Radial versus femoral access in patients with acute coronary syndromes with or without ST-segment elevation

A pre-specified analysis from the randomized minimizing adverse haemorrhagic events by transradial access site and systemic implementation of angioX (MATRIX access)

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Aims

To assess whether radial compared with femoral access is associated with consistent outcomes in patients with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndrome (NSTE-ACS).

Methods and results

In the Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX (MATRIX) programme patients were randomized to radial or femoral access, stratified by STEMI (2001 radial, 2009 femoral) and NSTE-ACS (2196 radial, 2198 femoral). The 30-day co-primary outcomes were major adverse cardiovascular events (MACE), defined as death, myocardial infarction, or stroke, and net adverse clinical events (NACE), defined as MACE or major bleeding. In the overall study population, radial access reduced the NACE but not MACE endpoint at the prespecified 0.025 alpha. MACE occurred in 121 (6.1%) STEMI patients with...
radial access vs. 126 (6.3%) patients with femoral access [rate ratio (RR) = 0.96, 95% CI = 0.75–1.24; P = 0.76] and in 248 (11.3%) NSTE-ACS patients with radial access vs. 303 (13.9%) with femoral access (RR = 0.80, 95% CI = 0.67–0.96; P = 0.016) (Pint = 0.25). NACE occurred in 142 (7.2%) STEMI patients with radial access and in 165 (8.3%) patients with femoral access (RR = 0.86, 95% CI = 0.68–1.08; P = 0.18) and in 268 (12.2%) NSTE-ACS patients with radial access compared with 321 (14.7%) with femoral access (RR = 0.82, 95% CI = 0.69–0.97; P = 0.023) (Pint = 0.76). All-cause mortality and access site-actionable bleeding favoured radial access irrespective of ACS type (Pint = 0.11 and Pint = 0.36, respectively).

**Conclusion**
Radial as compared with femoral access provided consistent benefit across the whole spectrum of patients with ACS, without evidence that type of presenting syndrome affected the results of the random access allocation.

**Keywords**
MATRIX • Radial • Femoral • STEMI • NSTE-ACS

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**Introduction**

Advances in antithrombotic therapy in patients with acute coronary syndrome (ACS), along with an early invasive strategy in high-risk patients, have reduced the incidence of recurrent ischaemic events but also increased bleeding complications.1 Bleeding is associated with short-term and long-term hazards for mortality, albeit the exact nature of this relationship remains speculative.1–3

The Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX (MATRIX) trial is the largest randomized trial to compare radial and femoral access in largely unslected patients with ACS with or without ST-segment elevation myocardial infarction (STEMI) undergoing coronary angiography and percutaneous coronary intervention (PCI). MATRIX-Access observed a numerical reduction of major adverse cardiovascular events (MACE) in favour of radial access, which did not reach the prespecified 0.025 alpha thresholds for statistical significance. However, the use of radial access significantly reduced the rate of net adverse clinical events (NACE), defined as the composite of MACE or major bleeding.

The RIVAL (A Trial of Trans-radial Versus Trans-femoral PCI Access Site Approach in Patients With Unstable Angina or Myocardial Infarction Managed With an Invasive Strategy) study reported inconsistent results in terms of the primary endpoint as well for mortality depending on presentation syndrome, namely non-ST-segment elevation ACS (NSTE-ACS) or STEMI.4 Therefore, it remains unclear whether radial access should be preferred over femoral access across the entire spectrum of ACS patients.

We had prespecified to analyse the consistency of risks and benefits of each access site in patients with NSTE-ACS and STEMI undergoing invasive management.

**Methods**

**Study design**
The MATRIX-Access was conceived as a randomized, multicentre, superiority trial-comparing radial with femoral access in patients with ACS with or without STE who were about to undergo coronary angiography and PCI, if indicated.1,7 This was the first of three trials of the MATRIX programme (registered with clinicaltrials.gov; Unique identifier: NCT01433627) and was performed in all patients with an ACS consenting to participate in the programme. The trial was approved by the institutional review board at each participating centre, and all patients gave written informed consent to participate.

**Study patients**

Patients were eligible if they had an ACS with or without ST-segment elevation (STE), were scheduled to undergo an invasive approach, and the interventional cardiologist was willing to proceed with either radial or femoral access with expertise for both, including at least 75 coronary interventions performed and at least 50% of interventions in ACS via the radial route during the previous year. Patients presenting with NSTE-ACS were eligible if they had a history consistent with new or worsening ischaemia, occurring at rest or with minimal activity within 7 days before randomization, and fulfilled at least two high-risk criteria (detailed in the web extra material). Patients with STEMI were eligible if they presented within 12 h of the onset of symptoms or between 12 and 24 h after symptom onset if there was evidence of continued ischaemia or previous fibrinolytic treatment and if they had STE of at least 1 mm in two or more contiguous leads, new left bundle-branch block, or true posterior MI. The main inclusion and exclusion criteria were previously reported.1,6

**Study protocol and randomization**

Before the start of angiography, patients were randomly assigned 1:1 to radial or femoral access for diagnostic angiography and PCI, if indicated, using a web-based system to ensure adequate concealment of allocation. The randomization sequence was computer generated, blocked, and stratified by site, intended new or ongoing use of ticagrelor or prasugrel, type of ACS (STEMI or troponin-positive or -negative NSTE-ACS), and anticipated use of immediate PCI. Access site management during and after the diagnostic or therapeutic procedure was left to the discretion of the treating physician, and closure devices were allowed as per local practice. The use of anticoagulants outside the protocol of the MATRIX programme was not allowed. Bivalirudin administration was consistent with the approved product labeling, whereas unfractionated heparin was dosed at 70–100 U/kg in patients not receiving glycoprotein IIb/IIIa inhibitors and at 50–70 U/kg in patients receiving glycoprotein IIb/IIIa inhibitors. Use of all other antithrombotic medications, including oral antiplatelet agents and non-antithrombotic medications, such as beta-blockers, angiotensin-converting enzyme inhibitors, and other antihypertensive agents, were allowed as per guidelines.7

