Journal Pre-proof

Radial versus femoral access in ACS patients undergoing complex PCI is associated with consistent bleeding benefit and no excess of risks

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PII: S0828-282X(22)00394-4

DOI: https://doi.org/10.1016/j.cjca.2022.06.014

Reference: CJCA 4379

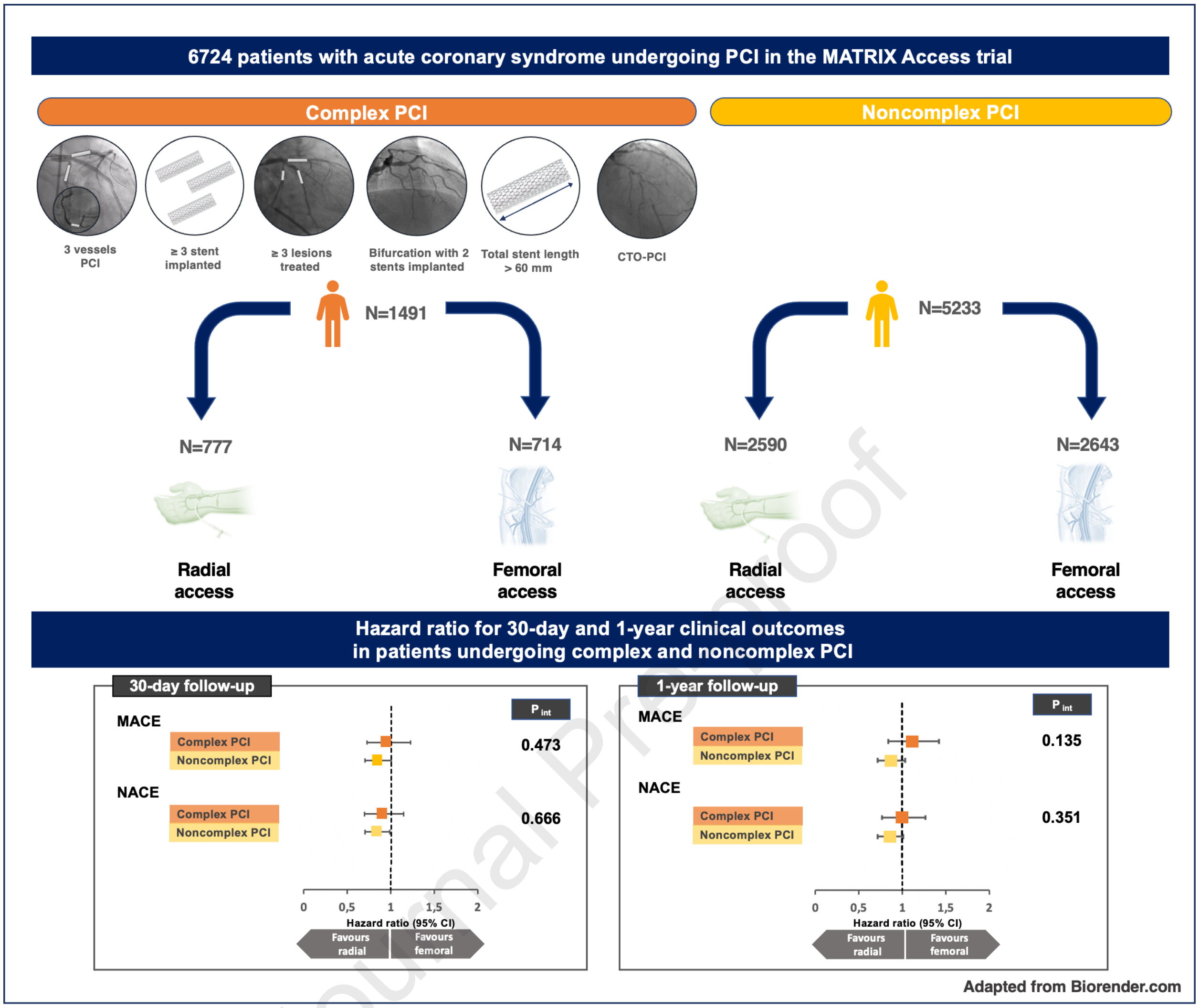
To appear in: *Canadian Journal of Cardiology*

Received Date: 20 January 2022

Revised Date: 15 June 2022

Accepted Date: 17 June 2022

Please cite this article as: Landi A, Branca M, Vranckx P, Leonardi S, Frigoli E, Heg D, Calabro P, Esposito G, Sardella G, Tumscitz C, Garducci S, Ando G, Limbruno U, Sganzerla P, Santarelli A, Briguori C, de la Torre Hernandez JM, Pedrazzini G, Windecker S, Valgimigli M, for the MATRIX Investigators, Radial versus femoral access in ACS patients undergoing complex PCI is associated with consistent bleeding benefit and no excess of risks, *Canadian Journal of Cardiology* (2022), doi: https://doi.org/10.1016/j.cjca.2022.06.014.


6724 patients with acute coronary syndrome undergoing PCI in the MATRIX Access trial
Complex PCI
Noncomplex PCI
3 vessels PCI
≥ 3 stent implanted
≥ 3 lesions treated
Bifurcation with 2 stents implanted
Total stent length > 60 mm
CTO-PCI
N=1491
N=5233
N=777
N=714
N=2590
N=2643
Radial access
Femoral access
Radial access
Femoral access
Hazard ratio for 30-day and 1-year clinical outcomes in patients undergoing complex and noncomplex PCI
30-day follow-up
1-year follow-up
P int
MACE
Complex PCI
Noncomplex PCI
0.473
NACE
0.666
0.135
0.351
0
0,5
1
1,5
2
Hazard ratio (95% CI)
Favours radial
Favours femoral
Adapted from Biorender.com

Radial versus femoral access in ACS patients undergoing complex PCI is associated with consistent bleeding benefit and no excess of risks

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Running title: Access site selection and complex PCI.

Word count (including title page, text, references, figure and table legends): 4,965

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ABSTRACT (244 words)

Background. The comparative effectiveness of transradial (TRA) compared with transfemoral access (TFA) in acute coronary syndrome (ACS) patients undergoing complex percutaneous coronary intervention (PCI) remains unclear.

Methods. Among 8,404 ACS patients in the *Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX* (MATRIX)-Access trial, 5,233 underwent noncomplex (TRA, n=2,590 and TFA, n=2,643) and 1,491 complex PCI (TRA, n=777 and TFA, n=714). Co-primary outcomes were major adverse cardiovascular events (MACE, the composite of all-cause mortality, myocardial infarction, or stroke) and the composite of MACE and BARC type 3-5 bleeding (net adverse cardiovascular events, NACE) at 30 days.

Results. Rates of 30-day MACE (hazard ratio [HR]:0.94; 95% confidence interval [CI]:0.72-1.22) or NACE (HR:0.89; 95% CI:0.69-1.14) did not significantly differ between groups in the complex PCI group, whereas both primary endpoints were lower (HR:0.84; 95% CI:0.70-1.00, HR:0.83; 95% CI:0.70-0.98, respectively) with TRA among noncomplex PCI patients, with negative interaction testing (P_{int} 0.473 and 0.666, respectively). Access-site BARC type 3 or 5 bleeding was lower with TRA, consistently among complex (HR:0.18; 95% CI:0.05-0.63) and noncomplex (HR:0.41; 95% CI:0.20-0.85) PCI patients, whereas the former group had a greater absolute risk reduction of 1.7% (number needed to treat: 59) due to their higher absolute risk.

Conclusions. Among ACS patients, PCI complexity does not affect the comparative efficacy and safety of TRA versus TFA, whereas the absolute risk reduction of access-site major bleeding was greater with TRA compared with TFA in complex as opposed to noncomplex PCI.

SUMMARY (74 words)

We evaluated the comparative efficacy and safety of transradial (TRA) compared with transfemoral access (TFA) in patients with acute coronary syndrome undergoing complex percutaneous coronary intervention (PCI). Among ACS patients, PCI complexity does not affect the comparative efficacy and safety of TRA versus TFA, whereas the absolute risk reduction of access-site major bleeding was greater with TRA compared with TFA in complex as opposed to noncomplex PCI.

INTRODUCTION

The adoption of transradial access (TRA) is recommended as default approach for the invasive management of patients with acute coronary syndrome (ACS) by current American and European guidelines (1,2), given the established benefit in reducing the risk of major bleeding and vascular complications compared with transfemoral access (TFA) (3–5). Furthermore, randomized clinical trials (RCT) have shown, albeit inconsistently, that TRA is associated with lower risk of all-cause mortality and acute kidney injury (AKI) (6,7) among ACS patients undergoing coronary angiography and/or percutaneous coronary intervention (PCI).

Patients undergoing complex PCI incur higher risks of ischemic and bleeding complications (8–10), owing to more frequent use of large bore catheters and higher prevalence of comorbidities such as peripheral artery disease (PAD) or chronic kidney disease (CKD). Therefore, TRA may be particularly advantageous among patients undergoing complex PCI. However, whether TRA is associated with similar procedural success and comparable clinical outcomes as well as lower major access site bleeding than TFA among patients undergoing complex PCI remains unclear. Recently, a randomized trial demonstrated the superiority of TRA over TFA in reducing the composite of clinically relevant access-site related bleeding or vascular complications in patients undergoing complex PCI with large-bore guiding catheters (11). Although not powered for ischemic outcomes, this trial demonstrated a numerical imbalance in major adverse cardiovascular events (MACE) events in favor of TFA (12), which may reflect greater challenges in accomplishing a complex PCI by means of TRA.

