ORIGINAL RESEARCH

Association Between Radial Versus Femoral Access for Percutaneous Coronary Intervention and Long-Term Mortality

Andrew Kei-Yan Ng, MBBS; Pauline Yeung Ng, MBBS; April Ip, MPH; Man-Hong Jim, MD; Chung-Wah Siu, MD

BACKGROUND: Percutaneous coronary intervention with radial arterial access has been associated with fewer occurrences of major bleeding. However, published data on the long-term mortality and major adverse cardiac events after percutaneous coronary intervention with radial or femoral arterial access are inconclusive.

METHOD AND RESULTS: This was a territory-wide retrospective cohort study including 26,022 patients who underwent first-ever percutaneous coronary intervention between January 1, 2010 and December 31, 2017 in Hong Kong. Among the 14,614 patients matched by propensity score (7,307 patients in each group), 558 (7.6%) and 787 (10.8%) patients died during the observation period in the radial group and femoral group, respectively, resulting in annualized all-cause mortality rates of 2.69% and 3.87%, respectively. The radial group had a lower risk of all-cause mortality compared with the femoral group up to 3 years after percutaneous coronary intervention (hazard ratio [HR], 0.70; 95% CI, 0.63–0.78; \(P<0.001\)). Radial access was associated with a lower risk of major adverse cardiac events (HR, 0.78; 95% CI, 0.73–0.83, \(P<0.001\)), myocardial infarction after hospital discharge (HR, 0.78; 95% CI, 0.70–0.87, \(P<0.001\)), and unplanned revascularization (HR, 0.76; 95% CI, 0.68–0.85, \(P<0.001\)). The risks of stroke were similar across the 2 groups (HR, 0.96; 95% CI, 0.82–1.13, \(P=0.655\)).

CONCLUSIONS: Radial access was associated with a significant reduction in all-cause mortality at 3 years compared with femoral access. Radial access was associated with reduced risks of myocardial infarction and unplanned revascularization, but not stroke. The benefits were sustained beyond the early postoperative period.

Key Words: mortality ■ percutaneous coronary intervention ■ radial artery catheter

In patients with coronary artery disease undergoing percutaneous coronary interventions (PCI), use of radial arterial access has been consistently shown to reduce major bleeding at the access site compared with femoral access in many randomized trials, especially those recruiting patients with acute coronary syndrome (ACS). However, there are still reservations about widespread adoption of transradial PCI, and its uptake in the United States is lagging. This may be partly contributed to by a longer learning curve, and thus requiring higher procedural volumes to achieve and maintain proficiency for transradial PCI. Another potential barrier is that the effects of radial access on mortality and major adverse cardiac events (MACE) have been variable across randomized and observational trials.

There is evidence that certain adverse events that are reduced by radial access have important prognostic implications on long-term mortality. For example, it has been demonstrated that bleeding events after PCI are associated with a 2- to 3-fold increase in long-term mortality. Radial access has also been associated with less acute kidney injury in a substudy from the MATRIX (Minimizing Adverse Hemorrhagic Events by Transradial Coronary Angiography and PCI) trial.
Ng et al Radial Access for PCI and Mortality

Transradial Access Site and Systemic Implementation of Angioplasty) randomized trial.16,17 Taken together, the effect on such adverse events as major bleeding and acute kidney injury may translate to decreased long-term mortality using a radial access approach.18,19

Our current knowledge on the relationship between access site for PCI and mortality has mainly come from observation and randomized studies with short- to midterm (1-year) follow-up,1–5,7,10,11,20 and the effects of access site on long-term mortality are largely unknown.

We hypothesized that use of radial access is associated with lower long-term mortality rates compared with use of femoral access in patients undergoing PCI.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population and Design

Data from all patients who underwent first-ever PCI between January 1, 2010 and December 31, 2017 from all 14 publicly funded hospitals that offer PCI in Hong Kong were reviewed. Patients’ baseline characteristics, exposures, and outcomes were retrieved from the Clinical Data and Analysis Reporting System, an electronic data repository that captures clinical parameters of all patients managed in publicly funded institutions in Hong Kong. The PCI Registry is part of the Clinical Data and Analysis Reporting System that systematically records patient and procedural characteristics related to PCI. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. Requirement for informed consent was waived because of the retrospective nature of the study.

We included all adult patients (18 years of age or older) who underwent PCI with documentation of femoral or radial arterial access use. Exclusion criteria were patients who had prior history of PCI, had concurrent radial and femoral accesses defined as both radial and femoral sheaths being placed, or required any mechanical circulatory support including intra-aorta balloon pump, percutaneous ventricular assist device, or extracorporeal membrane oxygenation.

Definitions of Exposure and Outcome Variables

The use of radial versus femoral arterial access site was defined as successful placement of an arterial sheath for PCI. The primary outcome was all-cause mortality in a time-to-event analysis up to 3 years from index PCI. The secondary outcomes were a composite outcome of MACE including all-cause mortality, myocardial infarction after hospital discharge, unplanned coronary revascularization, and stroke; and the individual components of the composite outcome, in a time-to-event analysis for up to 3 years from index PCI. Details of exposure and outcome definitions are shown in Data S1.

Statistical Analysis

All analyses were performed with prespecified end points and statistical methods. We constructed a propensity score that predicted the likelihood of radial versus femoral access with variables selected a priori based on data in the published literature and biological plausibility: sex, age, ethnicity (Chinese versus non-Chinese), tobacco use, diabetes mellitus, hypertension, dyslipidemia, cerebrovascular disease, chronic obstructive pulmonary disease,21,22 peripheral vascular disease,23 history of malignancy,24 cirrhosis,25 estimated glomerular filtration rate, white blood cell count >10^9/L,26 anemia (hemoglobin <13 g/dL for men, <12 g/dL for women),27 atrial fibrillation or flutter, oral anticoagulant use, previous myocardial infarction, prior coronary arterial bypass grafting, previous heart failure, decompensated heart failure on presentation (New York Heart Association Class III or IV), cardiogenic
Sensitivity Analyses

We performed sensitivity analysis by including all patients before propensity score matching. A multivariable Cox proportional hazards model adjusting for the same variables in the propensity score model was used to examine the association between access site and mortality in a time-to-event analysis.

Exploratory Analyses

We studied the effect modification on the relationship between access site and mortality by pre-defined clinical variables, and introduced interaction terms to the Cox regression model. We utilized the Acuity Score, which was validated to categorize the baseline bleeding risks of the patients.32

Data management and statistical analyses were performed with Stata software, version 16 (StataCorp LP). For the primary end point, a 2-tailed P value of <0.05 was considered statistically significant. For the secondary end points, Bonferroni correction was used to adjust for multiple testing, and a 2-tailed P value of <0.01 was considered statistically significant.

RESULTS

Patients and Characteristics

Between January 2010 and December 2017, a total of 26,022 patients were considered for inclusion: 1559 (6%) were excluded because of any of the following exclusion criteria: age younger than 18 years, access site unknown, concurrent radial and femoral accesses, or mechanical circulatory support required. Of the remaining 24,463 patients, a total of 1655 (6.7%) were excluded from the complete case analysis because of missing values in any of the variables used in the propensity score model. Characteristics of all patients (n=22,808) before propensity score matching are shown in Figures S1 and S2. The proportion of radial access increased monotonically from 33% in year 2010 to 70% in year 2017 (Figure S1).

Seven thousand three hundred seven matched pairs of patients were generated after 1:1 propensity score matching (Figure 1 in the main article and Figure S2). Table 1 shows the baseline characteristics of the study population. Patients in the radial group were less likely to have a history of cerebrovascular disease, reduced creatinine clearance, and anemia; and were more likely to have PCI done in institutions with a higher proportion of radial access use and in the more recent period. Table 2 shows the procedural and postprocedural characteristics of the study population. Of note, the radial group had a lower rate of drop in hemoglobin >2 g/dL and blood transfusion after PCI.