**Study outcomes**

Two co-primary 30-day composite outcomes were pre-specified: MACE, defined as the composite of all-cause mortality, MI, or stroke; and NACE, defined as the composite of non-coronary artery bypass grafting (CABG)-related major bleeding (Bleeding Academic Research Consortium, BARC type 3 or 5) or MACE.8 Secondary outcomes included each component of the composite outcomes, cardiovascular mortality, and stent thrombosis. Bleeding was also assessed and adjudicated on the basis of the TIMI and GUSTO scales.9,10 Stent thrombosis
Table 1  Baseline characteristics of the intention-to-treat population according to initial clinical presentation (STEMI, NSTE-ACS) and access site

| Baseline characteristics | STEMI | Femoral access | P-value | NSTE-ACS | Femoral access | P-value |
|--------------------------|-------|----------------|---------|----------|----------------|---------|
|                          | Radial access (n = 2001) | Femoral access (n = 2009) |         | Radial access (n = 2196) | Femoral access (n = 2198) |         |
| Age—years                | 63.7 ± 12.1 | 64.0 ± 12.1 | 0.43 | 67.2 ± 11.3 | 67.5 ± 11.3 | 0.33 |
| ≥75 years                | 424 (21.2) | 444 (22.1) | 0.48 | 644 (29.3) | 658 (29.9) | 0.66 |
| Male sex                 | 1552 (77.6) | 1541 (76.7) | 0.52 | 1574 (71.7) | 1505 (68.5) | 0.020 |
| Weight (kg)              | 77.4 ± 13.9 | 77.7 ± 13.4 | 0.52 | 77.4 ± 14.4 | 76.4 ± 13.7 | 0.024 |
| Body mass index (kg/m²)  | 26.9 ± 4.0 | 27.1 ± 4.1 | 0.22 | 27.2 ± 4.3 | 27.1 ± 4.3 | 0.22 |
| Diabetes mellitus        | 371 (18.5) | 352 (17.5) | 0.013 | 588 (26.8) | 592 (26.9) | 0.42 |
| Insulin-dependent        | 64 (3.2) | 91 (4.5) | 0.42 | 145 (6.6) | 166 (7.6) | 0.42 |
| Current smoker           | 821 (41.0) | 814 (40.5) | 0.90 | 638 (29.1) | 614 (27.9) | 0.64 |
| Hypertension             | 1093 (54.6) | 1141 (56.8) | 0.70 | 1532 (69.8) | 1545 (70.3) | 0.70 |
| Previous myocardial infarction | 198 (9.9) | 186 (9.3) | 0.49 | 387 (17.6) | 432 (19.7) | 0.084 |
| Previous PCI             | 215 (10.7) | 171 (8.5) | 0.017 | 395 (18.0) | 414 (18.8) | 0.47 |
| Radial access            | 38 (1.9) | 18 (0.9) | 0.0068 | 81 (3.7) | 66 (3.0) | 0.21 |
| Femoral access           | 94 (4.7) | 83 (4.1) | 0.38 | 182 (8.3) | 203 (9.2) | 0.27 |
| Both radial and femoral access | 8 (0.4) | 5 (0.2) | 0.40 | 28 (1.3) | 30 (1.4) | 0.79 |
| Access site unknown      | 75 (3.7) | 65 (3.2) | 0.38 | 104 (4.7) | 115 (5.2) | 0.45 |
| Previous CABG            | 27 (1.3) | 25 (1.2) | 0.77 | 84 (3.8) | 121 (5.5) | 0.0083 |
| Previous TIA or stroke   | 78 (3.9) | 94 (4.7) | 0.22 | 117 (5.3) | 136 (6.2) | 0.22 |
| Peripheral Vascular Disease | 106 (5.3) | 123 (6.1) | 0.26 | 235 (10.7) | 249 (11.3) | 0.51 |
| Chronic Obstructive Pulmonary Disease | 91 (4.5) | 94 (4.7) | 0.84 | 159 (7.2) | 189 (8.6) | 0.096 |
| History of renal failure | 14 (0.7) | 31 (1.5) | 0.011 | 32 (1.5) | 28 (1.3) | 0.60 |
| Dialysis                 | 1 (0.0) | 2 (0.1) | 1.00 | 3 (0.1) | 2 (0.1) | 0.69 |
| Clinical presentation    |                  |                  |         |                  |                  |         |
| Cardiac arrest           | 71 (3.5) | 68 (3.4) | 0.78 | 14 (0.6) | 15 (0.7) | 0.85 |
| Killip class             |                  |                  |         |                  |                  |         |
| I                        | 1775 (88.7) | 1817 (90.4) | 0.072 | 2021 (92.0) | 1983 (90.2) | 0.035 |
| II                       | 142 (7.1) | 144 (7.2) | 0.93 | 126 (5.7) | 157 (7.1) | 0.058 |
| III                      | 45 (2.2) | 22 (1.1) | 0.0044 | 43 (2.0) | 57 (2.6) | 0.16 |
| IV                       | 39 (1.9) | 26 (1.3) | 0.10 | 6 (0.3) | 1 (0.0) | 0.070 |
| Previous lytic therapy   | 94 (4.7) | 103 (5.1) | 0.53 | 0 (0.0) | 1 (0.0) | 1.00 |
| Systolic arterial pressure (mmHg) | 136.0 ± 27.0 | 136.2 ± 26.9 | 0.76 | 140.8 ± 23.9 | 141.2 ± 24.2 | 0.58 |
| Heart rate (min⁻¹)       | 77.2 ± 17.3 | 77.0 ± 17.1 | 0.78 | 75.6 ± 15.8 | 75.1 ± 16.5 | 0.38 |
| Left ventricular ejection fraction (%) | 49.2 ± 9.5 | 48.6 ± 9.5 | 0.030 | 53.2 ± 9.2 | 52.9 ± 9.9 | 0.44 |
| eGFR                     | 85.2 ± 25.7 | 84.5 ± 25.6 | 0.36 | 83.2 ± 25.2 | 82.3 ± 25.4 | 0.21 |
| eGFR < 60                | 310 (15.7) | 298 (15.0) | 0.55 | 390 (17.8) | 417 (19.1) | 0.29 |
| eGFR < 30                | 18 (0.9) | 27 (1.4) | 0.18 | 17 (0.8) | 22 (1.0) | 0.42 |
| Medications administered before the cath-Lab |                  |                  |         |                  |                  |         |
| Aspirin                  | 1865 (93.2) | 1881 (93.6) | 0.59 | 2091 (95.2) | 2073 (94.3) | 0.18 |
| Clopidogrel              | 734 (36.7) | 738 (36.7) | 0.97 | 1281 (58.3) | 1259 (57.3) | 0.48 |
| Prasugrel                | 402 (20.1) | 395 (19.7) | 0.73 | 83 (3.8) | 73 (3.3) | 0.41 |
| Ticagrel                | 378 (18.9) | 394 (19.6) | 0.56 | 600 (27.3) | 635 (28.9) | 0.25 |
| Enoxaparin              | 57 (2.8) | 91 (4.5) | 0.0048 | 630 (28.7) | 651 (29.6) | 0.50 |
| Fondaparinux            | 55 (2.7) | 68 (3.4) | 0.24 | 373 (17.0) | 400 (18.2) | 0.29 |
| ACE inhibitors           | 273 (13.6) | 278 (13.8) | 0.86 | 980 (44.6) | 1023 (46.5) | 0.20 |
| Angiotensin II receptor antagonist | 135 (6.7) | 141 (7.0) | 0.73 | 315 (14.3) | 321 (14.6) | 0.81 |
| Statins                 | 403 (20.1) | 410 (20.4) | 0.83 | 1409 (64.2) | 1453 (66.1) | 0.18 |
| Beta blockers            | 412 (20.6) | 432 (21.5) | 0.48 | 1282 (58.4) | 1343 (61.1) | 0.066 |
| Warfarin                | 20 (1.0) | 16 (0.8) | 0.50 | 52 (2.4) | 48 (2.2) | 0.68 |

