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# Transradial Versus Transfemoral Access for Bifurcation Percutaneous Coronary Intervention Using Second-Generation Drug-Eluting Stent

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**Trial Registration**ClinicalTrials.gov Identifier: [NCT03068494](https://clinicaltrials.gov/ct2/show/study/NCT03068494)<sup>20</sup>Division of Cardiology, Department of Internal Medicine, Ajou University Hospital, Ajou University College of Medicine, Suwon, Korea<sup>21</sup>Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, Chonnam National University College of Medicine, Gwangju, Korea<sup>22</sup>Division of Cardiology, Department of Internal Medicine, Bucheon Sejong Hospital, Bucheon, Korea**ABSTRACT**

**Background:** The benefits of transradial access (TRA) over transfemoral access (TFA) for bifurcation percutaneous coronary intervention (PCI) are uncertain because of the limited availability of device selection. This study aimed to compare the procedural differences and the in-hospital and long-term outcomes of TRA and TFA for bifurcation PCI using second-generation drug-eluting stents (DESs).

**Methods:** Based on data from the Coronary Bifurcation Stenting Registry III, a retrospective registry of 2,648 patients undergoing bifurcation PCI with second-generation DES from 21 centers in South Korea, patients were categorized into the TRA group (n = 1,507) or the TFA group (n = 1,141). After propensity score matching (PSM), procedural differences, in-hospital outcomes, and device-oriented composite outcomes (DOCOs; a composite of cardiac death, target vessel-related myocardial infarction, and target lesion revascularization) were compared between the two groups (772 matched patients each group).

**Results:** Despite well-balanced baseline clinical and lesion characteristics after PSM, the use of the two-stent strategy (14.2% vs. 23.7%,  $P = 0.001$ ) and the incidence of in-hospital adverse outcomes, primarily driven by access site complications (2.2% vs. 4.4%,  $P = 0.015$ ), were significantly lower in the TRA group than in the TFA group. At the 5-year follow-up, the incidence of DOCOs was similar between the groups (6.3% vs. 7.1%,  $P = 0.639$ ).

**Conclusion:** The findings suggested that TRA may be safer than TFA for bifurcation PCI using second-generation DESs. Despite differences in treatment strategy, TRA was associated with similar long-term clinical outcomes as those of TFA. Therefore, TRA might be the preferred access for bifurcation PCI using second-generation DES.

**Trial Registration:** ClinicalTrials.gov Identifier: [NCT03068494](https://clinicaltrials.gov/ct2/show/study/NCT03068494)**Keywords:** Transradial Approach; Bifurcation; Percutaneous Coronary Intervention; Drug-Eluting Stent**INTRODUCTION**

Several randomized controlled trials have demonstrated that transradial access (TRA), compared to transfemoral access (TFA), offers similar procedural success rates while reducing vascular complications and mortality, particularly in patients with acute coronary syndrome.<sup>1-3</sup> Current guidelines recommend TRA over TFA for patients with acute coronary syndrome and endorse TRA for patients with stable ischemic heart disease.<sup>4,5</sup>

Recent technological advances in percutaneous coronary intervention (PCI) devices have made TRA the default route for treating complex coronary artery diseases. However, several operators advocate TFA over TRA during complex PCIs, likely because of the greater backup support with a large-bore guiding catheter and the availability of larger devices. Furthermore, no clear evidence or guidelines exist regarding the clinical benefits of TRA

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**Disclosure**

The authors have no potential conflicts of interest to disclose.

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Conceptualization: Lee JH, Youn YJ. Data curation: Lee JH, Youn YJ. Formal analysis: Lee JH, Youn YJ. Funding acquisition: Youn YJ, Gwon HC. Investigation: Lee JH, Youn YJ, Jeon HS, Lee JW, Ahn SG. Methodology: Lee JH, Youn YJ, Jeon HS, Lee JW, Ahn SG. Software: Lee JH, Youn YJ. Validation: Lee JH, Youn YJ, Jeon HS, Lee JW, Ahn SG. Visualization: Lee JH, Youn YJ. Writing - original draft: Lee JH, Youn YJ. Writing - review & editing: Lee JH, Youn YJ, Jeon HS, Lee JW, Ahn SG, Yoon J, Gwon HC, Song YB, Choi KH, Kim HS, Chun WJ, Hur SH, Nam CW, Cho YK, Han SH, Rha SW, Chae IH, Jeong JO, Heo JH, Lim DS, Park SJ, Hong MK, Doh JH, Cha KS, Kim DI, Lee SY, Chang K, Hwang BH, Choi SY, Jeong MH, Lee HJ.

over TFA for complex PCI, such as bifurcation PCI, which accounts for approximately 15% of all PCI cases.<sup>6,7</sup> TRA is a feasible alternative, even for left main (LM) bifurcation treatment, in previous Coronary Bifurcation Stenting (COBIS) registries.<sup>8,9</sup> However, these registries involved first-generation drug-eluting stents (DESs). This study compared the procedural differences and in-hospital and long-term outcomes of TRA and TFA for bifurcation PCI using second-generation DESs.