Primary Outcome

The primary outcome of all-cause mortality developed in 558 (7.6%) and 787 (10.8%) patients in the radial group and femoral group, respectively, with annualized mortality rates of 2.7% and 3.9%. Patients in the radial group had a lower risk of all-cause mortality compared with the femoral group up to 3 years after PCI (hazard ratio [HR], 0.70; 95% CI, 0.63–0.78; P<0.001), as shown in Table 3 and Figure 2. The radial group also had a lower risk of cardiovascular mortality up to 3 years (HR, 0.67; 95% CI, 0.57–0.79; P<0.001). Between 0 and 30 days, all-cause mortality occurred in 93 (1.3%) and 146 (2.0%) patients in the radial and femoral group, respectively (HR, 0.63; 95% CI, 0.49–0.82; P=0.001). Between 30 days and 3 years, all-cause mortality occurred in 465 (annualized risk 2.3%) and 641 (annualized risk 3.2%) patients in the radial and femoral group, respectively (HR, 0.71; 95% CI, 0.63–0.80; P<0.001).
Secondary Outcomes
Radial access was associated with lower risks of MACE (HR, 0.78; 95% CI, 0.73–0.83; P<0.001), myocardial infarction after hospital discharge (HR, 0.78; 95% CI, 0.70–0.87; P<0.001), and unplanned revascularization (HR, 0.76; 95% CI, 0.68–0.85; P<0.001). The risks of stroke were similar across the 2 groups (HR, 0.96; 95% CI, 0.82–1.13; P=0.655). These results are shown in Table 3 and Figure 3A through 3D.

Sensitivity Analyses
We analyzed the outcomes of all 22,808 patients with complete information before propensity score matching. All-cause mortality occurred in 872 and 1256 patients in the radial and femoral group, respectively, corresponding to an annual risk of 2.39% and 4.57%, respectively (unadjusted HR, 0.52; 95% CI, 0.48–0.57; P<0.001). In the multivariable Cox regression model adjusting for all previously mentioned variables, the risk of all-cause mortality remained lower in the radial group compared with the femoral group (HR, 0.67; 95% CI, 0.61–0.73; P<0.001).

Falsification testing showed that the risks of cancer diagnosed after PCI (HR, 0.87; 95% CI, 0.7–1.05; P=0.148) and gastrointestinal bleeding (HR, 0.79; 95% CI, 0.54–1.14; P=0.207) were not significantly different between the radial and femoral groups.
Table 1. Baseline Characteristics of Patients After Propensity Score Matching

| Characteristic                               | Radial Group | Femoral Group | P Value | Standardized Difference |
|----------------------------------------------|--------------|---------------|---------|-------------------------|
|                                              | N=7307       | N=7307        |         |                         |
| Female, n (%)                               | 1681 (23.0%) | 1740 (23.8%)  | 0.249   | 0.019                   |
| Age, y, mean (SD)                           | 64.6 (11.3)  | 64.8 (11.8)   | 0.257   | 0.019                   |
| Chinese, n (%)                              | 6924 (94.8%) | 6903 (84.5%)  | 0.442   | −0.013                  |
| Tobacco use, n (%)                          | 3400 (46.5%) | 3352 (45.9%)  | 0.426   | −0.013                  |
| Diabetes mellitus, n (%)                    | 2509 (34.3%) | 2569 (35.2%)  | 0.297   | 0.017                   |
| Hypertension, n (%)                         | 4835 (63.4%) | 4892 (64.2%)  | 0.326   | 0.016                   |
| Dyslipidemia, n (%)                         | 4614 (63.1%) | 4602 (63.0%)  | 0.837   | −0.033                  |
| Cerebrovascular disease, n (%)              | 668 (9.1%)   | 741 (10.1%)   | 0.041   | 0.034                   |
| Chronic obstructive pulmonary disease, n (%) | 169 (2.3%)   | 186 (2.5%)    | 0.361   | 0.015                   |
| Peripheral vascular disease, n (%)          | 88 (1.2%)    | 100 (1.4%)    | 0.378   | 0.015                   |
| History of malignancy, n (%)               | 369 (5.0%)   | 385 (5.3%)    | 0.550   | 0.010                   |
| Cirrhosis, n (%)                            | 21 (0.3%)    | 19 (0.3%)     | 0.752   | −0.005                  |
| eGFR, mL/min per 1.73 m², mean (SD)         | 82.8 (25.3)  | 81.3 (30.0)   | 0.002   | −0.051                  |
| eGFR <50 mL/min per 1.73 m², n (%)          | 646 (8.8%)   | 907 (12.4%)   | <0.001  | 0.116                   |
| White blood cell count, 10⁹/L, mean (SD)    | 8.2 (2.9)    | 8.2 (3.0)     | 0.653   | 0.007                   |
| Anemia, n (%)                               | 2173 (28.1%) | 2141 (21.7%)  | 0.011   | 0.042                   |
| Atrial fibrillation or flutter, n (%)       | 380 (5.2%)   | 401 (5.5%)    | 0.440   | 0.013                   |
| On anticoagulant before PCI, n (%)          | 182 (2.5%)   | 194 (2.7%)    | 0.531   | 0.010                   |
| Previous myocardial infarction, n (%)       | 880 (12.0%)  | 907 (12.4%)   | 0.495   | 0.011                   |
| Previous coronary artery bypass surgery, n (%) | 48 (0.6%)   | 42 (0.6%)     | 0.526   | −0.011                  |
| Previous heart failure, n (%)               | 546 (7.5%)   | 588 (8.0%)    | 0.194   | 0.021                   |
| NYHA class III–IV in last 2 wk before PCI, n (%) | 286 (3.9%)  | 297 (4.1%)    | 0.642   | 0.008                   |
| Cardiogenic shock, n (%)                    | 136 (1.9%)   | 126 (1.7%)    | 0.533   | −0.010                  |
| Ventricular tachycardia in <48 h before PCI, n (%) | 156 (2.1%) | 157 (2.1%)    | 0.984   | 0.001                   |
| PCI urgency, n (%)                          |              |               | 0.231   | 0.028                   |
| Elective                                    | 4276 (58.5%) | 4209 (57.6%)  |         |                         |
| Urgent                                      | 2156 (29.5%) | 2157 (29.5%)  |         |                         |
| Emergent                                    | 893 (12.2%)  | 972 (13.3%)   |         |                         |
| Indication for PCI, n (%)                   |              |               | 0.254   | 0.033                   |
| Stable angina                               | 1413 (19.3%) | 1373 (18.8%)  |         |                         |
| Unstable angina                             | 1534 (21.0%) | 1523 (20.8%)  |         |                         |
| Non–ST-segment–elevation myocardal infarction| 3467 (47.4%) | 3439 (47.1%)  |         |                         |
| ST-segment–elevation myocardal infarction   | 893 (12.2%)  | 972 (13.3%)   |         |                         |
| Number of major epicardial artery involved, n (%) | 3336 (45.7%) | 3295 (45.1%)  | 0.710   | 0.014                   |
| One-vessel disease                          | 3336 (45.7%) | 3295 (45.1%)  |         |                         |
| Two-vessel disease                          | 2465 (33.7%) | 2470 (33.8%)  |         |                         |
| Three-vessel disease                        | 1506 (20.6%) | 1542 (21.1%)  |         |                         |
| Proportion of radial access use by institution, n (%) | <0.001 | −0.165       |         |                         |
| First quantile (lowest radial use)          | 2787 (38.1%) | 3205 (43.9%)  |         |                         |
| Second quantile                             | 2019 (27.6%) | 2069 (28.3%)  |         |                         |
| Third quantile                              | 1009 (13.8%) | 987 (13.5%)   |         |                         |
| Fourth quantile (highest radial use)        | 1492 (20.4%) | 1046 (14.3%)  |         |                         |
| Year of PCI, n (%)                          |              |               | <0.001  | −0.073                  |
| 2010–2013                                   | 2796 (38.3%) | 3058 (41.9%)  |         |                         |
| 2014–2017                                   | 4511 (61.7%) | 4249 (58.1%)  |         |                         |

Note: Comparison by Pearson χ² test for categorical data and by Student t tests for continuous data. eGFR indicates glomerular filtration rate; NYHA, New York Heart Association; and PCI, percutaneous coronary intervention.
A total of 8 variables in the propensity score matching model had missing data. Tobacco use, the variable that had the largest amount of missing data, had 1546 (6.3%) missing values. Multiple imputation was conducted, and the imputed cohort included all 1655 (6.7%) patients who were excluded because of missing values in any of the variables used in the model. The association between radial access and all-cause mortality from the imputed data set remained consistent with the complete case cohort (HR, 0.65; 95% CI, 0.59–0.71; P<0.001).

