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Original Research

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Feasibility of Distal Radial Access in High Bleeding Risk Patients Who Underwent Percutaneous Coronary Intervention

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AUTHOR'S SUMMARY

The distal radial access (DRA) has emerged as an alternative to the trans-radial approach for coronary angiography and percutaneous coronary intervention, reducing radial artery occlusion (RAO) and access site complications. We found that DRA-related bleeding and access site complications were not significantly different between high bleeding risk (HBR) and non-HBR groups. No Bleeding Academic Research Consortium major bleeding occurred, and less than 1% of patients experienced distal or conventional RAO at the 1-month follow-up in the total study population. DRA may be considered a safe access approach for HBR patients, with major complications of DRA being rare even in HBR patients.

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Conflict of Interest
The authors have no financial conflicts of interest.

Data Sharing Statement
The data generated in this study is available from the corresponding authors upon reasonable request.

Author Contributions
Conceptualization: Lee OH, Kim Y; Data curation: Roh JW, Lee OH, Im E, Cho DK, Lee JW, Lee BK, Yoo SY, Lee SY, Kim CJ, Jin HY, Park JS, Heo JH, Kim DH, Lee JB, Kim DK, Bae JH, Lee SY, Lee SH, Kim Y; Formal analysis: Jin

ABSTRACT

Backgrounds and Objectives: The distal radial access (DRA), a potential alternative to the trans-radial approach (TRA), may offer advantages in terms of access site complications due to its smaller vessel diameter, especially for high bleeding risk (HBR) patients. This study aims to investigate the feasibility of DRA in HBR patients.
Methods: Based on data from the KODRA registry, a prospective, multicenter cohort, this study analyzed 1,586 patients who underwent successful percutaneous coronary intervention (PCI) via DRA. Patients were categorized into HBR and non-HBR groups. The primary endpoint of the study is DRA-related bleeding, and the secondary endpoints of the study are overall access site complications and each component of the access site complications. To reduce the effect of potential confounders, a multivariable adjustment analysis was performed.
Results: The mean age of the total population was 71.1±10.8 years, and 40.3% of patients were female. Both DRA-related bleeding (odds ratio [OR], 1.15; 95% confidence interval [CI], 0.67–1.97; p=0.616) and overall access site complications (OR, 1.08; 95% CI, 0.67–1.72; p=0.761) were not significantly different between the HBR group and non-HBR group after multivariable adjustment. No major bleeding before discharge was observed in both groups. Furthermore, the incidence of distal and conventional radial artery occlusion was less than 1% at 1-month follow-up in both groups.
Conclusions: Our study results showed the safety of DRA for both DRA-related bleeding and access site complications among HBR patients who underwent PCI.

Trial Registration: ClinicalTrials.gov Identifier: NCT04080700

Keywords: Radial artery; Percutaneous coronary intervention; Hemorrhage; Coronary artery disease

INTRODUCTION

Major bleeding complications are a concern for patients undergoing invasive coronary angiography (CAG), and a significant proportion of the bleeding occurs at the vascular access site.[1] Several randomized controlled trials (RCTs) and meta-analyses comparing the trans-radial approach (TRA) with the trans-femoral approach (TFA) have shown that TRA can reduce major bleeding complications and major adverse cardiovascular events (MACE).[2-4] As a result, current guidelines recommend TRA when performing CAG as a Class I recommendation, and TRA is the preferred approach in high bleeding risk (HBR) patients.[5][6]

Distal radial access (DRA), an emerging alternative to the TRA, uses the anatomical snuffbox or dorsum of the hand as the puncture site to establish vascular access.[7] Several RCTs and meta-analyses have been investigated on DRA compared with TRA. DRA has advantages over TRA in reducing radial artery occlusion (RAO) and shortening hemostasis time without serious access site complications.[8-11] In addition, the recently published KODRA (Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach) trial, a large real-world prospective registry from Korea, demonstrated high success rates of CAG and percutaneous coronary intervention (PCI) with low rates of access site complications and bleeding events.[12]

Considering the smaller vessel size of the distal radial artery compared to the proximal radial artery, a potential advantage for bleeding complications may be expected, especially in HBR

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patients.[13] However, studies on bleeding complications of the DRA in HBR patients are still lacking. Therefore, the aim of this study is to evaluate the safety of DRA in HBR patients.