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was defined as the definite or probable occurrence of a stent-related thrombotic event according to the Academic Research Consortium classification.11 All outcomes were pre-specified.5 An independent clinical events committee blinded to treatment allocation adjudicated all suspected outcome events by reviewing relevant medical records after site monitoring by Trial Form Support (Lund, Sweden) in Italy and the Netherlands, FLS-Research Support (Barcelona, Spain) in Spain, and Gothia Forum (Västra Götaland) in Sweden.

Statistical analysis
Statistical analyses were performed by an academic statistical group led by two of the authors, who had access to the full de-identified data set. All analyses were performed according to the intention-to-treat principle, including all patients in the analysis according to the allocated access. Events up to 30 days post-randomization were considered. We analyzed primary and secondary outcomes separately for STEMI and NSTE-ACS as time to first event using the Mantel–Cox method, accompanied by log-rank tests to calculate corresponding two-sided P-values.

Results
The MATRIX trial enrolled 8404 patients with ACS from 78 centres in Italy, the Netherlands, Spain, and Sweden between October 2011 and July 2014. Of these patients, 4010 (47.8%) fulfilled the definition for STEMI (radial: 2001, 23.8%; femoral: 2009, 23.9%) (see Supplementary material online, eFigure S1 and S2), and 4394 (52.2%) patients presented with NSTE-ACS (radial 2196, 26.1%; femoral 2198, 26.1%). Complete follow-up throughout 30 days was available in 4191 radial and 4196 femoral patients. Baseline characteristics were generally well balanced between randomization groups according to access site, considering the initial clinical presentation (STEMI and NSTE-ACS) (Table I).

Procedural results according to clinical presentation and access site are presented in Supplementary material online, eTable S1. PCI
### Table 2  Adjudicated and non-adjudicated clinical outcome at 30 days

