Transradial versus transfemoral intervention in non-ST-segment elevation acute coronary syndrome patients undergoing percutaneous coronary intervention: the Korean transradial intervention registry of 1 285 patients

Min-Ho Lee, Duk Won Bang, Byung Won Park, Byung-Ryul Cho, Seung-Woon Rha, Myung Ho Jeong, Junghan Yoon, Jon Suh, Kyoo-Rok Han, Min Su Hyon

Abstract
Introduction: Although the implementation of transradial intervention (TRI) has increased over the last few years, there are limited data on the impact of TRI on efficacy and safety in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). We sought to compare one-year clinical outcomes and bleeding complications of TRI with those of transfemoral intervention (TFI) in patients with NSTE-ACS.

Methods: The Korean TRI registry was a cohort of 20 centres from 2012 to 2015. The primary efficacy endpoint was major adverse cardiovascular events (MACE), defined as a composite of cardiac death (CD), non-fatal myocardial infarction (MI) and repeat revascularisation (RR). Among the 1 319 patients with NSTE-ACS, 1 285 were finally analysed after excluding 34 due to lack of follow-up data. The patients were divided into TRI and TFI groups according to the final access site.

Results: At one-year follow up, the TRI group showed a significantly lower rate of MACE, and a marginally significantly lower rate of CD than the TFI group in the crude population. However, in propensity-score matched analysis, the rate of MACE did not differ between the TRI and TFI groups. Regarding bleeding complications, the TRI group was associated with significantly lower rates of major bleeding in both the crude and matched populations. Independent predictors of MACE were chronic kidney disease (CKD) and multi-vessel disease (MVD).

Conclusions: In patients with NSTE-ACS, TRI was associated with favourable one-year clinical outcomes and lower bleeding complications compared to TFI. Independent predictors of MACE were clinical and angiographic profiles (CKD, MVD) rather than vascular access sites.

Keywords: radial artery, femoral artery, acute coronary syndrome, myocardial infarction, percutaneous coronary intervention

Division of Cardiology, Department of Internal Medicine, Soonchunhyang University Hospital, Seoul, Korea
Min-Ho Lee, MD, neoich@gmail.com
Duk Won Bang, MD, PhD
Byung Won Park, MD
Min Su Hyon, MD, PhD, mshyon@schmc.ac.kr

Division of Cardiology, Department of Internal Medicine, Kangwon National University Hospital, Chuncheon, Korea
Byung-Ryul Cho, MD, PhD

Division of Cardiology, Department of Internal Medicine, Korea University Guro Hospital, Seoul, Korea
Seung-Woon Rha, MD, PhD

Division of Cardiology, Department of Internal Medicine, Chonnam National University Hospital, Gwangju, Korea
Myung Ho Jeong, MD, PhD

Division of Cardiology, Department of Internal Medicine, Yonsei University Wonju Severance Christian Hospital, Wonju, Korea
Junghan Yoon, MD, PhD

Division of Cardiology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Korea
Jon Suh, MD, PhD

Division of Cardiology, Department of Internal Medicine, Kangdong Sacred Heart Hospital, Seoul, Korea
Kyoo-Rok Han, MD, PhD, krheart@hallym.or.kr

Compared with the femoral artery, the radial artery is more superficial, smaller in diameter, it lacks important adjacent structures or potential spaces, and is easily compressed. Therefore, although femoral access has traditionally been used for percutaneous coronary intervention (PCI), radial access has gained increasing popularity with evolving technology and the increasing experience of interventional cardiologists over the past few years.
Risks related to PCI comprise ischaemic complications, including cardiac death (CD), myocardial infarction (MI), stent thrombosis and stroke, as well as vascular complications such as bleeding.1 Bleeding complications are associated with subsequent morbidity and mortality rates, 30 to 70% of which are related to the vascular access site.5

A recent meta-analysis of 76 studies involving a total of 761 919 patients concluded that transradial intervention (TRI) was associated with a 78% reduction in rate of bleeding and 80% reduction in transfusion rates, regardless of the clinical indication for PCI, compared with transfemoral intervention (TFI).4 This is consistent with results from the largest randomised trial done to date.6 However, the clinical outcomes of TRI varied according to the clinical settings of the studies, including the inclusion criteria.

