Radial Versus Femoral Access With or Without Vascular Closure Device in Patients With Acute Myocardial Infarction

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Compared with transradial intervention (TRI), it is unclear whether transfemoral intervention (TFI) with vascular closure device (VCD) improves major adverse cardiocerebrovascular events (MACCE) in patients with acute myocardial infarction (AMI). The aim of this study is to compare TRI versus TFI with or without VCD for reducing MACCEs. We examined 11,596 patients who underwent TRI or TFI from the Korean AMI Registry − National Institute of Health database. The MACCE at 1-year was defined as death, nonfatal MI, repeat revascularization, cerebrovascular accident, hospitalizations, and major bleedings. Because the patients were not randomly assigned to vascular access sites, propensity-score (PS) matching was performed. In the PS-matched cohorts, compared with TFI, TRI significantly reduced 1-year MACCEs (7.1% vs 10.1%; log-rank p < 0.001) through a reduction in major bleeding (0.6% vs 2.2%; p < 0.001). Compared with TRI, 1-year MACCEs (11.3% vs 7.9%, log-rank p < 0.001) and major bleedings (0.6% vs 2.2%; p < 0.001) were significantly greater in TFI without VCD, whereas TFI with VCD was comparable in 1-year MACCEs (7.5% vs 8.1%, log-rank p = 0.437) and major bleeding (0.7% vs 1.0%; p = 0.409). In conclusion, the use of VCD could be an alternative to avoid major bleeding and to improve clinical outcomes, particularly in high-risk patients who are not suitable for TRI.   © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:742−749)

Potent antiplatelet agents, anticoagulants, and percutaneous coronary intervention (PCI) are crucial to improve outcome in patients with acute myocardial infarction (AMI).[1,2] However, they increase bleeding complications which are related to clinical events. Therefore, it is important to balance thrombotic events and bleeding complications to improve outcome. In the recent randomized trials, radial access for PCI reduced major bleeding, and improved net adverse clinical events in patients with AMI.[3,4] It has been known that vascular closure devices (VCD) can effectively reduce major and minor bleeding complications after PCI.[5,6]

However, it is unclear whether radial compared with femoral access with VCD improves major adverse cardiocerebrovascular event (MACCE) after AMI. Accordingly, the aim of this study is to investigate whether femoral access with VCD would improve MACCEs compared with radial access in patients with AMI.

Methods

The Korean AMI Registry is a Korean, prospective, open, observational, multicenter, and online registry of AMI established with support of the National Institute of Health since November 2011. AMI was diagnosed on the basis of characteristic clinical presentation, serial changes on electrocardiography suggesting infarction, and increase in cardiac enzymes.[7] Patient and procedural details were recorded at the time of admission. All data are collected prospectively at each hospital, electronically encrypted, and recorded on an electronic web page-based case report form in National Institute of Health database. This research was supported by a fund (2013-E63005-02) by Research of Korea Centers for Disease Control and Prevention. The protocol was approved by the ethics committee of each participating institution, and all patients gave written informed consent to participate.

Initially, 13,104 patients (9,686 men; mean age = 64.0 ± 12.6-year-old) with a diagnosis of AMI at admission were registered in November 2011 to December 2015. Among them, 11,728 patients were identified as patients with AMI

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who underwent PCI. A total of 135 patients were recorded as having both radial and femoral access, and were excluded from this analysis. Finally, 11,596 patients were analyzed in this study (Figure 1).

All procedures were performed with standard interventional techniques. Access site selection before the diagnostic or therapeutic procedure was at the discretion of the treating physician. Decision of access site management after the procedure was made by the treating physician. VCD was used as per local practice. Antiplatelet therapy and periprocedural anticoagulation followed the standard regimen. Before the procedure, all patients received a loading dose of aspirin (300 mg) and clopidogrel (300 mg or 600 mg) or prasugrel (60 mg) or ticagrelor (180 mg) at the discretion of the attending physician. In the catheterization laboratory, anticoagulation with a bolus of unfractionated heparin (75 to 100 U/kg) was administered to achieve an activated clotting time >300 seconds. Routine use of postprocedure unfractionated heparin was not recommended unless patients requiring an intra-aortic balloon pump. Glycoprotein IIb/IIIa receptor inhibitor was left to the discretion of the attending interventional cardiologist. After the procedure, use of guideline directed medical therapy was mandatory, and the duration of dual antiplatelet agents was at the operator's discretion.

The 1-year MACCEs were defined as composite of death, nonfatal MI, repeat revascularization, cerebrovascular accident, rehospitalizations, and major bleeding. Major bleeding was defined as any observed bleeding which results in 5g/dL or more hemoglobin decrease, 15% or more hematocrit decrease, or intracranial hemorrhage. During the follow-up period, clinical outcome data were obtained by reviewing medical records, and interviewing patients by telephone.

