

ORIGINAL RESEARCH

Distal Radial Access and Women: Implications for Access Site Outcomes in Coronary Procedures

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BACKGROUND: We investigated the sex-specific variations in distal radial access (DRA)-associated outcomes, as well as the factors influencing these outcomes, by utilizing a comprehensive real-world registry.

METHODS: In this post-hoc analysis of the KODRA (Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach) trial, we selected 4608 patients who underwent successful coronary procedures, including percutaneous coronary intervention or coronary angiography, via DRA. Primary end points were overall DRA site outcomes including bleeding, radial artery occlusion, tenderness, hand edema, numbness, perforation, and dissection. We performed both propensity score matching and multivariable logistic regression to evaluate sex-specific differences in DRA-associated outcomes. Moreover, a multivariable analysis using logistic regression was also performed to evaluate the independent associated factors of DRA site outcomes.

RESULTS: The mean age was 66.5±11.8 years, and 67.8% (3125 men and 1483 women) were male among 4608 enrolled patients. The incidence of overall DRA site outcomes was significantly higher in women than in men (7.5% versus 4.1%, $P<0.001$). However, there was no major bleeding in both groups. In the multivariable analysis, female sex was a significant risk factor of overall DRA site outcomes, along with body mass index, chronic kidney disease, percutaneous coronary intervention procedure, use of potent P2Y₁₂ inhibitor, and unfractionated heparin dose.

CONCLUSIONS: This subgroup analysis of the KODRA trial by sex showed that overall DRA site outcomes following coronary procedures via DRA were more common in women than in men. However, no major bleeding was observed in either men or women.

REGISTRATION: URL: <https://www.clinicaltrials.gov>; Unique identifier: NCT04080700.

Key Words: coronary artery angiography ■ distal radial access ■ percutaneous coronary intervention ■ women

Several studies have shown that women with coronary artery disease undergoing percutaneous coronary intervention (PCI) exhibit worse clinical

outcomes than men.^{1,2} In addition, women have been significantly associated with higher rates of bleeding complications, even after adjustment for confounders.³

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CLINICAL PERSPECTIVE

What Is New?

- This study shows a sex difference in distal radial access (DRA) outcomes, with women experiencing higher rates of access site outcomes compared with men; however, these differences are limited to minor bleeding without significant difference in serious outcomes, such as major Bleeding Academic Research Consortium bleeding; in coronary procedures with DRA, women had more access site outcomes, primarily bleeding outcomes, compared with the male patients; however, there were no cases of major bleeding requiring surgical treatment in either men or women.
- In multivariable and propensity score matching analysis, being female was an important factor associated with the occurrence of access-site outcomes in coronary procedures using DRA.

What Are the Clinical Implications?

- Recently, DRA for coronary procedures has received more attention due to reduced rates of radial artery occlusion and bleeding outcomes.
- Careful monitoring for access site is highly recommended when performing DRA in women.

Nonstandard Abbreviations and Acronyms

DRA	distal radial access
KODRA	Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach
RAO	radial artery occlusion

Because women undergoing PCI tend to be older and it may lead to them having more underlying medical conditions than men, the reasons for the underlying sex differences are unclear.

In contemporary clinical practice, the utilization of distal radial access (DRA) in coronary procedures has emerged as an alternative to conventional radial access. Numerous studies have shown the benefits of this approach, including a lower incidence of bleeding and access site outcomes compared with conventional radial access.^{4–6} Furthermore, recent randomized trials have demonstrated the safety and efficacy of DRA, evidenced by the lower incidence of radial artery occlusion (RAO).^{7–9} More recently, the KODRA (Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach) registry, a large-scale real-world study, has shown an extremely low

rate of RAO, reinforcing the clinical benefits of DRA in patients undergoing coronary procedures.¹⁰ However, there are no comparative data regarding sex-specific outcomes associated with the DRA procedure.

This study aimed to investigate the sex-specific differences in the outcomes associated with the DRA using a real-world large-scale registry.

METHODS

The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Study Design and Population

The KODRA was a prospective, multicenter registry designed to evaluate the feasibility and safety of DRA for coronary angiography and PCI.¹⁰ The KODRA registry (NCT04080700) screened patients from 14 hospitals between September 2019 and September 2021; patients were aged ≥ 20 years and scheduled to undergo coronary angiography or PCI with a palpable DRA. The detailed study design and rationale of the KODRA trial have been published previously.¹⁰ A total of 4977 patients were enrolled in this KODRA registry, of whom 94.4% (4698/4977) underwent a successful puncture. In this post-hoc analysis of the KODRA registry, 4608 patients who successfully underwent coronary angiography or PCI via DRA were finally enrolled among 4698 patients. Data were analyzed separately by sex (Figure 1). The study protocol was approved by the institutional review board of each participating hospital, and written informed consent was obtained from all enrolled patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Study End Points and Definitions

The primary end points were overall DRA site outcomes including bleeding, RAO, tenderness, hand edema, numbness, perforation, and dissection. The secondary end points were defined as DRA-related bleeding according to Bleeding Academic Research Consortium (BARC) criteria and DRA site hematoma according to the modified EASY (Early Discharge After Trans-radial Stenting of Coronary Arteries Study) criteria.³ Both the primary and secondary end points were analyzed according to sex.