Recent large, randomised trials have demonstrated that TRI reduced mortality rates in patients with ST-segment elevation myocardial infarction (STEMI).7,8 By contrast, for treatment of non-ST-segment elevation acute coronary syndrome (NSTE-ACS), the clinical benefits of TRI remain less well defined. Although there have been a few studies comparing results between TRI and TFI in patients with NSTE-ACS, the only available data were derived from a subgroup analysis or post hoc analysis of those studies.9,10 Therefore our main objective was to compare one-year clinical outcomes and bleeding complications of TRI with those of TFI in patients with NSTE-ACS, using data from the Korean TRI registry (KOTRI registry).

Methods

The KOTRI registry was an observational cohort over six months (February to July 2014) in 20 centres in Korea. However, due to different processing times for institutional review board (IRB) approval at the participating centres, the entire study population was enrolled from May 2012 to January 2015.10

All patients were included if they had NSTE-ACS, non-ST-segment elevation myocardial infarction (NSTEMI) or unstable angina, an invasive approach was proposed, and the interventional cardiologist was willing to proceed with radial access. Patients were required to have intact dual circulation of the hand, as assessed by an Allen’s test, and radial and femoral artery access were based on the reported final access site.

At the time of admission, patients gave written consent for the storing of their information in the hospital’s medical records. This study was approved by the IRB of Soonchunhyang University Hospital, Seoul, Korea, as well as by all participating centres, and was conducted according to the principals of the Declaration of Helsinki.

The primary efficacy endpoint of this study was major adverse cardiovascular events (MACE), defined as a composite of CD, non-fatal MI and repeat revascularisation (RR). The secondary efficacy endpoints included individual components of MACE. All deaths were considered to have a cardiac cause unless a non-cardiac origin was definitively documented. MI was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel.

Bleeding complications were recorded during admission and defined according to the Bleeding Academic Research Consortium (BARC) criteria.12 Major bleeding was defined as BARC type 2 or above (any overt, actionable sign of haemorrhage that meets at least one of the following criteria: (1) requiring non-surgical, medical intervention by a healthcare professional, (2) leading to hospitalisation or increased level of care, or (3) prompting evaluation). Minor bleeding was defined as BARC type 1 (bleeding that is not actionable and does not cause the patient to seek unscheduled performance of studies, hospitalisation or treatment by a healthcare professional).

All patients were pre-treated with aspirin and a platelet P2Y12 inhibitor. The selection of angioplasty equipment, including the choice of drug-eluting stents (DES) and the use of glycoprotein IIb/IIIa inhibitors during the procedure were left to the operator’s discretion, as was the use of vascular closure devices. After the procedure, all patients received aspirin indefinitely and a P2Y12 inhibitor for at least 12 months.

After the index PCI, one-, six-, nine- and 12-month follow-ups were recommended. Clinical, angiographic, procedural and outcome data were collected by independent nurses and researchers who were unaware of the purpose of the study. Patient data were reviewed via electronic medical records.

Statistical analysis

The analysis was performed in two parts. First, analyses were conducted in the crude population. Data are presented as numbers and frequencies for categorical variables and as mean ± SD for continuous variables. For between-group comparisons, the chi-squared test or Fisher’s exact test were used for categorical variables, and the independent samples t-test was used for continuous variables. A Kaplan–Meier analysis was performed to calculate the cumulative incidence of clinical outcomes, and differences were assessed using the log-rank test. A multivariate Cox proportional hazards regression model was used to identify independent predictors of MACE. Factors entered into the multivariate model included those with p-values < 0.10 in the univariate analysis, and variables with known prognostic value.

In the second part of the analysis, a propensity-score matched population was selected to adjust for the uneven distribution of baseline characteristics and a 3:1 matched analysis was performed. In brief, propensity scores representing the probabilities of TRI were calculated using a multiple logistic regression model, based on the 11 measured baseline covariates. The adjusted variables were as follows: age, gender, hypertension, diabetes mellitus, dyslipidaemia, chronic kidney disease (CKD), current smoker, history of ischaemic heart disease (IHD), history of peripheral artery disease (PAD), initial diagnosis, and extent of disease.