| Clinical outcomes                                                                 | STEMI       | NSTE-ACS    | P-value | P-value for interaction |
|----------------------------------------------------------------------------------|-------------|-------------|---------|-------------------------|
|                                                                                  | Radial access | Femoral access | Radial access | Femoral access | Radial access | Femoral access | Radial access | Femoral access |
|                                                                                  | (n = 2001)  | (n = 009)   | (n = 2196) | (n = 2198)   | (n = 2196)  | (n = 2198)   | (n = 2196)  | (n = 2198)   |
| Co-primary composite endpoint of all-cause mortality, MI, or stroke              | 121 (6.1)   | 126 (6.3)   | 0.96 (0.75–1.24) | 0.76     | 248 (11.3)   | 303 (13.9)   | 0.80 (0.67–0.96) | 0.016    | 0.25                   |
| Co-primary composite endpoint of all-cause mortality, MI, stroke, or BARC 3 or 5 | 142 (7.2)   | 165 (8.3)   | 0.86 (0.68–1.08) | 0.18     | 268 (12.2)   | 321 (14.7)   | 0.82 (0.69–0.97) | 0.023    | 0.76                   |
| Composite of all-cause mortality, MI, stroke, urgent TVR, definite stent thrombosis or BARC 3 or 5 | 148 (7.5)   | 170 (8.5)   | 0.87 (0.69–1.08) | 0.21     | 271 (12.3)   | 321 (14.7)   | 0.83 (0.70–0.98) | 0.033    | 0.75                   |
| All-cause mortality                                                             | 48 (2.4)    | 55 (2.7)    | 0.87 (0.59–1.29) | 0.49     | 18 (0.8)     | 36 (1.7)     | 0.50 (0.28–0.88) | 0.014    | 0.11                   |
| Cardiovascular death                                                             | 46 (2.3)    | 53 (2.6)    | 0.87 (0.58–1.29) | 0.48     | 18 (0.8)     | 32 (1.5)     | 0.56 (0.31–1.00) | 0.046    | 0.22                   |
| Myocardial infarction                                                            | 66 (3.4)    | 65 (3.3)    | 1.02 (0.72–1.43) | 0.92     | 233 (10.6)   | 265 (12.1)   | 0.87 (0.72–1.05) | 0.13     | 0.42                   |
| Stroke                                                                          | 10 (0.5)    | 9 (0.5)     | 1.11 (0.45–2.73) | 0.82     | 6 (0.3)      | 7 (0.3)      | 0.85 (0.29–2.54) | 0.78     | 0.72                   |
| Transient ischaemic attack                                                       | 3 (0.2)     | 6 (0.3)     | 0.50 (0.12–2.00) | 0.32     | 2 (0.1)      | 7 (0.3)      | 0.28 (0.06–1.37) | 0.095    | 0.60                   |
| Urgent target vessel revascularization                                           | 34 (1.7)    | 31 (1.6)    | 1.10 (0.67–1.79) | 0.71     | 15 (0.7)     | 9 (0.4)      | 1.67 (0.73–3.81) | 0.22     | 0.39                   |
| Definite stent thrombosis                                                        | 22 (1.1)    | 18 (0.9)    | 1.22 (0.66–2.28) | 0.53     | 8 (0.4)      | 9 (0.4)      | 0.89 (0.34–2.30) | 0.80     | 0.58                   |
| Acute definite stent thrombosis                                                  | 17 (0.9)    | 9 (0.5)     | 1.90 (0.84–4.27) | 0.12     | 4 (0.2)      | 3 (0.1)      | 1.33 (0.30–5.96) | 0.71     | 0.68                   |
| Subacute definite stent thrombosis                                               | 6 (0.3)     | 9 (0.5)     | 0.66 (0.24–1.87) | 0.44     | 4 (0.2)      | 6 (0.3)      | 0.66 (0.19–2.36) | 0.52     | 1.00                   |
| Definite or probable stent thrombosis                                            | 30 (1.5)    | 22 (1.1)    | 1.37 (0.79–2.37) | 0.27     | 12 (0.5)     | 16 (0.8)     | 0.75 (0.35–1.58) | 0.45     | 0.20                   |
| Acute definite or probable stent thrombosis                                      | 19 (1.0)    | 10 (0.5)    | 1.91 (0.88–4.11) | 0.094    | 5 (0.2)      | 4 (0.2)      | 1.25 (0.33–4.66) | 0.74     | 0.59                   |
| Subacute definite or probable stent thrombosis                                   | 12 (0.6)    | 12 (0.6)    | 1.00 (0.45–2.22) | 0.99     | 8 (0.4)      | 12 (0.6)     | 0.66 (0.27–1.62) | 0.37     | 0.51                   |
| Bleeding                                                                         | 186 (9.4)   | 321 (16.3)  | 0.56 (0.46–0.67) | <0.0001  | 164 (7.5)    | 285 (13.1)   | 0.55 (0.46–0.68) | <0.0001  | 1.00                   |
| BARC Type 1                                                                       | 90 (4.5)    | 159 (8.1)   | 0.55 (0.43–0.72) | <0.0001  | 78 (3.6)     | 147 (6.8)    | 0.52 (0.39–0.69) | <0.0001  | 0.75                   |
| Type 2                                                                           | 66 (3.3)    | 109 (5.5)   | 0.60 (0.44–0.81) | 0.0009   | 61 (2.8)     | 106 (4.9)    | 0.57 (0.41–0.78) | 0.0004   | 0.82                   |
| Type 3abc                                                                        | 28 (1.5)    | 50 (2.6)    | 0.56 (0.35–0.89) | 0.012    | 26 (1.2)     | 34 (1.6)     | 0.76 (0.46–1.27) | 0.29     | 0.38                   |
| Type 3a                                                                          | 13 (0.7)    | 26 (1.4)    | 0.50 (0.26–0.97) | 0.036    | 16 (0.7)     | 18 (0.8)     | 0.89 (0.45–1.74) | 0.72     | 0.23                   |
| Type 3b                                                                          | 13 (0.7)    | 22 (1.1)    | 0.59 (0.30–1.17) | 0.13     | 10 (0.5)     | 15 (0.7)     | 0.66 (0.30–1.48) | 0.31     | 0.83                   |
| Type 3c                                                                          | 2 (0.1)     | 3 (0.2)     | 0.67 (0.11–3.98) | 0.65     | 0 (0.0)      | 1 (0.0)      | 0.33 (0.01–8.10) | 1.00     | 0.44                   |