METHODS

Ethical statement

The KODRA registry was approved by the Institutional Review Board (IRB) of Yongin Severance Hospital (IRB No. 9-2020-0027) and other participating institutions. All studies adhered to the tenets of the Declaration of Helsinki (2013). All patients provided informed consent and were registered at ClinicalTrial.gov (NCT04080700).

Study design and patient population

The population of our study was recruited from the KODRA registry,[12] the prospective multicenter registry involving 14 centers that enrolled 4,977 patients to evaluate the safety and feasibility of the DRA for CAG and PCI.

Figure 1 shows the study design. Of the 4,698 patients in the KODRA registry who had successful DRA punctures, 1,586 patients who underwent successful PCI via DRA were included in this subgroup analysis. The HBR group was defined by the following items from the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria[14]: age, hemoglobin level, estimated glomerular filtration rate (eGFR), and use of oral anticoagulants (OAC). Data not available from the KODRA registry were excluded: thrombocytopenia, history of intracranial hemorrhage, liver cirrhosis, or malignancy, and use of steroid or non-

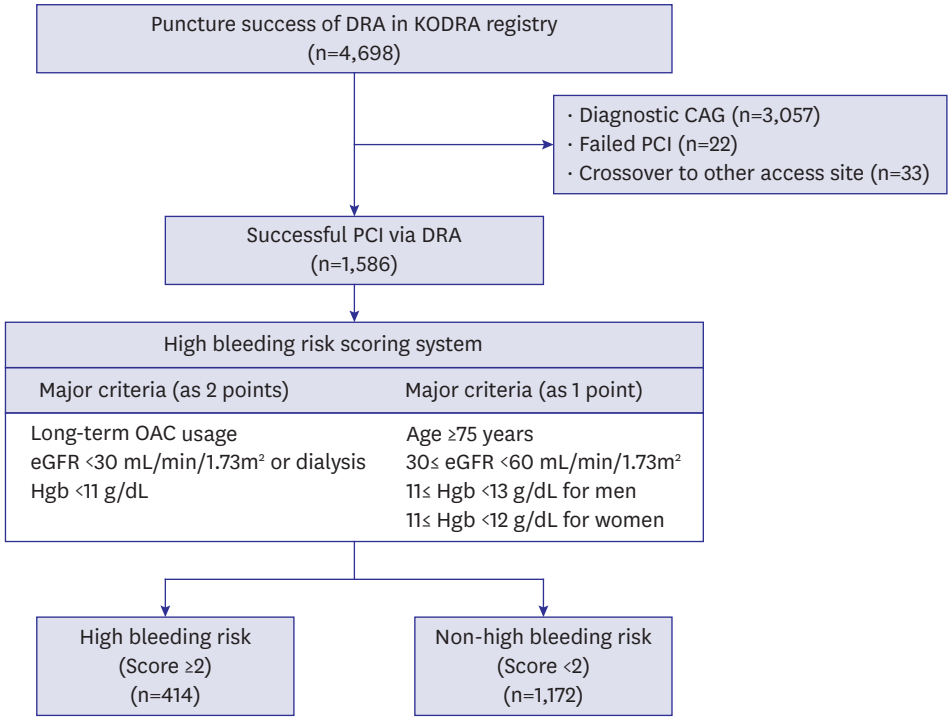

Figure 1. Study flowchart.
CAG = coronary angiography; DRA = distal radial access; eGFR = estimated glomerular filtration rate; Hgb = hemoglobin; KODRA = Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach; OAC = oral anti-coagulants; PCI = percutaneous coronary intervention.

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steroidal anti-inflammatory drugs. Patients with a score of 2 or more were assigned to the HBR group, with 414 patients in the HBR group and 1,172 patients in the non-HBR group.

Study procedures

The puncture procedure of the distal radial artery was performed as described at the KODRA trial.[12] Arterial puncture was performed either in the anatomical snuffbox or on the dorsum of the hand using a 20-gauge venipuncture catheter needle or a 21-gauge open steel needle following local anesthesia with subcutaneous lidocaine. Subsequently, a mini-guidewire was inserted into the artery, followed by the deployment of an introducer sheath. The loading and maintenance dose of anti-platelet agents and the dose of peri-procedural unfractionated heparin followed the protocols of each hospital. The diagnostic CAG was performed in the usual manner, and patients who underwent PCI were treated as the operator's decision. Hemostasis was done through adhesive tape fixation, elastic banding wrapping, a compression device, and manual compression at the operator's preference. The appropriate compression pressure and minimizing compression time for successful hemostasis were strongly recommended.