**METHODS****Study population**

The COBIS III Registry, a multicenter, observational, real-world registry, includes 2,648 patients treated for bifurcation lesions using second-generation DESs between January 2010 and December 2014 at 21 PCI centers in South Korea. Patients were categorized into two groups based on the vascular access: TRA, 1,507 (56.9%) patients; TFA, 1,141 (43.1%) patients.

The major inclusion criteria were any bifurcation lesions treated solely with second-generation DESs; a main vessel diameter  $\geq 2.5$  mm; and a side branch diameter  $\geq 2.0$  mm, confirmed with core laboratory quantitative coronary angiography analysis. The major exclusion criteria were cardiogenic shock, cardiac arrest with successful resuscitation during hospitalization, protected LM disease, and severe left ventricular dysfunction (i.e., ejection fraction  $< 30\%$ ). The COBIS III Registry has been previously described.<sup>10</sup>

**Procedural details**

PCI procedures were performed using current standard guidelines and conventional techniques. All patients received a loading dose of aspirin (300 mg) and P2Y12 inhibitors (clopidogrel [300–600 mg], prasugrel [60 mg], or ticagrelor 180 mg) at least 12 hours before PCI.<sup>4,5</sup> The vascular access route was selected by the attending physicians. Stenting techniques, including one- or two-stent strategies, final kissing balloon (FKB), proximal optimization technique (POT), or re-POT, and the DES were selected at the operators' discretion. Intravascular ultrasound-guided intervention was recommended to obtain optimal stent expansion and apposition. The type, dose, and duration of dual antiplatelet therapy and cardiovascular medications were decided by the physician.

**Data collection and quantitative coronary angiography analysis**

A web-based reporting system collected data on the patients' demographics, medications, laboratory findings, and angiographic and procedure details. Follow-up outcomes were collected from medical records or telephone interviews in cases of follow-up loss. An angiographic core laboratory (Heart Vascular Stroke Institute in Samsung Medical Center, Seoul, Korea) quantitatively analyzed baseline and procedural coronary angiograms using an automated edge-detection system (Centricity CA 1000; GE Healthcare, Waukesha, WI, USA).<sup>10</sup> Bifurcation lesions were divided into three segments; proximal main vessel, distal main vessel, and side branch. Those with Medina Classifications<sup>11</sup> of 1.1.1, 1.0.1, and 0.1.1 were considered true bifurcations.

**Study endpoints**

The primary endpoint was the incidence of device-oriented composite outcome (DOCO), defined as the composite of cardiac death, target vessel-related myocardial infarction (MI), and target lesion revascularization. The secondary endpoints included the individual components

of the DOCO, patient-oriented composite outcome (i.e., a composite of death from any cause, any MI, and any revascularization), and target vessel revascularization. In-hospital outcomes were evaluated based on periprocedural complications, which included access site complications, periprocedural MI, emergent repeat procedures, cardiogenic shock, and acute heart failure. All clinical events were verified by an independent clinical event adjudicating committee composed of interventional cardiology experts not involved in patient enrolment, as previously described.<sup>10</sup>

### Statistical analysis

Data are presented as number (%) or mean  $\pm$  standard deviation. Continuous variables were compared using Student's *t*-tests. Categorical variables were compared using  $\chi^2$  or Fisher's exact tests. The cumulative events of clinical outcomes were assessed using Kaplan–Meier estimates and compared with log-rank tests. All clinical endpoints were analyzed until the date of an endpoint event, loss to follow-up, or up to 5 years after the index procedure.

Propensity scores were estimated using multivariate logistic regression analyses on all covariates listed in **Tables 1** and **2**. Nearest-neighbor matching with a caliper of 0.005 was used and considered satisfactory when the standardized mean differences were  $< 10\%$  (**Supplementary Fig. 1**). The propensity scores yielded a C-statistic of 0.714, which indicated a good ability to differentiate between both groups. In subgroup analysis, adjusted hazard rates were calculated by means of multivariate Cox regression with clinical and lesion characteristics among propensity scores-matched populations.