SPSS version 18.0 (SPSS Inc, Chicago, Illinois) and the R programming language, version 2.8.0 (R Foundation for Statistical Computing) were used for all statistical analyses. Two-sided p-values < 0.05 were considered to be statistically significant.

Results

The KOTRI registry included 1 319 consecutive patients with NSTE-ACS from 20 centres who were successfully revascularised using DES from May 2012 to January 2015. Of these patients, 1 285 were eligible for the study and 34 were excluded due to lack of follow-up data. Among them, 983 patients were divided into the TRI group and 302 into the TFI group, according to final vascular access site.
Baseline clinical and angiographic characteristics are shown in Table 1. Compared with the TFI group, the TRI group had more favourable baseline characteristics, such as lower frequency of diabetes mellitus and CKD, and history of IHD and PAD, except for dyslipidaemia, which was more common in the TRI group. Other baseline characteristics, such as lower frequency of history of PAD, history of IHD, and smoking were also less frequent in the TRI group than in the TFI group. However, there were no differences in rates of MI (0.5 vs 0.0%, p = 0.045), which was mainly driven by the lower rate of CD in the TRI group (0.9 vs 2.3%, p = 0.050). However, there were no differences in rates of MI (5.5 vs 6.6%, p = 0.247) between two groups at one year.

The cumulative clinical outcomes in the crude population at one year are presented in Table 2 and Fig. 1. The rate of MACE was significantly lower in the TRI group than in the TFI group (4.2 vs 7.0%, p = 0.045), which was mainly driven by the lower rate of CD in the TRI group (0.9 vs 2.3%, p = 0.050). However, there were no differences in rates of MI (5.5 vs 6.6%, p = 0.247) and RR (3.3 vs 4.6%, p = 0.247) between two groups at one year.

Bleeding occurred in 27 patients (2.2%) in the crude population and was significantly less frequent in the TRI group (1.3 vs 5.1%, p < 0.001). This difference was mainly

### Table 1. Baseline characteristics of the crude population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n = 1285)</th>
<th>TRI group (n = 983)</th>
<th>TFI group (n = 302)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.6 ± 11.2</td>
<td>65.4 ± 11.2</td>
<td>66.5 ± 11.3</td>
<td>0.128</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>857 (66.7)</td>
<td>667 (67.9)</td>
<td>190 (62.9)</td>
<td>0.125</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>836 (65.2)</td>
<td>640 (65.2)</td>
<td>196 (65.1)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>432 (33.8)</td>
<td>306 (31.2)</td>
<td>126 (42.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>246 (19.3)</td>
<td>204 (20.9)</td>
<td>42 (14.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>Chronic kidney disease, n</td>
<td>52 (4.1)</td>
<td>7 (0.7)</td>
<td>45 (15.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>350 (27.4)</td>
<td>276 (28.3)</td>
<td>74 (24.6)</td>
<td>0.210</td>
</tr>
<tr>
<td>History of IHD, n (%)</td>
<td>331 (25.8)</td>
<td>223 (22.7)</td>
<td>108 (35.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>History of PAD, n (%)</td>
<td>29 (2.4)</td>
<td>10 (1.1)</td>
<td>19 (6.5)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Table 2. Clinical outcomes at one year