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Table 2  Continued

| Clinical outcomes                      | STEMI          |                      | NSSTE-ACS       |                      |
|----------------------------------------|----------------|---------------------|-----------------|---------------------|
|                                        | Radial access  | Femoral access      | Risk ratio      | P-value             |
|                                        | (n = 2001)     | (n = 009)           | (95% CI)        | P-value             |
| Type 4                                 | 2 (0.1)        | 3 (0.2)             | 0.67 (0.11–3.98) | 0.65                |
| Type 5ab                               | 8 (0.4)        | 8 (0.4)             | 1.00 (0.37–2.66) | 1.00                |
| Type 5a                                | 4 (0.2)        | 7 (0.4)             | 0.57 (0.17–1.95) | 0.36                |
| Type 5b                                | 4 (0.2)        | 1 (0.1)             | 4.00 (0.45–35.85)| 0.18                |
| Type 3 or 5                            | 36 (1.9)       | 58 (3.0)            | 0.62 (0.41–0.94) | 0.022               |
| Type 3 or 5 related to access site     | 8 (0.4)        | 29 (1.5)            | 0.27 (0.13–0.60)| 0.0005              |
| Type 3 or 5 not related to access site | 28 (1.5)       | 29 (1.5)            | 0.96 (0.57–1.62) | 0.89                |
| Type 2, 3, or 5                        | 100 (5.1)      | 166 (8.4)           | 0.59 (0.46–0.76) | <0.001              |
| Type 2, 3, or 5 related to access site | 32 (1.6)       | 104 (5.3)           | 0.30 (0.20–0.45) | <0.0001             |
| Type 2, 3, or 5 not related to access site | 69 (3.5)    | 66 (3.3)            | 1.05 (0.74–1.47) | 0.80                |
| TIMI                                    |                |                     |                 |                     |
| Major bleeding                         | 19 (1.0)       | 24 (1.2)            | 0.79 (0.43–1.44) | 0.44                |
| Minor bleeding                         | 11 (0.6)       | 19 (1.0)            | 0.58 (0.27–1.21) | 0.14                |
| Major or minor bleeding                | 30 (1.6)       | 43 (2.2)            | 0.69 (0.44–1.11) | 0.13                |
| GUSTO                                  |                |                     |                 |                     |
| Severe bleeding                        | 16 (0.8)       | 17 (0.9)            | 0.94 (0.47–1.86) | 0.86                |
| Moderate bleeding                      | 7 (0.4)        | 19 (1.0)            | 0.37 (0.15–0.87) | 0.018               |
| Mild bleeding                          | 163 (8.2)      | 285 (14.5)          | 0.55 (0.45–0.67) | <0.0001             |
| Severe or moderate bleeding            | 23 (1.2)       | 36 (1.8)            | 0.64 (0.38–1.07) | 0.087               |
| Composite of surgical access site repair or blood products transfusion | 17 (0.9)       | 28 (1.4)            | 0.60 (0.33–1.10) | 0.097               |
| Surgical access site repair            | 4 (0.2)        | 11 (0.6)            | 0.36 (0.12–1.14) | 0.070               |
| Blood products transfusion             | 14 (0.7)       | 19 (1.0)            | 0.73 (0.37–1.46) | 0.38                |

Percentages are cumulative incidence estimates. BARC, Bleeding Academic Research Consortium; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; MI, myocardial infarction; NSTE-ACS, non-ST-segment elevation acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction; TVR, target vessel revascularization.
was attempted in more than 90% in STEMI and in ~70% of NSTE-ACS patients in both access groups. There was a highly significant qualitative interaction between crossover rates and clinical presentation [$P$-value for interaction ($P_{int}$) < 0.0001], with 4.5% of the NSTE-ACS patients and 7.2% of the STEMI patients who received intervention via femoral access against the original random allocation to radial as compared with 2.9% of the NSTE-ACS patients and 1.6% of the STEMI patients who received intervention via radial access in the femoral group (see Supplementary material online, eTable S1).

There were significant interactions noted for left main coronary artery lesion location, which underwent slightly more frequent treatment in the radial arm of STEMI patients ($P_{int} = 0.024$), and for TIMI 2 flow post procedure ($P_{int} = 0.033$) being more frequently observed in STEMI as compared with NSTE-ACS patients irrespective of the allocated access group.

Medications at presentation (Table 1), during intervention (see Supplementary material online, eTable S1), or at discharge (see Supplementary material online, eTable S2) were well matched with the only exception for sub-therapeutic dosing of unfractionated heparin (<50 U/kg), which was more often implemented in NSTE-ACS patients in both access site groups as compared with STEMI ($P_{int} < 0.0001$).

**Clinical outcomes**

For the co-primary outcomes of major adverse cardiac events and NACE, there were no significant interactions between the access site and type of ACS (STEMI or NSTE-ACS patients) ($P_{int} = 0.25$ and 0.76, respectively) (Figure 1, see Supplementary material online, eFigure S3).

In particular, the first co-primary outcome MACE occurred in 121 (6.1%) STEMI patients with radial access and in 126 (6.3%) patients...
with femoral access [rate ratio (RR) = 0.96, 95% CI = 0.75–1.24]. Among NSTE-ACS patients, MACE events occurred in 248 (11.3%) patients randomly assigned to radial access, compared with 303 (13.9%) patients assigned to femoral access (RR = 0.80, 95% CI = 0.67–0.96) (Table 2). The second co-primary outcome NACE was observed in 142 (7.2%) patients with radial access vs. in 165 (8.3%) patients with femoral access (RR = 0.86, 95% CI = 0.68–1.08) among the STEMI group, and in 268 (12.2%) patients with radial access vs. 321 (14.7%) patients with femoral access (RR = 0.82, 95% CI = 0.69–0.97) in the NSTE-ACS population (see Supplementary material online, eFigure S4 and Table 2).

There was no significant interaction between access site and clinical presentation with respect to any other ischaemic secondary endpoint. All-cause and cardiovascular mortality, which numerically favoured the radial access, were significantly reduced in in the NSTE-ACS group undergoing radial access (RR = 0.50, 95% CI = 0.28–0.88; P = 0.014 and RR = 0.56, 95% CI = 0.31–1.00; P = 0.046, respectively) but not in STEMI patients (RR = 0.87, 95% CI = 0.59–1.29; P = 0.49 and RR = 0.87, 95% CI = 0.58–1.29; P = 0.48), with negative interaction testing (Table 2). The risks of stroke, MI, stent thrombosis, or urgent target vessel revascularization were not affected by access site, with no signal of heterogeneity with respect to the initial clinical presentation (Table 2 and see Supplementary material online, eFigure S4).