The modified EASY classification is as follows: Hematoma 1a refers to hand hematomas, and is categorized into 4 grades based on the distance from the puncture site: grade 1 (< 2 cm), grade 2 (2–5 cm), grade 3 (> 5 cm), and grade 4 (hand swelling). Hematoma 1b and above refers to wrist or arm hematomas: 1b is defined as wrist hematomas < 5 cm, II as wrist hematomas ≥ 5 and < 10 cm, III as hematomas extending to

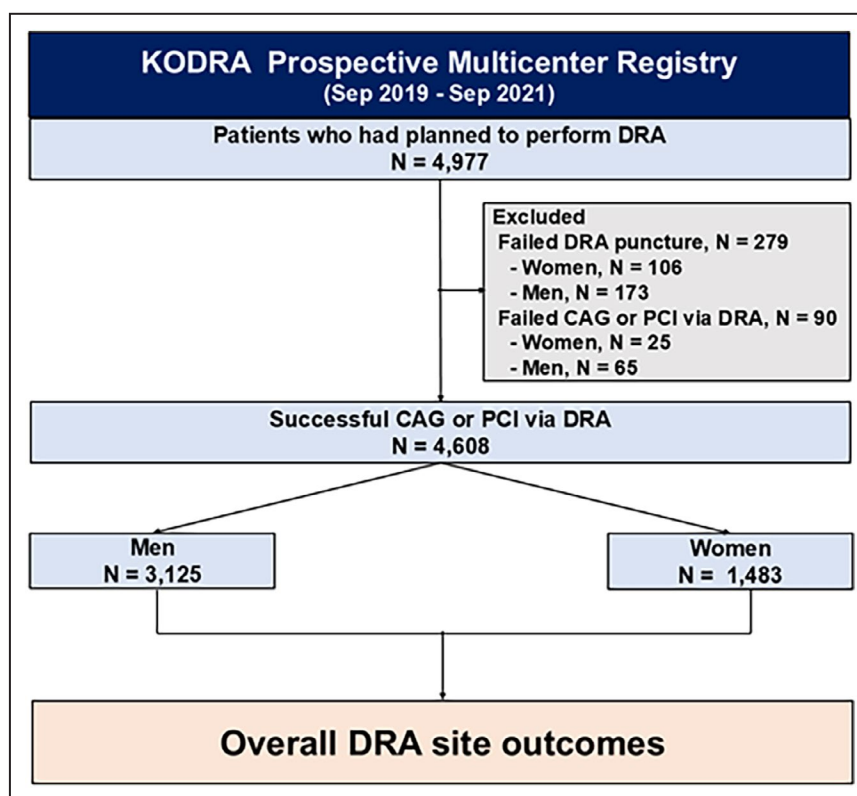


Figure 1. Study flow chart.

Overall DRA site outcomes include DRA-related bleeding, RAO on palpation, tenderness, hand edema, numbness, perforation, and dissection. CAG indicates coronary angiography; DRA, distal radial access; KODRA, The Korean Prospective Registry for Evaluating the Safety and Efficacy of Distal Radial Approach; PCI, percutaneous coronary intervention; and RAO, radial artery occlusion.

the forearm, and IV as hematomas reaching the upper arm. Total hemostasis time was defined as the time from the start of compression to the complete removal of compressive materials.

Statistical Analysis

Categorical variables are presented as counts and percentages, while continuous variables are presented as mean±SD. Independent 2-sample *t* test or Fisher exact test were used to compare differences in continuous or category variables between men and women. To investigate the risk factors of overall DRA site outcomes, we performed univariate and multivariable logistic regression analyses to evaluate factors associated with these outcomes. Since there was no study on the access site outcome of DRA after PCI, we tried to include as many factors as possible in the multivariable analysis, referring to the studies on the factors affecting radial or femoral access site outcomes after PCI.¹¹ As a sensitivity analysis, we conducted a propensity score matching analysis to evaluate sex difference in overall DRA site outcomes (Figure S1). The significance level was set at $P < 0.05$. All statistical

analyses were performed with R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Baseline and Procedural Characteristics