Study endpoints and definitions

The primary endpoint of the study is DRA-related bleeding. DRA-related bleeding was categorized into major and minor bleeding according to the Bleeding Academic Research Consortium (BARC) criteria.[15] Hematoma was graded according to the modified EASY (Early Discharge After Transradial Stenting of Coronary Arteries Study) criteria proposed by Tsigkas et al.[16] Grade Ia hematoma was subclassified from the puncture site into 4 groups (grade 1, <2 cm; grade 2, 2–5 cm; grade 3, >5 cm; grade 4, hand swelling). Grade Ib is defined as wrist hematoma <5 cm, II as wrist hematoma ≥5 and <10 cm, III as hematoma reaching the forearm, and IV as hematoma extending to the upper arm. The secondary endpoints of the study are overall access site complications, including DRA-related bleeding, distal RAO, conventional RAO, access site tenderness, numbness, swelling, perforation, and dissection prior to discharge. Each component of overall access site complications was also evaluated. In addition, distal RAO, conventional RAO, tenderness, numbness, swelling, and hand dysfunction were evaluated at the 1-month follow-up. Both distal and conventional radial arteries were assessed by the physicians' manual palpation, with the absence of pulsation being defined as RAO. Assessment with ultrasonography for the radial arteries at 1-month follow-up was optional and at the physicians' discretion.

Statistical analysis

All data were expressed as the mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables. Student's t-test was used to compare differences in continuous variables between the two groups. Categorical variables were compared using the χ^2 test or Fisher's exact test. Due to the rare occurrence of endpoints with an incidence of less than 10%, Firth's logistic regression was used to analyze the odds ratio (OR) with a 95% confidence interval (CI) for each endpoint.[17][18] Comparison of OR between the two groups was estimated using the Wald test.

The multivariable adjustment analysis was performed to reduce the effect of bias caused by potential confounders. After excluding those variables used to define the HBR group, the following covariates, which showed significant differences in baseline characteristics between the HBR and the non-HBR group, were included as variables in the multivariable adjustment analysis: Sex, body mass index (BMI), hypertension, diabetes, current smoking,

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previous revascularization including PCI and coronary artery bypass surgery, previous cerebrovascular accident (CVA), multivessel PCI, clinical presentation as acute coronary syndrome (ACS), use of potent $P2Y_{12}$ inhibitor, administered dose of unfractionated heparin (per 1,000 U), and total hemostasis time.

Data manipulation and statistical analysis were performed with R software (version 4.2.3; R Foundation for Statistical Computing, Vienna, Austria) using the stats and logistic packages for Firth's logistic regression. All tests were 2-tailed, and statistical significance was defined as p value less than 0.05.

RESULTS

Baseline clinical and procedural characteristics

Of the 1,586 patients who underwent PCI via DRA, patients were divided into the HBR group (n=414) and the non-HBR group (n=1,172). The baseline clinical characteristics of both groups are summarized in **Table 1**. The HBR group was older than the non-HBR group, had a higher proportion of females, had a lower BMI, and had a lower proportion of current smokers. The HBR group also had a higher prevalence of other comorbidities such as hypertension, diabetes, chronic kidney disease (CKD), previous revascularization, previous CVA, and anemia with hemoglobin levels below 11 g/dL. However, the proportion of ACS

Table 1. Baseline characteristics of patients undergoing percutaneous coronary intervention