**Table 1.** Baseline characteristics

Characteristics	Total population				PS-matched population			
	TRA (n = 1,507)	TFA (n = 1,141)	P value	SMD	TRA (n = 772)	TFA (n = 772)	P value	SMD
Age, yr	63.5 $\pm$ 10.7	64.0 $\pm$ 11.4	0.232	0.047	64.2 $\pm$ 10.6	63.4 $\pm$ 11.1	0.157	0.072
Male sex	1,170 (77.6)	843 (73.9)	0.025	0.088	583 (75.5)	581 (75.3)	0.906	0.006
Hypertension	817 (54.2)	687 (60.2)	0.002	0.121	446 (57.8)	457 (59.2)	0.570	0.029
Diabetes mellitus	513 (34.0)	392 (34.4)	0.866	0.007	249 (32.3)	269 (34.8)	0.281	0.055
Insulin-dependent	34 (2.3)	51 (4.5)	0.001	0.123	23 (3.0)	24 (3.1)	0.882	0.008
Dyslipidemia	475 (31.5)	534 (46.8)	$< 0.001$	0.317	326 (42.2)	322 (41.7)	0.837	0.010
Current smoking	427 (28.3)	371 (32.5)	0.020	0.091	229 (29.7)	243 (31.5)	0.439	0.039
Chronic kidney disease	31 (2.1)	78 (6.8)	$< 0.001$	0.233	27 (3.5)	28 (3.6)	0.891	0.007
Dialysis dependent	9 (0.6)	35 (3.1)	$< 0.001$	0.185	9 (1.2)	13 (1.7)	0.390	0.044
Previous MI	69 (4.6)	44 (3.9)	0.362	0.036	37 (4.3)	27 (3.5)	0.429	0.040
Previous PCI	187 (12.4)	136 (11.9)	0.703	0.015	103 (13.3)	94 (12.2)	0.492	0.035
Previous CVA	79 (5.2)	98 (8.6)	0.001	0.132	48 (6.2)	50 (6.5)	0.835	0.011
Stable ischemic heart disease	620 (41.1)	409 (35.8)			306 (39.6)	301 (39.0)		
NSTE-ACS	794 (52.7)	531 (46.5)			394 (51.0)	387 (50.1)		
STEMI	93 (6.2)	201 (17.6)			72 (9.3)	84 (10.9)		
<b>Medications at discharge</b>								
Aspirin	1,480 (98.4)	1,122 (98.3)	0.889	0.063	762 (98.7)	763 (98.8)	0.817	0.012
P2Y12 inhibitor	1,483 (98.6)	1,125 (98.6)	0.990	0.063	770 (99.7)	770 (99.7)	$> 0.999$	$< 0.001$
Clopidogrel	1,369 (92.0)	1,062 (94.0)	0.051	0.063	722 (93.5)	724 (93.8)	0.835	0.011
Prasugrel	61 (4.1)	39 (3.5)	0.391	0.063	26 (3.4)	27 (3.5)	0.889	0.007
Ticagrelor	55 (3.7)	24 (2.1)	0.020	0.064	22 (2.8)	19 (2.5)	0.635	0.024
$\beta$ -blocker	879 (58.4)	741 (64.9)	0.001	0.063	489 (63.3)	476 (61.7)	0.494	0.035
ACE inhibitor or ARB	887 (59.0)	736 (64.6)	0.003	0.029	483 (62.6)	481 (62.3)	0.916	0.005
Statin	1,347 (89.6)	1,022 (89.6)	0.994	0.063	702 (90.9)	700 (90.7)	0.860	0.009

Data are presented as number (%) or mean  $\pm$  standard deviation.

TRA = transradial access, TFA = transfemoral access, SMD = standardized mean difference, PS = propensity score, MI = myocardial infarction, PCI = percutaneous coronary intervention, CVA = cerebrovascular attack, NSTE-ACS = non-ST-segment-elevation-acute coronary syndrome, STEMI = ST-segment-elevation myocardial infarction, ACE = angiotensin converting enzyme, ARB = angiotensin II receptor blocker.