Between September 2019 and September 2021, a total of 4977 patients who attempted to undergo procedures via DRA were enrolled in 14 hospitals in Korea in this KODRA registry. Of the total 4977 patients initially enrolled, 279 experienced a failed puncture. Among them, 106 were women, representing a failure rate of 6.6% in female patients. Additionally, of the 90 patients who failed to undergo a successful procedure, 25 were women, indicating a procedure failure rate of 1.7% among 1508 female patients (Table S1). Finally, 4608 patients (3125 men and 1483 women) who successfully underwent coronary angiography or PCI via DRA were enrolled in the present study (Figure 1); PCI was performed in 1586 patients. The baseline characteristics of the patients are shown in Table 1. The mean age of the men was 64.62 ± 11.83 years, while the mean

Table 1. Demographic Characteristics

Variable	Total (n=4608)	Men (n=3125)	Women (n=1483)	P value
Age	66.47±11.84	64.62±11.83	70.36±10.89	<0.001
Height, cm	162.46±9.29	167.07±6.56	152.75±6.22	<0.001
Weight, kg	66.17±12.15	70.00±11.29	58.11±9.69	<0.001
Body surface area, m ²	1.72±0.19	1.80±0.17	1.57±0.15	<0.001
Body mass index, kg/m ²	24.93±3.54	24.98±3.42	24.85±3.79	0.276
Systolic blood pressure	133.41±20.52	132.82±20.07	134.64±21.38	0.006
Diastolic blood pressure	78.20±12.41	78.58±12.41	77.41±12.37	0.003
Heart rate	74.72±14.90	74.29±14.99	75.61±14.69	0.005
Hypertension	2934 (63.7)	1921 (61.5)	1013 (68.3)	<0.001
Diabetes	1687 (36.6)	1135 (36.3)	552 (37.2)	0.575
Dyslipidemia	2612 (56.7)	1729 (55.3)	883 (59.5)	0.008
Peripheral artery disease	98 (2.1)	73 (2.3)	25 (1.7)	0.187
Chronic kidney disease (eGFR <60 mL/min per 1.73 m ²)	335 (7.3)	226 (7.2)	109 (7.3)	0.934
Hemoglobin levels	13.47±2.02	13.95±2.01	12.47±1.65	<0.001
Atrial fibrillation	0.07±0.25	0.06±0.24	0.07±0.26	0.310
Previous myocardial infarction	537 (11.7)	430 (13.8)	107 (7.2)	<0.001
Previous percutaneous coronary intervention	1101 (23.9)	825 (26.4)	276 (18.6)	<0.001
Old cerebral vascular accident	345 (7.5)	242 (7.7)	103 (6.9)	0.367
Clinical diagnosis				0.043
Stable angina	1231 (26.7)	814 (26.0)	417 (28.1)	
Unstable angina	1028 (22.3)	704 (22.5)	324 (21.8)	
AMI (NSTEMI+STEMI)	679 (14.7)	508 (16.3)	171 (11.5)	
Others	1670 (36.2)	1099 (35.2)	571 (38.5)	
Medication				
Aspirin	2612 (56.7)	1764 (56.4)	848 (57.2)	0.662
Clopidogrel	1962 (42.6)	1281 (41.0)	681 (45.9)	0.002
Potent P2Y ₁₂ inhibitors (ticagrelor+prasugrel)	701 (15.2)	520 (16.6)	181 (12.2)	0.179
Anticoagulant	153 (3.3)	104 (3.3)	49 (3.3)	0.989

Values are mean±SD or n (%). AMI indicates acute myocardial infarction; eGFR, estimated glomerular filtration rate; and NSTEMI, non-ST-segment-elevation myocardial infarction.

age of the women was 70.36±10.89 years. The mean weight of the women was 58.11±9.69 kg, which was lower than that of the men, which was 70.00±11.29 kg. The mean systolic blood pressure and heart rate were slightly higher in women, while the mean diastolic blood pressure was slightly higher in men. Women had a significantly higher prevalence of hypertension and dyslipidemia than did men. Contrastingly, men had a significantly greater incidence of previous myocardial infarction, previous PCI, and acute coronary syndrome with lower clopidogrel use.

The procedural characteristics of patients according to sex are shown in Table 2. Left DRA was performed more frequently in women than in men, while multivessel disease was observed more often in men. A significantly higher dose of unfractionated heparin was injected with a longer total hemostasis time in men than in women. Additionally, there was a greater use of 6-Fr and 7-Fr sheath insertion and elastic bandage

use in men. A greater proportion of women required additional hemostasis after coronary DRA procedures than did men; a similar pattern was observed for PCI via DRA (Table S2).