<table>
<thead>
<tr>
<th>Variables</th>
<th>TRI group (n = 983)</th>
<th>TFI group (n = 302)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude population</td>
<td>904 (70.4)</td>
<td>723 (73.6)</td>
<td>0.810</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>381 (29.6)</td>
<td>260 (26.4)</td>
<td>0.120</td>
</tr>
<tr>
<td>Disease extent, n (%)</td>
<td>536 (42.7)</td>
<td>420 (43.9)</td>
<td>0.120</td>
</tr>
<tr>
<td>1VD</td>
<td>416 (33.1)</td>
<td>323 (33.8)</td>
<td>0.120</td>
</tr>
<tr>
<td>2VD</td>
<td>304 (24.2)</td>
<td>214 (22.4)</td>
<td>0.120</td>
</tr>
<tr>
<td>Culprit lesion, n (%)</td>
<td>372 (29.5)</td>
<td>291 (30.6)</td>
<td>0.120</td>
</tr>
<tr>
<td>LAD</td>
<td>134 (17.5)</td>
<td>102 (17.7)</td>
<td>0.120</td>
</tr>
<tr>
<td>LCX</td>
<td>226 (28.5)</td>
<td>167 (28.2)</td>
<td>0.120</td>
</tr>
<tr>
<td>LM</td>
<td>35 (4.6)</td>
<td>26 (4.5)</td>
<td>0.120</td>
</tr>
</tbody>
</table>

TRI = transradial intervention; TFI = transfemoral intervention; IHD = ischaemic heart disease; PAD = peripheral artery disease; NSTEMI = non-ST-segment elevation myocardial infarction; VD = vessel disease; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; LM = left main.

### Table 3. Bleeding complications at one year

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n = 1285)</th>
<th>TRI group (n = 983)</th>
<th>TFI group (n = 302)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable angina, n (%)</td>
<td>904 (70.4)</td>
<td>723 (73.6)</td>
<td>181 (59.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Major bleeding, n (%)</td>
<td>536 (42.7)</td>
<td>420 (43.9)</td>
<td>116 (38.8)</td>
<td>0.023</td>
</tr>
<tr>
<td>Minor bleeding, n (%)</td>
<td>416 (33.1)</td>
<td>323 (33.8)</td>
<td>93 (31.1)</td>
<td>0.091</td>
</tr>
<tr>
<td>Culprit lesion, n (%)</td>
<td>304 (24.2)</td>
<td>214 (22.4)</td>
<td>90 (30.1)</td>
<td>0.091</td>
</tr>
</tbody>
</table>

TRI = transradial intervention; TFI = transfemoral intervention; IHD = ischaemic heart disease; PAD = peripheral artery disease; NSTEMI = non-ST-segment elevation myocardial infarction; VD = vessel disease; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; LM = left main.

### Table 4. Baseline characteristics of the propensity-score matched population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall (n = 624)</th>
<th>TRI group (n = 421)</th>
<th>TFI group (n = 243)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.6 ± 11.7</td>
<td>66.2 ± 11.6</td>
<td>66.6 ± 11.3</td>
<td>0.507</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>414 (65.9)</td>
<td>155 (64.3)</td>
<td>159 (65.2)</td>
<td>0.690</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>204 (32.7)</td>
<td>86 (35.7)</td>
<td>38 (15.7)</td>
<td>0.433</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>150 (34.8)</td>
<td>137 (31.8)</td>
<td>13 (5.8)</td>
<td>0.422</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>91 (14.6)</td>
<td>35 (14.5)</td>
<td>&gt; 0.999</td>
<td>0.299</td>
</tr>
<tr>
<td>Chronic kidney disease, n</td>
<td>4 (0.6)</td>
<td>4 (1.7)</td>
<td>3 (1.2)</td>
<td>0.299</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>180 (28.8)</td>
<td>68 (28.2)</td>
<td>112 (46.1)</td>
<td>0.867</td>
</tr>
<tr>
<td>History of IHD, n (%)</td>
<td>176 (28.2)</td>
<td>76 (31.5)</td>
<td>90 (37.5)</td>
<td>0.359</td>
</tr>
<tr>
<td>History of PAD, n (%)</td>
<td>9 (1.4)</td>
<td>7 (2.9)</td>
<td>2 (0.8)</td>
<td>0.164</td>
</tr>
</tbody>
</table>

TRI = transradial intervention; TFI = transfemoral intervention; IHD = ischaemic heart disease; PAD = peripheral artery disease; NSTEMI = non-ST-segment elevation myocardial infarction; VD = vessel disease; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; LM = left main.