	Total population (n=1,586)	HBR patients (n=414)	Non-HBR patients (n=1,172)	p value
Age (year)	66.7±11.8	75.8±9.9	63.5±10.7	<0.001
Female sex	399 (25.2)	195 (47.1)	204 (17.4)	<0.001
BMI	24.9±3.4	24.0±3.4	25.2±3.4	<0.001
Hypertension	1,017 (64.1)	331 (80.0)	686 (58.5)	<0.001
Diabetes mellitus	640 (40.4)	223 (53.9)	417 (35.6)	<0.001
Dyslipidemia	924 (58.3)	244 (58.9)	680 (58.0)	0.745
CKD (eGFR <60 mL/min/1.73 m^2)	132 (8.3)	116 (28.0)	16 (1.4)	<0.001
CKD stage III (30 ≤ eGFR <60 mL/min/1.73 m^2)	65 (4.1)	49 (11.8)	16 (1.4)	
CKD stage IV (15 ≤ eGFR <30 mL/min/1.73 m^2)	27 (1.7)	27 (6.5)	0 (0.0)	
CKD stage V or dialysis (eGFR <15 mL/min/1.73 m^2)	40 (2.5)	40 (9.7)	0 (0.0)	
Current smoker	434 (27.4)	44 (10.6)	390 (33.3)	<0.001
Previous MI	162 (10.2)	52 (12.6)	110 (9.4)	0.067
Previous revascularization*	329 (20.7)	105 (25.4)	224 (19.1)	0.007
Previous CVA	139 (8.8)	62 (15.0)	77 (6.6)	<0.001
Hemoglobin	13.6±2.1	11.4±2.0	14.4±1.5	<0.001
Hemoglobin <11 g/dL	172 (10.9)	174 (42.0)	0 (0.0)	<0.001
Clinical presentation				0.002
SAP	308 (19.4)	88 (21.3)	220 (18.8)	
ACS	1,155 (72.8)	279 (67.4)	876 (74.7)	
Others	123 (7.8)	47 (11.4)	76 (6.5)	
Anti-thrombotic agents				
Aspirin	1,214 (76.5)	308 (74.4)	906 (77.3)	0.230
$P2Y_{12}$ inhibitor				
Clopidogrel	806 (50.8)	249 (60.1)	557 (47.5)	<0.001
Potent $P2Y_{12}$ inhibitor†	450 (28.4)	64 (15.5)	386 (32.9)	<0.001
Warfarin	6 (0.4)	6 (1.4)	0 (0.0)	<0.001
NOAC	27 (1.7)	27 (6.5)	0 (0.0)	<0.001

Data are presented as the mean ± standard deviation or number (%).
ACS = acute coronary syndrome; BMI = body mass index; CKD = chronic kidney disease; CVA = cerebrovascular accident; eGFR = estimated glomerular filtration rate; HBR = high bleeding risk; MI = myocardial infarction; NOAC = new oral anti-coagulants; SAP = stable angina pectoris.
*Includes previous percutaneous coronary intervention and previous coronary artery bypass surgery.
†Includes ticagrelor and prasugrel.

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Table 2. Lesion and procedural characteristics of patients undergoing PCI

	Total population (n=1,586)	HBR patients (n=414)	Non-HBR patients (n=1,172)	p value
PCI via left DRA	1,019 (64.2)	288 (69.6)	731 (62.4)	0.009
Puncture experience of DRA				0.146
<100 cases	349 (22.0)	93 (22.5)	256 (21.8)	
100–499 cases	408 (25.7)	120 (29.0)	288 (24.6)	
≥500 cases	829 (52.3)	201 (48.6)	628 (53.6)	
Target lesion				0.137
Left main	42 (2.6)	9 (2.2)	33 (2.8)	
LAD	866 (54.6)	226 (54.6)	640 (54.6)	
LCX	226 (14.2)	55 (13.3)	171 (14.6)	
RCA	439 (27.7)	124 (30.0)	315 (26.9)	
Ramus intermediate	13 (0.8)	0 (0.0)	13 (1.1)	
Multivessel PCI	407 (25.7)	125 (30.2)	282 (24.1)	0.014
Final sheath size				0.488
5-Fr	78 (5.1)	36 (8.7)	88 (7.5)	
6-Fr	1,232 (80.7)	312 (75.4)	921 (78.6)	
7-Fr	101 (6.6)	28 (6.8)	78 (6.7)	
Sheathless	115 (7.5)	38 (9.2)	85 (7.3)	
Unfractionated heparin dose	8,394.2±2,240.9	8,110.0±2,503.6	8,494.2±2,132.9	0.004
Hemostasis time (minutes)	226.9±142.4	211.2±130.8	232.5±145.9	<0.001
Hemostasis method				
Adhesive tape fixation	916 (57.8)	241 (58.2)	675 (57.6)	0.890
Elastic bandage	651 (41.0)	164 (39.6)	487 (41.6)	0.585
Others	19 (1.2)	9 (2.2)	10 (0.9)	0.044
Additional hemostasis	84 (5.3)	31 (7.5)	53 (4.5)	0.921
Total hemostasis time (minutes)	242.6±191.1	224.4±149.5	249.0±203.5	<0.001

Data are presented as the mean ± standard deviation or number (%).
DRA = distal radial access; HBR = high bleeding risk; LAD = left anterior descending artery; LCX = left circumflex artery; PCI = percutaneous coronary intervention; RCA = right coronary artery.

was lower in the HBR group. Patients in the HBR group more frequently used OACs but less frequently used potent $P2Y_{12}$ inhibitors. The baseline lesion and procedural characteristics of both groups are presented in **Table 2**. The HBR group more frequently used the left DRA as the access site and less frequently performed multivessel PCI, used less unfractionated heparin, and had a shorter total hemostasis time.