Data are expressed as mean ± standard deviation for continuous variables and as percentages for categorical variables. Comparisons between baseline variables were assessed with a Student t test for continuous variables and a Pearson chi-square test for categorical variables. Patients were divided into transfemoral intervention (TFI) and transradial intervention (TRI) groups. Because the patients were not randomly assigned to vascular access sites, propensity-score (PS) matching was performed to reduce the effect of treatment-selection bias and potential confounding factors in this observational study. For each patient, a PS indicating the likelihood of using radial access during PCI was calculated using a nonparsimonious multivariable logistic regression model with covariates including baseline and angiographic characteristics,[8] leaving 3,528 TRI versus 3,528 TFI groups. TFI groups were further divided into TFI with VCD and TFI without VCD groups. PS matching was performed again for each patient, leaving 2,590 TRI versus 2,590 TFI without VCD, and 2,198 TRI versus 2,198 TFI with VCD, respectively. Goodness of fit of the PS was evaluated using the c-statistic and the Hosmer-Lemeshow test. To determine predictors for MACCEs and major bleeding, Cox proportional hazards regression models were used to provide adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). Variables with $p < 0.05$ in univariate analyses were included in multivariate analysis model. The MACCEs and major bleeding were compared by Kaplan-Meier survival curves for both unmatched and PS-matched cohorts. Landmark analyses were performed to determine whether any difference in long-term outcomes were because of maintenance of short-term effects or additional effects beyond 30 days. For all analyses, a two-sided $p < 0.05$ was considered statistically significant. Statistical analysis was performed using SAS version 9.1. (SAS Institute Inc., Cary, NC).
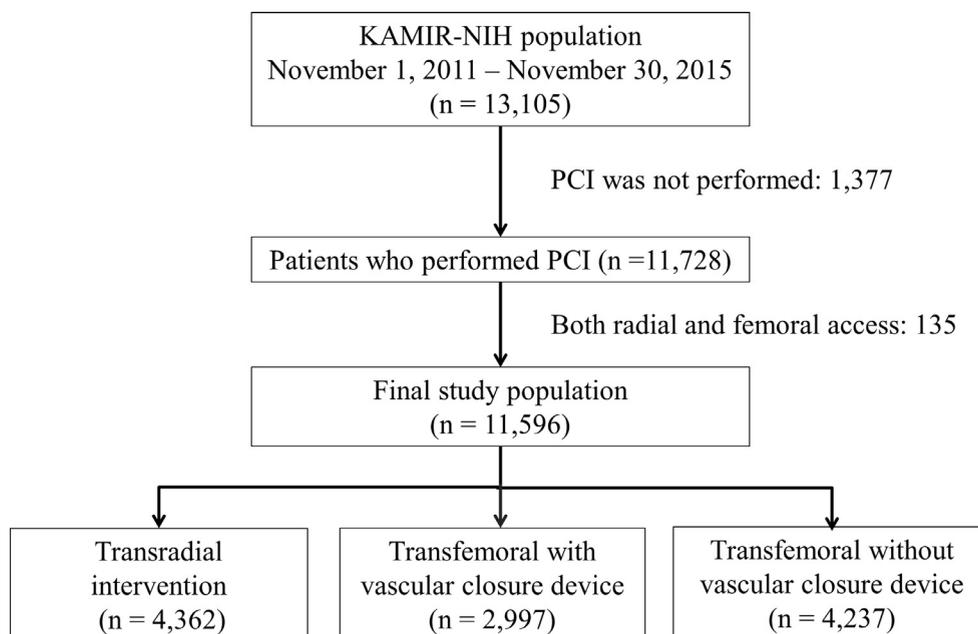

Figure 1. Flow diagram of the study subjects.
PCI = Percutaneous coronary intervention

Results

Baseline, angiographic, and procedural characteristics are presented in Supplementary Table 1 and 2, respectively. Mean age was 63.6±12.5 year-old and 8,723 were men. There were 4,362 patients in the TRI group and 7,234 patients in the TFI groups including 4,237 patients in the TFI without VCD group and 2,997 patients in the TFI with VCD group. Patients in the TRI groups had low-risk clinical and angiographic features such as young age, lower prevalence of ST-elevation MI, Killip class >1, cardiogenic shock hypertension, diabetes mellitus, hyperlipidemia, previous MI, less left main complex lesion, and pre-TIMI flow 0. Clinical outcomes were presented in Supplementary Table 3. The overall MACCEs were significantly lower in the TRI group compared with TFI group (6.6% vs 14.1%, p < 0.001) which was mainly driven by major bleeding (0.6% vs 2.7%, p < 0.001). When examining major bleeding, this was also lower in the TRI group compared with TFI without VCD group (0.6% vs 3.9%, p < 0.001), whereas there was no significant difference between TRI and TFI with VCD (0.6% vs 0.9%, p = 0.135).

Multivariable analysis identified TRI as predictor for 1-year MACCEs (HR 0.68, 95% CI 0.59 to 0.79; p < 0.001). TRI was also an independent predictor for major bleeding (HR 0.28, 95% CI 0.18 to 0.45; p < 0.001). Compared with TRI, TFI without VCD significantly increased 1-year MACCEs (HR 1.62, 95% CI 1.37 to 1.90; p < 0.001) and major bleeding (HR 4.78, 95% CI 3.02 to 7.58; p < 0.001), whereas TFI with VCD showed comparable outcomes in terms of 1-year MACCEs (HR 1.17, 95% CI 0.97 to 1.42; p = 0.093) and major bleeding (HR 1.27, 95% CI 0.69 to 2.31; p = 0.433). VCD was an independent predictor of major bleeding (HR 0.29, 95% CI 0.19 to 0.45; p < 0.001) and 1-year MACCEs (HR 0.67, 95% CI 0.57 to 0.79; p < 0.001) after adjusting confounding variables.