We sought therefore to investigate the comparative efficacy and safety of TRA versus TFA in ACS patients undergoing complex PCI from the *Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX* (MATRIX)-Access trial.

METHODS

Study design

This is a post-hoc analysis of the MATRIX trial, a program of 3 independent randomized controlled trials (ClinicalTrials.gov; NCT01433627) in patients with ACS undergoing invasive management (13). The first trial (MATRIX-Access) compared TRA versus TFA in 8,404 ACS patients (4,6), whereas MATRIX-

Antithrombin and MATRIX Treatment Duration (6,14) compared bivalirudin versus unfractionated heparin (UFH) and prolonged post-PCI bivalirudin infusion versus short-term bivalirudin administration in patients undergoing PCI. The trial was approved by the institutional review board at each participating site, and all patients gave written informed consent.

All participants enrolled in the MATRIX-Access trial were considered eligible for this analysis.

Complex PCI was defined as PCI with at least one of the following characteristics: three-vessels PCI, ≥3 implanted stents, ≥3 treated lesions, bifurcation intervention with 2 stents implanted, total stent length > 60 mm or chronic total occlusion (CTO)-PCI. These criteria were previously defined by Giustino et al (8) and are frequently used in clinical studies (9,10,15). Patients undergoing PCI without any of the above-mentioned criteria were classified as noncomplex PCI.

Follow-up and study outcomes

The endpoints of the MATRIX-Access trial have been previously reported (4,6). The two co-primary outcomes were MACE (the composite of all-cause mortality, myocardial infarction [MI], or stroke) and net adverse clinical events (NACE), defined as the composite of MACE or major bleeding not related to coronary artery bypass grafting (Bleeding Academic Research Consortium [BARC] type 3 or 5) at 30-days. Secondary outcomes included the composite of all-cause mortality, MI, stroke, urgent target vessel revascularization (TVR) or definite stent thrombosis, each component of the co-primary outcomes and cardiovascular mortality. Key secondary outcome was access site-related BARC type 3 or 5 bleeding at 30 days. Bleeding was also assessed and adjudicated on the basis of the Thrombolysis In Myocardial Infarction (TIMI) and Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) scales. As secondary endpoints, ischemic and bleeding events were also assessed at 1 year.

Sensitivity analyses were performed excluding patients with any crossover of the randomized access site or subjects undergoing staged procedures (i.e. only patients who underwent index PCI). An independent clinical events committee, blinded to treatment allocation, adjudicated all adverse events.

Statistical analysis

All analyses were performed according to the intention-to-treat principle. Differences across groups were assessed using the student t-test in case of continuous variables and the chi-square or Fisher exact test in case of categorical data. The cumulative incidence of the primary and secondary endpoints was estimated by the Kaplan-Meier method. Hazard ratios (HRs) and 95% confidence intervals (CIs) were generated with Cox proportional-hazards models. The consistency of the treatment effect of TRA versus TFA between the complex and noncomplex PCI subgroups was evaluated with formal interaction testing. We performed stratified logistic regressions by subgroups, including center's annual volume of PCI, center's proportion of radial PCI, clinical presentation, age, gender, access sheath size, body mass index, diabetes mellitus, CKD, PAD, randomization to bivalirudin or UFH. Continuous relation between procedure duration and MACE was assessed using restricted cubic splines. The analyses were done using Stata release 16.1 (StataCorp LLC, College Station, Texas).

RESULTS

Study population

Among 8,404 patients enrolled in the MATRIX-Access trial, 6,724 patients underwent PCI (**Supplemental Figure S1**). Of those, 1,491 (22.2%) patients underwent complex PCI and 5,233 (77.8%) subjects noncomplex PCI. In the complex PCI group 777 underwent TRA and 714 subjects TFA, whereas in the noncomplex PCI group 2,590 and 2,643 patients underwent TRA and TFA, respectively.

Baseline and procedural characteristics

Patients undergoing complex PCI were older and presented more frequently diabetes, previous MI, PAD and NSTE-ACS (**Supplemental Table S1**). Patients who underwent complex PCI had more frequently lesions involving the left coronary system (particularly the left main) and had longer fluoroscopy and procedural times compared with the noncomplex PCI group (**Supplemental Table S2**).

Baseline demographics and clinical presentation according to PCI complexity and randomly assigned access site were well matched (**Table 1**). Patients allocated to TRA experienced crossover more frequently than those randomized to TFA, in either complex (10% vs 3%) or noncomplex PCI groups (5% vs 2%). 6 Fr was the most used sheath size in both randomized access sites, although a higher use of 7 Fr sheaths was observed in patients randomized to TFA in either complex or noncomplex PCI groups. Angiographic and procedural characteristics, stratified by PCI complexity, were otherwise well balanced between groups (**Table 2)**, as medications at discharge (**Supplemental Table S3**). The prevalence of complex PCI features was also well balanced between the two access sites (**Supplemental Figure S2)**.

Clinical outcomes in patients with complex PCI

Thirty-day and 1-year clinical outcomes in patients undergoing complex PCI are shown in **Figure 1** and **Supplemental Table S4**. Complex PCI was associated with a higher risk of MACE (HR:1.56; 95% CI:1.33 to 1.82; P < 0.001) and NACE (HR 1.54, 95% CI: 1.32 to 1.79; p < 0.001) at 30 days, which was driven by an increased risk of all-cause mortality and MI. The risk of BARC type 3 or 5 bleeding was numerically increased in the complex PCI group at 30 days (HR: 1.38; 95% CI: 0.96 to 1.97; P= 0.083) and complex PCI resulted in a significantly higher risk of access site-related BARC 3 or 5 bleeding (HR: 1.82; 95% CI: 1.03 to 3.22; P= 0.039) at 30 days.

Clinical outcomes according to the randomized access site and PCI complexity

Table 3 and **Supplemental Table S5** summarize the primary and secondary outcomes at 30 days and 1 year according to PCI complexity and randomized access site.

Primary outcomes

There was no evidence of significant interactions for the treatment effects on co-primary outcomes between the complex and noncomplex PCI groups (P_{int} for MACE=0.473, P_{int} for NACE=0.666). Among patients who underwent complex PCI, 30-day MACE occurred in 112 (14.4%) patients assigned to TRA and 109 (15.3%) patients assigned to TFA (HR: 0.94; 95% CI: 0.72 to 1.22; P=0.643), and NACE occurred in 121 (15.6%) patients assigned to TRA and 124 (17.4%) patients assigned to TFA (HR: 0.89; 95% CI: 0.69 to 1.14; P=0.349) (**Table 3, Figure 2**). In the noncomplex PCI group, 30-day MACE occurred in 229 (8.8%) assigned to TRA and 278 (10.5%) assigned to TFA (HR: 0.84; 95% CI: 0.70 to 1.00; P=0.046), and NACE occurred in 257 (9.9%) assigned to TRA and 314 (11.9%) assigned to TFA (HR: 0.83; 95% CI: 0.70 to 0.98; P=0.028) (**Table 3, Figure 2**). The rates of co-primary outcomes at 1 year are shown in **Figure 3** and **Supplemental Table S5**.

Sensitivity analyses of the two coprimary outcomes excluding patients with crossover to a non-randomized access (**Supplemental Table S6**) or subjects undergoing staged procedures (**Supplemental Table S7**) were consistent with the main analyses.

Secondary outcomes

There was no statistically significant heterogeneity of treatment effect on all-cause and cardiovascular mortality at 30 days according to PCI complexity (P_{int}= 0.096 and 0.135 respectively, **Table 3, Figure 2**). Yet, TRA was associated with fewer all-cause and cardiovascular death rates compared with TFA in patients with noncomplex (HR: 0.61; 95% CI: 0.39 to 0.96; P= 0.033; HR: 0.62; 95% CI: 0.39 to 0.99; P=0.046; respectively), but not in those with complex PCI (HR: 1.13; 95% CI: 0.64 to 1.98; P=0.675; HR: 1.10; 95% CI: 0.61 to 2.00; P= 0.747; respectively). MI and definite stent thrombosis did not differ between groups within the complex and noncomplex PCI strata, with negative interaction testing (P_{int} =0.671 and 0.824, respectively**)**.

There was no significant heterogeneity of the treatment effect on stroke according to PCI complexity at 30 days. The treatment effect on stroke was directionally opposite at 1 year (P_{int} = 0.029), with TRA being associated with a lower risk of stroke compared with TFA in patients undergoing complex PCI (HR: 0.11; 95% CI: 0.01 to 0.92; P=0.041) and a similar risk in subjects who underwent noncomplex PCI (HR: 1.33; 95% CI: 0.65 to 2.74; P=0.437).

There was no evidence of interaction for the treatment effects on BARC, TIMI or GUSTO bleeding across PCI complexity strata (**Table 3).** Compared with TFA, TRA was associated with significantly lower rates of BARC type 3 or 5 bleeding in patients undergoing complex PCI (HR: 0.42; 95% CI: 0.22 to 0.81; P=0.010) and numerically lower rates among noncomplex PCI patients (HR: 0.72; 95% CI: 0.49 to 1.06; P=0.097). Of note, TRA resulted in lower rates of BARC type 2, 3 or 5 bleeding in both groups.