The proportion of each component of the HBR score

The proportion of each component of the HBR score is shown in **Supplementary Figure 1**. In the HBR group, the major criterion with the largest proportion was anemia with a hemoglobin level below 11 g/dL, observed in 10.9% of the group, followed by patients with CKD stage IV or V (eGFR below 30 mL/min/1.73 m^2 or on dialysis), and the use of OACs. For the minor criteria, approximately 70% of the HBR group were patients aged 75 years or older, and approximately 43% had CKD stage III (30 ≤ eGFR <60 mL/min/1.73 m^2). Meanwhile, in the non-HBR group, 15.1% were patients aged 75 years or older, and 4.6% had CKD stage III.

DRA-related bleeding and access site complications

DRA-related bleeding, other access site complications, and their ORs were compared between the HBR group and the non-HBR group, as shown in **Table 3**. Although there were no cases of BARC major bleeding or type 3a bleeding in either the HBR or non-HBR groups, HBR patients had a significantly higher risk of DRA-related bleeding (OR, 1.87; 95% CI, 1.23–2.82; p=0.004) and overall access site complications (OR, 1.71; 95% CI, 1.17–2.46; p=0.006) compared to non-HBR patients. However, these differences became non-significant after multivariable adjustment for both DRA-related bleeding (OR, 1.15; 95% CI, 0.66–1.97; p=0.616) and overall access site complications (OR, 1.08; 95% CI, 0.67–1.72;

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Table 3. Event rates and logistic regression (OR) of access site complications

	HBR patients (n=414)	Non-HBR patients (n=1,172)	Univariate analysis		Multivariable analysis*	
			OR (95% CI)	p value	OR (95% CI)	p value
DRA-related bleeding	39 (9.4)	62 (5.3)	1.87 (1.23–2.82)	0.004	1.15 (0.66–1.97)	0.616
BARC major bleeding	0 (0.0)	0 (0.0)	-		-	
BARC minor bleeding						
BARC type 1	14 (3.4)	20 (1.7)	2.04 (1.01–4.00)	0.047	1.33 (0.54–3.18)	0.534
BARC type 2	25 (6.0)	42 (3.6)	1.74 (1.04–2.86)	0.036	1.09 (0.55–2.09)	0.811
BARC type 3a	0 (0.0)	0 (0.0)	-		-	
Access site hematoma (modified EASY criteria)						
1a	34 (8.2)	59 (5.0)	1.70 (1.09–2.61)	0.020	1.02 (0.57–1.80)	0.938
<2 cm	11 (2.7)	29 (2.5)	1.11 (0.53–2.15)	0.779	0.74 (0.29–1.71)	0.487
2–5 cm	9 (2.2)	9 (0.8)	2.87 (1.14–7.21)	0.026	2.72 (0.77–9.81)	0.118
>5 cm	1 (0.2)	7 (0.6)	0.56 (0.06–2.59)	0.497	0.24 (0.02–1.35)	0.110
Hand swelling	13 (3.1)	14 (1.2)	2.69 (1.25–5.72)	0.012	1.63 (0.58–4.58)	0.352
1b	1 (0.2)	2 (0.2)	1.70 (0.16–12.80)	0.618	0.42 (0.00–8.71)	0.588
2	1 (0.2)	0 (0.0)	-		-	
3	3 (0.7)	1 (0.1)	6.64 (1.09–68.68)	0.040	6.13 (0.67–76.16)	0.108
Overall access site complications	48 (11.6)	84 (7.2)	1.71 (1.17–2.46)	0.006	1.08 (0.67–1.72)	0.761
Other access site complications						
Before discharge						
Distal radial artery occlusion by palpation	6 (1.4)	1 (0.1)	1.33 (0.24–5.52)	0.718	0.96 (0.14–5.39)	0.964
Radial artery occlusion by palpation	3 (0.7)	0 (0.0)	-		-	
Tenderness	13 (3.1)	19 (1.6)	1.99 (0.96–3.99)	0.062	1.19 (0.52–2.63)	0.680
Hand edema	19 (4.6)	37 (3.2)	1.49 (0.84–2.58)	0.169	0.95 (0.46–1.91)	0.896
Numbness	2 (0.5)	9 (0.8)	0.74 (0.14–2.63)	0.667	0.32 (0.03–1.70)	0.195
Perforation	2 (0.5)	1 (0.1)	4.73 (0.63–51.83)	0.127	4.40 (0.52–48.60)	0.167
Dissection	1 (0.2)	3 (0.3)	1.21 (0.12–7.39)	0.846	0.77 (0.07–5.76)	0.807
1-Month follow up						
Distal radial artery occlusion by palpation	2 (0.5)	5 (0.4)	1.33 (0.24–5.52)	0.718	0.96 (0.14–5.39)	0.964
Radial artery occlusion by palpation	1 (0.3)	5 (0.4)	0.79 (0.08–3.99)	0.798	0.71 (0.06–4.62)	0.730
Patients evaluated for radial artery occlusion using ultrasound	139 (35.2)	399 (34.5)	-		-	
Distal radial artery occlusion by ultrasound	1 (0.7)	1 (0.3)	2.88 (0.23–35.65)	0.372	1.71 (0.13–24.09)	0.671
Radial artery occlusion by ultrasound	1 (0.7)	1 (0.3)	2.88 (0.23–35.65)	0.372	1.71 (0.13–24.09)	0.671
Tenderness	1 (0.3)	3 (0.3)	1.25 (0.12–7.64)	0.821	0.39 (0.00–5.47)	0.541
Hand edema	1 (0.3)	7 (0.6)	0.58 (0.06–2.67)	0.523	0.30 (0.03–1.92)	0.215
Numbness	4 (1.0)	13 (1.1)	0.97 (0.29–2.65)	0.960	0.96 (0.17–3.86)	0.959
Hand dysfunction	0 (0.0)	3 (0.3)	-		-	