**Table 2.** Lesion characteristics

Characteristics	Total population				PS-matched population			
	TRA (n = 1,507)	TFA (n = 1,141)	P value	SMD	TRA (n = 772)	TFA (n = 772)	P value	SMD
Diseased vessel <sup>a</sup>			< 0.001	0.178			0.950	0.007
1 vessel	617 (40.9)	384 (33.7)			280 (36.3)	285 (36.9)		
2 vessels	611 (40.5)	477 (41.8)			326 (42.2)	320 (41.5)		
3 vessels	279 (18.5)	280 (24.5)			166 (21.5)	167 (21.6)		
Bifurcation location			< 0.001	0.190			0.506	0.063
Left main	472 (31.3)	463 (40.6)			306 (39.6)	283 (36.7)		
LAD/diagonal	734 (48.7)	474 (41.5)			333 (43.1)	349 (45.2)		
LCX/OM	213 (14.1)	137 (12.0)			92 (11.9)	104 (13.5)		
RCA (PL/PDA)	88 (5.8)	67 (5.9)			41 (5.3)	36 (4.7)		
Medina classification			< 0.001	0.038			0.215	0.005
1.1.1	492 (32.6)	347 (30.4)			256 (33.2)	228 (29.5)		
1.0.1	100 (6.6)	68 (6.0)			47 (6.1)	52 (6.7)		
0.1.1	110 (7.3)	138 (12.1)			67 (8.7)	92 (11.9)		
1.0.0	181 (12.0)	115 (10.1)			83 (10.8)	86 (11.1)		
1.1.0	258 (17.1)	169 (14.8)			122 (15.8)	108 (14.0)		
0.1.0	324 (21.5)	251 (22.0)			171 (22.2)	170 (22.0)		
0.0.1	42 (2.8)	53 (4.6)			26 (3.4)	36 (4.7)		
In-stent restenosis lesion	32 (2.1)	44 (3.9)	0.008	0.102	20 (2.6)	19 (2.5)	0.871	0.008
Moderate to severe calcification	308 (20.4)	238 (20.9)	0.791	0.010	169 (21.9)	163 (21.1)	0.710	0.019
Chronic total occlusion	130 (8.6)	159 (13.9)	< 0.001	0.168	80 (10.4)	79 (10.2)	0.933	0.004
Thrombotic lesion	27 (1.8)	44 (3.9)	0.001	0.125	17 (2.2)	17 (2.2)	> 0.999	< 0.001

Data are presented as number (%).

TRA = transradial access, TFA = transfemoral access, SMD = standardized mean difference, PS = propensity score, LAD = left anterior descending artery, LCX = left circumflex artery, OM = obtuse marginal artery, RCA = right coronary artery, PL = posterolateral artery, PDA = posterior descending artery.

<sup>a</sup>A diseased vessel was defined as a vessel with at least 50% stenosis.

Statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R Statistical Software version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). *P* values < 0.05 was considered statistically significant.

### Ethics statement

The Institutional Review Board approved this study (Wonju Severance Christian Hospital IRB, CR316133). The requirement for patient-informed consent was waived owing to the retrospective nature of the study.

## RESULTS

### Baseline characteristics

In the total study population, patients in the TRA group were more likely to be male than those in the TFA group, and less likely to have a history of cardiovascular risk factors such as hypertension, insulin-dependent diabetes, dyslipidemia, chronic kidney disease, and previous cerebrovascular accident (**Table 1**). In addition, patients with ST-segment elevation MI were less likely to be treated via TRA. After conducting propensity score matching (PSM), no statistical differences existed between the two groups with respect to baseline clinical variables, clinical presentation, and medications at discharge.

### Lesion characteristics

In the total study population, the prevalence of complex lesions was lower in the TRA group than in the TFA group (**Table 2**). Specifically, the TRA group had a lower incidence of multivessel disease, LM bifurcation lesions, in-stent restenosis lesions, chronic total

occlusion, and thrombotic lesions. However, after PSM, all lesion characteristics were similar between the two groups.

### Procedural characteristics and in-hospital adverse outcomes

In the total study population, patients in the TRA were more likely to be treated with the one-stent strategy, whereas patients in the TFA were more likely to be treated with the two-stent strategy (Table 3). Thus, the TRA group had a significantly lower number of stents used, less use of FKB inflation, and greater use of POT or re-POT than the TFA group. After PSM, differences remained with regard to the proportion of patients being treated with the two-stent strategy in the TRA group versus the TFA group (14.2% vs. 23.7%,  $P < 0.001$ ), number of stents used ( $1.8 \pm 0.9$  vs.  $1.9 \pm 1.1$ ,  $P < 0.001$ ), and use of FKB (27.5% vs. 36.5%,  $P < 0.001$ ).