After PS-matching, baseline characteristics (Table 1) and angiographic characteristics (Table 2) were well balanced with no statistically significant differences in TRI versus TFI, TRI versus TFI with VCD, and TRI versus TFI without VCD, respectively. Clinical outcomes in the PS-matched cohort were presented in Table 3. The Kaplan-Meier curves for 30-day and 1-year MACCEs for PS-matched cohorts are shown in Figure 2. Compared with TFI, TRI was associated with significant reduction in MACCEs at 30 days (2.6% vs 3.9%; log-rank p = 0.002; Figure 2A) and at 1 year (7.1% vs 10.1%; log-rank p < 0.001; Figure 2B). The curves diverge over a short-term period and become almost parallel. The difference was mainly driven by reduced major bleeding (0.6% vs 2.2%; p < 0.001) within 30 days and reduced revascularization rates (1.4% vs 2.3%, p < 0.001) between 30 days and 1 year (Supplementary Table 4). When we divided the TFI into TFI with or without VCD, MACCEs were significantly greater in TFI without VCD compared with TRI at 30 days (5.2% vs 3.2%, log-rank p < 0.001; Figure 3A) and at 1 year (11.3% vs 7.9%, log-rank p < 0.001; Figure 3B), and the difference was mainly driven by reduced major bleeding (0.6% vs 2.2%; p < 0.001). However, there were no significant differences in MACCEs between TRI and TFI with VCD at 30 days (2.6% vs 3.9%; log-rank p = 0.057; Figure 4A) and at 1 year (7.5% vs 8.1%, log-rank p = 0.437; Figure 4B). There was no significant difference in major bleeding between 2 groups (0.7% vs 1.0%; p = 0.409).

Discussion

This study sought to investigate the association of vascular access site with outcome in patients with or without ST elevation MI. The main findings of this study are as follows. First, TRI significantly improves outcome compared with TFI. Second, reduction in clinical events in TRI is associated with reduced major bleeding. Third, the use of VCD in TFI is associated with a reduction in major bleeding and clinical events. Fourth, the long-term prognostic benefit conferred by TRI seems to be related to the reduction of early vascular complication such as major bleeding after the PCI.

The most intriguing finding of this study is that differences in terms of clinical events between TRI and TFI narrowed because major bleeding is comparable between 2 groups when VCD was used. In the previous studies, TRI showed less bleedings and vascular complications compared with TFI.[3,4,9] Although the mortality benefit with TRI has only been consistently demonstrated in patients with ST-segment elevation MI,[10] the benefit of TRI seemed to be apparent in terms of bleeding. The advantage of TRI mainly arises from anatomical position of radial artery, which is a superficial artery that is readily compressible, and is easier to achieve hemostasis compared with the femoral artery. However, not all patients are suitable for TRI despite its benefit. In the previous studies, crossover rate varied from 3.7% to 5.3% according to the experience of operators with TRI.[3,11−13] Therefore, the primary concern in our study is that how to improve outcome in patients who are not suitable for TRI. In the present study, TRI was superior to the TFI both in the unmatched and PS-matched cohort. However, when VCD was used with TFI, outcome was comparable between TRI and TFI in the PS-matched cohort because of reduced major bleeding. Therefore, the use of VCD could be an alternative option to avoid access site bleeding in TFI.

In the present study, compared with TRI, outcomes in the TFI were bifurcated according to the use of VCD; TRI was better than TFI without VCD, whereas it was comparable to the TFI with VCD. However, it is not consistent with the results of previous studies comparing VCDs and manual compression.[14] There are 2 plausible explanations. First, the differences in baseline characteristics between TRI and TFI without VCD may affect our results. In our study, patients in TFI without VCD have more high-risk clinical features such as cardiogenic shock, higher Killip class, and lower left ventricular ejection fraction. Therefore, the risk of clinical events and major bleeding may be higher than those of TRI group despite PS-matching. Second, low body mass index in Asian population may explain our result. The location of a femoral artery of Western population is much deeper than those of Asian population because of higher body mass index. Therefore, it is easier for Asian population to achieve hemostasis using VCDs. Although practice guidelines recommend