Exploratory Analyses
We explored effect modification of the access site–mortality association by various patient and procedural parameters (Table 4 and Figure 4). There were significantly greater benefits attributable to radial access in PCI that were performed in 2014 to 2017 compared with 2010 to 2013 (P for interaction=0.024), in institutions with higher use of radial access (P for interaction=0.002), and in patients with higher predicted bleeding risk by Acuity Score (P for interaction=0.041).

DISCUSSION
In this cohort of 14 614 propensity score matched adult patients undergoing first-ever PCI, we showed that radial arterial access was associated with a reduction in risk of all-cause mortality within 3 years of the procedure compared with femoral arterial access, adding to previous knowledge about benefits of radial access on shorter-term mortality and bleeding complications. The access site–mortality association remained consistent after adjustment for factors potentially affecting the choice of access site and multiple sensitivity analyses. Specifically, radial access was associated with lower adjusted risks of MACE, myocardial infarction after discharge, and unplanned coronary revascularization, but similar risks of strokes.

Radial access has been consistently shown to reduce major bleeding at access site in several randomized trials representing a wide range of clinical syndromes.\(^1\)\(^-\)\(^5\) However, its effects on mortality and MACE are less conclusive and further limited by a follow-up period of no more than 1 year. In the MATRIX trial and RIVAL (Radial Versus Femoral Access for...
Coronary Intervention) trials, no benefits in mortality or MACE were shown for radial access.\textsuperscript{1,2} In contrast, in the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) trial, which exclusively focused in patients with STEMI, a mortality benefit at 30 days was shown.\textsuperscript{3} In a meta-analysis of 24 randomized trials, all-cause mortality was reduced with radial access only for patients with STEMI, and the follow-up period was limited to either in-hospital or 30 days.\textsuperscript{5} Since randomized studies have strict inclusion criteria and require operators to be competent in both access options, it is imperative to confirm the findings in real-world populations. A registry of 44,804 patients found a mortality benefit with radial access for patients with STEMI.\textsuperscript{33} Similarly, in a meta-analysis inclusive of 17 cohort studies for ACS (14 for STEMI exclusively), radial access was associated with short-term mortality benefit.\textsuperscript{20} However, no mortality benefit was observed in several large cohort studies unrestricted on clinical

| Outcomes                          | Annualized Rate | Hazard Ratio | 95% CI     | P Value |
|-----------------------------------|-----------------|--------------|------------|---------|
|                                   | Radial Group    | Femoral Group|            |         |
| Primary                           |                 |              |            |         |
| All-cause mortality               | 2.69%           | 3.87%        | 0.70       | 0.63–0.78 | <0.001  |
| Cardiovascular mortality          | 1.13%           | 1.70%        | 0.67       | 0.57–0.79 | <0.001  |
| Secondary                         |                 |              |            |         |
| Major adverse cardiac events      | 8.19%           | 10.60%       | 0.78       | 0.73–0.83 | <0.001  |
| Myocardial infarction             | 3.10%           | 4.00%        | 0.78       | 0.70–0.87 | <0.001  |
| Unplanned revascularization       | 2.61%           | 3.48%        | 0.76       | 0.68–0.85 | <0.001  |
| Stroke                            | 1.52%           | 1.58%        | 0.96       | 0.82–1.13 | 0.655   |

Comparison by Cox proportional hazards regression.

Figure 2. Primary outcome; estimated probabilities of all-cause mortality stratified by access site.
All-cause mortality at 3 years developed in 558 (7.6%) and 787 (10.8%) patients in the radial and femoral group, respectively. Patients in the radial group had a lower risk of all-cause mortality compared with the femoral group (hazard ratio, 0.70; 95% CI, 0.63–0.78; $P<0.001$). PCI indicates percutaneous coronary intervention.
presentsations, or restricted to non–ST-segment-elevation myocardial infarction. To the best of our knowledge, these are the first real-world data showing a mortality benefit from radial access across a diverse population; the benefit was seen at 30 days, and further accrued for up to 3 years.

One plausible mechanism for the long-term effect on mortality is through the reduction in post-PCI bleeding events, blood transfusions, and major vascular complications in using radial artery access. These complications, such as femoral bleeding and blood transfusion, have been associated with increased mortality up to 6 years after PCI. In a sub study of the HORIZONS-AMI (The Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, patients with post-PCI bleeding during an in-hospital stay were associated with 4-fold risks of mortality at 3 years with consistent associations across different landmark analyses; and the excess risks of late mortality from post-PCI bleeding continued to monotonically accrue over time. In agreement with these findings, our data showed that radial access was associated with lower rates of clinical bleeding such as groin and retroperitoneal hematoma that did not necessitate major surgery. Not surprisingly, we also found that the
mortality benefit of radial access was different in patients depending on the Acuity Score; patients with greater risks of bleeding benefitted more from radial access. Another known benefit of radial access was lower volumes of radiographic contrast use,40 and lower rates of acute kidney injury after PCI.16,41 This was also observed in our cohort. Since acute kidney injury after PCI is associated with increased long-term mortality,18,19 this may be another mechanism underlying the effect of radial access on survival. Finally, potent P2Y12 inhibitors have been shown to improve survivals after PCI in patients with ACS.42 The reduction in bleeding risk by radial access may have facilitated the more liberal use of potent P2Y12 inhibitors, hence explaining the continuing accrual of survival benefit beyond the early post-PCI phase.

In our secondary analysis, myocardial infarction and unplanned coronary revascularization were less frequent in the transradial group. This may be attributed to the reported association between post-PCI bleeding and subsequent myocardial infarction.12,43 Post-PCI bleeding and blood transfusion lead to a proinflammatory state, platelet aggregation, and activation of coagulation cascade, increasing the risk of thrombotic events.44–46 Interruption of therapies including dual antiplatelet and/or antithrombotic therapy after bleeding complications also results in more ischemic events.47,48 Furthermore, less access site bleeding during the PCI procedure may enable operators to focus their attention on optimization of results (eg, by the use of intravascular imaging), which may result in better long-term outcomes.49 In our data, intravascular imaging was more frequently used in the radial group, although this should be interpreted with caution as it may be confounded by operators’ expertise and preference.

The current European Society of Cardiology guidelines have a class I, level of evidence A, recommendation for use of radial access for PCI in patients with ACS.50 The American Heart Association also supports a “radial first” strategy for patients with ACS.7 Our data support these recommendations and invite future randomized trials to evaluate the mortality benefit in patients with stable coronary artery disease. Moreover, we observed that radial access was more beneficial when institutions or operators had accumulated more experience and procedural volumes, which was consistent with the known learning curve required to optimize outcomes.9 We also observed that the mortality benefits of radial access were more pronounced in recent years, which paralleled a growing portion of transradial PCI. However, such mortality benefit was also significant in hospitals and time periods with less radial experience.