Similarly, there was no significant interaction between access and type of ACS with respect to bleeding endpoints, with the only exception for GUSTO moderate (Pint = 0.034) but neither GUSTO severe nor the composite of moderate-to-severe GUSTO bleeding. Radial access reduced BARC 2–5 and BARC 3–5 bleeding, owing to a significant reduction of access site haemorrhagic complications (Table 2). Fatal bleeding was rare, and it did not differ across access groups within type of ACS.

| Composite endpoint: death, MI or stroke | Radial access | Femoral access | Risk Ratio (95% CI) | p Value | p Value for trend or interaction |
|----------------------------------------|--------------|---------------|-------------------|---------|-------------------------------|
| Centre’s annual volume of PCI          | Low (247-544)| 36/677        | 53/685            | 0.68 (0.44–1.04) | 0.074 |
|                                        | Intermediate (548-991)| 42/723       | 36/718            | 1.16 (0.74-1.82) | 0.51  |
|                                        | High (1000-1950)| 43/601       | 37/606            | 1.18 (0.75–1.83) | 0.47  |
| Centre’s proportion of radial PCI      | Low (14.9-64.4%)| 44/686    | 28/740            | 1.73 (1.07–2.78) | 0.023 |
|                                        | Intermediate (65.4-79.0%)| 37/719    | 44/725            | 0.84 (0.54–1.30) | 0.44  |
|                                        | High (80.0-98.0%) | 40/596      | 54/544            | 0.66 (0.44–1.00) | 0.050 |
| Age                                    | ≥75 yr       | 52/424        | 51/444            | 1.07 (0.72–1.59) | 0.73  |
|                                        | <75 yr       | 69/1577       | 75/1565           | 0.91 (0.65–1.27) | 0.58  |
| Gender                                  | Women       | 31/449        | 42/468            | 0.75 (0.47–1.20) | 0.23  |
|                                        | Men         | 50/1552       | 42/1541           | 1.07 (0.79–1.44) | 0.67  |
| BMI                                     | ≥25 kg/m²    | 81/1317       | 78/1841           | 1.06 (0.77–1.45) | 0.73  |
|                                        | <25 kg/m²    | 40/684        | 48/680            | 0.81 (0.53–1.24) | 0.32  |
| Intended start or continuation of prasugrel or ticagrelor | Yes | 75/1358     | 71/1353           | 1.05 (0.76–1.46) | 0.75  |
|                                        | No          | 46/643        | 55/636            | 0.85 (0.57–1.26) | 0.41  |
| Diabetes                                | Yes         | 39/371        | 32/352            | 1.15 (0.72–1.85) | 0.36  |
|                                        | No          | 82/1630       | 94/1857           | 0.89 (0.66–1.19) | 0.42  |
| Estimated glomerular filtration rate (eGFR) | ≤60 mL/min  | 77/1670       | 84/1692           | 0.93 (0.68–1.27) | 0.65  |
|                                        | >60 mL/min  | 37/210        | 37/218            | 0.94 (0.59–1.49) | 0.78  |
| History of peripheral vascular disease  | Yes         | 16/106        | 16/123            | 1.17 (0.58–2.37) | 0.66  |
|                                        | No          | 105/1895      | 110/1886          | 0.95 (0.72–1.24) | 0.70  |
| Previous UFH                            | Yes         | 41/952        | 51/949            | 0.80 (0.53–1.21) | 0.28  |
|                                        | No          | 80/1049       | 75/1060           | 1.08 (0.76–1.48) | 0.64  |
| Planned GPI                             | Yes         | 19/128        | 15/285            | 1.11 (0.56–2.19) | 0.77  |
|                                        | No          | 102/1673      | 111/1724          | 0.94 (0.72–1.24) | 0.68  |
| Randomization to anti-thrombin type     | Bivalirudin  | 58/1002       | 60/1010           | 0.97 (0.68–1.40) | 0.89  |
|                                        | UFH         | 63/999        | 66/999            | 0.95 (0.67–1.35) | 0.77  |
Subgroup and sensitivity analyses

Figures 2 and 3 demonstrate the consistency of the two co-primary outcomes in patients with NSTE-ACS and STEMI across predefined subgroups. The effect of radial vs. femoral access appeared consistent across age, sex, BMI, planned or actual use of prasugrel or ticagrelor vs. clopidogrel, diabetes, renal function, history of peripheral vascular disease, and tertiles of the centres’ annual volume of PCI.

Among STEMI but not NSTE-ACS patients, there was a signal for heterogeneity for both co-primary outcomes across tertiles of the centres’ percentage of radial PCI (see Supplementary material online, eTable S3, overall volume of PCI and radial PCI per centre and tertiles boundaries). Similar findings were noted for all-cause mortality (see Supplementary material online, eFigure S5) but not for bleeding (see Supplementary material online, eFigure S6). Finally, no interaction was noted between prior administration of UFH and the occurrence of ST in the study groups, both in STEMI or NST-EACS populations.