The cumulative clinical outcomes in the crude population at one year are presented in Table 2 and Fig. 1. The rate of MACE was significantly lower in the TRI group than in the TFI group (4.2 vs 7.0%, p = 0.045), which was mainly driven by the lower rate of CD in the TRI group (0.9 vs 2.3%, p = 0.050). However, there were no differences in rates of MI (5.5 vs 6.6%, p = 0.247) and RR (3.3 vs 4.6%, p = 0.247) between two groups at one year.

Bleeding occurred in 27 patients (2.2%) in the crude population and was significantly less frequent in the TRI group (1.3 vs 5.1%, p < 0.001). This difference was mainly
driven by the lower frequency of major bleeding in the TRI group (0.4 vs 3.4%, \( p < 0.001 \)). However, there was no significant difference in minor bleeding rates between the two groups (0.8 vs 1.7%, \( p = 0.199 \)) (Table 3).

To minimise allocation bias and better describe the treatment impact of TRI in NSTE-ACS patients, propensity-score matching was done. After 3:1 propensity-score matching, 624 of 983 patients in the TRI group (63.5%) were successfully matched to 241 patients in the TFI group. The baseline characteristics of the two groups were well balanced after matching (Table 4).

The clinical outcomes of the matched population were different from those of the crude population (Table 2, Fig. 2). The rate of MACE was not different between the TRI and TFI groups (4.0 vs 5.4%, \( p = 0.333 \)). Also, there were no significant differences in rates of CD, MI and RR between the two groups.

Bleeding complications of the matched population were similar to those of the crude population. Bleeding occurred in 20 patients (2.4%) and was significantly less frequent in the TRI group (1.0 vs 6.0%, \( p < 0.001 \)), which was mainly attributable to the lower frequency of major bleeding in the TRI group (0.3 vs 3.8%, \( p < 0.001 \)). However, there was no significant difference in minor bleeding rates between the two groups (0.7 vs 2.1%, \( p = 0.126 \)) (Table 3).

To identify independent predictors of MACE after successful PCI in this registry, Cox proportional hazard regression analysis was performed (Table 5). Significant independent predictors were CKD (HR: 4.172, 95% CI: 1.822–9.551, \( p = 0.021 \)) and MVD (HR: 2.619, 95% CI: 1.146–4.843, \( p = 0.002 \)). However, TRI was not an independent predictor of MACE (HR: 1.106, 95% CI: 0.532–1.939, \( p = 0.963 \)).
Subgroup analysis regarding MACE was performed according to older age ($\geq 65$ years), gender, hypertension, diabetes mellitus, dyslipidaemia, CKD, current smoker, history of IHD, history of PAD, presence of NSTEMI and MVD. Results in the various subgroups were similar to those observed in the entire population (Fig. 3). There were no significant differences in clinical outcomes between the two groups, and the results were consistent across all subgroups, without any significant interactional $p$-value.