Data are presented as the mean ± standard deviation or number (%).
BARC = bleeding academic research consortium; CI = confidential interval; DRA = distal radial access; EASY = Early Discharge After Transradial Stenting of Coronary Arteries Study; HBR = high bleeding risk; OR = odds ratio.
*The confounding factors considered in the adjusted hazard ratio are sex, body mass index, hypertension, diabetes, current smoking, previous revascularization, previous cerebrovascular accident, multivessel percutaneous coronary intervention, clinical presentation as acute coronary syndrome, use of potent $P2Y_{12}$ inhibitor, dose of unfractionated heparin (per 1,000 U), and total hemostasis time.

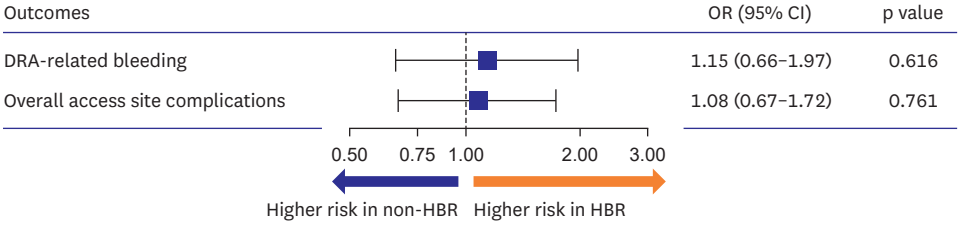

Figure 2. Feasibility of DRA in HBR patients who underwent PCI.
CI = confidence interval; DRA = distal radial access; HBR = high bleeding risk; OR = odds ratio.

p=0.761) (**Figure 2**). Among the overall access site complications, the incidences of distal RAO and conventional RAO at the time of discharge were 1.4% and 0.7% in the HBR group, respectively, compared to 0.1% and 0% in the non-HBR group. The incidences of distal RAO and conventional RAO by palpation and ultrasonography at 1-month follow-up were also rare

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in both groups, which showed no significant difference between the two groups. Similarly, none of the components of access site complications showed a significant difference, with rare incidences of less than 5% in both groups.

DISCUSSION

The present subgroup analysis of the large, multi-center, prospective observational registry evaluating DRA for CAG and PCI showed that there was no significant difference in DRA-related bleeding and overall access site complications between the HBR and the non-HBR groups in patients who underwent successful PCI via DRA after multivariable adjustment analysis, indicating the safety of DRA in HBR patients. In the total study population, there was no BARC major bleeding or even BARC type 3a bleeding, and less than 1% experienced distal or conventional RAO at the 1-month follow-up after discharge.