Discussion

The results of this prespecified sub-analysis of the MATRIX-Access trial and type of ACS suggest that the overall trial results remain largely consistent in patients with NSTE-ACS and STEMI at presentation. There was no significant interaction for any of the explored outcomes between the access strategy (radial or femoral artery access) and initial clinical presentation in terms of type of ACS (NSTE-ACS, STEMI). In patients with NSTE-ACS, the use of radial access significantly reduced both co-primary outcomes of MACE and NACE, as well as all-cause mortality and cardiac mortality. In patients presenting with STEMI, the use of radial access did not formally reduce all-cause or cardiac mortality.
albeit each endpoint numerically consistently favoured the radial access, and no signal of heterogeneity was observed. As expected, the overall event frequencies differ between NSTE-ACS and STEMI patients (for radial and femoral group combined). That is STEMI patients have more deaths, fewer MIs, more stent thrombosis and more bleeds. The use of radial access for coronary angiography followed by PCI significantly reduced the rate of BARC-actionable (BARC 2–5) bleeding events across the entire spectrum of ACS irrespective of NSTE-ACS or STEMI at the time of presentation.

MATRIX-access is the largest ($n = 8404$) randomized trial to compare radial and femoral access, including unselected patients at high baseline and procedural risk. Our study results differ from those observed in the Radial Vs femorAL access for coronary intervention (RIVAL) study, that reported a possible mortality benefit in STEMI but not in NSTE-ACS patients with radial access, with positive interaction testing. This observation triggered concern within the interventional cardiology community, given the relatively scarce comparative outcome data on radial vs. femoral access among patients with NSTE-ACS before the landmark RIVAL trial was published, particularly as mortality even tended to be higher in patients undergoing invasive management for NSTE-ACS via radial access. In MATRIX-Access, a prerandomization stratification by type of ACS (STEMI ($n = 4010$ patients) and NSTE-ACS ($n = 4394$ patients) resulted in two study groups largely balanced for clinical and angiographic characteristics. At variance with RIVAL, MATRIX-Access did not provide any signal that NSTE-ACS patients may derive less benefit than STEMI patients with radial as compared with femoral access. Hence, the finding of a more favourable effect with radial access in STEMI patients in RIVAL may be explained by random variation. An alternative hypothesis is that operators who recruited patients with NSTE-ACS in RIVAL had lower proficiency towards radial intervention than those who recruited patients with STEMI.

The proportion of PCIs undertaken via radial access emerged as a potential effect modifier in the overall MATRIX population for both
co-primary endpoints of MACE and NACE and overall mortality. However, no such treatment modification effect was observed in our current stratified analysis when NSTE-ACS patients were considered separately. In addition, although the total volume of radial PCI-procedures was higher for operators who recruited NSTE-ACS as opposed to STEMI patients in RIVAL, the interaction between pre-randomization diagnosis (STEMI vs. NSTE-ACS) and access site allocation (radial vs. femoral access) remained highly significant (P = 0.0001) in a multivariable model of predictors of mortality, even after adjustment for baseline variables, operator, and centre experience, suggesting that it was independent of operator and centre radial access experience. Unlike for patients with NSTE-ACS, the present analysis confirmed that for patients with STEMI the proportion of PClIs undertaken via radial access emerged as a treatment modifier with respect to both co-primary endpoints and mortality. This suggests that superiority in efficacy of radial over femoral access in STEMI patients requires considerable expertise that can be met only by high-volume radial operators.

Our present observations lend support to findings from previous position articles, expert opinion papers from Europe and North America, which endorse the preferential use of radial over femoral access but caution against the unrestricted use of radial for STEMI among inexperienced operators. The available data strongly suggest that more efforts should be directed at increasing the adoption of radial vascular access and training operators to acquire the necessary skills. As any procedure or interventions, there is a learning curve with radial interventions, although several studies suggest that the curve is not steep. Since radial access is beneficial across the entire spectrum of ACS, operators may acquire experience in elective cases before engaging in more complex and acute cases.

Limitations of our analysis need to be considered. Although reported subgroups were prespecified in the protocol and statistical analysis plan, we did not adjust for multiple comparisons, increasing the risk of type I error. Bleeding is an outcome that is dependent according to various definitions. Using the BARC consensus definitions for major bleeding, there were substantial reductions in bleeding in both the STEMI and NSTE-ACS cohorts in MATRIX. Moreover, these results were consistent when the GUSTO bleeding definitions were applied. In addition, most centres participating in the MATRIX trial were highly experienced in the radial technique; similar outcomes may not apply in centres performing lower volumes of radial access.

In conclusion, our results show that in unselected patients undergoing invasive management for treatment of ACS, the use of radial compared with femoral access provided consistent benefit across the whole spectrum of ACS without evidence that type of presenting syndrome affected the results of the random access allocation. Adequate operator experience emerged as treatment modifier in STEMI but not NSTE-ACS patients, suggesting that operators willing to transition from a default femoral to a default radial access should first accrue enough transradial volume in elective cases.

**Supplementary material**

Supplementary material is available at European Heart Journal online.

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**Conflict of interest**

Pascal Vranckx reports receiving payment or consulting fees from AstraZeneca, Bayer Health Care, Boehringer-Ingelheim, Daiichi-Sankyo, and The Medicines Co. outside the submitted work. Giuseppe Ando reports receiving payment or consulting fees from AstraZeneca, Bayer Health Care, Menarini, Daiichi-Sankyo, Abbott Vascular and Biotronik outside the submitted work. Francesco Tomassini reports receiving payment or consulting fees from Bayer Health Care and Daiichi-Sankyo outside the submitted work. Peter Juni has received research grants to the institution from Astra Zenea, Biotronik, Biosensors International, Eli Lilly and The Medicines Company, and serves as unpaid member of the steering group of trials funded by Astra Zenea, Biotronik, Biosensors, St Jude Medical and The Medicines Company. Stephan Windecker reports receiving has received research grants to the institution from Astra Zenea and speaking or consulting fees from MATRIX outside the submitted work. Marco Valgimigli reports grants from The Medicines Company, grants from Terumo, during the study; grants from AstraZeneca, and personal fees from Terumo, St Jude Vascular, and Abbott Vascular, outside the submitted work.

**References**

1. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. Circulation 2006;114:774–782.