Access-site BARC type 3 or 5 bleeding was lower with TRA, consistently among complex (HR 0.18; 95% CI: 0.05 to 0.63; P=0.007) and noncomplex (HR 0.41; 95% CI: 0.20 to 0.85; P= 0.016) PCI patients, whereas the former group had a greater absolute risk reduction of 1.7% (number needed to treat to benefit [NNTB]: 59) due to their higher absolute risk. Among noncomplex PCI patients, TRA was still associated with a significant almost 60% risk reduction for access-site related BARC 3 or 5 bleeding with an absolute risk difference of 0.5% between the two access groups, corresponding to a NNTB of 200.

Subgroup analysis and spline functions

The effects of TRA versus TFA for the co-primary outcomes of MACE (**Figure 4**) or NACE (**Figure 5**) in the complex PCI and noncomplex PCI groups were largely consistent across pre-specified subgroups, with no significant interaction. **Supplemental Figure S3 and S4** show the stratified analysis of all-cause mortality and BARC type 3 or 5 bleeding, which were consistent with the main analysis. Access sheath size was the only subgroup variable demonstrating a significant interaction with the randomized access site (P_{int} =0.046) for all-cause mortality in patients undergoing complex PCI, suggesting higher mortality rates with TRA than TFA with 6-french but not with > 6-french sheath sizes. Conversely, we found positive tests for trend across tertiles of the centers percentage of radial PCI and randomized antithrombotic therapy for all-cause mortality ($P_{int} \leq$ 0.041) in the noncomplex PCI group, with a more pronounced benefit of TRA in centers that did 80% or more radial PCI or in patients allocated to UFH.

Spline functions of 30-day and 1-year MACE in patients undergoing complex and noncomplex PCI did not demonstrate a significant impact of procedure duration on outcomes in the two study groups, as shown in the **Supplemental Figure S5**.

Clinical outcomes according to type and numbers of complex criteria fulfilled

The effect of TRA versus TFA for MACE, NACE and all-cause mortality (**Supplemental Figure S6 and S7**) was consistent across the components of the complex PCI definition; results were also stratified according to progressive number of complex PCI criteria fulfilled.

DISCUSSION

The relationship between complex PCI, ischemic and bleeding outcomes is multifactorial in etiology, relying on patient's comorbidities, the extent of coronary artery disease, completeness of revascularization and optimal antithrombotic strategies (16,17). Beyond these contributing factors, access site selection remains key in mitigating the risk of bleeding while adequately supporting revascularization technique (12). To the best of our knowledge, this is the largest study investigating TRA versus TFA in ACS patients undergoing complex PCI. The main findings of the current analysis can be summarized as follows:

1. The complexity of PCI did not affect the comparative efficacy and safety of TRA versus TFA, which is supported by negative interaction testing for the co-primary or major secondary endpoints.
2. While NACE and MACE and mortality were lower with TRA among noncomplex PCI patients, these endpoints did not significantly differ in patients who had undergone complex PCI, with rates of events numerically favoring TRA for both co-primary endpoints at 30 days, but disfavoring TRA for MACE at 1 year and mortality at both 30 days and 1 year, with negative interaction testing across complexity strata for all-cause death at 30 days (P_{int}=0.096).
3. Among complex PCI patients, TRA reduced major access-site bleeding with greater absolute and relative risk benefit compared with noncomplex PCI.

Several studies have recently focused on patients undergoing complex interventions. However, the vast majority of these studies has mainly investigated on the optimal revascularization and/or antithrombotic strategies (8,9,18,19), with significant heterogeneity in the definition of complex PCI. A small number of studies analyzed the role of access site selection, in the context of patients with chronic coronary syndrome (CCS) undergoing PCI of CTO, heavily calcified lesions, left main or complex bifurcations (11). Conversely, this is the first study on complex PCI reporting the use of TRA versus TFA in ACS patients, who typically exhibit higher risk of ischemic events especially following complex procedures. In the present study, we used the previously introduced definition of complex PCI by Giustino et al. (8) since it integrates features of procedural complexity and has been extensively adopted by multiple investigations (9,10,15). To this aim, the original complex PCI definition was applied, including CTO PCI which is not frequently performed at index procedure in ACS patients. However, our complex PCI definition also took into account staged procedures which were performed during or after hospitalization.

The COLOR trial (11) investigated the value of TRA versus TFA in 388 patients undergoing complex PCI with large-bore guiding catheters (≥7 Fr). Our present analysis extends previous observations by showing that TRA mitigates not only minor, but also major BARC bleeding compared with TFA among patients undergoing complex PCI, in whom the absolute bleeding risk is higher and leading to a greater absolute benefit of TRA compared with TFA. A recent meta-analysis of observational studies investigating the use of TRA versus TFA in CTO-PCI also found that TRA was associated with fewer access-site complications and major bleeding with similar procedural success compared with TFA (20). Notably, excluding patients with IABP, dual access (e.g. radial plus femoral, radial plus radial or femoral plus femoral) was not used for CTO-PCI in the MATRIX trial. Possible explanations for these findings might reside into the selection of non-complex CTO for PCI or the choice of attempting a simple, single-access approach shortly after the index event, leveraging a typical dual-access planned CTO procedure in case of unsuccessful initial PCI. An unexpected finding from the COLOR trial was a borderline higher rate of MACE at 30 days with TRA compared with TFA. The results of our study are reassuring as they do not show a significant increased rate of MACE among complex PCI patients who underwent TRA compared with TFA, albeit a slight numerical higher rate of MACE disfavored TRA at 1 year follow-up. Additional evidence supporting similar effectiveness between TFA and TRA with respect to MACE among complex PCI patients comes from the lack of relationship between the duration of the procedure (as a proxy of procedural complexity) and outcomes in the two study groups. Finally, when each of the PCI complexity components where separately appraised, we did not see heterogeneity with respect to the treatment effects between TRA and TFA. Although our findings are reassuring in showing that PCI complexity does not affect the comparative effectiveness of TRA versus TFA, they should be interpreted taking into account that operators qualified for the participation in the MATRIX trial if had performed ≥50% of intervention in ACS patients through TRA in the previous 12 months, with an absolute number of trans-radial coronary interventions of more than 75. The benefit in terms of MACE and mortality which were observed in the entire study cohort were no longer evident among complex PCI patients. These observations may simply reflect the lack of power to detect treatment effects in the complex PCI patient subset. This interpretation is supported by the negative interaction testing between TRA and TFA across PCI complexity strata. Moreover, the rates of MI or stroke were not higher with TRA compared with TFA in complex PCI patients. The only component of the co-primary endpoints which numerically favored TFA among complex PCI patients was 30-day or 1-year mortality, with negative interaction testing.

It is intriguing that the numerical excess of mortality for TRA among complex PCI patients apparently accrued entirely from patients who were intervened upon with 6-french guiding catheters, in whom there was a numerical excess of fatal events with TRA compared with TFA (HR:1.52; 95% CI: 0.92 to 2.45) whereas no fatal event occurred among patients who received > 6-French access sheath size, with positive interaction testing. This observation should be interpreted with great caution, taking into account that it originates from subgroup analyses of a secondary endpoint and few patients used greater than 6-French access sheath size, especially in the TRA group. Yet, it is interesting that TRA was associated to 3-fold less frequent use of large-bore access site compared with TFA among complex PCI patients. These findings reinforce the notion that adequate sheath size choice remains key to optimize PCI results and clinical outcomes, irrespective of access site selection.

A significant interaction effect between randomized access site compared with qualifying complexity of PCI on stroke was found at 1 year, but not at 30 days. Given the low number of events, in absence of any plausible biological explanation, it might represent a spurious finding.

Study limitations

Although the present analysis is the largest evaluating patients undergoing complex PCI through TRA or TFA, the MATRIX-Access was not powered to explore differences in outcomes across subgroups. In addition, randomization was not stratified by PCI complexity and stratification of the population in complex and noncomplex PCI groups led to subgroups which are relatively underpowered. Third, these results are not generalizable to all patients undergoing complex PCI, due to the high operator's expertise in the MATRIX trial and the complex PCI definition used for this analysis, which has been mainly validated in CCS patients. Finally, the low number of ACS patients with severe hemodynamic instability and/or cardiogenic shock in the MATRIX trial highlights the need to interpret our results in the context of patients in whom both radial and femoral access are feasible and felt to be in potential equipoise. We cannot not exclude that some very complex lesions (grafts, heavily calcified lesions requiring atherectomy, CTO requiring dual access) were under-represented in the trial due to operators' preference not randomize these patients. Yet, randomization took place before knowing the coronary anatomy.

CONCLUSIONS

PCI complexity did not affect the comparative efficacy and safety of TRA versus TFA in ACS patients, based on consistently negative interaction testing across complex or noncomplex PCI strata for both co-primary endpoints of NACE and MACE and other explored secondary endpoints. The benefits of TRA in terms of reduced access site bleeding were entirely preserved among complex PCI patients who derived greater relative and absolute bleeding risk reduction with TRA than TFA compared with noncomplex PCI patients.