Access Site-Related Outcomes

The incidence of overall DRA site outcomes was significantly higher in women than in men (7.5% versus 4.1%, $P<0.001$), largely due to a higher rate of minor bleeding. DRA-related bleeding was also significantly more common in women than in men (4.9% versus 2.5%, $P<0.001$) (Figure 2). This difference was exclusively due to minor BARC type 1 and 2 bleeding, whereas there were no cases of major BARC bleeding in either group (Figure S2). Regarding the degree of DRA site hematoma, analyzed using the modified EASY criteria, a significantly higher incidence of Ia hematoma was observed in women (4.6% versus 2.4%,

Table 2. Procedure Characteristics

	Total (n=4608)	Men (n=3125)	Women (n=1483)	P value
Total access time, s	151.28±149.63	150.72±146.78	152.45±155.50	0.720
Left DRA	2766 (60.0)	1816 (58.1)	950 (64.1)	<0.001
Ultraound-guided puncture	293 (6.4)	213 (6.8)	80 (5.4)	0.075
Multivessel disease	1465 (31.8)	1103 (35.3)	362 (24.4)	<0.001
Unfractionated heparin dose	5281.42±2802.35	5506.42±2870.52	4807.29±2590.67	<0.001
Final sheath size				<0.001
4-Fr	613 (13.3)	359 (11.5)	254 (17.1)	
5-Fr	1804 (39.1)	1226 (39.2)	578 (39.0)	
6-Fr	1968 (42.7)	1387 (44.4)	581 (39.2)	
7-Fr	104 (2.3)	80 (2.6)	24 (1.6)	
Sheathless	119 (2.6)	73 (2.3)	46 (3.1)	
Hemostasis time, min	189.88±110.08	195.45±118.14	178.14±89.69	<0.001
Hemostasis method				<0.001
Adhesive tape fixation	2402 (52.1)	1573 (50.3)	829 (55.9)	
Elastic bandage wrapping	2159 (46.9)	1528 (48.9)	631 (42.5)	
Others	47 (1.0)	24 (0.8)	23 (1.6)	
Additional hemostasis	171 (3.7)	97 (3.1)	74 (5.0)	0.002
Hemostatis total time, min	197.61±136.15	202.90±147.74	186.47±106.90	<0.001

Values are mean±SD or n (%). DRA indicates distal radial access; and Fr, French.

$P<0.001$) than in men; it was predominantly constituted of <2 cm hematoma (1.3% versus 2.3%, $P=0.020$) (Table 3, Figure S2). No significant differences were

observed in any of the remaining predischarge complications, including RAO on palpation, tenderness, hand edema, numbness, perforations, and dissection.