Table 1
Baseline characteristics in the matched cohort

Variable	Transfemoral intervention (n = 3,528)	Transradial intervention (n = 3,528)	p	Transfemoral intervention with vascular closure device (n = 2,198)	Transradial intervention (n = 2,198)	p	Transfemoral intervention without vascular closure device (n = 2,590)	Transradial intervention (n = 2,590)	p
Age (year)	63.4 ± 12.4	63.3 ± 12.5	0.858	62.9 ± 12.3	62.5 ± 12.6	0.323	63.9 ± 12.5	63.9 ± 12.6	0.928
Male	2706 (76.7%)	2682 (76.0%)	0.501	1679 (76.4%)	1690 (76.9%)	0.695	1953 (75.4%)	1947 (75.2%)	0.847
Body mass index (kg/m^2)	24.2 ± 3.4	24.2 ± 3.3	0.930	24.2 ± 3.4	24.3 ± 3.2	0.633	24.1 ± 3.3	24.1 ± 3.3	0.994
Initial presentation									
Systolic blood pressure (mmHg)	133.2 ± 28.0	133.2 ± 26.9	0.999	134.0 ± 26.9	133.7 ± 27.5	0.691	130.7 ± 28.9	131.2 ± 27.0	0.488
Heart rate (beats/min)	77.9 ± 18.1	78.1 ± 17.0	0.725	77.9 ± 18.5	77.5 ± 17.3	0.539	78.4 ± 18.5	78.2 ± 17.9	0.692
Chest pain	3133 (88.8%)	3132 (88.8%)	0.970	1971 (89.7%)	1973 (89.8%)	0.921	2263 (87.4%)	2264 (87.4%)	0.967
Dyspnea	733 (20.8%)	727 (20.6%)	0.860	540 (2.6%)	567 (25.8%)	0.348	512 (19.8%)	515 (19.9%)	0.917
ST-elevation myocardial infarction	1485 (42.1%)	1524 (43.2%)	0.343	1055 (48.0%)	1098 (50.0%)	0.179	1386 (53.5%)	1395 (53.9%)	0.802
Killip class >1	518 (14.7%)	507 (14.4%)	0.710	386 (17.6%)	360 (16.4%)	0.296	432 (16.7%)	434 (16.8%)	0.936
Cardiogenic shock	164 (4.6%)	138 (3.9%)	0.126	116 (5.3%)	110 (5.0%)	0.682	156 (6.0%)	136 (5.3%)	0.228
Hypertension*	1732 (49.1%)	1734 (49.1%)	0.962	1113 (50.6%)	1088 (49.5%)	0.451	1290 (49.8%)	1261 (48.7%)	0.420
Diabetes mellitus	936 (26.5%)	939 (26.6%)	0.936	573 (26.1%)	569 (25.9%)	0.891	720 (27.8%)	703 (27.1%)	0.597
Hyperlipidemia†	391 (11.1%)	396 (11.2%)	0.850	320 (14.6%)	314 (14.3%)	0.797	263 (10.2%)	242 (9.3%)	0.325
Current smoker	1450 (41.1%)	1439 (40.8%)	0.790	920 (41.9%)	935 (42.5%)	0.647	1042 (40.2%)	1042 (40.2%)	>0.999
Previous myocardial infarction	241 (6.8%)	239 (6.8%)	0.925	146 (6.6%)	134 (6.1%)	0.459	183 (7.1%)	189 (7.3%)	0.747
Previous angina pectoris	312 (8.8%)	303 (8.6%)	0.704	191 (8.7%)	192 (8.7%)	0.957	240 (9.3%)	233 (9.0%)	0.736
Left ventricular ejection fraction by volume (%)	52.4 ± 10.5	52.7 ± 10.5	0.212	52.8 ± 10.6	52.8 ± 10.5	0.946	51.7 ± 10.5	51.6 ± 10.8	0.747
Serum glucose (mg/dL)	162.8 ± 73.9	163.0 ± 75.1	0.910	163.7 ± 75.9	163.1 ± 76.5	0.809	169.7 ± 78.2	166.4 ± 77.9	0.140
Estimated glomerular filtration rate (mL/min)	85.5 ± 37.8	86.4 ± 30.7	0.286	82.5 ± 39.5	83.5 ± 29.3	0.332	85.5 ± 35.9	85.9 ± 32.3	0.613
Peak creatine kinase-MB (mg/dL)	114.2 ± 41.5	114.8 ± 39.1	0.996	115.7 ± 156.1	117.1 ± 138.4	0.768	121.9 ± 176.2	123.2 ± 143.1	0.776
Total cholesterol (mg/dL)	180.4 ± 45.0	180.8 ± 44.8	0.711	183.9 ± 46.9	183.5 ± 44.8	0.799	179.3 ± 45.6	178.7 ± 44.6	0.630
Low-density lipoprotein cholesterol (mg/dL)	114.2 ± 41.5	114.8 ± 39.1	0.596	113.3 ± 38.3	115.5 ± 41.0	0.084	114.4 ± 41.7	113.9 ± 38.5	0.689
Medical therapy									
Aspirin	3525 (99.9%)	3524 (99.9%)	0.705	2195 (99.9%)	2194 (99.8%)	0.705	2588 (99.9%)	2587 (99.9%)	0.655
Clopidogrel	2683 (76.0%)	2687 (76.2%)	0.911	1765 (80.3%)	1762 (80.2%)	0.910	1971 (76.1%)	1970 (76.1%)	0.974
Prasugrel	440 (12.5%)	459 (13.0%)	0.498	187 (8.5%)	195 (8.9%)	0.668	374 (14.4%)	393 (15.2%)	0.457
Ticagrelor	913 (25.9%)	912 (25.9%)	0.978	450 (20.5%)	445 (20.2%)	0.851	653 (25.2%)	631 (24.4%)	0.479
Beta-blockers	3025 (85.7%)	3037 (86.1%)	0.681	1876 (85.4%)	1880 (85.5%)	0.864	2220 (85.7%)	2207 (85.2%)	0.608
Angiotensin converting enzyme inhibitors / Angiotensinogen type II receptor blockers	2871 (81.4%)	2880 (81.6%)	0.783	1749 (79.6%)	1768 (80.4%)	0.474	2101 (81.1%)	2098 (81.0%)	0.915
Ca-channel blockers	219 (6.2%)	218 (6.2%)	0.961	136 (6.2%)	141 (6.4%)	0.756	146 (5.6%)	156 (6.0%)	0.553
Statin	3349 (94.9%)	3346 (94.8%)	0.871	2071 (94.2%)	2075 (94.4%)	0.794	2424 (93.6%)	2440 (94.2%)	0.353

Data expressed as mean ± SD or number (percent)

* Defined as previously diagnosed by a physician and/or receiving medication to lower blood pressure.