Funding

The trial was sponsored by the Società Italiana di Cardiologia Invasiva (GISE, a non-profit organisation), which received grant support from The Medicines Company and Terumo. This substudy did not receive any direct or indirect funding.

Disclosures

Dr. Branca, Dr. Frigoli and Dr. Heg are with CTU Bern, University of Bern, which has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. In particular, pharmaceutical and medical device companies provide direct funding to some of these studies. For an up-to-date list of CTU Bern's conflicts of interest see http://www.ctu.unibe.ch/research/declaration_of_interest/index_eng.html

Prof. Vranckx reports personal fees from Bayer, personal fees from Daiichi Sankyo, and personal fees from CLS Behring.

Dr. Leonardi received personal fees for advisory board participation from AstraZeneca, Bayer, Chiesi, BMS-Pfizer and educational grants from AstraZeneca.

Dr. Andò reports personal fees and non-financial support from Bayer, Daiichi Sankyo, Pfizer - Bristol Myers Squibb, Boeringer Ingelheim, personal fees from Menarini, AstraZeneca, Chiesi, and Biosensors, and non-financial support from Amgen, outside the submitted work.

Dr. Jose M. de la Torre Hernandez reports grants from Abbott Medical, Biosensors, Bristol Myers Squibb, Amgen, honoraria or consultation fees from Boston Scientific, Medtronic, Biotronik, AstraZeneca, Daiichi-Sankyo.

Prof. Windecker reports research and educational grants to the institution from Abbott, Amgen, Astra Zeneca, BMS, Bayer, Biotronik, Boston Scientific, Cardinal Health, CardioValve, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Johnson & Johnson, Medicure, Medtronic, Novartis, Polares, OrPha Suisse, Pfizer, Regeneron, Sanofi-Aventis, Sinomed, Terumo, V-Wave. Prof. Windecker serves as unpaid advisory board member and/or unpaid member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, Bayer. BMS, Boston Scientific, Biotronik, Cardiovalve, Edwards Lifesciences, MedAlliance, Medtronic, Novartis, Polares, Sinomed, Terumo, V-Wave and Xeltis, but has not received personal payments by pharmaceutical companies or device manufacturers. He is also member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration.

Prof. Valgimigli reports grants and personal fees from Abbott, personal fees from Chiesi, personal fees from Bayer, personal fees from Daiichi Sankyo, personal fees from Amgen, grants and personal fees from Terumo, personal fees from Alvimedica, grants from Medicure, grants and personal fees from AstraZeneca, personal fees from Biosensors, personal fees from Idorsia, outside the submitted work. The other authors report no relationships relevant to the contents of this paper to disclose.

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FIGURE LEGENDS

Figure 1. Clinical outcomes in patients undergoing complex and noncomplex PCI at 30 days (panel A) and 1 year (panel B). *Abbreviations: PCI= percutaneous coronary intervention; MACE= major adverse cardiovascular events; NACE= net adverse clinical events; CV= cardiovascular; MI= myocardial infarction; TVR= target vessel revascularization; ST= stent thrombosis; BARC= Bleeding Academic Research Consortium.*

Figure 2. Radial versus femoral access in patients undergoing complex or noncomplex percutaneous coronary intervention (PCI). Complex PCI was defined as any of the following: three-vessel PCI, ≥ 3 implanted stents, ≥ 3 treated lesions, bifurcation with 2 stents implanted, total stent length > 60 mm or chronic total occlusion (CTO)-PCI. Abbreviations: *MACE= major adverse cardiovascular events; NACE= net adverse clinical events; MI, myocardial infarction; BARC= Bleeding Academic Research Consortium; CI= confidence interval; NNTB= number needed to treat to benefit.*

Figure 3. Kaplan-Meier estimates and HRs for major adverse clinical events (MACE) (panel A) and net adverse clinical events (NACE) (panel B) at 12 months comparing radial versus femoral access in patients undergoing complex and noncomplex PCI. *HR= hazard ratio; CI= confidence interval;*

Figure 4. Sub-groups analysis for major adverse cardiovascular events (MACE) in patients undergoing complex and noncomplex PCI. *PCI=percutaneous coronary intervention. ACS=acute coronary syndrome. STEMI=ST-segment elevation myocardial infarction. NSTE-ACS=non-ST-segment elevation acute coronary syndrome; BMI= body mass index; CKD= chronic kidney disease; UFH= unfractionated heparin; CI= confidence interval.* *p values are for trend across ordered groups.

Figure 5. Sub-groups analysis for net adverse clinical events (NACE) in patients undergoing complex and noncomplex PCI. *PCI=percutaneous coronary intervention. ACS=acute coronary syndrome. STEMI=ST-segment elevation myocardial infarction. NSTE-ACS=non-ST-segment elevation acute coronary syndrome; BMI= body mass index; CKD= chronic kidney disease; UFH= unfractionated heparin; CI= confidence interval.* *p values are for trend across ordered groups.

TABLES

Table 1. Baseline characteristics in patients undergoing complex and noncomplex PCI randomized to radial versus femoral access. *Abbreviations: BMI, body mass index; CAD, coronary artery disease; MI, myocardial infarction; PCI= percutaneous coronary intervention; CABG= coronary artery bypass grafting; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease; STE-ACS= ST-segment elevation acute coronary syndrome; NSTE-ACS= non-ST elevation acute coronary syndrome; LVEF= left ventricular ejection fraction; eGFR, estimated glomerular filtration rate.*

	Complex PCI (n=1,491)			Noncomplex PCI (n= 5,233)		
	Radial Access (n= 777)	Femoral Access (n=714)	P-value	Radial Access (n=2,590)	Femoral Access (n=2,643)	P-value
Age ≥ 75 years	217 (28%)	200 (28%)	1.000	607 (23%)	645 (24%)	0.418
Male sex	613 (79%)	550 (77%)	0.416	2021 (78%)	1992 (75%)	0.024
BMI, kg/m^2	27.0 ± 4.0	27.1 ± 4.1	0.466	27.2 ± 4.1	27.1 ± 4.1	0.561
Diabetes mellitus	232 (30%)	176 (25%)	0.027	541 (21%)	552 (21%)	1.000
Smoker	434 (56%)	381 (53%)	0.349	1485 (57%)	1523 (58%)	0.845
Hypercholesterolemia	338 (44%)	331 (46%)	0.274	1116 (43%)	1186 (45%)	0.200
Hypertension	500 (64%)	461 (65%)	0.957	1582 (61%)	1647 (62%)	0.363
Family history of CAD	211 (27%)	181 (25%)	0.444	729 (28%)	751 (28%)	0.830
Previous MI	131 (17%)	119 (17%)	0.945	335 (13%)	365 (14%)	0.372
Previous PCI	128 (16%)	108 (15%)	0.479	377 (15%)	364 (14%)	0.428
Previous CABG	38 (5%)	32 (4%)	0.715	53 (2%)	83 (3%)	0.015
Previous CVA	48 (6%)	45 (6%)	1.000	108 (4%)	130 (5%)	0.208
Peripheral Vascular Disease	85 (11%)	65 (9%)	0.263	170 (7%)	209 (8%)	0.062
COPD	43 (6%)	54 (8%)	0.116	136 (5%)	169 (6%)	0.087
Anemia*	187 (24%)	152 (21%)	0.216	458 (18%)	483 (18%)	0.589
Clinical presentation						
STEMI	334 (43%)	306 (43%)	1.000	1506 (58%)	1512 (57%)	0.502
NSTE-ACS	414 (53%)	360 (50%)	0.276	972 (38%)	1012 (38%)	0.588
Cardiac arrest	17 (2%)	12 (2%)	0.575	66 (3%)	56 (2%)	0.315
Killip class III or IV	47 (6%)	28 (4%)	0.075	58 (2%)	50 (2%)	0.383
Systolic arterial pressure, mmHg	137.0 ± 26.7	139.2 ± 27.6	0.115	138.4 ± 25.5	138.8 ± 25.5	0.580
LVEF (<35%)	86/751 (11%)	76/692 (11%)	0.803	190/2503 (8%)	213/2534 (8%)	0.299
eGFR at baseline	83.6 ± 26.1	82.9 ± 24.9	0.571	84.6 ± 25.1	84.2 ± 25.2	0.606
Medications administered before catheterization						
Lytic therapy	13 (2%)	14 (2%)	0.702	72 (3%)	80 (3%)	0.622
Aspirin	737 (95%)	681 (95%)	0.719	2443 (94%)	2498 (95%)	0.810
Clopidogrel	376 (48%)	351 (49%)	0.795	1170 (45%)	1192 (45%)	0.978
Prasugrel	74 (10%)	73 (10%)	0.665	370 (14%)	354 (13%)	0.357

Ticagrelor	203 (26%)	177 (25%)	0.592	603 (23%)	649 (25%)	0.285
Enoxaparin	125 (16%)	148 (21%)	0.023	362 (14%)	404 (15%)	0.184
Fondaparinux	77 (10%)	88 (12%)	0.160	225 (9%)	239 (9%)	0.662
Unfractionated heparin	197 (25%)	182 (25%)	0.953	918 (35%)	908 (34%)	0.417
Triple antithrombotic therapy at admission	9 (1%)	10 (1%)	0.818	25 (1%)	16 (1%)	0.159

Values are mean ± SD or n (%). * Hb <12 g/dl for women, <13 g/dl for men.