**Discussion**

This study examined the role of vascular access site exclusively, in patients with NSTE-ACS undergoing PCI from the KOTRI registry, which is a large, observational cohort to describe the
Although recent ACCF/AHA/SCAI PCI practice guidelines led to the inevitable debate on preferred vascular access site. clinical outcomes after intervention for NSTE-ACS. rather than vascular access site are important in determining NSTE-ACS, suggesting that clinical and angiographic profiles MVD were independent predictors of MACE in patients with group in both the crude and matched populations; (4) CKD and bleeding complications were lower in the TRI than the TFI two groups after propensity-score matching; (3) rates of major in the crude population at one-year follow up; (2) there were no group had a lower rate of MACE and CD than the TFI group with TRI. The major findings of this analysis are: (1) the TRI association between clinical outcomes and bleeding complications in patients with STEMI. Also in the RIVAL trial, TRI was associated with significant clinical benefits in the primary outcome (a composite of CD, stroke, MI, TLR and bleeding) (13.6 vs 21.0%, p = 0.003) and cardiac mortality rate (5.2 vs 9.2%, p = 0.020) at 30 days in patients with STEMI. Consistent with these results, Karrowni et al. concluded from their meta-analysis, including 12 randomised trials, that TRI was associated with favourable outcomes in STEMI patients and should be the preferred approach for experienced radial operators.6 However, in contrast to STEMI, the clinical benefits of TRI in NSTE-ACS have not been fully demonstrated. In subgroup analysis of the RIVAL trial, TRI did not show any clinical benefits in the primary outcome (HR: 1.11, 95% CI: 0.83–1.48; p = 0.49) and mortality rate (HR: 1.66, 95% CI: 0.94–2.92; p = 0.082) at 30 days. Post hoc analysis of the EARLY-ACS trial revealed no significant differences in 30-day death/MI (12.6 vs 11.2%, p = 0.162) or 30-day death (1.8 vs 2.3%, p = 0.283, respectively), nor were the rates of one-year MACE and CD. Therefore our data corroborate previous findings and extend the observations to one year. Regarding bleeding complications, the subgroup analysis of the PRESTO-ACS trial revealed that TRI was associated with a significant decrease in TIMI bleeding (0.7 vs 2.7%, p = 0.03) at one year in patients with NSTE-ACS.7 Also, subgroup analysis of the RIVAL trial showed lower rate of ACUITY-defined bleeding with TRI in the NSTE-ACS cohort.7 However, the results in the previous two studies were derived from subgroup analysis, which had the potential for false-positive errors.8 Furthermore, the former study was conducted without any sensitivity analysis despite uneven distribution of baseline clinical, procedural and pharmacological characteristics between the TRI and TFI groups.8 In our study, the rates of 30-day MACE and CD were no different between the TRI and TFI groups (0.8 vs 0.4%, p = 0.545; 0.5 vs 0.0%, p = 0.283, respectively), nor were the rates of one-year MACE and CD. Therefore our data corroborate previous findings and extend the observations to one year. Regarding bleeding complications, the subgroup analysis of the PRESTO-ACS trial revealed that TRI was associated with a significant decrease in TIMI bleeding (0.7 vs 2.7%, p = 0.03) at one year in patients with NSTE-ACS.7 Also, subgroup analysis of the RIVAL trial showed lower rate of ACUITY-defined bleeding with TRI in the NSTE-ACS cohort.7 However, the results in the previous two studies were derived from subgroup analysis, which had the potential for false-positive errors.8 Furthermore, the former study was conducted without any sensitivity analysis despite uneven distribution of baseline clinical, procedural and pharmacological characteristics between the TRI and TFI groups.8 Corroborating previous findings, our analysis was in line with earlier results, using different bleeding criteria (BARC criteria) in a significantly larger TRI cohort, although bleeding is an outcome that is definition dependent.9 Therefore, our study strongly supports the benefit of TRI with regard to bleeding complications in intervention for NSTE-ACS and may be more reflective of real-world clinical practice. For the paradigm shift from ‘femoral access first’ to ‘radial access first’ in the middle of the debate on the preferred vascular access site in PCI, there should be enough clinical evidence supporting the efficacy and safety of TRI to TFI. However, there is an incomplete evidence base for overall superiority of the radial approach over the femoral approach.