† Defined as previously diagnosed by a physician and/or receiving lipid-lowering drugs.

Table 2
Angiographic characteristics in the matched cohort

Variable	Transfemoral intervention (n = 3,528)	Transradial intervention (n = 3,528)	p	Transfemoral intervention with vascular closure device (n = 2,198)	Transradial intervention (n = 2,198)	p	Transfemoral intervention without vascular closure device (n = 2,590)	Transradial intervention (n = 2,590)	p
No. of narrowed coronary arteries									
1	1701 (48.2%)	1722 (48.8%)	0.617	1065 (48.5%)	1045 (47.5%)	0.546	1272 (49.1%)	1297 (50.1%)	0.487
2	1070 (30.3%)	1039 (29.5%)	0.420	629 (28.6%)	653 (29.7%)	0.426	744 (28.7%)	750 (29.0%)	0.854
3	597 (16.9%)	605 (17.1%)	0.800	413 (18.8%)	411 (18.7%)	0.938	450 (17.4%)	424 (16.4%)	0.335
Left main, isolated*	20 (0.6%)	15 (0.4%)	0.397	8 (0.4%)	10 (0.5%)	0.637	12 (0.5%)	9 (0.3%)	0.512
Left main, complex[†]	140 (4.0%)	147 (4.2%)	0.673	83 (3.8%)	79 (3.6%)	0.749	112 (4.3%)	110 (4.2%)	0.891
Target coronary artery			0.564			0.636			0.827
Left anterior descending	1676 (47.5%)	1648 (46.7%)		1022 (46.5%)	1006 (45.8%)		1238 (47.8%)	1198 (46.3%)	
Left circumflex	684 (19.4%)	686 (19.4%)		414 (18.8%)	417(19.0%)		410 (15.8%)	459 (17.7%)	
Right	1089 (30.9%)	1122 (31.8%)		724 (32.9%)	737 (33.5%)		875 (33.8%)	880 (34.0%)	
Left main	79 (2.2%)	71 (2.0%)		38 (1.7%)	38 (1.7%)		67 (2.6%)	52 (2.0%)	
Lesion type			0.823			0.687			0.791
Type A	67 (1.9%)	39 (1.1%)		56 (2.5%)	34 (1.5%)		26 (1.0%)	24 (0.9%)	
Type B1	463 (13.1%)	384 (10.9%)		396 (18.0%)	255 (11.6%)		239 (9.2%)	260 (10.0%)	
Type B2	1227 (34.8%)	1453 (41.2%)		532 (24.2%)	858 (39.1%)		1079 (41.7%)	1055 (40.8%)	
Type C	1771 (50.2%)	1649 (46.8%)		1214 (55.2%)	1050 (47.8%)		1246 (48.1%)	1249 (48.3%)	
Pre TIMI 0	1473 (41.8%)	1522 (43.2%)	0.234	1004 (45.7%)	1048 (47.7%)	0.183	1190 (45.9%)	1212 (46.8%)	0.531
Stent type									
Baremetal stent	28(0.8%)	28 (0.8%)	>0.999	20 (0.9%)	18 (0.8%)	0.745	19 (0.7%)	16 (0.6%)	0.611
Everolimus eluting stent	1538 (43.6%)	1546 (43.8%)	0.848	1020 (46.4%)	1014 (46.1%)	0.856	1128 (43.6%)	1134 (43.8%)	0.867
Zotarolimus eluting stent	692 (19.6%)	716 (20.3%)	0.475	473 (21.5%)	473 (21.5%)	>0.99	506 (19.5%)	506 (19.5%)	>0.999
Biolimus eluting stent	664 (18.8%)	625 (17.7%)	0.230	402 (18.3%)	407 (18.5%)	0.846	462 (17.8%)	453 (17.5%)	0.743
Other drug-eluting stent	342 (9.7%)	341 (9.7%)	0.968	150 (6.8%)	152 (6.9%)	0.905	275 (10.6%)	283 (10.9%)	0.720
Stent No. (mg/dL)	1.37 ± 0.85	1.38 ± 0.82	0.853	1.39 ± 0.85	1.41 ± 0.82	0.482	1.37 ± 0.84	1.38 ± 0.82	0.675
Stent length (mm)	24.8 ± 7.3	24.9 ± 7.4	0.810	25.0 ± 7.2	25.0 ± 7.4	0.944	24.9 ± 7.4	24.8 ± 7.3	0.708

Data expressed as mean ± SD or number (percent)

* There is a lesion only in left main coronary artery without other epicardial coronary arteries.

[†] There are lesions in both left main coronary artery and other epicardial coronary arteries.

Table 3
Outcome in the matched cohort

Variable	Transfemoral intervention (n = 3,528)	Transradial intervention (n = 3,528)	p	Transfemoral intervention with vascular closure device (n = 2,198)	Transradial intervention (n = 2,198)	p	Transfemoral intervention without vascular closure device (n = 2,590)	Transradial intervention (n = 2,590)	p
Major adverse cerebrocardiovascualar event	249 (7.1%)	356 (10.1%)	<0.001	164 (7.5%)	179 (8.1%)	0.399	204 (7.9%)	292 (11.3%)	<0.001
Death	157 (4.5%)	148 (4.2%)	0.598	101 (4.6%)	73 (3.3v)	0.03	134 (5.2%)	132 (5.1%)	0.900
Cardiac death	109 (3.1%)	97 (2.7%)	0.396	76 (3.5%)	47 (2.1%)	0.008	91 (3.5%)	92 (3.6%)	0.940
Noncardiac death	48 (1.4%)	51 (1.4%)	0.761	25 (1.1%)	26 (1.2%)	0.888	43 (1.7%)	40 (1.5%)	0.740
Myocardial infarction	53 (1.5%)	55 (1.6%)	0.846	31 (1.4%)	28 (1.3%)	0.694	42 (1.6%)	38 (1.5%)	0.652
Revascularization	57 (1.6%)	84 (2.4%)	0.022	35 (1.6%)	60 (2.7v)	0.01	41 (1.6%)	49 (1.9v)	0.395
Repeat percutaneous coronary intervention	48 (1.4%)	73 (2.1%)	0.022	30 (1.4%)	51 (2.3%)	0.019	36 (1.4%)	43 (1.7v)	0.427
Coronary artery bypass grafting	9 (0.3%)	11 (0.3%)	0.654	5 (0.2%)	9 (0.4%)	0.284	5 (0.2%)	6 (0.2%)	0.763
Cerebrovascular accident	11 (0.3%)	14 (0.4%)	0.548	5 (0.2%)	7 (0.3%)	0.563	8 (0.3%)	9 (0.3v)	0.808
Rehospitalization	57 (1.6%)	83 (2.4%)	0.026	40 (1.8%)	45 (2.0%)	0.584	55 (2.1%)	68 (2.6%)	0.235
Major bleeding	21 (0.6v)	80 (2.3%)	<0.001	16 (0.7%)	21 (1.0%)	0.409	17 (0.7%)	76 (2.9%)	<0.001

Data expressed as number (percent)

VCDs for early haemostasis and faster ambulation, but do not recommend for the purpose of decreasing bleeding, further studies are required to identify specific population who may have a benefit from VCDs.

Our study has several potential limitations. First, the KAMIR − NIH was an observational study. Although propensity analysis was performed to control a large number of confounding factors, we cannot completely exclude the possibility of residual confounding factors. Therefore, our results should only be regarded as hypothesis generating. Second, we were not able to control unmeasured factors, such as sheath size and individual operator experience, which may affect outcomes, especially with TRI. Third, bleeding complications were not categorized using classic bleeding scores. However, to reduce potential variability in

definitions of a bleeding complication between the centers, we only included clinically meaningful major bleeding category. Fourth, the details regarding vascular access such as planned initial access, crossover rate, and specific type of VCDs were not available in this observational study. However, the limitations of the study should not undermine our strength of this study that includes patients with cardiogenic shock, peripheral vascular disease, and previous bypass surgery and thus representative of patients encountered in day-to-day clinical practice. In conclusion, compared with TRI, TFI with VCD was comparable in outcomes through a reduction in major bleeding. Therefore, the use of VCD could be an alternative to avoid major bleeding and to improve outcomes, particularly in high-risk patients who are not suitable for TRI.
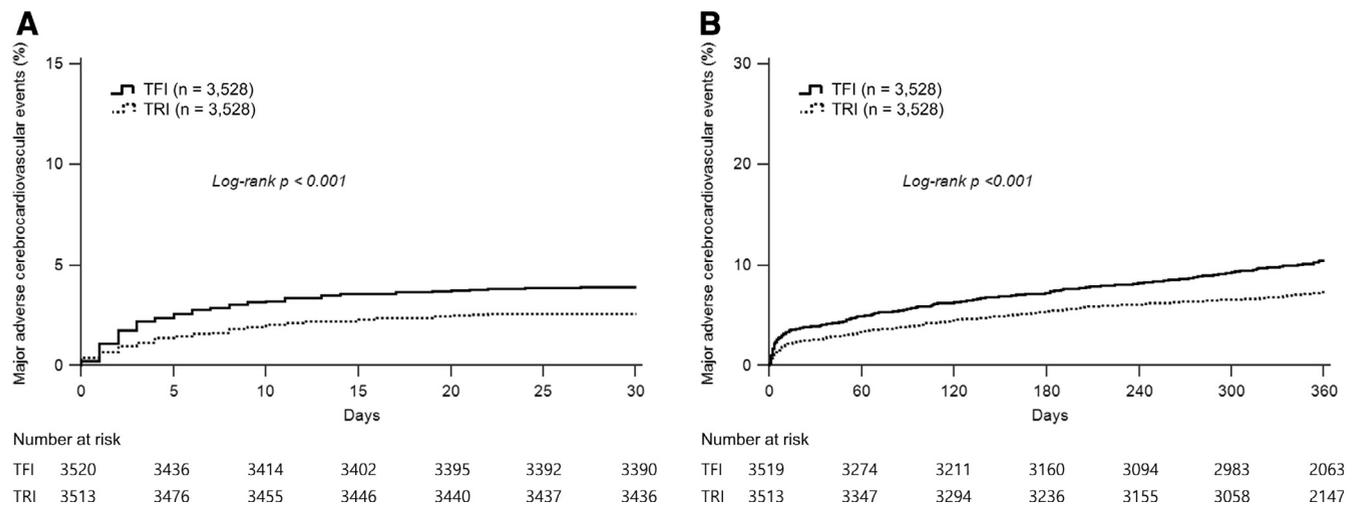