Table 2. Angiographic and procedural characteristics. *PCI= percutaneous coronary intervention; GPI= glycoprotein IIb/IIIa inhibitors; UFH= unfractionated heparin; TIMI= thrombolysis in myocardial infarction.*

	Complex PCI (n=1,491)			Noncomplex PCI (n= 5,233)		
	Radial Access (n= 777)	Femoral Access (n=714)	P-Value	Radial Access (n=2,590)	Femoral Access (n=2,643)	P-Value
Any crossover during index hospitalization	75 (10%)	19 (3%)	<0.001	131 (5%)	58 (2%)	<0.001
Intra-aortic balloon pump	44 (6%)	46 (6%)	0.587	27 (1%)	40 (2%)	0.141
Sheath size						
5Fr	6 (1%)	5 (1%)	1.000	24 (1%)	24 (1%)	1.000
6Fr	750 (97%)	638 (89%)	<0.001	2553 (99%)	2499 (95%)	<0.001
7Fr	20 (3%)	66 (9%)	<0.001	12 (0%)	106 (4%)	<0.001
8Fr	0 (0%)	5 (1%)	0.025	0 (0%)	14 (1%)	<0.001
Medication used during catheterization						
Aspirin	52 (7%)	65 (9%)	0.101	166 (6%)	182 (7%)	0.506
Clopidogrel	54 (7%)	54 (8%)	0.690	209 (8%)	193 (7%)	0.300
Prasugrel	59 (8%)	49 (7%)	0.618	273 (11%)	235 (9%)	0.045
Ticagrelor	90 (12%)	100 (14%)	0.163	284 (11%)	281(11%)	0.722
Planned GPI	99 (13%)	89 (12%)	0.876	318 (12%)	281 (11%)	0.062
Bailout GPI	45 (6%)	37 (5%)	0.650	108 (4%)	109 (4%)	0.945
UFH	428 (55%)	374 (52%)	0.299	1391 (54%)	1358 (51%)	0.097
UFH total dose, U/kg	80.6 ± 33.1	80.8 ± 32.1	0.937	74.6 ± 29.7	73.9 ± 27.2	0.523
Bivalirudin	379 (49%)	352 (49%)	0.876	1282 (49%)	1314 (50%)	0.890
Prolonged infusion post-PCI	190 (24%)	176 (25%)	0.952	648 (25%)	661 (25%)	1.000
Full bivalirudin regimen post-PCI	68 (9%)	56 (8%)	0.574	239 (9%)	228 (9%)	0.467
Low bivalirudin regimen post-PCI	122 (16%)	120 (17%)	0.574	409 (16%)	433 (16%)	0.573
Full procedural success	701 (90%)	640 (90%)	0.731	2421 (93%)	2476 (94%)	0.778
Treated vessel(s)						
Left main coronary artery	134 (17%)	102 (14%)	0.119	18 (1%)	17 (1%)	0.866
Left anterior descending a.	446 (58%)	414 (58%)	0.875	1239 (48%)	1235(47%)	0.422
Left circumflex artery	285 (37%)	258 (36%)	0.829	619 (24%)	651 (25%)	0.540
Right coronary artery	277 (36%)	271 (38%)	0.389	839 (32%)	852 (32%)	0.906
Bypass graft	10 (1%)	8 (1%)	0.816	10 (0%)	28 (1%)	0.005
Overall stent length, mm	52.8 ± 25.0	54.1 ± 26.4	0.344	25.3 ± 11.0	25.1 ± 10.7	0.534
Fluoroscopy time, min	20.3 ± 12.9	25.0 ±135.1	0.347	13.2 ± 8.9	13.4 ± 48.2	0.852
Duration of procedure, min	67.7 ± 36.5	68.6 ± 35.2	0.641	51.6 ± 24.4	49.9 ± 24.1	0.013
Lesions treated with PCI	n= 1,332	n = 1,234		n = 2,919	n=2,969	
At least one DES	980 (74%)	898 (73%)	0.656	1836 (63%)	1897 (64%)	0.433
At least one BMS	225 (17%)	207 (17%)	0.958	837 (29%)	797 (27%)	0.123
TIMI flow pre-procedure						
0 or 1	452 (34%)	437 (35%)	0.430	1179 (40%)	1188 (40%)	0.770
2	143 (11%)	140 (11%)	0.659	388 (13%)	390 (13%)	0.878

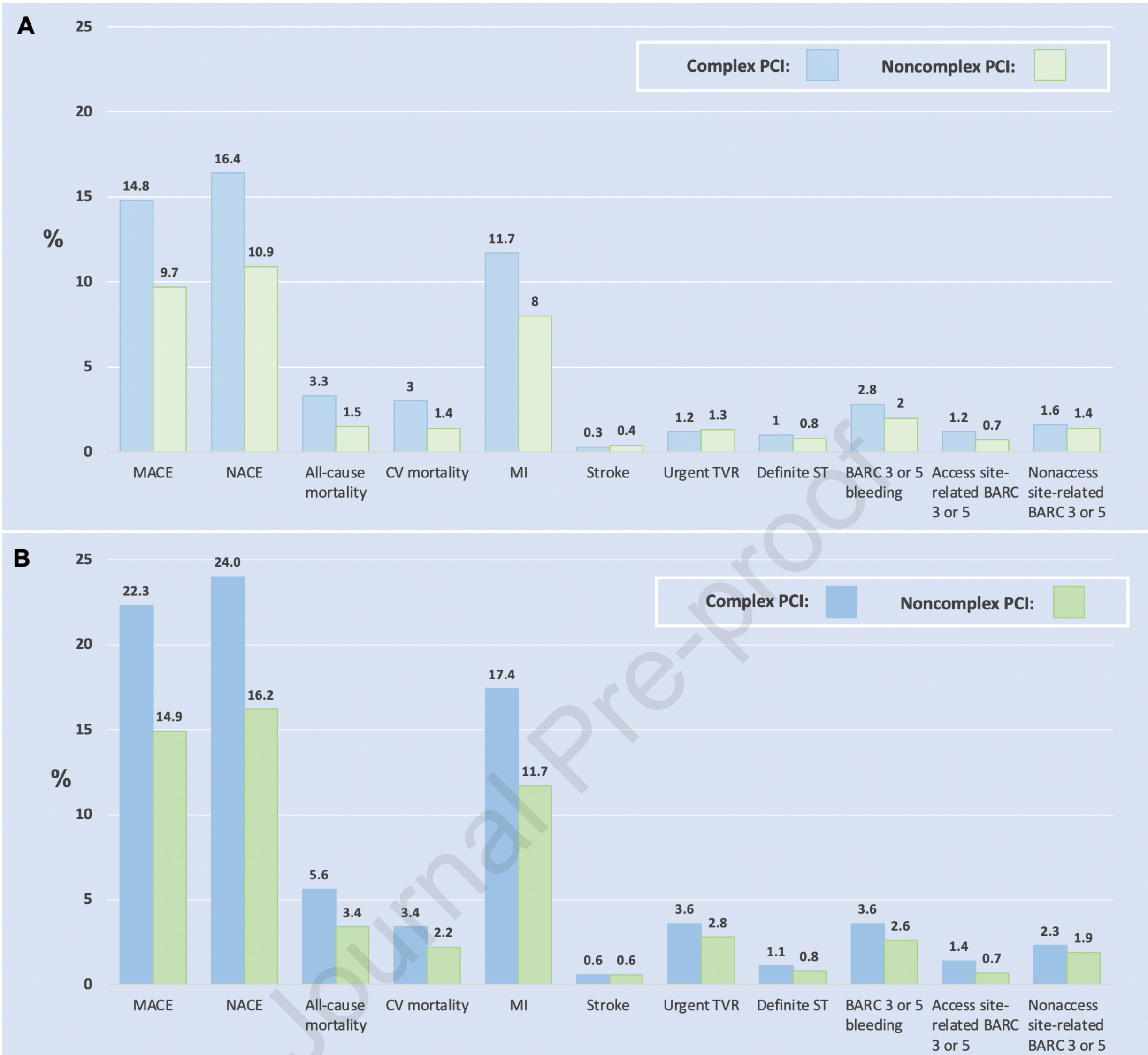
3	735 (55%)	655 (53%)	0.302	1352 (46%)	1391 (47%)	0.695
TIMI flow post-procedure						
0 or 1	36 (3%)	29 (2%)	0.616	41 (1%)	44 (1%)	0.828
2	32 (2%)	28 (2%)	0.896	73 (3%)	73 (2%)	0.933
3	1262 (95%)	1175 (95%)	0.583	2805 (96%)	2852 (96%)	0.947
Coronary stenosis less than 30% per treated lesion	1269 (95%)	1174 (95%)	0.925	2816 (96%)	2863 (96%)	0.944

Values are mean ± SD, or n (%).