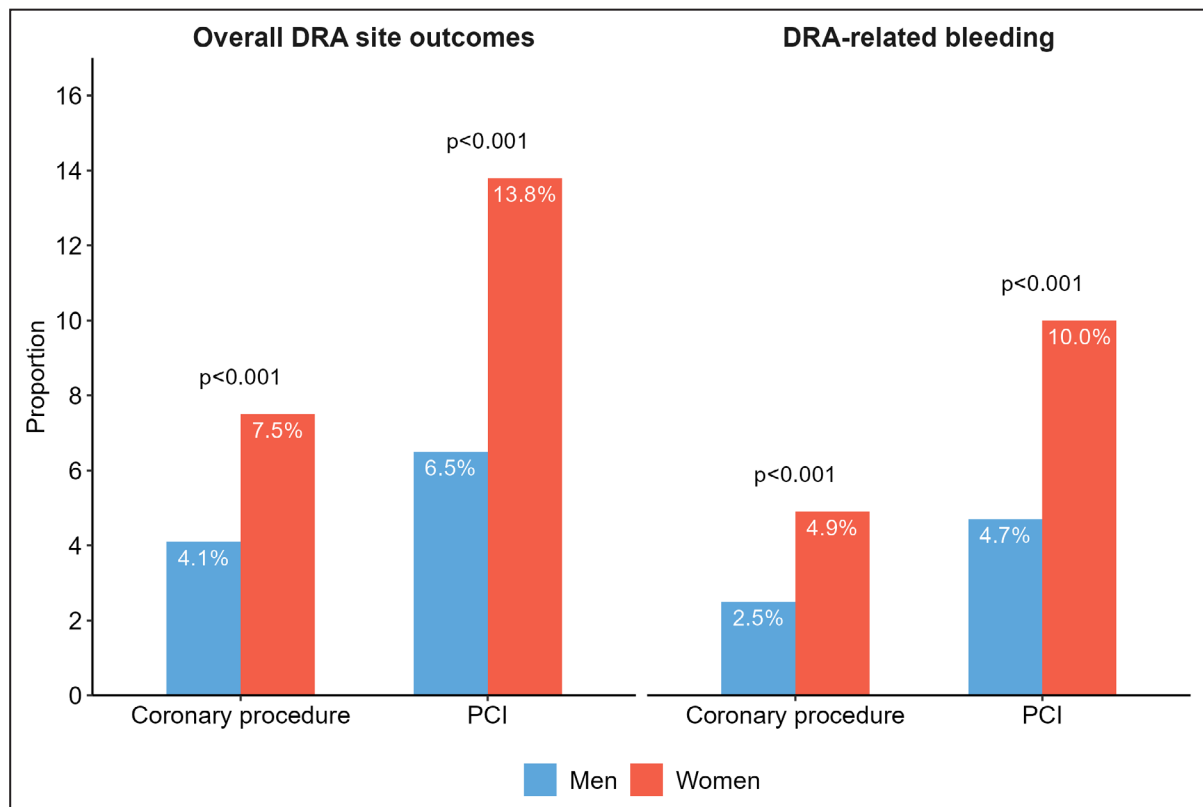


Figure 2. Outcomes of distal radial access between men and women. DRA indicates distal radial access; and PCI, percutaneous coronary intervention.

Table 3. Distal Radial Access Site Outcomes During Coronary Procedures Before and After Propensity Score Matching Analysis

Variables	Crude				PS-matched			
	Total (n=4608)	Men (n=3125)	Women (n=1483)	P value	Total (n=2966)	Men (n=1483)	Women (n=1483)	P value
Overall DRA site outcomes	240 (5.2)	129 (4.1)	111 (7.5)	<0.001	174 (5.9)	63 (4.2)	111 (7.5)	<0.001
DRA-related bleeding	149 (3.2)	77 (2.5)	72 (4.9)	<0.0001	110 (3.7)	38 (2.6)	72 (4.9)	0.001
BARC major bleeding	0 (0.0)	0 (0.0)	0 (0.0)	—	0 (0.0)	0 (0.0)	0 (0.0)	—
BARC minor bleeding								
BARC Type 1	49 (1.1)	25 (0.8)	24 (1.6)	0.015	38 (1.3)	14 (0.9)	24 (1.6)	0.144
BARC Type 2	100 (2.2)	52 (1.7)	48 (3.2)	<0.001	72 (2.4)	24 (1.6)	48 (3.2)	0.006
BARC Type 3a	0 (0.0)	0 (0.0)	0 (0.0)	—	0 (0.0)	0 (0.0)	0 (0.0)	—
DRA site hematoma degree (modified EASY criteria)								
Ia	142 (3.1)	74 (2.4)	68 (4.6)	<0.001	105 (3.5)	37 (2.5)	68 (4.6)	0.003
<2 cm	75 (1.6)	41 (1.3)	34 (2.3)	0.020	55 (1.9)	21 (1.4)	34 (2.3)	0.106
2–5 cm	25 (0.5)	12 (0.4)	13 (0.9)	0.056	20 (0.7)	7 (0.5)	13 (0.9)	0.264
>5 cm	7 (0.2)	2 (0.1)	5 (0.3)	0.069	7 (0.2)	2 (0.1)	5 (0.3)	0.450
Hand swelling	35 (0.8)	19 (0.6)	16 (1.1)	0.124	23 (0.8)	7 (0.5)	16 (1.1)	0.095
Ib	5 (0.1)	2 (0.1)	3 (0.2)	0.394	4 (0.1)	1 (0.1)	3 (0.2)	0.617
II	1 (0.0)	0 (0.0)	1 (0.1)	0.703	1 (0.0)	0 (0.0)	1 (0.1)	>0.999
III	1 (0.0)	1 (0.0)	0 (0.0)	>0.999	0 (0.0)	0 (0.0)	0 (0.0)	—
IV	0 (0.0)	0 (0.0)	0 (0.0)	—	0 (0.0)	0 (0.0)	0 (0.0)	—
Other complications before discharge								
Radial artery occlusion by palpation	8 (0.2)	3 (0.1)	5 (0.3)	0.145	6 (0.2)	1 (0.1)	5 (0.3)	0.221
Tenderness	67 (1.5)	38 (1.2)	29 (2.0)	0.066	52 (1.8)	23 (1.6)	29 (2.0)	0.488
Hand edema	74 (1.6)	46 (1.5)	28 (1.9)	0.355	45 (1.5)	17 (1.1)	28 (1.9)	0.136
Numbness	13 (0.3)	6 (0.2)	7 (0.5)	0.169	9 (0.3)	2 (0.1)	7 (0.5)	0.182
Perforation	7 (0.2)	4 (0.1)	3 (0.2)	0.841	5 (0.2)	2 (0.1)	3 (0.2)	>0.999
Dissection	9 (0.2)	3 (0.1)	6 (0.4)	0.063	7 (0.2)	1 (0.1)	6 (0.4)	0.131

Values are n (%). BARC indicates Bleeding Academic Research Consortium; DRA, distal radial access; EASY, Early Discharge After Trans-radial Stenting of Coronary Arteries Study; and PS, propensity score.