This study had several strengths. First, it captured representative territory-wide data with robust long-term outcomes and minimal loss to follow-up, because nearly all patients continued to receive care under the same healthcare system. Second, unlike in randomized trials, which are conducted in highly selected

### Table 4. Subgroup Analysis Examining Differential Effects of Access Site on the Primary Outcome

| Subgroup                        | Hazard Ratio | 95% CI     | P Value for Interaction |
|---------------------------------|--------------|------------|-------------------------|
| All patients                    | 0.70         | 0.63–0.78  |                         |
| Sex                             |              |            | 0.363                   |
| Male                            | 0.68         | 0.60–0.77  |                         |
| Female                          | 0.76         | 0.62–0.93  |                         |
| Age group                       |              |            | 0.224                   |
| Age <65 y                       | 0.62         | 0.50–0.77  |                         |
| Age ≥65 y                       | 0.72         | 0.64–0.82  |                         |
| Diabetes mellitus               |              |            | 0.777                   |
| No diabetes mellitus            | 0.71         | 0.61–0.83  |                         |
| With diabetes mellitus          | 0.69         | 0.59–0.80  |                         |
| Previous CABG                   |              |            | 0.228                   |
| No previous CABG                | 0.69         | 0.62–0.77  |                         |
| Previous CABG                   | 1.24         | 0.47–3.27  |                         |
| Baseline renal function         |              |            | 0.195                   |
| eGFR >50 mL/min per 1.73 m²     | 0.81         | 0.70–0.92  |                         |
| eGFR ≤50 mL/min per 1.73 m²     | 0.69         | 0.58–0.83  |                         |
| Indication for PCI              |              |            | 0.266                   |
| Stable coronary artery disease  | 0.82         | 0.60–1.12  |                         |
| Acute coronary syndrome         | 0.68         | 0.61–0.77  |                         |
| Primary PCI                     |              |            | 0.325                   |
| Nonprimary PCI                  | 0.68         | 0.61–0.77  |                         |
| Primary PCI                     | 0.79         | 0.61–1.02  |                         |
| Cardiogenic shock               |              |            | 0.067                   |
| No cardiogenic shock            | 0.71         | 0.63–0.79  |                         |
| Cardiogenic shock               | 0.47         | 0.29–0.76  |                         |
| PCI date                        |              |            | 0.024                   |
| 2010–2013                       | 0.82         | 0.68–0.99  |                         |
| 2014–2017                       | 0.63         | 0.55–0.72  |                         |
| Radial use by institution       |              |            | 0.002                   |
| Low use                         | 0.78         | 0.68–0.89  |                         |
| High use                        | 0.55         | 0.46–0.65  |                         |
| Radial use by institution and year |          |            | 0.029                   |
| Low use                         | 0.82         | 0.65–1.05  |                         |
| High use                        | 0.58         | 0.47–0.71  |                         |
| Predicted bleeding risk         |              |            | 0.041                   |
| Low risk                        | 0.85         | 0.69–1.06  |                         |
| High risk                       | 0.66         | 0.58–0.75  |                         |

Comparison by Cox proportional hazards regression. CABG indicates coronary artery bypass surgery; eGFR, glomerular filtration rate; and PCI, percutaneous coronary intervention.

*Cardiogenic shock without mechanical circulatory support.
centers competent in both transradial and transfemoral PCI, we showed that the mortality benefit of radial access was appreciable even in real-world settings with no restriction with regard to clinical scenarios, institutions, and operators. Third, our data were retrieved from a population-based electronic database with

### Figure 4. Subgroup analysis.
Effect modification was significant across PCI date, radial use by institution alone and by institution-year, and predicted bleeding risk. CABG indicates coronary artery bypass surgery; CAD, coronary artery disease; and PCI, percutaneous coronary intervention.
comprehensive information on vascular access and subsequent events recorded a priori, thus minimizing the selection, information, and recall biases. Fourth, this was a territory-wide study with a large sample size, enabling us to control for many potential confounders. The results were also consistent across primary, secondary, and sensitivity analysis.

This study had some limitations. First, the observational nature of the study conferred risks of unmeasured confounding and bias, but we had adjusted extensively by propensity score matching for potential confounders that may affect the choice of access site and outcomes, and the findings were consistent in many sensitivity analyses. In falsification analysis, the absence of exposure effect on risks of cancer and gastrointestinal bleeding suggests minimal residual confounding. Nonetheless, differences in use of intravascular imaging and patterns of medication prescription after discharge could potentially represent intermediate mechanisms of the association under study. Second, adjustment was made for choice of access site at institutional but not individual operator’s level; hence, the study results may only be applicable to operators with levels of technical proficiency similar to operators in this study. Nevertheless, we used individual institution and time period as surrogates, and found that the benefit of radial access was still significant across different levels of radial experience albeit for a different magnitude. Third, the radial paradox, where benefits conferred by transradial PCI are accompanied by a paradoxical increase in vascular complications driven by complications in transfemoral PCI, could potentially exaggerate the benefits of radial access.51

Fourth, this study predominantly included patients of Asian descent and may not be generalizable across all PCI patients.

In conclusion, we showed that use of radial access in PCI was associated with a significant reduction in all-cause mortality at 3 years after PCI. Radial access was associated with reduced risks of MI and unplanned revascularization, but not stroke. Our findings suggest that the benefits of radial access extend beyond the early postoperative period.

ARTICLE INFORMATION
Received February 10, 2021; accepted June 7, 2021.

Affiliations
Cardiac Medical Unit, Grantham Hospital, Hong Kong SAR, China (A.K.N., M.J.); Department of Adult Intensive Care, Queen Mary Hospital, Hong Kong SAR, China (P.Y.N.); Division of Respiratory and Critical Care Medicine, Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China (P.Y.N.); and Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong SAR, China, (C.S.).

Acknowledgments
Author contributions: A. K. Ng and C. Siu were responsible for the conception and design of the study. A. K. Ng analyzed the data collected by A. Ip.

REFERENCES
1. Valgimigli M, Frigoli E, Leonardi S, Vranckx P, Rothenbühler M, Tebaldi M, Variella F, Calabrò P, Garucci S, Rubartelli P, et al. Radial versus femoral access and bivalirudin versus unfractionated heparin in invasively managed patients with acute coronary syndrome (MATRIX): final 1-year results of a multicentre, randomised controlled trial. Lancet. 2018;392:835–848. DOI: 10.1016/S0140-6736(18)31714-8.
2. Jolly SS, Yusuf S, Cairns J, Niemelä K, Xavier D, Widimsky P, Budaj A, Niemelä M, Valentín V, Lewis BS, et al. 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. DOI: 10.1016/S0140-6736(11)60404-2.
3. Romagnoli E, Biondi-Zoccai G, Sciabrini A, Politi L, Rigattieri S, Pendenza G, Summaria F, Patrizi R, Borghi A, Di Russo C, et al. 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. DOI: 10.1016/j.jacc.2012.06.017.
4. Bernat I, Horak D, Stasek J, Mates M, Pesek J, Ostadal P, Hrabos V, Dusek J, Koza J, Sembera Z, et al. 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. DOI: 10.1016/j.jacc.2013.08.1651.
5. Ferrante G, Rao SV, Jüni P, Da Costa BR, Reimers B, Condorelli G, Anzurini A, Jolly SS, Bertrand OF, Krucoff MW, et al. Radial versus femoral access for coronary interventions across the entire spectrum of patients with coronary artery disease: a meta-analysis of randomized trials. JACC Cardiovasc Interv. 2016;9:1419–1434. DOI: 10.1016/j.jcint.2016.04.014.
6. Feldman DN, Swaminathan RV, Kaltenbach CA, Baklanov DV, Kim LK, Wong SC, Minutello RM, Messenger JC, Moussa I, Garratt KN, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the National Cardiovascular Data Registry (2007–2012). Circulation. 2013;127:2295–2306. DOI: 10.1161/CIRCULATIONAHA.112.000536.
7. Mason PJ, Shah B, Tamis-Holland JE, Bittl JA, Cohen MG, Saffirstein J, Drachman DE, Valle JA, Rhodes D, Gilchrist IC, et al. An update on radial artery access and best practices for transradial coronary angiography and intervention in acute coronary syndrome: a scientific statement from the American Heart Association, Circ Cardiovasc Interv. 2018;11:e000335. DOI: 10.1161/HCV.0000000000000335.
8. Caputo RP, Tremmel JA, Rao S, Gilchrist IC, Pyne C, Poncholy S, Fraser D, Gulati R, Skelding K, Bertrand O, et al. Transradial arterial access for coronary and peripheral procedures: executive summary by the transradial committee of the SCA. Catheter Cardiovasc Interv. 2011;78:823–839. DOI: 10.1002/ccd.23052.
9. Hess CN, Peterson ED, Neely ML, Dai D, Hillegas WB, Krucoff MW, Kutcher MA, Messenger JC, Poncholy S, Piana RN, et al. The learning curve for transradial percutaneous coronary intervention among operators in the United States: a study from the National Cardiovascular Data Registry. Circulation. 2014;129:2277–2286. DOI: 10.1161/CIRCULATIONAHA.113.006356.
10. Alnasser SM, Bagai A, Jolly SS, Cantor WJ, Dehghani P, Rao SV, Cheema AN. Transradial approach for coronary angiography and
intervention in the elderly: a meta-analysis of 777,841 patients. Int J Cardiol. 2017;228:45–51. DOI: 10.1016/j.ijcard.2016.11.207.