Table 3. Adjudicated bleeding and ischemic events at 30 days according to randomized access site and PCI complexity. *PCI= percutaneous coronary intervention; MI= myocardial infarction; BARC= Bleeding Academic Research Consortium; TVR= target vessel revascularization; TIMI= Thrombolysis in Myocardial Infarction; GUSTO= Global Use of Strategies to Open Occluded Arteries; CI= confidence interval.*

	Complex PCI (n=1,491)				Noncomplex PCI (n= 5,233)				
	Radial Access (n= 777)	**Femoral Access (n=714)**	**Hazard Ratio (95% CI)**	**P-value**	**Radial Access (n=2,590)**	**Femoral Access (n=2,643)**	**Hazard Ratio (95% CI)**	**P-value**	**P-value for interaction**
Co-primary composite endpoint of all-cause mortality, MI or stroke	112 (14.4%)	109 (15.3%)	0.94 (0.72-1.22)	0.643	229 (8.8%)	278 (10.5%)	0.84 (0.70-1.00)	0.046	0.473
Co-primary composite endpoint of all-cause mortality, MI, stroke, or BARC 3 or 5 bleeding	121 (15.6%)	124 (17.4%)	0.89 (0.69-1.14)	0.349	257 (9.9%)	314 (11.9%)	0.83 (0.70-0.98)	0.028	0.666
Composite of all-cause mortality, MI, stroke, urgent TVR, definite stent thrombosis	123 (15.8%)	126 (17.7%)	0.89 (0.69-1.14)	0.344	262 (10.1%)	317 (12.0%)	0.84 (0.71-0.99)	0.036	0.712
All-cause mortality	27 (3.5%)	22 (3.1%)	1.13 (0.64-1.98)	0.675	30 (1.2%)	50 (1.9%)	0.61 (0.39-0.96)	0.033	0.096
Cardiovascular death	24 (3.1%)	20 (2.8%)	1.10 (0.61-2.00)	0.747	28 (1.1%)	46 (1.7%)	0.62 (0.39-0.99)	0.046	0.135
MI	88 (11.4%)	85 (12.0%)	0.95 (0.71-1.28)	0.737	194 (7.5%)	224 (8.5%)	0.88 (0.73-1.07)	0.194	0.671
Stroke	0 (0.0%)	4 (0.6%)	0.10 (0.01-1.85)	0.052	11 (0.4%)	10 (0.4%)	1.12 (0.48-2.64)	0.796	1.000
Urgent TVR	11 (1.4%)	6 (0.9%)	1.69 (0.62-4.57)	0.302	34 (1.3%)	33 (1.3%)	1.05 (0.65-1.70)	0.840	0.400
Definite stent thrombosis	8 (1.0%)	6 (0.9%)	1.22 (0.42-3.53)	0.708	22 (0.9%)	21 (0.8%)	1.07 (0.59-1.94)	0.830	0.824
Acute definite stent thrombosis	2 (0.3%)	2 (0.3%)	0.92 (0.13-6.53)	0.933	19 (0.7%)	10 (0.4%)	1.94 (0.90-4.17)	0.091	0.488
Subacute definite stent thrombosis	6 (0.8%)	4 (0.6%)	1.38 (0.39-4.88)	0.620	4 (0.2%)	11 (0.4%)	0.37 (0.12-1.16)	0.088	0.131
Definite or probable stent thrombosis	13 (1.7%)	10 (1.4%)	1.19 (0.52-2.72)	0.672	27 (1.0%)	27 (1.0%)	1.02 (0.60-1.74)	0.944	0.751
Acute definite or probable stent thrombosis	3 (0.4%)	3 (0.4%)	0.92 (0.19-4.55)	0.918	21 (0.8%)	10 (0.4%)	2.14 (1.01-4.55)	0.048	0.349