Similar results were observed when analyzed using propensity score matching, with overall DRA site outcomes and DRA-related bleeding being more prevalent in women (Table 3). Regarding PCI, women had a significantly greater incidence of DRA site outcomes and DRA-related bleeding. Additionally, 2 to 5 cm and >5 cm hematoma, hand swelling, RAO, and tenderness were significantly more common in women (Table 4). However, major BARC bleeding or extensive hematoma of DRA did not occur in either PCI group (Table 4, Figure S3).

Risk Factors of Overall DRA Site Outcomes

The results of the multivariable analysis, using the factors evaluated in the univariate analysis, performed to determine the risk factors of overall DRA site outcomes are shown in Table 5. Female sex was a significant

factor influencing access site outcomes (odds ratio [OR], 2.08 [95% CI, 1.58–2.74]; $P<0.001$). Body mass index (OR, 0.94 [95% CI, 0.91–0.98]), chronic kidney disease (OR, 2.00 [95% CI, 1.30–3.00]), PCI procedure (OR, 1.48 [95% CI, 1.09–2.00]; $P=0.011$), use of potent P2Y₁₂ inhibitors (OR, 2.54 [95% CI, 1.81–3.60]; $P<0.001$), and unfractionated heparin dose (OR, 1.09 [95% CI, 1.03–1.15]) were also significant factors influencing the occurrence of overall DRA site outcomes. In sensitivity analysis, female sex was also a significant factor of overall DRA site outcomes after propensity score matching (OR, 1.82 [95% CI, 1.33–2.51]; $P<0.001$) (Figure 3).

DISCUSSION

This study provides a comprehensive analysis of sex differences in DRA site outcomes by examining a

Table 4. Distal Radial Access Site Outcomes During Percutaneous Coronary Intervention

Variable	Total (n=1586)	Men (n=1187)	Women (n=399)	P value
Overall DRA site outcomes	132 (8.3)	77 (6.5)	55 (13.8)	<0.001
DRA related bleeding	96 (6.1)	56 (4.7)	40 (10.0)	<0.001
BARC major bleeding	0 (0.0)	0 (0.0)	0 (0.0)	...
BARC minor bleeding				
BARC Type 1	33 (2.1)	19 (1.6)	14 (3.5)	0.018
BARC Type 2	63 (4.0)	37 (3.1)	26 (6.5)	0.006
BARC Type 3a	0 (0.0)	0 (0.0)	0 (0.0)	...
DRA site hematoma degree (modified EASY criteria)				
Ia	92 (5.8)	54 (4.5)	38 (9.5)	<0.001
<2 cm	40 (2.5)	28 (2.4)	12 (3.0)	0.596
2–5 cm	18 (1.1)	9 (0.8)	9 (2.3)	0.032
>5 cm	7 (0.4)	2 (0.2)	5 (1.3)	0.017
Hand swelling	27 (1.7)	15 (1.3)	12 (3.0)	0.035
Ib	3 (0.2)	2 (0.2)	1 (0.3)	>0.999
II	1 (0.1)	0 (0.0)	1 (0.3)	0.567
III	0 (0.0)	0 (0.0)	0 (0.0)	...
IV	0 (0.0)	0 (0.0)	0 (0.0)	...
Other complications before discharge				
Radial artery occlusion by palpation	3 (0.2)	0 (0.0)	3 (0.8)	0.021
Tenderness	28 (1.8)	15 (1.3)	13 (3.3)	0.016
Hand edema	56 (3.5)	35 (2.9)	21 (5.3)	0.044
Numbness	11 (0.7)	7 (0.6)	4 (1.0)	0.609
Perforation	3 (0.2)	2 (0.2)	1 (0.3)	0.876
Dissection	4 (0.3)	2 (0.2)	2 (0.5)	0.569

Values are n (%). DRA indicates distal radial access; BARC, Bleeding Academic Research Consortium; and EASY, Early Discharge After Transradial Stenting of Coronary Arteries Study.

composite end point that evaluates a range of event intensities, from minor to major access site outcomes. Our results indicate that while the overall incidence of DRA site outcomes was higher in women, this difference was primarily driven by minor bleeding events. No significant differences were observed in major complications, highlighting that sex differences in coronary DRA procedures are largely related to minor events rather than major outcomes.

Sex differences in patients undergoing coronary procedures remain controversial. Several studies on coronary procedures have reported that the risk of mortality and complications is higher in women than in men.^{12,13} In particular, many studies have also shown that bleeding is more common in women after PCI, with bleeding being a well-known factor in future ischemic cardiovascular events associated with the discontinuation of antiplatelet therapy.^{14,15}

Typically, access site selection for coronary procedures is widely acknowledged as an important factor influencing the occurrence of bleeding complications. When comparing radial and femoral PCI, bleeding and mortality were significantly lower with radial access, a trend more pronounced in women than in men.^{16,17} Furthermore, in a large meta-analysis comparing radial and femoral artery access coronary procedures, it was reported that major vascular complications requiring surgical treatment occurred more in the femoral artery than in the radial artery.¹⁸ Given these advantages, the current rate of all-comer PCI through the conventional radial artery access is reported to be up to 80%.¹⁹ However, when performing coronary procedures via the radial artery, RAO is also an important complication, and it is reported that women have more RAO due to their smaller diameter, and associated with this, the proportion of radial artery coronary procedures is lower than that of men.^{20–22}

Recently, the DRA has attracted attention because of its advantages in terms of reduced rates of RAO and bleeding complications.^{4–6} While RAO incidence during coronary procedures via the radial artery can range from 0.8% to as high as 38%,²³ DRA procedures typically exhibit a markedly lower RAO rate, often <1.0% within 24 hours postprocedure.⁹ Moreover, evaluations using optical coherence tomography have shown no acute vascular injuries of the radial artery following PCI via DRA.²⁴ In our study, the predischARGE RAO rate remained remarkably low, <1.0% for coronary procedures and PCI, regardless of patient sex. However, there was a higher incidence of RAO in women than in men during PCI via DRA (0.8% versus 0.0%, $P=0.021$).

The smaller diameter of the DRA compared with that of the conventional radial artery presents several obstacles, including a learning curve during DRA procedures. Female sex is a predictor of small distal radial artery diameter and also a predictor of DRA failure.^{25–27} In our study, puncture failures were also significantly higher in women, 6.6% compared with 5.1% in men, with a P value of 0.048. The current study showed that women had a significantly higher rate of DRA site outcomes, and in particular, DRA-related minor bleeding was also more common in women. In addition, women were evaluated by multivariable analysis, and propensity score matching was found to be an important factor associated with the occurrence of DRA site outcomes in coronary procedures. Despite the smaller diameter of the distal radial artery in women, which is expected for less DRA-related bleeding, the higher incidence of access site bleeding outcomes in our study might be explained by the time to hemostasis. The KODRA trial did not propose a hemostasis time for DRA during coronary procedures, and hemostasis was achieved according to each hospital's protocol. Therefore, a lower dose of heparin was used in women

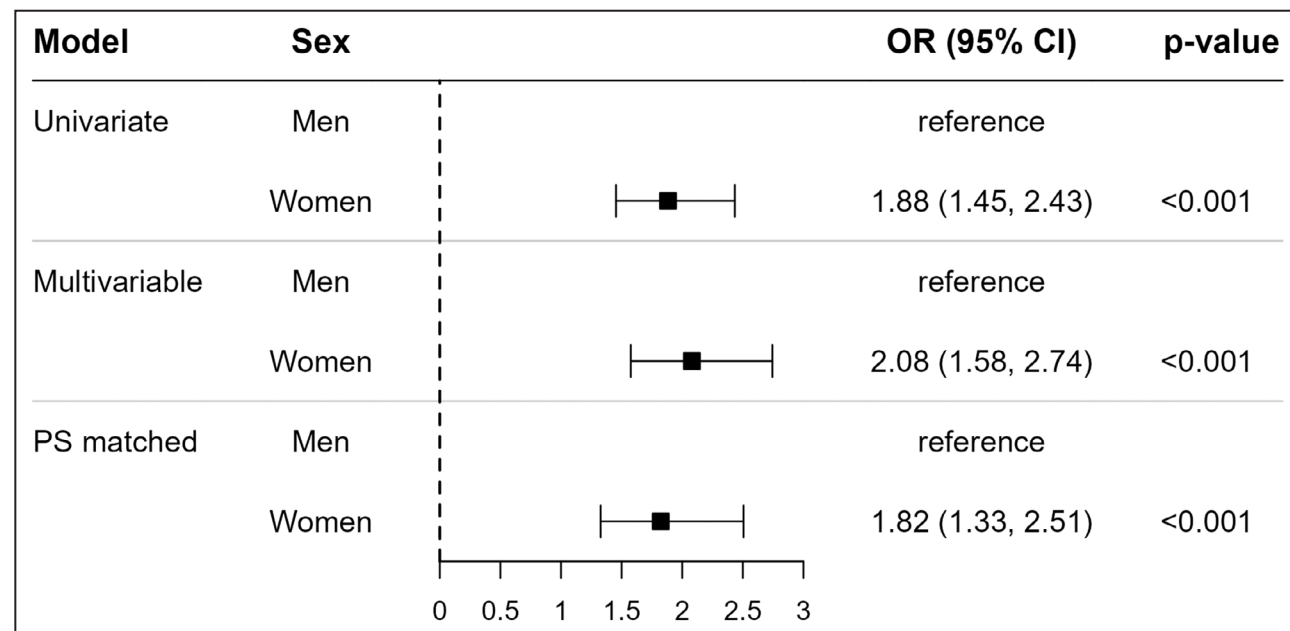
Table 5. Factors Associated With Overall Distal Radial Access Site Outcomes