2. Mehran R, Pocock S, Nikolsky E, Dangas GD, Clayton T, Claessens BE, Caixeta A, Fes T, Manoukian SV, White H, Bertrand M, Ohman EM, Parish H, Lansky AJ, Lincoff AM, Stone GW. Impact of bleeding on mortality after percutaneous coronary intervention results from a patient-level pooled analysis of the REPLACE-2 (randomized evaluation of PCI linking angiomax to reduced clinical events), ACUITY (acute catheterization and urgent intervention triage strategy), and HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trials. JACC Cardiovasc Interv 2011;4:654–664.

3. Rao SV, O’grady K, Pepeer KS, Granger CB, Newby LK, Mahaffey KW, Moliternino DJ, Lincoff AM, Armstrong PW, Van de Werf F, Califf RM, Harrington RA. A comparison of the clinical impact of bleeding measured by two different classifications among patients with acute coronary syndromes. J Am Coll Cardiol 2006;47:809–816.

4. Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P, Budaj A, Niemela M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afsal R, Jliner CD, Chrolavicius S, Mehta SR. 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.

5. Valgimigli M, Calabro P, Cortese B, Frigoli E, Garducci S, Rubartelli P, Ando G, Santarelli A, Gali M, Garbo R, Repetto A, Imaa S, Briguori C, Limbruno U, Vielini R, Gagnor A, Scientifie foundation and possible implications for practice of the Minimizing Adverse Haemorrhagic Events by Transradial Access Site andSystemic Implementation of AngioX (MATRIX) trial. J Cardiovasc Transl Res 2014;7:101–111.

6. Valgimigli M, Gagnor A, Calabro P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briiguori C, Ando G, Repetto A, Limbruno U, Cortese B, Siganzeara P, Lupi A, Gali M, Colangelo S, Imaa S, Assiello P, Prerstedero P, Sardella G, Varbella F, Esposto G, Santarelli A, Tressoli S, Nazzaro M, Zingarelli A, de Cesare N, Rigatelli S, Tosi P, Palmieri C, Brugiatella S, Rao SV, Heg D, Rothenbuhler M, Vranckx P, Juni P. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015;385:2465–2476.

7. Steg PG, James SK, Airo DD, Badano LP, Blomstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Gruentzig PP, Halvorsen S, Huber K, Juni P, Kastrati A, Knauth J, Lenzen MJ, Mahaffey KW, Valgimigli M, van ’T Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012;33:2569–2619.

8. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V, Valgimigli M, Vranckx P, Taggart D, Sabik JF, Cutlip DE, Krucoff MW, Ohman EM, Steg PG, White H. Standardized bleeding definitions for cardiovascular clinical trials: a consensus
report from the Bleeding Academic Research Consortium. Circulation 2011;123:2736–2747.
9. An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. The GUSTO investigators. N Engl J Med 1993;329:673–682.
10. Rao AK, Pratt C, Berke A, Jaffe A, Ockene I, Schreiber TL, Bell WR, Kratzerud G, Robertson TL, Ternin ML. Thrombolysis in Myocardial Infarction (TIMI) Trial–phase I: hemorrhagic manifestations and changes in plasma fibrinogen and the fibrinolytic system in patients treated with recombinant tissue plasminogen activator and streptokinase. J Am Coll Cardiol 1988;11:1–11.
11. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hannon M, Krucoff MW, Serruys PW. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007;115:2344–2351.
12. Hamon M, Pristipino C, Di Mario C, Nolan J, Ludwig J, Tubaro M, Sabate M, Muri-Ferre J, Huber K, Niemela K, Haude M, Wijns W, Dudek D, Fajadet J, Kiemeneij F. Consensus document on the radial approach in percutaneous cardiovascular interventions: position paper by the European Association of Percutaneous Cardiovascular Interventions and Working Groups on Acute Cardiac Care® and Thrombosis of the European Society of Cardiology. EuroIntervention 2013;8:1242–1251.
13. Dauerman HL, Rao SV, Resnic FS, Applegate RJ. Bleeding avoidance strategies. Consensus and controversy. J Am Coll Cardiol 2011;58:1–10.
14. Caputo RP, Tremmel JA, Rao S, Gilchrist IC, Pyne C, Pancholy S, Frazier D, Gulati R, Shelding K, Bertrand O, Patel T. Transradial arterial access for coronary and peripheral procedures: executive summary by the Transradial Committee of the SCAI. Catheter Cardiovasc Interv 2011;78:823–839.
15. Eleid MF, Rihal CS, Gulas R, Bell MR. Systematic use of transradial PCI in patients with ST-segment elevation myocardial infarction: a call to “arms”. JACC Cardiovasc Interv 2013;6:1145–1148.
16. Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehills J, Mkhayer J, Storey RF, Windecker S, Baumgartner H, Gaemperli O, Achenbach S, Agewall S, Badimon L, Baret J, Bueno H, Bugiardini R, Carerj S, Casselman F, Cuijper T, Erol C, Fitzsimons D, Halle M, Hamm C, Hillick-Smith D, Huber K, Ilodromitis E, James S, Lewis BS, Lip GY, Piepoli MF, Richter D, Rosemann T, Sechtem U, Steg PG, Vrints C, Luis Zamorano J. 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. Eur Soc Cardiol (ESC) Eur Heart J 2016;37:267–315.
17. Hess CN, Peterson ED, Neely ML, Dai D, Hillegas WB, Krucoff MW, Kuchler MA, Messenger JC, Pancholy S, Piana RN, Rao SV. 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.
18. Ball WT, Shanell W, Jolly SS, Hong T, Kutryk MJ, Graham JJ, Fam NP, Chisholm RJ, Cheema AN. Characterization of operator learning curve for transradial coronary interventions. Circ Cardiovasc Interv 2011;4:336–341.