Subacute definite or probable stent thrombosis	10 (1.3%)	7 (1.0%)	1.31 (0.50-3.45)	0.580	8 (0.3%)	17 (0.6%)	0.48 (0.21-1.11)	0.085	0.122
Bleeding									
BARC classification									
Type 1	32 (4.2%)	71 (10.0%)	0.41 (0.27-0.62)	<0.001	114 (4.4%)	202 (7.7%)	0.57 (0.45-0.71)	<0.001	0.168
Type 2	37 (4.8%)	45 (6.3%)	0.75 (0.49-1.16)	0.201	75 (2.9%)	136 (5.2%)	0.56 (0.42-0.74)	<0.001	0.257
Type 3	10 (1.3%)	26 (3.7%)	0.35 (0.17-0.73)	0.005	37 (1.4%)	50 (1.9%)	0.75 (0.49-1.15)	0.189	0.075
Type 3a	2 (0.3%)	11 (1.6%)	0.17 (0.04-0.75)	0.020	25 (1.0%)	30 (1.1%)	0.85 (0.50-1.44)	0.542	0.046
Type 3b	8 (1.0%)	15 (2.1%)	0.49 (0.21-1.15)	0.101	11 (0.4%)	17 (0.6%)	0.66 (0.31-1.41)	0.280	0.609
Type 3c	0 (0.0%)	1 (0.1%)	0.31 (0.01-7.60)	0.479	1 (0.0%)	3 (0.1%)	0.34 (0.04-3.26)	0.349	-
Type 4	0 (0.0%)	0 (0.0%)	-	-	1 (0.0%)	0 (0.0%)	3.06 (0.12-75.08)	0.495	-
Type 5	3 (0.4%)	2 (0.3%)	1.38 (0.23-8.24)	0.726	7 (0.3%)	12 (0.5%)	0.59 (0.23-1.51)	0.273	0.413
Type 5a	2 (0.3%)	2 (0.3%)	0.92 (0.13-6.52)	0.932	4 (0.2%)	8 (0.3%)	0.51 (0.15-1.69)	0.270	0.615
Type 5b	1 (0.1%)	0 (0.0%)	2.76 (0.11-67.64)	1.000	3 (0.1%)	4 (0.2%)	0.76 (0.17-3.41)	0.724	-
Type 3 or 5	13 (1.7%)	28 (4.0%)	0.42 (0.22-0.81)	0.010	44 (1.7%)	62 (2.4%)	0.72 (0.49-1.06)	0.097	0.168
Related to access site	3 (0.4%)	15 (2.1%)	0.18 (0.05-0.63)	0.007	10 (0.4%)	25 (0.9%)	0.41 (0.20-0.85)	0.016	0.277
Type 2, 3 or 5	50 (6.5%)	71 (10.0%)	0.64 (0.44-0.92)	0.015	118 (4.6%)	197 (7.5%)	0.60 (0.48-0.76)	<0.001	0.805
Related to access site	22 (2.8%)	47 (6.6%)	0.43 (0.26-0.71)	0.001	40 (1.5%)	120 (4.6%)	0.34 (0.24-0.48)	<0.001	0.452
TIMI classification									
Major bleeding	4 (0.5%)	9 (1.3%)	0.41 (0.13-1.32)	0.135	14 (0.5%)	18 (0.7%)	0.79 (0.39-1.59)	0.513	0.341
Minor bleeding	3 (0.4%)	8 (1.1%)	0.34 (0.09-1.29)	0.115	20 (0.8%)	25 (1.0%)	0.81 (0.45-1.47)	0.493	0.245
Major or minor bleeding	7 (0.9%)	17 (2.4%)	0.38 (0.16-0.91)	0.029	34 (1.3%)	43 (1.6%)	0.80 (0.51-1.26)	0.343	0.131
GUSTO classification									
Severe bleeding	5 (0.7%)	7 (1.0%)	0.66 (0.21-2.06)	0.470	14 (0.5%)	18 (0.7%)	0.79 (0.39-1.59)	0.512	0.782
Moderate bleeding	3 (0.4%)	10 (1.4%)	0.27 (0.08-1.00)	0.050	14 (0.5%)	20 (0.8%)	0.71 (0.36-1.41)	0.330	0.200
Severe or moderate bleeding	8 (1.0%)	17 (2.4%)	0.43 (0.19-1.00)	0.049	28 (1.1%)	38 (1.4%)	0.75 (0.46-1.22)	0.247	0.261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MACE
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Stroke
Urgent TVR
Definite ST
BARC 3 or 5 bleeding
Access site-related BARC 3 or 5
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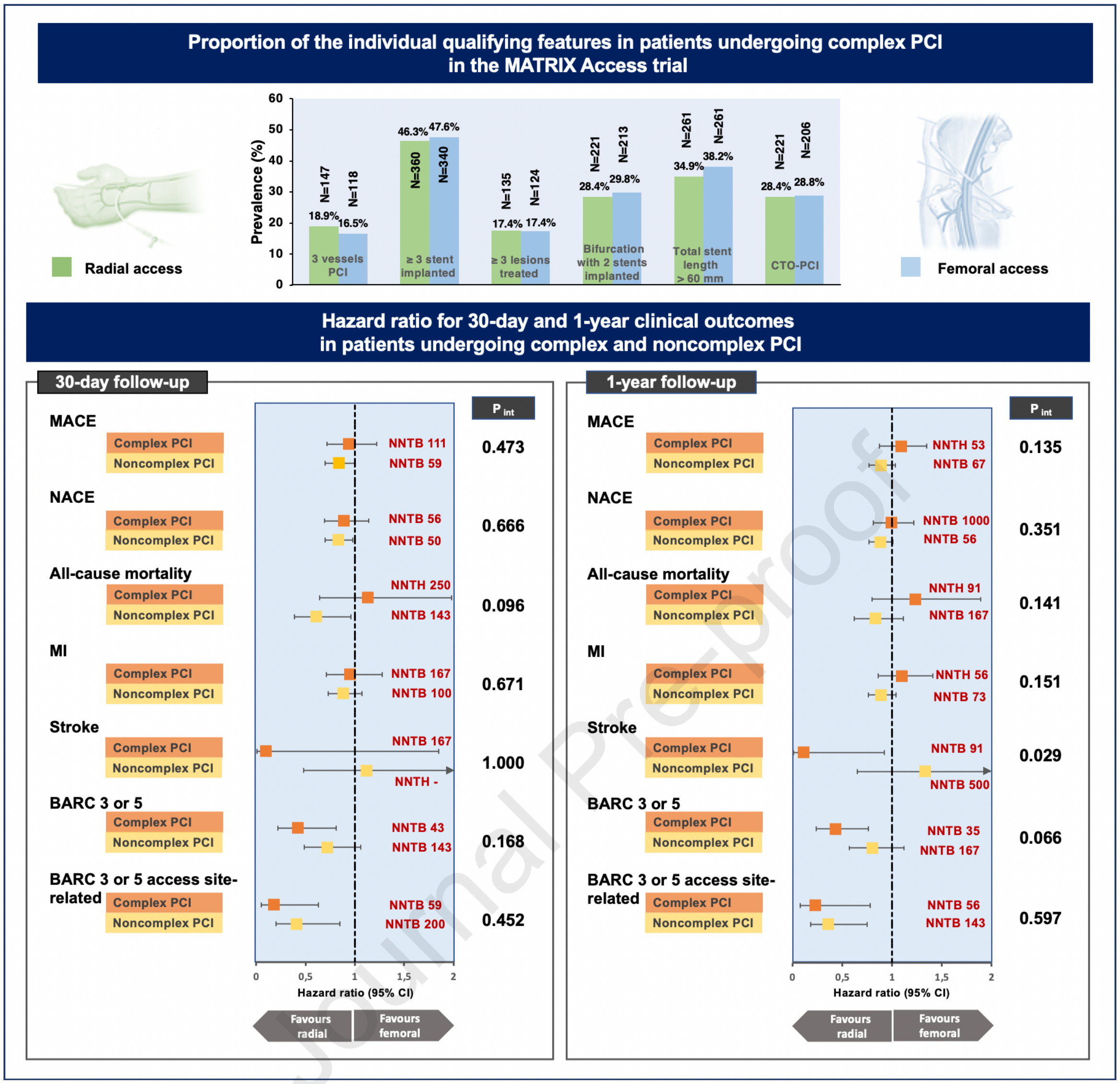
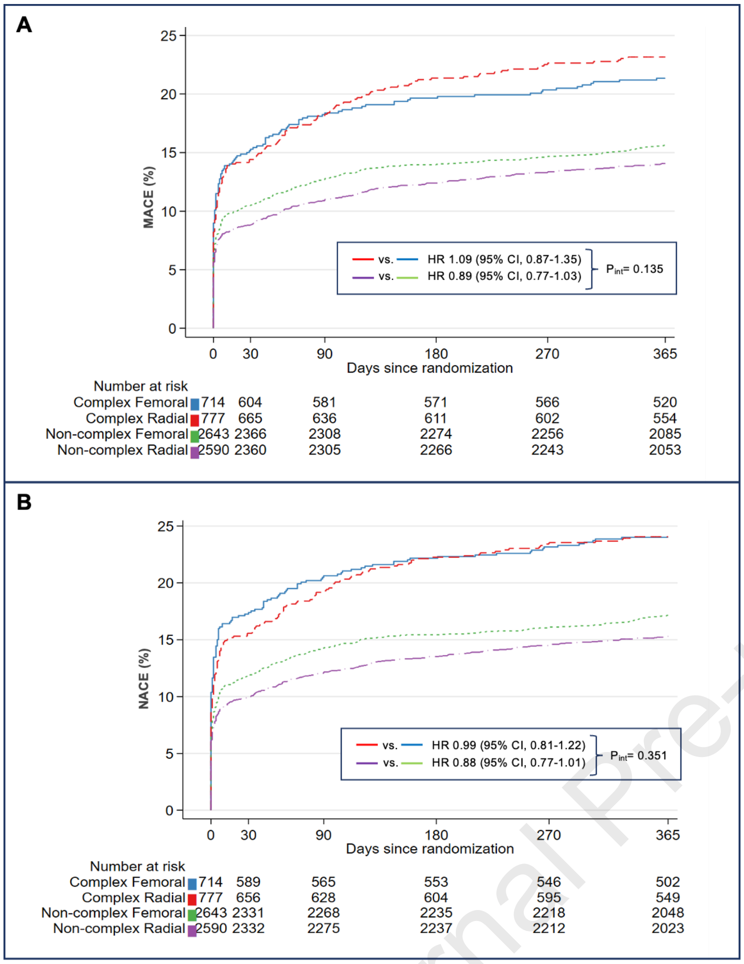
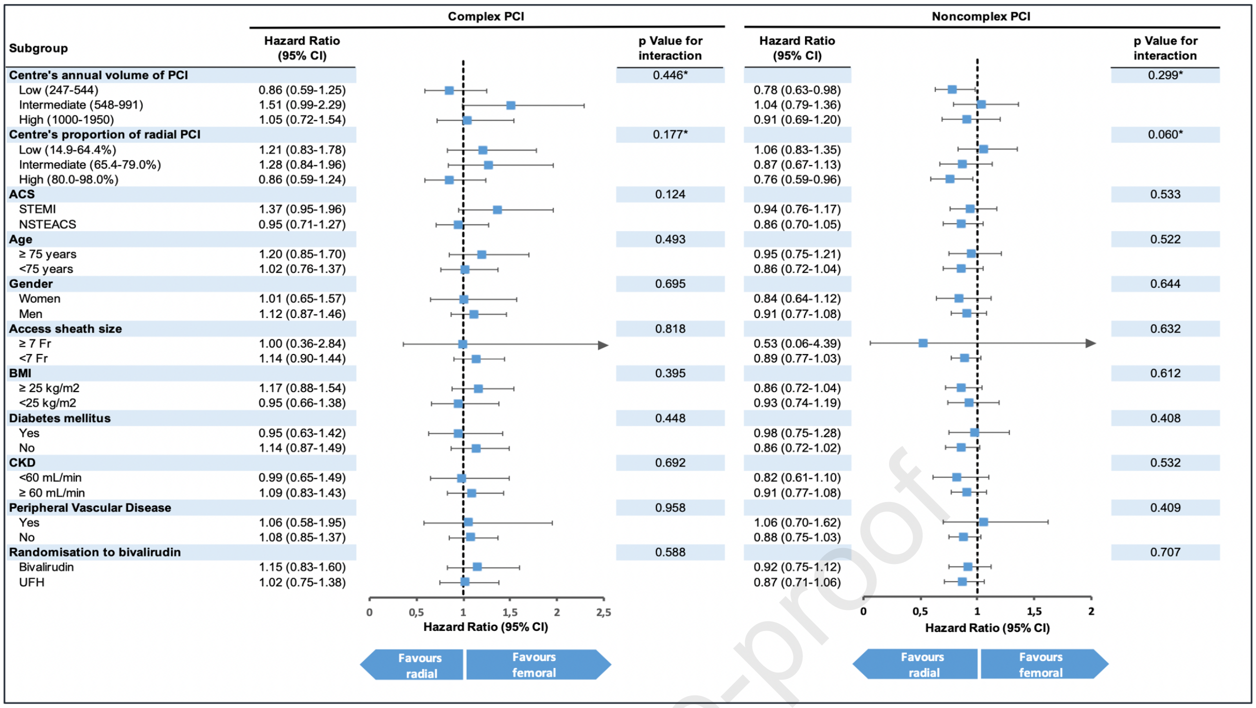
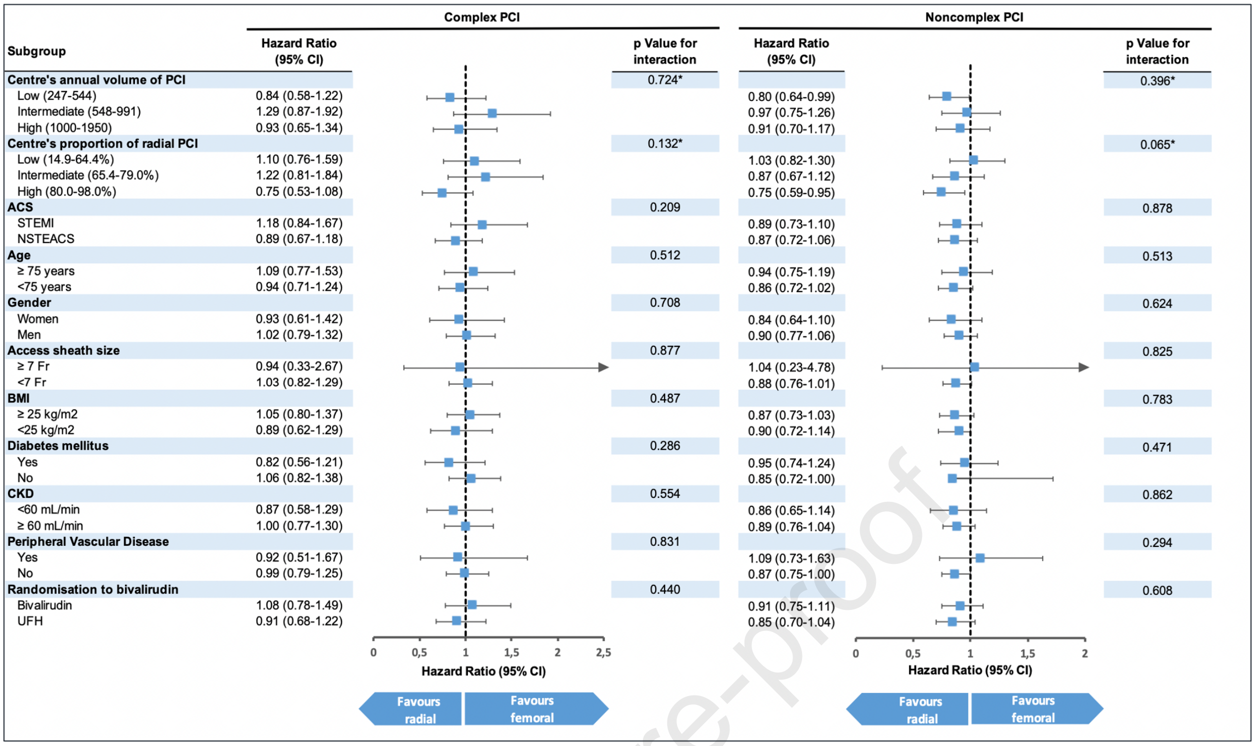
2.3
1.9