Recently, two randomised, controlled trials were published regarding clinical outcomes of TRI in patients with ACS.3 The RIVAL trial showed the clear benefit of TRI in terms of primary outcome (a composite of death, MI, stroke and major bleeding) (HR: 0.60, 95% CI: 0.38–0.94; p = 0.026) and mortality (HR: 0.39, 95% CI: 0.20–0.76; p = 0.006) at 30 days in patients with STEMI.1 In the RIVAL trial, TRI did not show any clinical benefits in the primary outcome (a composite of death, MI, TLR and bleeding) (13.6 vs 21.0%, p = 0.003) and cardiac mortality rate (5.2 vs 9.2%, p = 0.020) at 30 days in patients with STEMI.1 Consistent with these results, Karrowni et al. concluded from their meta-analysis, including 12 randomised trials, that TRI was associated with favourable outcomes in STEMI patients and should be the preferred approach for experienced radial operators.6 However, in contrast to STEMI, the clinical benefits of TRI in NSTE-ACS have not been fully demonstrated. In subgroup analysis of the RIVAL trial, TRI did not show any clinical benefits in the primary outcome (HR: 1.11, 95% CI: 0.83–1.48; p = 0.49) and mortality rate (HR: 1.66, 95% CI: 0.94–2.92; p = 0.082) at 30 days. Post hoc analysis of the EARLY-ACS trial revealed no significant differences in 30-day death/MI (12.6 vs 11.2%, p = 0.162) or 30-day death (1.8 vs 2.3%, p = 0.283) between the TRI and TFI groups.8 In our study, the rates of 30-day MACE and CD were no different between the TRI and TFI groups (0.8 vs 0.4%, p = 0.545; 0.5 vs 0.0%, p = 0.283, respectively), nor were the rates of one-year MACE and CD. Therefore our data corroborate previous findings and extend the observations to one year. Regarding bleeding complications, the subgroup analysis of the PRESTO-ACS trial revealed that TRI was associated with a significant decrease in TIMI bleeding (0.7 vs 2.7%, p = 0.03) at one year in patients with NSTE-ACS.7 Also, subgroup analysis of the RIVAL trial showed lower rate of ACUITY-defined bleeding with TRI in the NSTE-ACS cohort.7 However, the results in the previous two studies were derived from subgroup analysis, which had the potential for false-positive errors.8 Furthermore, the former study was conducted without any sensitivity analysis despite uneven distribution of baseline clinical, procedural and pharmacological characteristics between the TRI and TFI groups.8 Corroborating previous findings, our analysis was in line with earlier results, using different bleeding criteria (BARC criteria) in a significantly larger TRI cohort, although bleeding is an outcome that is definition dependent.9 Therefore, our study strongly supports the benefit of TRI with regard to bleeding complications in intervention for NSTE-ACS and may be more reflective of real-world clinical practice. For the paradigm shift from ‘femoral access first’ to ‘radial access first’ in the middle of the debate on the preferred vascular access site in PCI, there should be enough clinical evidence supporting the efficacy and safety of TRI to TFI. However, there is an incomplete evidence base for overall superiority of the radial approach over the femoral approach.

Recently, two randomised, controlled trials were published regarding clinical outcomes of TRI in patients with ACS.3 The RIVAL trial showed the clear benefit of TRI in terms of primary outcome (a composite of death, MI, stroke and major bleeding) (HR: 0.60, 95% CI: 0.38–0.94; p = 0.026) and mortality (HR: 0.39, 95% CI: 0.20–0.76; p = 0.006) at 30 days in patients with STEMI.1 In the RIVAL trial, TRI did not show any clinical benefits in the primary outcome (a composite of death, MI, TLR and bleeding) (13.6 vs 21.0%, p = 0.003) and cardiac mortality rate (5.2 vs 9.2%, p = 0.020) at 30 days in patients with STEMI.1 Consistent with these results, Karrowni et al. concluded from their meta-analysis, including 12 randomised trials, that TRI was associated with favourable outcomes in STEMI patients and should be the preferred approach for experienced radial operators.6 However, in contrast to STEMI, the clinical benefits of TRI in NSTE-ACS have not been fully demonstrated. In subgroup analysis of the RIVAL trial, TRI did not show any clinical benefits in the primary outcome (HR: 1.11, 95% CI: 0.83–1.48; p = 0.49) and mortality rate (HR: 1.66, 95% CI: 0.94–2.92; p = 0.082) at 30 days. Post hoc analysis of the EARLY-ACS trial revealed no significant differences in 30-day death/MI (12.6 vs 11.2%, p = 0.162) or 30-day death (1.8 vs 2.3%, p = 0.257) between the TRI and TFI groups.8 In our study, the rates of 30-day MACE and CD were no different between the TRI and TFI groups (0.8 vs 0.4%, p = 0.545; 0.5 vs 0.0%, p = 0.283, respectively), nor were the rates of one-year MACE and CD. Therefore our data corroborate previous findings and extend the observations to one year. Regarding bleeding complications, the subgroup analysis of the PRESTO-ACS trial revealed that TRI was associated with a significant decrease in TIMI bleeding (0.7 vs 2.7%, p = 0.03) at one year in patients with NSTE-ACS.7 Also, subgroup analysis of the RIVAL trial showed lower rate of ACUITY-defined bleeding with TRI in the NSTE-ACS cohort.7 However, the results in the previous two studies were derived from subgroup analysis, which had the potential for false-positive errors.8 Furthermore, the former study was conducted without any sensitivity analysis despite uneven distribution of baseline clinical, procedural and pharmacological characteristics between the TRI and TFI groups.8 Corroborating previous findings, our analysis was in line with earlier results, using different bleeding criteria (BARC criteria) in a significantly larger TRI cohort, although bleeding is an outcome that is definition dependent.9 Therefore, our study strongly supports the benefit of TRI with regard to bleeding complications in intervention for NSTE-ACS and may be more reflective of real-world clinical practice. For the paradigm shift from ‘femoral access first’ to ‘radial access first’ in the middle of the debate on the preferred vascular access site in PCI, there should be enough clinical evidence supporting the efficacy and safety of TRI to TFI. However, there is an incomplete evidence base for overall superiority of the radial approach over the femoral approach.
In this study, we clearly demonstrated that TRI shows comparable one-year clinical outcomes and lower bleeding complications compared to TFI. In addition, for NSTE-ACS patients, more will be on the more potent antiplatelet agents such as prasugrel and ticagrelor, which have higher bleeding risks than clopidogrel. Therefore, TRI might become the vascular access site of choice and the best option to decrease bleeding complications, with favourable clinical outcomes in NSTE-ACS intervention.

Study limitations
This study has several limitations. First, there may have been an allocation bias based on uneven distribution of risk factors and clinical and anatomical conditions of the patients, since this was a non-randomised, observational study and the selection of vascular access site was left to the operator’s discretion. To overcome this, we used robust statistical methods, including propensity-score matching and multivariate Cox proportional hazards regression.

Second, we did not account for the cross-over rate and exact reasons for it, since these measures were not fully collected. Third, we were unable to study the impact of the recent improvement in the femoral technique, such as the reduction of endovascular device diameter, early removal of the arterial introducer, and preference for the femoral puncture technique guided by fluoroscopy or ultrasound, which might translate into a lower incidence of vascular complications.

Finally, the rate of bleeding complications may have been low because operators participating in the KOTRI registry were highly experienced in both the radial and femoral approaches. Therefore, our results may not apply to all centres performing radial procedures.

Conclusion
In the large, observational cohort of the KOTRI registry, TRI was associated with favourable one-year clinical outcomes and lower bleeding complications compared to TFI in patients with NSTE-ACS undergoing PCI. Independent predictors of MACE were clinical and angiographic profiles (CKD, MVD) rather than vascular access sites. These data suggest that TRI may be the preferred option in patients with NSTE-ACS.

This study was supported by the Soonchunhyang University Research Fund. The funder had no role in the study design, data collection and analysis, decision to publish, or manuscript preparation.

Clinical centres of the KOTRI registry: Catholic University Bucheon St Mary’s Hospital, Bucheon; Catholic University Daejeon St Mary’s Hospital, Daejeon; Chonnam National University Hospital, Gwangju; Chungnam National University Hospital, Daejeon; Chungang University Hospital, Seoul; Daegu Catholic University Medical Centre, Daegu; Eulji University Hospital, Daejeon; Gangneung Asan Hospital, Gangneung; Hallym University Kangdong Sacred Heart Hospital, Seoul; Hanyang University Hospital, Seoul; Inha University Hospital, Incheon; Inje University Haeundae Paik Hospital, Busan; Korea University Guro Hospital, Seoul; Konyang University Hospital, Daejeon; Kangwon National University Hospital, Chuncheon; Myongji Hospital, Goyang; Soonchunhyang University Hospital, Seoul; Soonchunhyang University Bucheon Bucheon Hospital, Bucheon; Pusan National University Hospital, Busan; and Yonsei University Wonju Severance Christian Hospital, Wonju, Korea.

References