Figure 2. Kaplan-Meier survival curves for major adverse cerebrocardiovascular events at (A) 30 days and (B) 1-year between TRI and TFI in the propensity score-matched cohorts.
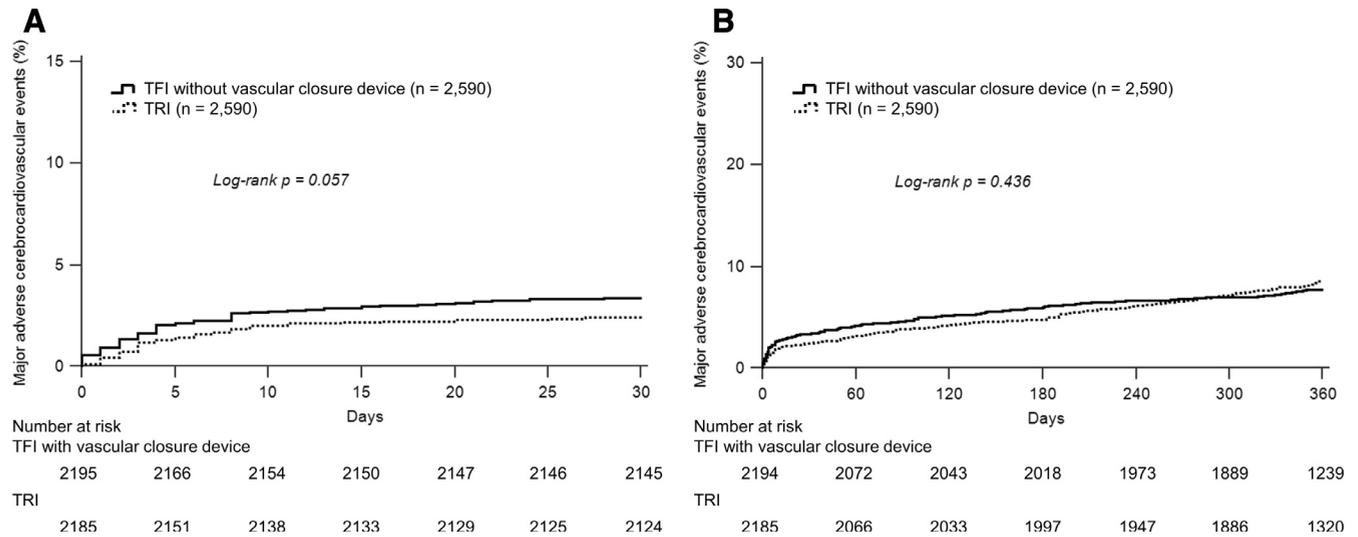TRI = transradial intervention; TFI = transfemoral intervention

Figure 3. Kaplan-Meier survival curves for major adverse cerebrocardiovascular events at (A) 30 days and (B) 1-year between TRI and TFI without VCD in the propensity score-matched cohorts.
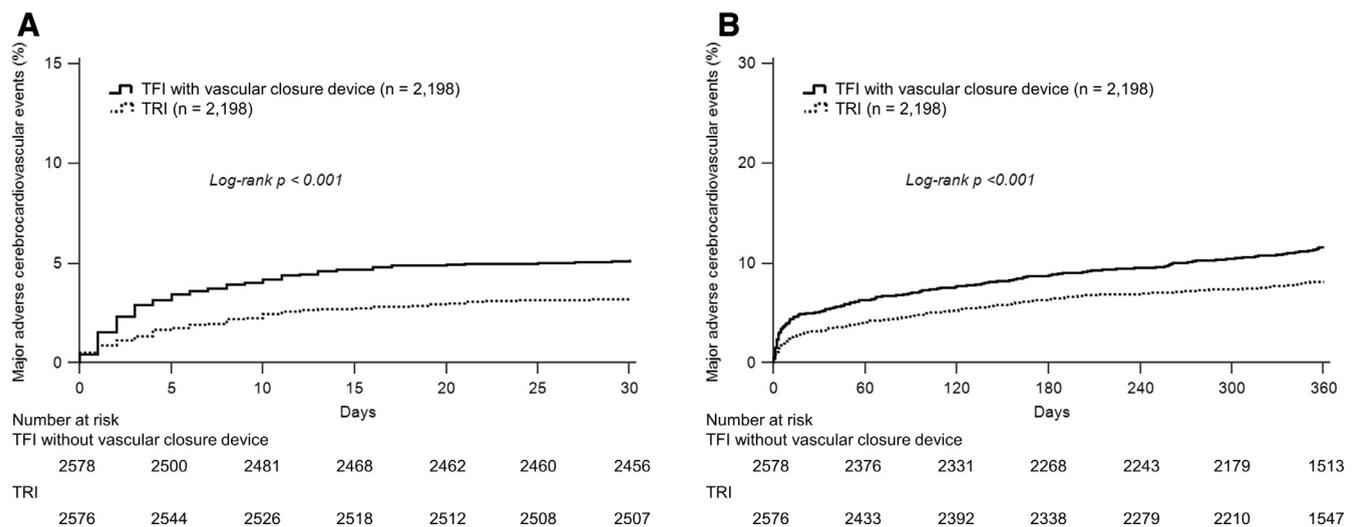TRI = transradial intervention; TFI = transfemoral intervention; VCD = vascular closure device