Proportion of the individual qualifying features in patients undergoing complex PCI in the MATRIX Access trial
Radial access
Femoral access
Prevalence (%)
3 vessels PCI
≥ 3 stent implanted
≥ 3 lesions treated
Bifurcation with 2 stents implanted
Total stent length > 60 mm
CTO-PCI
Hazard ratio for 30-day and 1-year clinical outcomes in patients undergoing complex and noncomplex PCI
30-day follow-up
1-year follow-up
MACE
NACE
All-cause mortality
MI
Stroke
BARC 3 or 5
BARC 3 or 5 access site-related
Complex PCI
Noncomplex PCI
P int
Hazard ratio (95% CI)
Favours radial
Favours femoral


A
MACE (%)
25
20
15
10
5
0
vs. HR 1.09 (95% CI, 0.87-1.35)
vs. HR 0.89 (95% CI, 0.77-1.03)
P_{int}= 0.135
0 30 90 180 270 365
Days since randomization
Number at risk
Complex Femoral 714 604 581 571 566 520
Complex Radial 777 665 636 611 602 554
Non-complex Femoral 2643 2366 2308 2274 2256 2085
Non-complex Radial 2590 2360 2305 2266 2243 2053
B
NACE (%)
25
20
15
10
5
0
vs. HR 0.99 (95% CI, 0.81-1.22)
vs. HR 0.88 (95% CI, 0.77-1.01)
P_{int}= 0.351
0 30 90 180 270 365
Days since randomization
Number at risk
Complex Femoral 714 589 565 553 546 502
Complex Radial 777 656 628 604 595 549
Non-complex Femoral 2643 2331 2268 2235 2218 2048
Non-complex Radial 2590 2332 2275 2237 2212 2023


Complex PCI
Noncomplex PCI
Subgroup
Hazard Ratio (95% CI)
p Value for interaction
Hazard Ratio (95% CI)
p Value for interaction
Centre's annual volume of PCI 0.446* 0.299*
Low (247-544) 0.86 (0.59-1.25) 0.78 (0.63-0.98)
Intermediate (548-991) 1.51 (0.99-2.29) 1.04 (0.79-1.36)
High (1000-1950) 1.05 (0.72-1.54) 0.91 (0.69-1.20)
Centre's proportion of radial PCI 0.177* 0.060*
Low (14.9-64.4%) 1.21 (0.83-1.78) 1.06 (0.83-1.35)
Intermediate (65.4-79.0%) 1.28 (0.84-1.96) 0.87 (0.67-1.13)
High (80.0-98.0%) 0.86 (0.59-1.24) 0.76 (0.59-0.96)
ACS 0.124 0.533
STEMI 1.37 (0.95-1.96) 0.94 (0.76-1.17)
NSTEACS 0.95 (0.71-1.27) 0.86 (0.70-1.05)
Age 0.493 0.522
≥ 75 years 1.20 (0.85-1.70) 0.95 (0.75-1.21)
<75 years 1.02 (0.76-1.37) 0.86 (0.72-1.04)
Gender 0.695 0.644
Women 1.01 (0.65-1.57) 0.84 (0.64-1.12)
Men 1.12 (0.87-1.46) 0.91 (0.77-1.08)
Access sheath size 0.818 0.632
≥ 7 Fr 1.00 (0.36-2.84) 0.53 (0.06-4.39)
<7 Fr 1.14 (0.90-1.44) 0.89 (0.77-1.03)
BMI 0.395 0.612
≥ 25 kg/m2 1.17 (0.88-1.54) 0.86 (0.72-1.04)
<25 kg/m2 0.95 (0.66-1.38) 0.93 (0.74-1.19)
Diabetes mellitus 0.448 0.408
Yes 0.95 (0.63-1.42) 0.98 (0.75-1.28)
No 1.14 (0.87-1.49) 0.86 (0.72-1.02)
CKD 0.692 0.532
<60 mL/min 0.99 (0.65-1.49) 0.82 (0.61-1.10)
≥ 60 mL/min 1.09 (0.83-1.43) 0.91 (0.77-1.08)
Peripheral Vascular Disease 0.958 0.409
Yes 1.06 (0.58-1.95) 1.06 (0.70-1.62)
No 1.08 (0.85-1.37) 0.88 (0.75-1.03)
Randomisation to bivalirudin 0.588 0.707
Bivalirudin 1.15 (0.83-1.60) 0.92 (0.75-1.12)
UFH 1.02 (0.75-1.38) 0.87 (0.71-1.06)
0
0,5
1
1,5
2
2,5
Hazard Ratio (95% CI)
Favours radial
Favours femoral
0
0,5
1
1,5
2
Hazard Ratio (95% CI)
Favours radial
Favours femoral


Complex PCI
Noncomplex PCI
Subgroup
Hazard Ratio (95% CI)
p Value for interaction
Hazard Ratio (95% CI)
p Value for interaction
Centre's annual volume of PCI 0.724* 0.396*
Low (247-544) 0.84 (0.58-1.22) 0.80 (0.64-0.99)
Intermediate (548-991) 1.29 (0.87-1.92) 0.97 (0.75-1.26)
High (1000-1950) 0.93 (0.65-1.34) 0.91 (0.70-1.17)
Centre's proportion of radial PCI 0.132* 0.065*
Low (14.9-64.4%) 1.10 (0.76-1.59) 1.03 (0.82-1.30)
Intermediate (65.4-79.0%) 1.22 (0.81-1.84) 0.87 (0.67-1.12)
High (80.0-98.0%) 0.75 (0.53-1.08) 0.75 (0.59-0.95)
ACS 0.209 0.878
STEMI 1.18 (0.84-1.67) 0.89 (0.73-1.10)
NSTEACS 0.89 (0.67-1.18) 0.87 (0.72-1.06)
Age 0.512 0.513
≥ 75 years 1.09 (0.77-1.53) 0.94 (0.75-1.19)
<75 years 0.94 (0.71-1.24) 0.86 (0.72-1.02)
Gender 0.708 0.624
Women 0.93 (0.61-1.42) 0.84 (0.64-1.10)
Men 1.02 (0.79-1.32) 0.90 (0.77-1.06)
Access sheath size 0.877 0.825
≥ 7 Fr 0.94 (0.33-2.67) 1.04 (0.23-4.78)
<7 Fr 1.03 (0.82-1.29) 0.88 (0.76-1.01)
BMI 0.487 0.783
≥ 25 kg/m2 1.05 (0.80-1.37) 0.87 (0.73-1.03)
<25 kg/m2 0.89 (0.62-1.29) 0.90 (0.72-1.14)
Diabetes mellitus 0.286 0.471
Yes 0.82 (0.56-1.21) 0.95 (0.74-1.24)
No 1.06 (0.82-1.38) 0.85 (0.72-1.00)
CKD 0.554 0.862
<60 mL/min 0.87 (0.58-1.29) 0.86 (0.65-1.14)
≥ 60 mL/min 1.00 (0.77-1.30) 0.89 (0.76-1.04)
Peripheral Vascular Disease 0.831 0.294
Yes 0.92 (0.51-1.67) 1.09 (0.73-1.63)
No 0.99 (0.79-1.25) 0.87 (0.75-1.00)
Randomisation to bivalirudin 0.440 0.608
Bivalirudin 1.08 (0.78-1.49) 0.91 (0.75-1.11)
UFH 0.91 (0.68-1.22) 0.85 (0.70-1.04)
0
0,5
1
1,5
2
2,5
Hazard Ratio (95% CI)
0
0,5
1
1,5
2
Hazard Ratio (95% CI)
Favours radial
Favours femoral
Favours radial
Favours femoral