In the total study population, the TRA group, compared to the TFA group, had significantly lower rates of periprocedural complications (2.2% vs. 4.9%,  $P < 0.001$ ), primarily driven by the lower rate of access site complications (0.5% vs. 1.7%,  $P = 0.002$ ). These differences

**Table 3.** Procedural characteristics and in-hospital adverse outcomes

Characteristics	Total population			PS-matched population		
	TRA (n = 1,507)	TFA (n = 1,141)	P value	TRA (n = 772)	TFA (n = 772)	P value
Treatment strategy			< 0.001			< 0.001
One-stent strategy	1,320 (87.6)	840 (73.6)		654 (84.7)	567 (73.4)	
1-stent without side branch ballooning	1,043 (69.2)	642 (56.3)		508 (65.8)	434 (56.2)	
1-stent with side branch ballooning	277 (18.4)	198 (17.4)		146 (18.9)	133 (17.2)	
Two-stent strategy	174 (11.5)	267 (23.4)		110 (14.2)	183 (23.7)	
Crush	103 (6.8)	141 (12.4)		63 (8.2)	96 (12.4)	
T-stenting or TAP	52 (3.5)	73 (6.4)		37 (4.8)	48 (6.2)	
Culottes	9 (0.6)	22 (1.9)		2 (0.3)	16 (2.1)	
Kissing or V-stenting	10 (0.7)	31 (2.7)		8 (1)	23 (3)	
Other	10 (0.7)	34 (3.0)		8 (1)	22 (2.8)	
No. of stents used	1.7 ± 0.9	1.9 ± 1.0	< 0.001	1.8 ± 0.9	1.9 ± 1.1	< 0.001
Stent type			< 0.001			< 0.047
Everolimus-eluting stent	543 (47.6)	733 (48.6)		372 (48.2)	362 (46.9)	
Zotarolimus-eluting stent	361 (31.6)	375 (24.9)		243 (31.5)	216 (28.0)	
Biolimus-eluting stent	177 (15.5)	337 (22.4)		119 (15.4)	160 (20.7)	
Mixed or other stent	60 (5.3)	62 (4.1)		38 (4.9)	34 (4.4)	
Maximal stent diameter, mm						
Main vessel	3.22 ± 0.44	3.18 ± 0.44	0.029	3.26 ± 0.44	3.19 ± 0.44	0.001
Side branch	2.97 ± 0.49	2.93 ± 0.52	0.456	3.00 ± 0.50	2.91 ± 0.52	0.227
Stent length, mm						
Main vessel	28.5 ± 13.1	29.7 ± 14.7	0.037	29.4 ± 14.0	28.5 ± 12.6	0.203
Side branch	21.8 ± 8.1	20.7 ± 7.9	0.223	21.8 ± 8.5	20.9 ± 8.1	0.434
Final kissing balloon	380 (25.2)	409 (35.8)	< 0.001	212 (27.5)	282 (36.5)	< 0.001
POT or re-POT	487 (32.3)	313 (27.4)	0.007	248 (32.1)	216 (28.0)	0.076
NC balloon use	301 (20.0)	233 (20.4)	0.776	185 (19.7)	149 (19.3)	0.847
IVUS guidance	609 (40.4)	477 (41.8)	0.470	318 (41.2)	340 (44.0)	0.258
Rotational atherectomy	5 (0.3)	11 (1.0)	0.038	5 (0.6)	7 (0.9)	0.562
Periprocedural complication	33 (2.2)	56 (4.9)	< 0.001	17 (2.2)	34 (4.4)	0.015
Access site complication	7 (0.5)	19 (1.7)	0.002	2 (0.3)	14 (1.8)	0.003
Access site hematoma or oozing	3 (0.2)	10 (0.9)	0.014	1 (0.1)	7 (0.9)	0.070
Access site dissection	4 (0.3)	9 (0.8)	0.056	1 (0.1)	7 (0.9)	0.070
Periprocedural MI	8 (0.5)	7 (0.6)	0.779	5 (0.6)	4 (0.5)	0.738
Emergent repeat procedure	5 (0.3)	6 (0.5)	0.442	3 (0.4)	3 (0.4)	> 0.999
Cardiogenic shock	3 (0.2)	5 (0.4)	0.302	1 (0.1)	3 (0.4)	0.317
Acute heart failure	4 (0.3)	5 (0.4)	0.512	2 (0.3)	2 (0.3)	> 0.999

Data are presented as number (%) or mean ± standard deviation.