11. Kadakia MB, Rao SV, McCoy L, Choudhari PS, Sherwood MW, Lilly S, Kobayashi T, Kolansky DM, Wlensky RL, Yeh RW, et al. Transradial versus transfemoral access in patients undergoing rescue percutaneous coronary intervention after fibrinolytic therapy. JACC Cardiovasc Interv. 2018;11:868–1876. DOI: 10.1016/j.jcin.2018.07.029.

12. Valje JA, Shetterly S, Maddox TM, Ho PM, Bradley SM, Sandhu A, Magid D, Tsai TT. Postdischarge bleeding after percutaneous coronary intervention and subsequent mortality and myocardial infarction: insights from the HMO Research Network-Stent Registry. Circ Cardiovasc Interv. 2016;9:e033519. DOI: 10.1161/CIRCI NTERVENTIO NS.115.033519.

13. Kucheryavsky S, Rao SV, Myint PK, Kaveany B, Nolan J, Ludman PF, de Belder MA, Loke Y, Mamas MA. Major bleeding after percutaneous coronary intervention and risk of subsequent mortality: a systematic review and meta-analysis. Open Heart. 2014;1:e000021. DOI: 10.1136/ope nhrt-2013-000021.

14. Chhatrivalia AK, Amin AP, Kennedy KF, House JA, Cohen DJ, Rao SV, Curtis JP, Parzynski CS, Messenger JC, Parise H, Fahy M, Manoukian SV, Feit F, et al. A risk score to predict in-hospital mortality for radial versus femoral access, bleeding and ischemic events in patients with acute coronary syndrome. J Am Coll Cardiol. 2017;70:3075–3091. doi:10.1016/j.jacc.2017.02.055.

15. Rao SV, O’Grady K, Pieper KS, Myint PK, Newby LK, Van de Werf F, Mahafey KW, Callist RM, Harrington RA. Impact of bleeding severity on clinical outcomes among patients with acute coronary syndromes. Am Heart J. 2014;168:1200–1206. DOI: 10.1016/j.ahj.2014.05.006.

16. Ando G, Cortese B, Russo F, Rothenbuhler M, Frigoli E, Gargiulo G, Briguori C, Vranckx P, Leonardi S, Guiducci V, et al. Acute kidney injury after radial or femoral access for invasive acute coronary syndrome management: AKI-MATRIX. J Am Coll Cardiol. 2017;69. S0735- 1097(17)36897-3. DOI: 10.1016/j.jacc.2017.02.070.

17. Kanic V, Kompara G, Suran D, Eckart R, Bevc S, Hojs R. Impact of kilogram-defined acute kidney injury on mortality after a randomized clinical trial of radial access for acute myocardial infarction. Cardiorenal Med. 2018;3:332–339. DOI: 10.1159/000492287.

18. Rothenbuhler M, Valigmig M, Oudtayo A, Frigoli E, Leonardi S, Vranckx P, Turturo M, Moretti L, Amico F, Ugucconi L, et al. Association of acute kidney injury and bleeding events with mortality after radial or femoral access in patients with acute coronary syndrome undergoing invasive management: secondary analysis of a randomized clinical trial. Eur Heart J. 2019;40:1226–1232. DOI: 10.1093/eurheartj/ehy660.

19. Roghi A, Savontti C, Cavallini A, Arriaga G, Angoli L, Castriota F, Bernardi G, Sansa M, De Servi S, Pitcheider W, et al. Impact of acute renal failure following percutaneous coronary intervention on long-term mortality. J Cardiovasc Med (Hagerstown). 2008;9:375–381. DOI: 10.2459/CM.0b013 e3282 eee979.

20. Fraga Rodriguez A, Astour A, Loliag G, Ziajadi KM, Abdel-Latif AK. Systematic review and meta-analysis of major cardiovascular outcomes for radial versus femoral access in patients with acute coronary syndrome. South Med J. 2016;109:61–76. DOI: 10.14423/SMJ.00000 00000000404.

21. Lin WC, Chen CW, Lu CL, Lai WW, Huang MH, Tsai LM, Li CY, Lai CH. The association between recent hospitalized copd exacerbations and adverse outcomes after percutaneous coronary intervention: a nationwide cohort study. Int J Chron Obstruct Pulmon Dis. 2019;14:169–179.

22. Enriquez JR, Parikh SV, Selzer F, Jacobs AK, Marroquin O, Mulukutla S, Kodaira M, Sawano M, Kuno T, Numasawa Y, Noma S, Suzuki M, Roghi A, Savonitto S, Cavallini C, Arraiz G, Angoli L, Castriota F, Berna MA, Koyama T, Nishihara H, Niikoh YM, et al. Impact of recent hospitalized copd exacerbations and adverse outcomes after percutaneous coronary intervention: a meta-analysis. BMC Cardiovasc Disord. 2018;18:75. DOI: 10.1186/ s12872-018-0926-6.

23. Wang X, Qiu M, Qi J, Li J, Wang H, Li Y, Han Y. Impact of anemia on long-term ischemic events and bleeding events in patients under- going percutaneous coronary intervention: a systematic review and meta-analysis. J Thorac Dis. 2017;9:2041–2052. DOI: 10.3978/j.issn.2072-1439.2016.11.56.

24. Mengya R, Zhaoyu L, Qihest J, Masa SS, Fadira J, Capodanno D, Magid D, Tsay IM, Dinh DT, Brennan A, Clark D, Cox N, Harper R, Addison D, Andrianopoulos N, Reid C, et al. Prevalence and outcomes: insights from the National Cardiovascular Data Registry. Circ Cardiovasc Qual Outcomes. 2017;10:552–559. DOI: 10.1016/j.circoutq.2016.09.069.

25. Tariwaki M, Stefanini GG, Silber S, Richardt G, Vranckx P, Serruys PW, Buszman PE, Kelbaek H, Windecker S, Investigators RA-C. 4- year clinical outcomes and predictors of repeat revascularization in patients treated with new-generation drug-eluting stents: a report from the RESOLUTION-4Comers trial (a randomized comparison of a zotarolimus-eluting stent with an everolimus-eluting stent for percutaneous coronary intervention). J Am Coll Cardiol. 2014;63:1617–1625. DOI: 10.1016/j.jacc.2013.12.036.

26. Mehra R, Pocock SJ, Nikolsky E, Clayton T, Dansag GD, Kirtane AJ, Parise H, Fahy M, Manoukian SV, Feit F, et al. A risk score to predict bleeding in patients with acute coronary syndromes. J Am Coll Cardiol. 2010;55:2556–2566. DOI: 10.1016/j.jacc.2009.09.076.