Variable	Univariate			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
Age $\geq$ 75 y	1.36	1.03–1.78	0.029	1.04	0.77–1.39	0.816
Female sex	1.88	1.44–2.44	<0.001	2.08	1.58–2.74	<0.001
Body mass index	0.94	0.91–0.98	0.003	0.94	0.91–0.98	0.005
Hypertension	1.08	0.83–1.43	0.564	0.99	0.74–1.33	0.942
Diabetes	1.00	0.76–1.31	0.985	0.92	0.69–1.22	0.576
Chronic kidney disease (eGFR <60 mL/min per 1.73 m ²)	2.15	1.44–3.11	<0.001	2.00	1.30–3.00	0.001
PCI procedure	1.22	0.91–1.63	0.179	1.48	1.09–2.00	0.011
Acute myocardial infarction (NSTEMI+STEMI)	1.40	0.99–1.93	0.048	0.88	0.61–1.25	0.485
6-Fr or 7-Fr sheath	1.61	1.24–2.10	<0.001	1.30	0.97–1.75	0.080
Potent P2Y ₁₂ inhibitor	2.88	2.12–3.98	<0.001	2.54	1.81–3.60	<0.001
Anticoagulant	1.14	0.53–2.14	0.703	1.30	0.60–2.50	0.460
Unfractionated heparin dose (per 1000 IU)	1.11	1.06–1.15	<0.001	1.09	1.03–1.15	0.001
Hemostasis method, elastic bandage wrapping	0.65	0.50–0.85	0.002	0.89	0.66–1.19	0.433
Hemostasis time, 30 min	1.00	0.96–1.03	0.838	0.99	0.95–1.03	0.713

eGFR indicates estimated glomerular filtration rate; Fr, French; OR, odds ratio; PCI, percutaneous coronary intervention; NSTEMI, non-ST-segment-elevation myocardial infarction; and STEMI, ST-segment-elevation myocardial infarction.

with relatively lower body weight compared with the men, which may have resulted in a shorter hemostasis time and consequently more additional hemostasis

required in real-world clinical settings. A prospective observational study showed that $\approx$ 180 minutes is the appropriate hemostasis time for PCI via DRA.²⁸ Based

**Figure 3. Forest plot of odds ratio for association between sex and overall DRA site outcomes.**

Multivariable logistic regression and PS matching were performed with covariates including age, sex, body mass index, hypertension, diabetes, chronic kidney disease, PCI procedure, acute myocardial infarction, 6-Fr or 7-Fr sheath, potent P2Y₁₂ inhibitor, anticoagulant, unfractionated heparin dose, hemostasis method, and hemostasis time. DRA indicates distal radial access; PCI, percutaneous coronary intervention; OR, odds ratio; and PS, propensity score.

on our findings, it is recommended that hemostasis time after coronary procedures via DRA should be relatively longer in women than in men to minimize DRA-related bleeding. In addition, lower body mass index, chronic kidney disease, PCI procedure, use of potent P2Y12 inhibitor, and unfractionated heparin dose were also significant factors influencing overall DRA site outcomes. Previous studies already have identified these factors as contributing to such vascular outcomes.²⁹ Therefore, our research suggests that when these factors are present during coronary procedures via DRA, more time may be required to achieve hemostasis.

Study Limitations

This study has several limitations. First, there may be a selection bias in the treatment of patients with DRA. Second, the baseline characteristics between the sexes differed, because this study was not originally designed to compare men and women; to address these discrepancies, multivariable analysis was performed. Third, RAO was primarily determined by palpation rather than Doppler ultrasound. This method of assessment may potentially obscure the exact incidence of RAO and related outcomes. Fourth, because each center was permitted to perform hemostasis in accordance with their established hemostasis protocol, this discrepancy in hemostasis may have been associated with the incidence of outcomes at the access site.

CONCLUSIONS

In this subgroup analysis of the large-scale KODRA trial regarding coronary DRA outcomes, we found that women had higher overall rates of access site events compared with men, but these differences were primarily limited to minor complications such as minor bleeding. Importantly, no significant sex differences were observed for more serious outcomes. These findings highlight that the DRA remains a safe alternative option for both men and women, but we need to be particularly careful when performing DRA procedures in women because female sex is associated with an increased risk of minor complications.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S2
Figures S1–S3

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