lesion complexity, clinical outcomes after bifurcation PCI have improved as a result of enhanced devices, better patient and lesion selection, simplified procedures, and the use of advanced procedural optimization techniques. The current results from 10 years of experience support the contemporary consensus statement about bifurcation PCI and imply that practice patterns are heading in the right direction to enhance patient outcomes.

expert consensus has recommended the provisional 1-stent strategy as the primary strategy for bifurcation lesions, not all lesions can be treated using this strategy.[1,2,4–6] Despite heterogeneous reports about the comparative prognoses with various 2-stent techniques,[4] procedural optimization techniques such as POT, FKB, and intravascular imaging have been considered as essential tools in any 2-stent strategy.[4] Conversely, no standard consensus has emerged regarding the role of procedural optimization techniques with the 1-stent strategy. The current results indicate that POT, FKB, and IVUS guidance offer prognostic benefit in patients treated with a 2-stent strategy but not in those treated with a 1-stent strategy. The limited benefit provided by optimization techniques with 1-stent procedures might be attributable to the relatively lower event rates and favorable prognoses of the 1-stent strategy. On the contrary, the 2-stent strategy requires better preprocedural planning, the selection of a specific stent technique appropriate to the bifurcation anatomy, optimal sizing, and sufficient expansion of the implanted stent to prevent procedural complications and adverse clinical events after PCI. Therefore, the higher effect size of the procedural optimization techniques in patients receiving 2-stent procedures might not be unexpected. In addition, the increased adoption of the optimization techniques could be another potential explanation for the improved clinical outcomes from the 2-stent strategy found in our data. The current results thus suggest that meticulous selection of a proper target lesion, better preprocedural planning, and high-quality post-PCI optimization could be more important than the selection of a specific 2-stent technique.

Limitations

This study has some limitations. First, although we secured a large sample size using the patient-pooled method to yield statistical power, the current study design was retrospective and our data could contain unmeasured confounders, such as temporal changes in procedural volume, operator experience and proficiency in bifurcation PCI, and reimbursement criteria. Second, considering a difference in the practice pattern for bifurcation PCI across countries,[36] generalizability of the current findings might be limited. Third, temporal changes in medical treatment and the resulting prognostic impact could not be evaluated. Fourth, we could not include temporal changes after 2015. Fifth, although the use of IVUS during bifurcation PCI was collected, specific timing of IVUS use (pre-PCI, post-PCI, or both) or whether an optimal post-PCI result was achieved could not be collected.

CONCLUSIONS

During the past decade of bifurcation PCI, major changes have occurred in patient and lesion characteristics, devices, PCI strategy including stent optimization techniques, and patient prognosis. Despite increased patient and lesion complexity, clinical outcomes after bifurcation PCI have improved, mainly because of better devices and more widespread adoption of procedural optimization techniques and appropriate treatment strategies. Our data from the past 10 years support the contemporary consensus statement about bifurcation PCI and imply that practice patterns are heading in the right direction to improve patient outcomes.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Table S1
Figure S1

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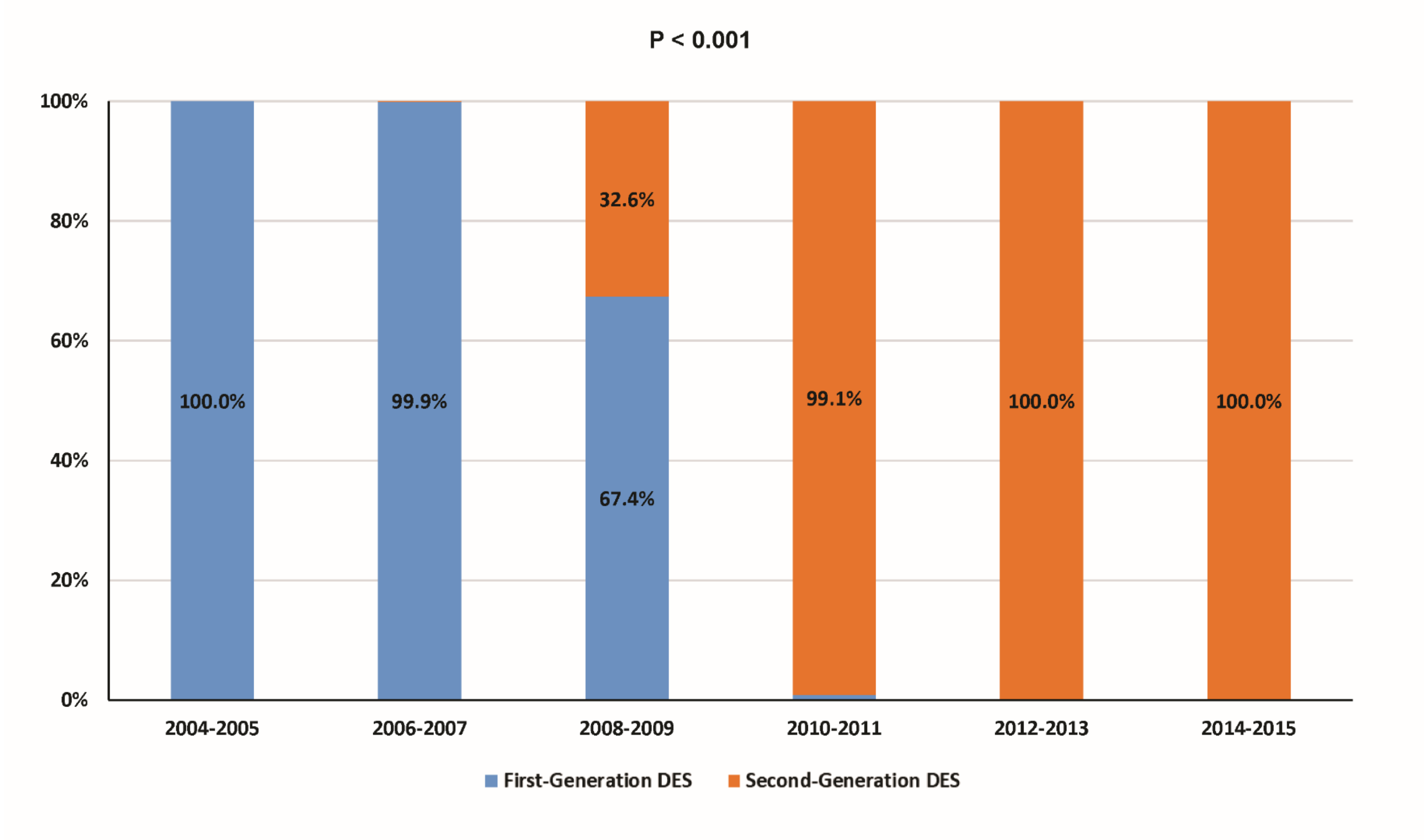
Supplemental Material

Table S1. Interaction of Changes in Trends between TVF risk and Covariables.

Covariables	Interaction P value
2nd generation DES	**<0.001**
True bifurcation	**0.013**
Age (per 1 year)	0.842
Male	0.280
Diabetes mellitus	0.679
Chronic kidney disease	0.114
Left main bifurcation	0.285
Multivessel disease	0.527
Radial access	0.574
Final kissing balloon	0.063
Proximal optimization technique	0.759
Image-guidance	0.479

DES, drug-eluting stent.

Figure S1. Annual Trends in Type of Stent Used.



Bar plots showing the proportion of stent types used. After 2010–2011, second-generation DES almost completely replaced first-generation DES. DES, drug-eluting stent.