TRA = transradial access, TFA = transfemoral access, PS = propensity score, TAP = T and small protrusion, POT = proximal optimization technique, NC = noncompliant, IVUS = intravascular ultrasound, MI = myocardial infarction.

were maintained after PSM, with access site complications of 0.3% and 1.8% ( $P = 0.003$ ) in the TRA and TFA groups, respectively. However, no significant differences existed between the TRA and TFA groups in other adverse events such as periprocedural MI, emergent repeat procedures, cardiogenic shock, and acute heart failure.

In addition, a temporal trend of increased use of TRA for bifurcation PCI was observed (Supplementary Fig. 2). The percentage of TRA procedures increased from 46.6% to 70.7% over the study period.

**Long-term clinical outcomes**

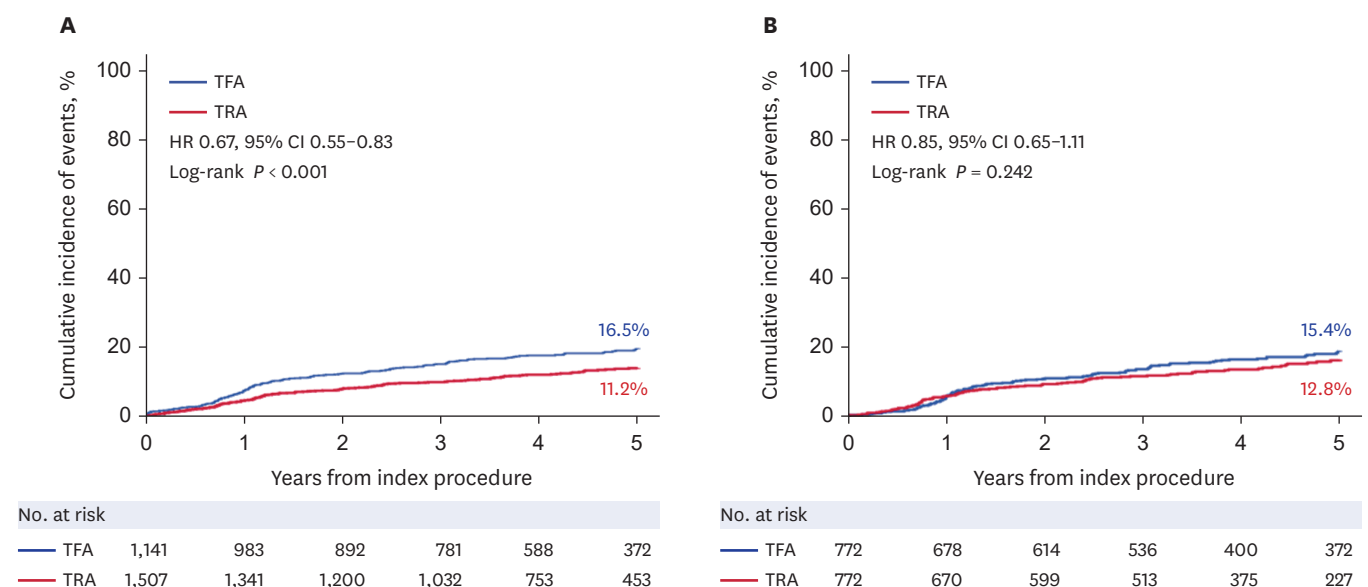
The median follow-up duration was 53 months. In the total population, the incidence of DOCO, the primary outcome, was significantly lower in the TRA group than in the TFA group (Table 4, Fig. 1A). In addition, the secondary outcomes patient-oriented composite outcome, target lesion revascularization, and target vessel revascularization were lower in the TRA group. However, the incidence of all adverse clinical events was similar between the two groups after PSM (Fig. 1B). The incidence of DOCO was not different between the TRA and