27. Demidova MM, Smith JG, Holmqvist F, Erlinge D, Piatetov P. Prognostic impact of early fibrillation in patients with ST-elevation myocardial infarction treated with primary PCI. Eur Heart J. 2012;31:302–311. DOI: 10.1093/eurheartj/ehs3553.

28. Asrar ul Haq M, Tsay IM, Dinh DT, Brennan A, Clark D, Cox N, Harper R, Nadurata V, Andrianopoulos N, Reid C, et al. Prevalence and outcomes of a national registry. J Am Coll Cardiol. 2016;109:61–76. DOI: 10.14423/SMJ.00000 00000000404.

29. Clayson P, Osmond D, McEvoy J, Passmore P. Viewpoint: lessons from the radial versus femoral access, bleeding and ischemic events in patients with acute coronary syndrome: insights from the HMO Research Network-Stent Registry. Circ Cardiovasc Interv. 2015;8:167–175.

30. Ng et al. Radial Access for PCI and Mortality in Patients with End-stage Liver Disease. Clin Med Insights Cardiovasc Med. 2020;14:179356820901941. DOI: 10.1177/179356820901491.

31. Zhang S, Diao J, Qi C, Jin J, Li L, Gao X, Gong L, Wu W. Predictive value of neutrophil to lymphocyte ratio in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention: a meta-analysis. BMC Cardiovasc Disord. 2018;18:75. DOI: 10.1186/ s12872-018-0926-6.
bleeding on late clinical outcomes after primary percutaneous coronary intervention in acute myocardial infarction the HORIZONS-AMI (harmonizing outcomes with stents in acute myocardial infarction) trial. J Am Coll Cardiol. 2011;58:1750–1756. DOI: 10.1016/j.jacc.2011.07.021.

40. Lim YH, Lee Y, Shin J, Yoon J, Lee SH, Rha SW, Lee JH, Jeong MH, Cho BR, Kim KG. Comparisons of clinical and procedural outcomes between transradial and transfemoral approaches in percutaneous coronary intervention (from the Korean Transradial Intervention Prospective Registry). Am J Cardiol. 2016;117:1272–1281. DOI: 10.1016/j.amjcard.2016.01.020.

41. Ando G, Gragnano F, Calabro P, Valgimigli M. Radial vs femoral access for the prevention of acute kidney injury (AKI) after coronary angiography or intervention: a systematic review and meta-analysis. Catheter Cardiovasc Interv. 2018;92:ES518–ES526. DOI: 10.1002/ccd.27903.

42. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009;361:1045–1057. DOI: 10.1056/NEJMoa0904327.

43. Ko DT, Yun L, Wijeysundera HC, Jackevicius CA, Rao SV, Austin PC, Marquis JF, Tu JV. Incidence, predictors, and prognostic implications of hospitalization for late bleeding after percutaneous coronary intervention for patients older than 65 years. Circ Cardiovasc Inter. 2010;3:140–147. DOI: 10.1161/CIRCINTERVENTIONS.109.928721.

44. Rao SV, Eikelboom JA, Garg G, Harrington RA, Califf RM, Bassand JP. Bleeding and blood transfusion issues in patients with non-ST-segment elevation acute coronary syndromes. Eur Heart J. 2007;28:1193–1204. DOI: 10.1093/eurheartj/ehm019.

45. Twomey KM, Rao SV, Becker RC. Proinflammatory, immunomodulating, and prothrombotic properties of anemia and red blood cell transfusions. J Thromb Thrombolysis. 2006;21:167–174. DOI: 10.1007/s11239-006-5206-4.

46. Kwok CS, Sherwood MW, Watson SM, Nasir SB, Sperrin M, Nolan J, Kinnaird T, Kiatchoosakun S, Ludman PF, de Belder MA, et al. Blood transfusion after percutaneous coronary intervention and risk of subsequent adverse outcomes: a systematic review and meta-analysis. JACC Cardiovasc Interv. 2015;8:436–446. DOI: 10.1016/j.jcin.2014.09.026.

47. Genéreux P, Rutledge DR, Palmieri T, Caixeta A, Kedhi E, Hermiller JB, Wang J, Krucoff MW, Jones-McMeans J, Sudhir K, et al. Stent thrombosis and dual antiplatelet therapy interruption with everolimus-eluting stents: insights from the Xience V coronary stent system trials. Circ Cardiovasc Interv. 2015;8:e001362. DOI: 10.1161/CIRCINTERVENTIONS.114.001362.

48. Stefanescu Schmidt AC, Steg PG, Yeh RW, Kerelakes DJ, Tanguay JF, Hsieh WH, Massaro JM, Mauri L, Cutlip DE; Investigators D. Interruption of dual antiplatelet therapy within six months after coronary stents (from the Dual Antiplatelet Therapy Study). Am J Cardiol. 2019;124:1813–1820. DOI: 10.1016/j.amjcard.2019.09.006.

49. Elgendy IY, Mahmoud AN, Elgendy AY, Bavry AA. Outcomes with intravascular ultrasound-guided stent implantation: a meta-analysis of randomized trials in the era of drug-eluting stents. Circ Cardiovasc Interv. 2016;9:e003700. DOI: 10.1161/CIRCINTERVENTIONS.116.003700.

50. Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:367–315. DOI: 10.1093/eurheartj/ehv020.

51. Azzalini L, Tosin K, Chabot-Blanchet M, Avram R, Ly HO, Gaudet B, Gallo R, Doucet S, Tanguay JF, Ibrahim R, et al. The benefits conferred by radial access for cardiac catheterization are offset by a paradoxical increase in the rate of vascular access site complications with femoral access: the Campeau radial paradox. JACC Cardiovasc Interv. 2015;8:1854–1864. DOI: 10.1016/j.jcin.2015.07.029.
Supplemental Material
ENDPOINT DEFINITIONS

Death

Deaths is classified as cardiovascular or non-cardiovascular. The cause of death will be determined by the principal condition that resulted in the death, not the immediate mode of death. Managing physicians will utilize all available information provided, along with clinical expertise, in their adjudication of the cause of death.

Cardiovascular death

Death due to cardiovascular causes. They include:

- death from acute myocardial infarction and its complications (e.g., arrhythmia, sudden arrest, heart failure)
- sudden cardiac death
- death from heart failure
- death from stroke
- death caused by complications of cardiovascular procedures
- death from cardiovascular hemorrhage (e.g., intracranial hemorrhage, non-procedural or non-traumatic vascular rupture (e.g., aortic aneurysm), or hemorrhage causing cardiac tamponade)
- death from other cardiovascular causes not included in the above categories but with a specific, known cardiovascular cause (e.g., pulmonary embolus or peripheral arterial disease)

Myocardial Infarction after hospital discharge

Any new diagnosis coding from the table below after hospital discharge for index PCI.

| 410  | Acute Myocardial Infarction                                      |
|------|-----------------------------------------------------------------|
| 410.0| Acute myocardial infarction, of anterolateral wall              |
| 410.1| Acute myocardial infarction, of other anterior wall             |
| 410.2| Acute myocardial infarction, of inferolateral wall              |
| 410.3| Acute myocardial infarction, of inferoposterior wall            |
| 410.4| Acute myocardial infarction, of other inferior wall             |
| 410.5| Acute myocardial infarction, of other lateral wall              |
| 410.6| Acute myocardial infarction, true posterior wall infarction     |
| 410.7| Acute myocardial infarction, subendocardial infarction         |
| 410.8| Acute myocardial infarction, of other specified sites          |
Acute myocardial infarction, unspecified sites
Acute myocardial infarction
Myocardial infarction

Other Acute and Subacute forms of Ischemic Heart Disease
Post myocardial infarction syndrome
Intermediate coronary syndrome
Other acute and subacute forms of ischemic heart disease
Other acute and subacute forms of ischemic heart disease

Stroke

Any new diagnosis coding from the table below after PCI.