Several RCTs comparing the TRA and the TFA have shown significant benefits of the TRA in reducing vascular complications, as well as improving major outcomes such as bleeding complications and cardiovascular death.[2)4)19)] Notably, the MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox) study demonstrated that these advantages for major bleeding and cardiovascular death extend beyond the peri-procedural phase.[4)] The reduction in bleeding and vascular access site complications is likely attributed to the smaller vessel diameter associated with the TRA. Although these advantages of TRA seem to be beneficial for HBR patients, studies investigating bleeding complications of TRA in HBR patients have not yet been performed. As DRA has established itself as an alternative option to TRA, it is expected to be performed safely in HBR patients due to the smaller vessel diameter compared to TRA.[20)21)] In addition, studies have demonstrated the feasibility and safety of DRA in patients undergoing hemodialysis,[22)23)] and DRA was feasible in patients with ST-elevation myocardial infarction (STEMI) requiring medication with potent antithrombotic agents such as the injection of glycoprotein IIb/IIIa inhibitors or ticagrelor or prasugrel.[24)] Furthermore, Lee et al.[25)] reported that DRA may be a feasible alternative access route without serious access site complications compared to TRA or TFA in the setting of STEMI. Based on these studies, DRA may be an alternative access site for a group of patients with a high tendency to bleed without any significant safety concerns.

In our study, DRA has no significant difference in complications other than bleeding between HBR and non-HBR patients. Access site complications, including distal or conventional RAO, were rarely observed, even though 77.5% of the HBR group underwent PCI with 6-Fr sheath. In a retrospective study, Kim et al.[26)] evaluated acute injuries to the conventional radial artery with optical coherent tomography in patients who underwent PCI via DRA with a 6-Fr sheath. This study found that acute injuries such as intimal tears (2.2%, 1 case of 46 enrolled patients) or dissections (0.0%) were rare, demonstrating that the 6-Fr sheath can be safely used in DRA. In our study, both distal and conventional RAO were estimated by physicians' manual palpation before discharge and by ultrasonography optionally used at the 1-month follow-up. In the HBR population, the incidences of distal RAO and conventional RAO before discharge were 1.4% and 0.7%, respectively. At 1-month follow-up, the incidences of distal RAO and conventional RAO were 0.5% and 0.3% when assessed by manual palpation and 0.7% and 0.3% when assessed by ultrasonography, respectively. These results were comparable to those reported in previous studies[8)27)] that used ultrasonography for RAO estimation, which showed distal RAO rates of 0.46% to 0.7% and conventional RAO

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rates of 0.31% before discharge. The favorable surrounding anatomy and small diameter of DRA, leading to the advantages in hemostasis and reduced vascular injury, are thought to contribute to these results.[13)28)]

Our study showed the safety of DRA in HBR patients, reaffirming that it can be used as an alternative access site to TRA without safety issues. Further RCTs comparing DRA with TRA are needed to confirm the feasibility of DRA as an alternative access site in the HBR population.

The first limitation of the study is insufficient data in calculating the HBR score to define the HBR group, as some variables from the ARC-HBR criteria were not assessed. Consequently, the number of HBR patients may have been underestimated. However, most of the missing data were related to past medical history, and aside from stroke, the prevalence of these conditions in real-world settings is generally low.[29)] Although the results may not be entirely generalizable in defining the HBR group, considering the prevalence of each criterion, they are likely to be sufficiently representative. Secondly, the study did not include a control group for different vascular access in HBR patients, which requires caution in the interpretation of the results, as it does not allow for direct comparison with other access methods. Third, due to the limitation of our study design and statistical power, it is difficult to directly interpret the outcomes of HBR patients as being equivalent or non-inferior to those of non-HBR patients. Lastly, distal RAO and conventional RAO might be underestimated due to being investigated by physicians' manual palpation rather than by ultrasonography.

Our study results demonstrate the safety of the use of DRA in terms of DRA-related bleeding and access site complications in HBR patients who undergoing PCI. These results suggest that DRA can be considered a safe access route for HBR patients.

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SUPPLEMENTARY MATERIAL

Supplementary Figure 1

The number and percentage of each component of HBR score in the (A) HBR group and (B) non-HBR group.

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