**Table 4.** Cumulative incidence of adverse events at 5 years

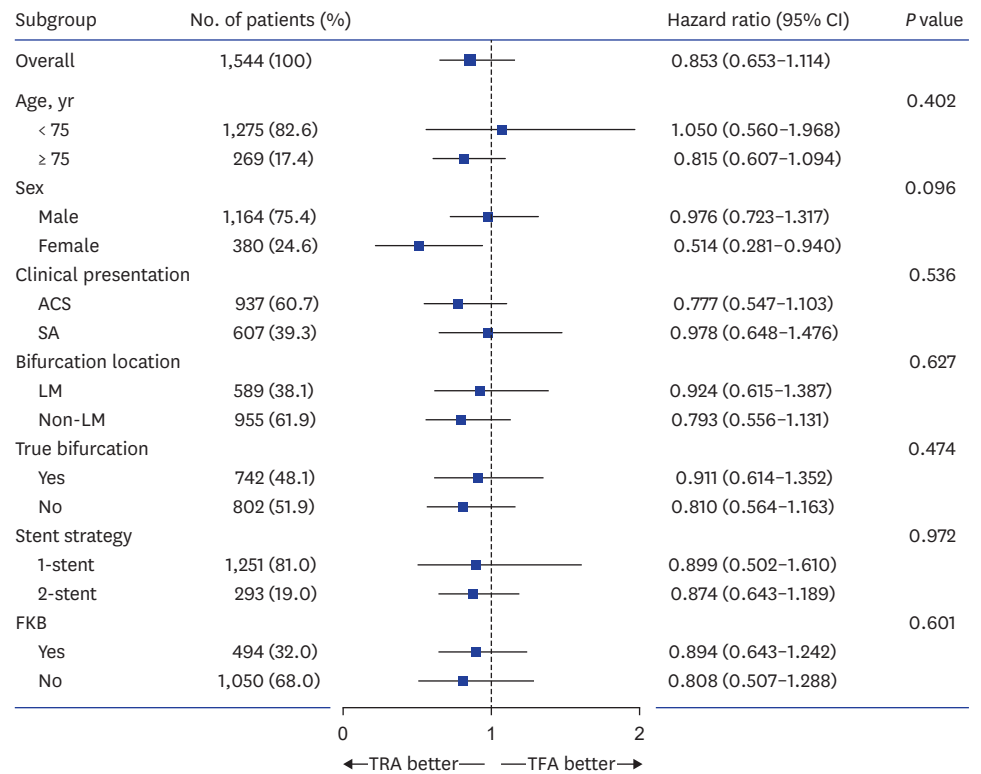
Variables	Total population			PS-matched population		
	TRA (n = 1,507)	TFA (n = 1,141)	Log rank P value	TRA (n = 772)	TFA (n = 772)	Log rank P value
Device-oriented composite outcome	80 (5.3)	89 (7.8)	0.010	49 (6.3)	55 (7.1)	0.639
Cardiac death	32 (2.1)	30 (2.6)	0.434	23 (3.0)	16 (2.1)	0.204
Target vessel-related MI	9 (0.6)	15 (1.3)	0.055	4 (0.5)	10 (1.3)	0.122
Target lesion revascularization	47 (3.1)	58 (5.1)	0.011	26 (3.4)	37 (4.8)	0.201
Patient-oriented composite outcome	169 (11.2)	188 (16.5)	< 0.001	99 (12.8)	119 (15.4)	0.242
Death from any cause	48 (3.2)	66 (5.8)	0.002	31 (4.0)	35 (4.5)	0.763
Any myocardial infarction	18 (1.2)	22 (1.9)	0.127	10 (1.3)	13 (1.7)	0.565
Any revascularization	116 (7.7)	119 (10.4)	0.013	66 (8.5)	81 (10.5)	0.297
Target vessel revascularization	76 (5.0)	88 (7.7)	0.005	44 (5.7)	59 (7.6)	0.172

Data are presented as number (%).

TRA = transradial access, TFA = transfemoral access, PS = propensity score, MI = myocardial infarction.



**Fig. 1.** Patient-oriented composite outcome based on vascular access in the total (A) and propensity score-matched populations (B). HR = hazard ratio, CI = confidence interval, TFA = transfemoral access, TRA = transradial access.



**Fig. 2.** Subgroup analysis of device-oriented composite outcome. CI = confidence interval, ACS = acute coronary syndrome, SA = stable angina, LM = left main, TRA = transradial access, TFA = transfemoral access.

TFA groups (6.3% vs. 7.1%,  $P = 0.639$ ). **Fig. 2** illustrates the results of the subgroup analysis of DOCO, based on vascular access, among the propensity score-matched population. There were no significant differences between access sites in the various subgroups. Furthermore, detailed subgroup analysis also revealed no significant differences between access sites based on bifurcation location, medina classification, and whether intravascular ultrasound was used (**Supplementary Fig. 3**).

## DISCUSSION

We evaluated procedural differences, in-hospital adverse outcomes, and long-term clinical outcomes during a 5-year follow-up between TRA and TFA for bifurcation PCI by using multicenter, observational, real-world registry data in the second-generation DES era. The major study findings were: 1) compared to TFA, TRA was associated with a simple strategy involving less use of the two-stent and FKB techniques; 2) TRA was associated with lower in-hospital adverse outcomes, especially access site complications; 3) TRA and TFA had similar long-term clinical outcomes, despite differences in treatment strategy; and 4) an increasing trend was noted for using TRA for bifurcation PCI.