| Code | Description                                      |
|------|--------------------------------------------------|
| 430  | Subarachnoid Haemorrhage, Non-traumatic          |
| 430 (0) | Subarachnoid haemorrhage, non-traumatic         |
| 430 (1) | Rupture arteriovenous malformation in brain     |
| 430 (2) | Subarachnoid haemorrhage, due to rupture aneurysm |
| 430 (3) | Subarachnoid haemorrhage, nontraumatic          |
| 430 (4) | Subarachnoid haemorrhage, due to ruptured mycotic aneurysm, non-traumatic |
| 430 (5) | Subarachnoid haemorrhage – spinal, non-traumatic |
| 430 (6) | Subarachnoid haemorrhage                        |
| 430 (7) | Subarachnoid haemorrhage from carotid siphon and bifurcation |
| 430 (8) | Subarachnoid haemorrhage from middle cerebral artery |
| 430 (9) | Subarachnoid haemorrhage from anterior communicating artery |
| 430 (10) | Subarachnoid haemorrhage from posterior communicating artery |
| 430 (11) | Subarachnoid haemorrhage from basilar artery    |
| 430 (12) | Subarachnoid haemorrhage from vertebral artery  |
| 430 (13) | Subarachnoid haemorrhage intracranial artery    |
| 430 (14) | Berry aneurysm                                  |
| 430 (15) | Haemorrhage due to ruptured congenital cerebral aneurysm |

Intracerebral Haemorrhage, Non-traumatic

| Code | Description                                      |
|------|--------------------------------------------------|
| 431  | Intracerebral Haemorrhage, Non-traumatic         |
| 431 (0) | Intracerebral haemorrhage, non-traumatic         |
| 431 (1) | Spontaneous intracerebral haemorrhage           |
| 431 (2) | Intracerebral haemorrhage, nontraumatic         |
| 431 (3) | Intracerebral haemorrhage – basilar, non-traumatic |
| 431 (4) | Intracerebral haemorrhage – cerebellar, non-traumatic |
| 431 (5) | Intracerebral haemorrhage – capsular, non-traumatic |
| 431 (6) | Intracerebral haemorrhage – pontine, non-traumatic |
| 431 (7) | Intracerebral haemorrhage – intra-ventricular, non-traumatic |
| 431 (8) | Haemorrhagic conversion of cerebral infarction   |
| 431 (9) | Intracerebral haemorrhage                        |
| Code  | Description                                           |
|-------|-------------------------------------------------------|
| 431 (10) | Intracerebral haemorrhage in hemisphere, cortical |
| 431 (11) | Bullbar haemorrhage                                   |
| 431 (12) | Intracerebral haemorrhage, multiple localized         |
| 431 (13) | Cerebral haemorrhage                                  |
| 431 (14) | Intracerebral haemorrhage in brain stem               |
| 431 (15) | Basalis haemorrhage                                   |
| 431 (16) | Ventricular haemorrhage of brain                      |
| 431 (17) | Intracerebral subcortical haemorrhage in hemisphere   |

**432.1**  
**Subdural Hemorrhage, Non-traumatic**

| Code  | Description                                           |
|-------|-------------------------------------------------------|
| 433   | Occlusion and Stenosis of Percerebral Arteries        |
| 433.0 | Occlusion and stenosis of basilar artery, w/o mention of cerebral infarction |
| 433.1 | Occlusion and stenosis of carotid artery              |
| 433.2 | Occlusion and stenosis of vertebral artery            |
| 433.3 | Occlusion and stenosis of multiple and bilateral precerebral, arteries |
| 433.8 | Occlusion and stenosis of other specified precerebral artery |
| 433.9 | Occlusion and stenosis of unspecified precerebral artery |
| 433 (0) | Occlusion and stenosis of precerebral arteries       |

| Code  | Description                                           |
|-------|-------------------------------------------------------|
| 434   | Occlusion of Cerebral Arteries                        |
| 434.0 | Cerebral thrombosis                                  |
| 434.1 | Cerebral embolism                                    |
| 434.9 | Cerebral artery occlusion, unspecified                |
| 434 (0) | Occlusion of cerebral arteries                        |

| Code  | Description                                           |
|-------|-------------------------------------------------------|
| 435   | Transient Cerebral Ischemia                           |
| 435.0 | Basilar artery syndrome                               |
| 435.1 | Vertebral artery syndrome                             |
| 435.2 | Subclavian steal syndrome                             |
| 435.8 | Other specified transient cerebral ischemias          |
| 435.9 | Unspecified transient cerebral ischemia               |
| 435 (0) | Transient cerebral ischemia                           |

| Code  | Description                                           |
|-------|-------------------------------------------------------|
| 436   | Acute, But Ill-defined Cerebrovascular Disease        |
| 436 (0) | Acute cerebrovascular disease                        |
| 436 (1) | Brain stem stroke syndrome                            |
| 436 (2) | Cerebellar stroke syndrome                            |
| 436 (3) | Stroke                                                |
| 436 (4) | Extension of cerebrovascular accident                 |
| 436 (5) | Cerebrovascular accident                              |
Unplanned Coronary Revascularization

Percutaneous coronary intervention (PCI) is defined as the placement of an angioplasty guidewire, balloon, or other device (eg, stent, atherectomy, brachytherapy, or thrombectomy catheter) into a native coronary artery or bypass graft for the purpose of mechanical coronary revascularization. The diagnostic assessment of coronary lesion severity by intravascular ultrasonography, coronary flow reserve, or fractional flow reserve is not considered a PCI procedure.

Coronary artery bypass grafting (CABG) is defined as a procedure performed to bypass partially or completely occluded coronary arteries with veins and/or arteries harvested from elsewhere in the body, thereby improving the blood supply to the coronary circulation supplying the myocardium.

Unplanned coronary revascularization is defined as any PCI or CABG performed not as a part of planned procedure upon the conclusion of index PCI.
BASELINE VARIABLES DEFINITIONS

Anemia

Anemia is defined as hemoglobin <13g/dL for men and hemoglobin <12g/dL for women.

PCI urgency

- Elective: Patient cardiac status has been stable in the days or weeks before the operation. The procedure can be deferred without increased risk of compromised cardiac outcome.

- Urgent: Procedure required during the same hospitalization to minimize chances of clinical deterioration or adverse outcome. Clinical conditions include (but are not limited to) acute or worsening chest pain, acute or worsening HF, acute MI, critical coronary stenosis, IABP support, UA with intravenous nitroglycerin, and rest angina.

- Emergency: Procedure required because of ongoing, refractory (difficult, complicated, and/or unmanageable), unrelenting cardiac compromise, with or without hemodynamic instability, and not responsive to any form of therapy except PCI.
Figure S1. Proportion of Radial Use by Year.

Proportion of Radial Access by Year

P for trend <0.001

| Year | Proportion |
|------|------------|
| 2010 | 33%        |
| 2011 | 37%        |
| 2012 | 51%        |
| 2013 | 57%        |
| 2014 | 59%        |
| 2015 | 59%        |
| 2016 | 65%        |
| 2017 | 70%        |
Figure S2. Propensity score distribution in the propensity score matched cohort.
Table S1. Baseline characteristics of all patients before propensity score matching.