Figure 4. Kaplan-Meier survival curves for major adverse cerebrocardiovascular events at (A) 30 days and (B) 1-year between TRI and TFI with VCD in the propensity score-matched cohorts.
TRI = transradial intervention; TFI = transfemoral intervention; VCD = vascular closure device

Disclosures

All authors have nothing to disclosure.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.amjcard.2018.11.040.

1. Cannon CP, Harrington RA, James S, Ardissino D, Becker RC, Emanuelsson H, Husted S, Katus H, Keltai M, Khurmi NS, Kontny F, Lewis BS, Steg PG, Storey RF, Wojdyla D, Wallentin L. PLATelet inhibition and patient Outcomes Investigators. Comparison of ticagrelor with clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO): a randomised double-blind study. Lancet 2010;375:283–293.

2. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM. TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2007;357:2001–2015.

3. Jolly SS, Yusuf S, Cairns J, Niemelä K, Xavier D, Widimsky P, Budaj A, Niemelä M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afzal R, Joyner CD, Chrolavicius S, Mehta SR. RIVAL trial group. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011;377:1409–1420.

4. Valgimigli M, Gagnor A, Calabró P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briguori C, Andò G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S,

Nazzaro M, Zingarelli A, de Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbühler M, Vranckx P, Jüni P. MATRIX Investigators. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. *Lancet* 2015;385:2465–2476.

5. Dangas G, Mehran R, Kokolis S, Feldman D, Satler LF, Pichard AD, Kent KM, Lansky AJ, Stone GW, Leon MB. Vascular complications after percutaneous coronary interventions following hemostasis with manual compression versus arteriotomy closure devices. *J Am Coll Cardiol* 2001;38:638–641.

6. Ward SR, Casale P, Raymond R, Kussmaul WG 3rd, Simpfendorfer C. Efficacy and safety of a hemostatic puncture closure device with early ambulation after coronary angiography. Angio-Seal Investigators. *Am J Cardiol* 1998;81:569–572.

7. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959–969.

8. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983;70:41–55.

9. Iqbal MB, Arujuna A, Ilsley C, Archbold A, Crake T, Firoozi S, Kalra S, Knight C, Lim P, Malik IS, Mathur A, Meier P, Rakhit RD, Redwood S, Whitbread M, Bromage D, Rathod K, Wragg A, MacCarthy P, Dalby M. London Heart Attack Centre (HAC) Group Investigators. Radial versus femoral access is associated with reduced complications and mortality in patients with non-ST-segment-elevation myocardial infarction: an observational cohort study of 10,095 patients. *Circ Cardiovasc Interv* 2014;7:456–464.

10. Mehta SR, Jolly SS, Cairns J, Niemela K, Rao SV, Cheema AN, Steg PG, Cantor WJ, Džavík V, Budaj A, Rokoss M, Valentin V, Gao P, Yusuf S. RIVAL Investigators. Effects of radial versus femoral artery access in patients with acute coronary syndromes with or without ST-segment elevation. *J Am Coll Cardiol* 2012;60:2490–2499.

11. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, Politi L, Rigattieri S, Pendenza G, Summaria F, Patrizi R, Borghi A, Di Russo C, Moretti C, Agostoni P, Loschiavo P, Lioy E, Sheiban I, Sangiorgi G. Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. *J Am Coll Cardiol* 2012;60:2481–2489.

12. Bernat I, Horak D, Stasek J, Mates M, Pesek J, Ostadal P, Hrabos V, Dusek J, Koza J, Sembera Z, Brtko M, Aschermann O, Smid M, Polansky P, Al Mawiri A, Vojacek J, Bis J, Costerousse O, Bertrand OF, Rokyta R. ST-segment elevation myocardial infarction treated by radial or femoral approach in a multicenter randomized clinical trial: the STEMI-RADIAL trial. *J Am Coll Cardiol* 2014;63:964–972.

13. Vink MA, Amoroso G, Dirksen MT, van der Schaaf RJ, Patterson MS, Tijssen JG, Kiemeneij F, Slagboom T. Routine use of the transradial approach in primary percutaneous coronary intervention: procedural aspects and outcomes in 2209 patients treated in a single high-volume centre. *Heart* 2011;97:1938–1942.

14. Tron C, Koning R, Eltchaninoff H, Douillet R, Chassaing S, Sanchez-Giron C, Cribier A. A randomized comparison of a percutaneous suture device versus manual compression for femoral artery hemostasis after PTCA. *J Interv Cardiol* 2003;16:217–221.