Previous large-scale randomized trials have revealed that TRA is superior to TFA in terms of access site bleeding, which ultimately reduced cardiac mortality, especially for patients with acute coronary syndrome.<sup>1-3</sup> To reduce bleeding complications, TRA is recommended as a default strategy across the whole spectrum of ischemic heart disease.<sup>12,13</sup> A recent meta-analysis<sup>14</sup> of LM



PCI also demonstrated that TRA was associated with reduced bleeding and lower access site or vascular complications compared with TFA. This is consistent with our findings.

Recent technological advances in PCI devices have allowed TRA to be used in complex coronary artery diseases. The preference for TRA over TFA in PCI is growing. However, many operators hesitate to use TRA, especially during a complex procedure, likely because of poor backup support and the limited availability of larger devices. Regarding the radial artery diameter, most patients can be treated with a conventional 6 French guide during TRA.<sup>15</sup> Nevertheless, the use of the two-stent strategy with a 6 French guide is limited, especially when two stents with larger diameters are inserted simultaneously. However, this limitation could be overcome by using a sheathless guide system or large-bore sheath, which provides a larger inner diameter without increasing the outer diameter.<sup>16,17</sup> Current guidelines recommend a one-stenting strategy with provisional side branch stenting as the initial approach for treating bifurcation lesions; the limitation of selecting the two-stent strategy should not affect clinical outcomes.<sup>18</sup> In this study, use of the two-stent strategy was significantly lower in the TRA group, followed by FKB, even after adjusting for baseline clinical and angiographic characteristics. Despite the limitations of the two-stent strategy during TRA, the clinical outcomes were similar between the two groups. These findings suggest that TRA operators tend to prefer simple procedures that do not result in poor clinical outcomes.

Previous studies have evaluated the clinical benefits of using TRA versus TFA for bifurcation PCI.<sup>8,9</sup> The COBIS I registry, which enrolled patients from 2004 to 2006, revealed no significant differences between TRA and TFA for non-LM lesions in procedural success rates or in long-term safety and efficacy.<sup>8</sup> The COBIS II Registry, which enrolled patients from 2003 to 2009 with LM and non-LM lesions, similarly demonstrated that TRA was superior to TFA in reducing bleeding complications and had comparable long-term clinical outcomes.<sup>9</sup> However, these studies used first-generation DESs and may therefore have limited applicability. Our study confirmed that TRA was superior to TFA in reducing vascular complications and had similar clinical outcomes to bifurcation PCI with second-generation DESs. In addition, the rate of TRA was 30.2% in the COBIS I registry, 24.9% in COBIS II, and 56.9% in this study, highlighting a growing preference for TRA in bifurcation PCI.

Our study had several limitations. First, this was a non-randomized, retrospective, observational study; therefore, the potential for selection bias exists. Thus, PSM was conducted to adjust for confounding variables. This registry did not have detailed information about sheath size or the use of a sheathless guide on TRA due to its retrospective nature. Second, the choice of access site was largely determined by operator preference or hospital policy, which led to differences in baseline clinical and angiographic variables between the TRA and TFA groups. Despite conducting PSM, residual confounding factors could have affected the results. Third, the COBIS III Registry does not provide data on the rate of crossover from TRA to TFA or vice versa during bifurcation PCI. It was possible to change access sites from TRA to TFA during bifurcation PCI due to unpredictable complications. Accordingly, future prospective studies might be required which include vascular access and the rate of crossover during bifurcation procedure. Fourth, data on non-access site bleeding were unavailable. Finally, the registry did not include data on physiology-guided PCI, which may have an impact on clinical outcomes.

In conclusion, TRA showed similar long-term clinical outcomes compared to TFA for bifurcation PCI using second-generation DESs. Furthermore, our study also suggested that

TRA enables operators to execute a simple strategy with fewer procedural complications compared to TFA. The use of TRA in bifurcation PCI is increasing. Nonetheless, further large randomized controlled studies are needed to confirm these findings. Overall, the results provide important clinical evidence to support the default use of TRA for bifurcation PCI.

## SUPPLEMENTARY MATERIALS

### Supplementary Fig. 1

Standardized mean difference before and after PSM.

### Supplementary Fig. 2

Temporal trend of the use of transradial access for bifurcation percutaneous coronary intervention.

### Supplementary Fig. 3

Further detailed subgroup analysis based on bifurcation location, medina classification, and whether intravascular ultrasound was used.

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