| Characteristic                                                                 | All Patients     | Radial Group   | Femoral Group  |
|-------------------------------------------------------------------------------|-----------------|----------------|----------------|
|                                                                               | N = 24463       | N = 11020      | N = 13430      |
| Female - no. (%)                                                              | 5652 (23.1%)    | 2817 (25.6%)   | 2826 (21.0%)   |
| Age - mean (SD)                                                               | 64.748922 (11.494138) | 65.4 (11.8)   | 64.2 (11.2)    |
| Chinese - no. (%)                                                             | 22997 (94.0%)   | 10299 (93.5%)  | 12685 (94.5%)  |
| Tobacco use - no. (%)                                                         | 10555 (46.1%)   | 4523 (44.7%)   | 6031 (47.1%)   |
| Diabetes mellitus - no. (%)                                                   | 8540 (34.9%)    | 4119 (37.4%)   | 4418 (32.9%)   |
| Hypertension - no. (%)                                                        | 15642 (63.9%)   | 7289 (66.1%)   | 8351 (62.2%)   |
| Dyslipidemia - no. (%)                                                        | 15451 (63.2%)   | 6908 (62.7%)   | 8539 (63.6%)   |
| Cerebrovascular disease - no. (%)                                             | 2360 (9.6%)     | 1286 (11.7%)   | 1073 (8.0%)    |
| Chronic obstructive pulmonary disease - no. (%)                              | 582 (2.4%)      | 279 (2.5%)     | 303 (2.3%)     |
| Peripheral vascular disease - no. (%)                                         | 348 (1.4%)      | 217 (2.0%)     | 131 (1.0%)     |
| History of malignancy - no. (%)                                               | 1281 (5.2%)     | 622 (5.6%)     | 659 (4.9%)     |
| Cirrhosis - no. (%)                                                           | 62 (0.3%)       | 29 (0.3%)      | 33 (0.2%)      |
| Estimated GFR - ml/min/1.73m2, mean (SD)                                     | 80.699677 (27.543228) | 77.2 (30.7)   | 83.6 (24.3)    |
| Estimated GFR < 50ml/min/1.73m2 - no. (%)                                    | 2778 (11.4%)    | 1770 (16.1%)   | 1008 (7.5%)    |
| White blood cell count - 10^9/L, mean (SD)                                   | 8.2533959 (3.0845965) | 8.3 (3.3)     | 8.2 (2.9)      |
| Anemia - no. (%)                                                              | 7679 (31.4%)    | 4003 (36.3%)   | 3674 (27.4%)   |
| Atrial fibrillation or flutter - no. (%)                                      | 1305 (5.3%)     | 659 (6.0%)     | 644 (4.8%)     |
| On anti-coagulant before PCI - no. (%)                                        | 627 (2.6%)      | 302 (2.7%)     | 323 (2.4%)     |
| Previous myocardial infarction - no. (%)                                      | 3048 (12.5%)    | 1474 (13.4%)   | 1574 (11.7%)   |
| Previous coronary artery bypass surgery - no. (%)                            | 422 (1.7%)      | 370 (3.4%)     | 52 (0.4%)      |
| Previous heart failure - no. (%)                                              | 1916 (7.8%)     | 1037 (9.4%)    | 878 (6.5%)     |
| NYHA class III-IV in last 2 weeks before PCI - no. (%)                        | 987 (4.0%)      | 567 (5.1%)     | 420 (3.1%)     |
| Cardiogenic shock - no. (%)                                                   | 581 (2.4%)      | 416 (3.8%)     | 165 (1.2%)     |
| Ventricular tachycardia in <48 hours before PCI - no. (%)                    | 672 (2.7%)      | 427 (3.9%)     | 245 (1.8%)     |
| PCI urgency - no. (%)                                                         |                 |                |                |
| Elective                                                                     | 14267 (58.3%)   | 6184 (56.1%)   | 8071 (60.1%)   |
| Urgent                                                                       | 6739 (27.6%)    | 2882 (26.2%)   | 3856 (28.7%)   |
| Emergent                                                                     | 3453 (14.1%)    | 1951 (17.7%)   | 1502 (11.2%)   |
| Indication for PCI - no. (%)                                                  |                 |                |                |
| Stable angina                                                                | 4646 (19.0%)    | 2014 (18.3%)   | 2626 (19.6%)   |
| Unstable angina                                                              | 5089 (20.8%)    | 2244 (20.4%)   | 2841 (21.2%)   |
| Non-ST elevation myocardial infarction                                       | 11271 (46.1%)   | 4868 (44.2%)   | 6400 (47.7%)   |
| ST elevation myocardial infarction | 3450 (14.1%) | 1890 (17.2%) | 1560 (11.6%) |
| Number of major epicardial artery involved - no. (%) | | | |
| One vessel disease | 11022 (45.2%) | 4680 (42.7%) | 6330 (47.1%) |
| Two vessel disease | 8164 (33.5%) | 3711 (33.9%) | 4452 (33.2%) |
| Three vessel disease | 5211 (21.4%) | 2567 (23.4%) | 2644 (19.7%) |
| Proportion of radial access use by institution - no. (%) | | | |
| 1st quantile (lowest radial use) | 9780 (40.0%) | 6055 (54.9%) | 3725 (27.7%) |
| 2nd quantile | 6917 (28.3%) | 2637 (23.9%) | 4279 (31.9%) |
| 3rd quantile | 3245 (13.3%) | 1095 (9.9%) | 2140 (15.9%) |
| 4th quantile (highest radial use) | 4521 (18.5%) | 1233 (11.2%) | 3286 (24.5%) |
| Year of PCI - no. (%) | | | |
| 2010-2013 | 10138 (41.4%) | 5704 (51.8%) | 4432 (33.0%) |
| 2014-2017 | 14325 (58.6%) | 5316 (48.2%) | 8998 (67.0%) |

SD, standard deviation; GFR, glomerular filtration rate; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.
Table S2. Procedural characteristics and medications on hospital discharge of patients before propensity score matching.

| Characteristic                              | All Patients | Radial Group | Femoral Group |
|---------------------------------------------|--------------|--------------|---------------|
|                                             | N = 24463    | N = 11020    | N = 13430     |
| Intravascular imaging - no. (%)            |              |              |               |
|                                            | 11972 (48.9%)| 4431 (40.2%) | 7539 (56.1%)  |
| Intravascular ultrasonography - no. (%)    |              |              |               |
|                                            | 8618 (35.2%) | 3294 (29.9%) | 5323 (39.6%)  |
| Optic coherence tomography - no. (%)       |              |              |               |
|                                            | 3502 (14.3%) | 1169 (10.6%) | 2331 (17.4%)  |
| Angiographic success - no. (%)             |              |              |               |
|                                            | 23830 (97.5%)| 10635 (96.7%)| 13183 (98.2%) |
| Drop in hemoglobin >2g/dL - no. (%)        |              |              |               |
|                                            | 4294 (17.6%) | 1850 (16.8%) | 2438 (18.2%)  |
| Anemia after PCI - no. (%)                 |              |              |               |
|                                            | 9967 (44.8%) | 5257 (50.6%) | 4706 (39.7%)  |
| Aspirin on discharge - no. (%)             |              |              |               |
|                                            | 23765 (97.1%)| 10696 (97.1%)| 13059 (97.2%) |
| P2Y12 inhibitor on discharge - no. (%)     |              |              |               |
|                                            | 24079 (98.4%)| 10816 (98.1%)| 13253 (98.7%) |
| Potent P2Y12 inhibitor on discharge - no. (%)|            |              |               |
|                                            | 3798 (15.5%) | 1364 (12.4%) | 2433 (18.1%)  |
| Proton pump inhibitor on discharge - no. (%)|            |              |               |
|                                            | 14779 (60.4%)| 6262 (56.8%) | 8508 (63.4%)  |
| P2Y12 inhibitor duration - median (IQR) in days |        |              |               |
|                                            | 366 (362, 408)| 365 (244, 415)| 366 (364, 404)|
| Statin on discharge - no. (%)              |              |              |               |
|                                            | 23275 (95.1%)| 10380 (94.2%)| 12887 (96.0%) |
| ACE inhibitor or ARB on discharge - no. (%) |            |              |               |
|                                            | 16735 (68.4%)| 7773 (70.5%) | 8959 (66.7%)  |
| Beta-blocker on discharge - no. (%)        |              |              |               |
|                                            | 17902 (73.2%)| 8358 (75.8%) | 9541 (71.0%)  |
| Anti-coagulant on discharge - no. (%)      |              |              |               |
|                                            | 906 (3.7%)   | 436 (4.0%)   | 468 (3.5%)    |

PCI, percutaneous coronary intervention, ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker.