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Transradial versus trans-femoral access site in high-speed rotational atherectomy in Sweden

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ABSTRACT

Background: Radial artery is the preferred access site in contemporary percutaneous coronary intervention (PCI). However, limited data exist regarding utilization pattern, safety, and long-term efficacy of transradial artery access (TRA) PCI in heavily calcified lesions using high-speed rotational atherectomy (HSRA).

Methods: All patients who underwent HSRA-PCI in Sweden between 2005 and 2016 were included. Outcomes were major adverse cardiac events (MACE, including death, myocardial infarction (MI) or target vessel revascularisation (TVR)), in-hospital bleeding and restenosis. Inverse probability of treatment weighting was used to adjust for the non-randomized access site selection.

Results: We included 1479 patients of whom 649 had TRA and 782 transfemoral artery access (TFA) HSRA-PCI. The rate of TRA increased significantly by 18% per year but remained lower in HSRA-PCI (60%) than in the overall PCI population (85%) in 2016.

TRA was associated with comparable angiographic success but significantly lower risk for major (adjusted OR 0.16; 95% CI 0.05–0.47) or any in-hospital bleeding (adjusted OR 0.32; 95% CI 0.13–0.78). At one year, the adjusted risk for MACE (HR 0.87; 95% CI 0.67–1.13) and its individual components did not differ between TRA and TFA patients. The risk for restenosis did not significantly differ between TRA and TFA HSRA-PCI treated lesions (adjusted HR 0.92; 95% CI 0.46–1.81).

Conclusion: HSRA-PCI by TRA was associated with significantly lower risk for in-hospital bleeding and equivalent long-term efficacy when compared with TFA. Our data support the feasibility and superior safety profile of TRA in HSRA-PCI.

Abbreviations and acronyms: ACS, acute coronary syndrome; CABG, coronary artery by-pass grafting; CTO, chronic total occlusion; DES, drug eluting stents; DM, diabetes mellitus; GFR, glomerular filtration rate; GPI, glycoprotein IIb/IIIa receptor inhibitors; HSRA, high speed rotational atherectomy; IPTW, inverse probability of treatment weighting; MACE, major adverse cardiac events; MI, myocardial infarction; PCI, percutaneous coronary intervention; PS, propensity score; SCAAR, Swedish Coronary and Angioplasty Registry; TFA, transfemoral artery access; TLT, target lesion thrombosis; TRA, transradial artery access; TVR, target vessel revascularisation.

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[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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1. Introduction

Percutaneous coronary intervention (PCI) of calcified lesions remains challenging with high risk for procedural failure and adverse events [1]. High speed rotational atherectomy (HSRA, Rotablator™ Boston Scientific, Natick, MA, USA) has been established as an important adjunctive tool in the treatment of heavily calcified lesions [2] with good long-term outcome in the era of drug eluting stents (DES) [3–5].

Compared with transfemoral artery access (TFA), transradial artery access (TRA) PCI reduces vascular and bleeding complications and improves outcomes across the entire spectrum of patients with coronary artery disease [6–8] and has been endorsed as the default access site by the recent European guidelines on myocardial revascularization [9].

Patients with severe calcified coronary lesions are also at high risk for bleeding complications [10], and may thus derive substantial benefits from TRA-PCI. However, in complex PCIs, such as those with HSRA, TRA is used less frequently compared with an unselected PCI population [11]. Furthermore, the use of TRA in HSRA-PCI considerably varies between different PCI sites and countries [5,11]. The individual operator's perception that the 6 French size guide catheter, routinely used during TRA-PCI, may provide suboptimal support for device delivery and restrict burr size selection might be a potential barrier for adoption of TRA in HSRA-PCI.

However, data on the impact of access site on HSRA-PCI are scarce and little is known about long-term outcomes in this patient group. Our aim was to evaluate temporal trends and long-term outcomes of HSRA-PCI by TRA vs TFA.

2. Methods

2.1. Study population

This was a retrospective analysis of prospectively collected data, using the Swedish Coronary and Angioplasty Registry (SCAAR) registry. Between January 2005 and December 2016, all patients in Sweden who underwent PCI with HSRA were identified. Patients were allocated to the TRA and the TFA group, based on the access site that was successfully used during the procedure (conversion from TRA to TFA was analyzed as TFA and vice versa). Cases with missing information regarding access site, bilateral access site including TRA and TFA access or other recorded vascular access sites, were excluded (supplementary file, methods). Complete follow-up was available until July 2017.

2.2. The SCAAR registry

The SCAAR registry is part of the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry and details about the database have been previously described. [12]. The SCAAR provides ~100% angiography and PCI coverage in Sweden. The PCI physicians enter more than 200 clinical and procedural characteristics, immediately after the procedure, using a web-based case-report platform. In-hospital complications and outcomes are also collected at discharge. Additionally, in patients undergoing any subsequent coronary angiography, and information about restenosis or thrombosis in any previously PCI-treated coronary lesion/segment are collected. External monitors have regularly evaluated registry data and agreement with the medical records has been over 95% [13].

2.3. Outcomes

Efficacy outcomes included the cumulative 1-year rate of major adverse cardiac events (MACE), defined as the composite of death, myocardial infarction (MI) or target vessel revascularisation (TVR), the individual components of MACE and clinically driven restenosis and target lesion thrombosis (TLT). Safety outcomes included the rate of in-hospital major non-coronary artery by-pass grafting (CABG) related bleeding, any in-hospital non-CABG related bleeding as well as other in-hospital complications.

Death was defined as death from any cause. MI was defined as any rehospitalisation identified by the International Classification of Diseases (ICD) codes I21 and I22. TVR was defined as a repeat revascularisation of any segment of the target vessel with PCI or decision about CABG during follow up. In case of CABG, TVR was presumed. PCI of the target vessel that was decided at the index procedure and performed within 60 days after the index procedure, was not included in TVR. Restenosis was defined as clinically relevant >50% stenosis in a previously treated segment assessed visually or by fractional flow reserve or instantaneous wave-free ratio in a subsequent coronary angiography. Definite TLT was defined as angiographic evidence of thrombosis in a previously treated lesion, with an acute clinical presentation. Major in-hospital non-CABG bleeding was defined (using a modification of The Thrombolysis in Myocardial Infarction (TIMI) bleeding major and minor criteria) as fatal or cerebral bleeding, bleeding leading to hemoglobin drop >4.0 g/dL without an overt bleeding or > 3.0 g/L with an overt bleeding, bleeding requiring surgical intervention, blood transfusion, pseudoaneurysm requiring treatment other than manual compression and a bleeding that led to early discontinuation of antiplatelet therapy. Any in-hospital non-CABG bleeding was defined as any bleeding requiring medical attention. Other in-hospital complications were defined as death from any cause, stroke, periprocedural MI, coronary vessel perforation, cardiac tamponade, urgent CABG, or re-PCI due to a PCI-related complication.

Information on vital status and MI were obtained by merging the SCAAR registry with the National Board of Health and Welfare's Cause of Death and the national registry of acute cardiac care (RIKS-HIA), respectively. Information on TVR, restenosis, TLT and in-hospital complications were derived from SCAAR. Outcomes were obtained from the registries and were not adjudicated.

2.4. Statistical analysis

To study temporal trends in access site selection, a logistic regression model was constructed with access site as the dependent variable and the year of the procedure as the independent variable. To study possible interactions between time trends in access site and selected patient subgroups, interactions terms were also included in the logistic regression model. Finally, to evaluate whether the operator's preference influenced the access site choice we selected the last five years of the study period, to encompass more contemporary interventional practice and we identified the 10 operators with the highest HSRA-PCI procedure volume for whom the proportion of access site stratified by operator is presented.

The total number of HSRA-PCI procedures were used to evaluate temporal trends in TRA use, during the study period. MACE, death, MI, TVR, in-hospital bleeding and in-hospital complications were analyzed on a patient level, in which only the first time a patient appeared in the registry was selected (to avoid double counting of outcomes). The total number of lesions treated with HSRA were used to assess restenosis and TLT.

The cumulative rate of 1-year outcomes were assessed using Kaplan–Meier curves. The proportional hazard assumption was verified by the Schoenfeld residuals test.

To study the association between TRA vs TFA and efficacy and safety outcomes, Cox proportional hazard models and logistic regression models were constructed and presented as hazard ratios (HR) and odds ratios (OR) with 95% confidence intervals (CI), respectively. In the unadjusted models, only access site was included as covariate. To account for the non-randomized selection of access site and adjust for differences between the groups inverse probability of treatment weighting (IPTW) was utilized. Two propensity score (PS) models were developed for patient- and lesion-level analyses, reflecting the

probability for TRA. The following covariates were included in the PS models: age, gender, smoking status, diabetes mellitus (DM), hypertension, hyperlipidemia, previous MI, previous PCI, previous CABG, renal failure (defined as estimated glomerular filtration rate (GFR) ≤60 mL/min/1.73m^2), indication for PCI (acute coronary syndrome (ACS) or not), angiographic findings (single vessel disease without left main (LM) vs multi-vessel disease and/or LM disease), procedural use of intra-aortic pump, insertion of temporary pacemaker, number of treated segments per procedure, stent use, DES use during the procedure, intravascular imaging, complete revascularization, treatment of at least one chronic total occlusion (CTO) during the procedure and periprocedural medications including aspirin, P2Y12 receptor inhibitors (none, clopidogrel or ticagrelor/prasugrel), fondaparinux, bivalirudin, low molecular weight heparin, unfractionated heparin or glycoprotein IIb/IIIa receptor inhibitors (GPI). In the PS model in lesion level analysis additional covariates included the type of procedure per lesion (HSRA without stent, HSRA with bare metal stent (BMS) or HSRA with DES), target vessel, stenosis type (de-novo vs restenosis lesion), stenosis class, lesion involving a bifurcation and CTO or not. Using the individual PS, we calculated the inverse probability of treatment weights (IPTW). Covariate balance between the groups before and after IPTW weighting was assessed using the standardized differences between the groups, with differences less than 0.10 indicating a good balance (supplementary file, table S1 and fig. S1 and S2). IPTW cox regression and logistic regression models were constructed including treatment and PCI-center as a clustering factor, to obtain a cluster-robust estimate. In the lesion level analyses, IPTW cox regression models were constructed including treatment and 2-level clustering to account for multiple devices used in one patient and patients treated in the same hospital (additional data are provided in supplementary file, methods, statistical analysis).

In a sensitivity analysis of bleeding complications, we excluded cases in which at least a CTO was treated during the procedure, to exclude cases with bilateral femoral or bilateral radial artery access, predominantly used in CTO-PCIs. In another analysis, cases with conversion from TRA to TFA and vice versa were also excluded. Finally, we evaluated bleeding complications in an intention to treat analysis in which conversion from TRA to TFA was analyzed as TRA and vice versa.

For the covariates included in the PS calculation, 27% of the patients had at least one missing value and 1.1% of the total values were missing. Missing at random was assumed and multiple missing values imputations was performed. All covariates used in PS models, year of the procedure and access site were included in the imputation model and five imputation datasets were created.

2.5. Ethics

Patients do not provide written consent but are informed about their participation in the SCAAR registry and can opt-out. The study was approved by the local ethical review board (Dnr 2017/16–31) and was conducted according to the 1975 declaration of Helsinki.

3. Results

The study population consisted of 1431 patients of whom 649 (45%) had TRA and 782 (55%) TFA. From 2005 to 2016, the rate of TRA significantly increased by 18% per year ($p < 0.01$ for trend), from 27% in 2005 to 60% in 2016. However, the use of TRA for HSRA-PCI was considerably lower than that reported in the overall PCI population in Sweden (supplementary file, fig. S3). Noteworthily, we found large differences regarding access site choice between the 10 highest HSRA-PCI procedure volume operators (supplementary file, fig. S4).

The rate of TRA increased in a similar fashion in all selected subgroups (in elderly, females, diabetics, patients with renal failure, previous CABG, in patients with an ACS as the indication for PCI, in patients with at least one CTO lesion treated during the procedure and in patients with LM disease) as in the whole population, without significant interactions (supplementary file, fig. S5).

3.1. Baseline and procedural characteristics

Patients in the TRA and the TFA group were well balanced in terms of sex, age, body mass index (BMI) and proportion of patients with DM. Patients in the TRA group were less likely to have a previous MI or a previous revascularization (Table 1). The proportion of patients with ACS and the angiographic findings did not differ significantly between the groups. In the TRA group, DES and intravascular imaging were more often used, complete revascularization was more often achieved, and a temporary pacemaker was less often inserted, as compared to the TFA group. The rate of glycoprotein IIb/IIIa receptor inhibitor administration, fluoroscopy time and contrast volume did not differ significantly between the groups (Table 1). Left anterior descending artery was the most common target vessel in both groups whereas the proportion of de novo lesions and lesions class B2/C that were treated with HSRA-PCI were higher in the TRA than in the TFA group. Angiographic success was high in both groups (supplementary file, Table 2).

3.2. In-hospital outcomes

HSRA-PCI by TRA was associated with lower risk for major bleeding (0.8% (5 events) vs 3.7% (29 events), adjusted OR 0.16; 95% CI 0.05–0.47) and overall bleeding complications (2.6% (17 events) vs 6.5% (51 events), adjusted OR 0.32; 95% CI 0.13–0.78) compared to TFA-PCI (Table 2 and Fig. 1. We found no association between the risk for other in-hospital complications and the access site, before or after adjustment (6.0% (39 events) vs 4.9% (38 events), adjusted OR 1.06; 95% CI 0.74–1.52) (Table 2, Fig. 1 and supplementary file, table S3). Similar results were obtained in all sensitivity analyses (supplementary file, results).

3.3. Long terms outcomes

The cumulative one-year MACE rate was 15.3% (97 events) vs 20.2% (156 events) in the TRA vs TFA patients, respectively (Fig. 2). In the unadjusted model, TRA was associated with a lower risk for MACE (HR 0.74; 95% CI 0.58–0.96). However, no significant difference remained after adjustment (adjusted HR 0.87; 95% CI 0.64–1.19) (Table 2).

The cumulative rate of death was 7.4% (47 events) vs 8.6% (67 events) in the TRA vs TFA patients, respectively (Fig. 2). We found no association between access site and the risk for death, before or after adjustment (TRA vs TFA, adjusted HR1.02; 95% CI 0.68–1.52). TRA was associated with lower unadjusted risk for MI, (5.7% (34 events) vs 9.0% (66 events)) but the difference was no longer significant after adjustment (adjusted HR 0.84; 95% CI 0.61–1.16). The risk for TVR did not significantly differ between the groups, before or after adjustment (TRA vs TFA, 5.7% (34 events) vs 6.6% (48 events), adjusted HR 1.01;95% CI 0.59–1.74) (Table 2 and Fig. 2).

The cumulative rate of restenosis was 3.1% (28 events) vs 5.0% (52 events) in the TRA vs TFA HSRA-PCI treated lesions. The unadjusted risk for restenosis was lower in lesions treated with HSRA-PCI by TRA than TFA. However, no significant difference remained after adjustment (TRA vs TFA, adjusted HR 0.92; 95% CI 0.46–1.81). The cumulative rate of TLT thrombosis was low in both groups (Table 2).

4. Discussion

This nationwide observational study of all patients who underwent PCI with HSRA in Sweden between 2005 and 2016 showed that TRA was associated with significantly lower risk for in-hospital bleeding without any difference in long-term efficacy, compared to TFA. It also demonstrated that HSRA-PCI by the TRA is feasible with similar angiographic success, radiation time and risk for other in-hospital complications, compared to TFA. Although the use of TRA significantly increased over

Table 1
Baseline and procedural characteristics.

	Radial access	Femoral access	P
Number of patients	649	782	
Age, years, mean (SD)	72.3 (9.2)	72.0 (9.3)	0.57
Body weight, kg, mean (SD)	81.8 (15.9)	80.4 (15.9)	0.12
Body mass index, kg/m^2, mean (SD)	27.8 (8.2)	27.5 (7.6)	0.43
Female sex	186 (28.7)	232 (29.7)	0.68
Diabetes	216 (33.5)	287 (36.9)	0.18
Insulin treatment*	116 (53.7)	144 (51.1)	0.56
Smoking			
Former smokers	309 (49.1)	347 (47.9)	0.56
Current smokers	67 (10.7)	68 (9.4)	
History of Hyperlipidemia	52.4 (81.1)	648 (83.7)	0.20
History of Hypertension	540 (83.2)	633 (82.0)	0.47
Previous myocardial infarction	273 (42.9)	387 (52.2)	<0.01
Previous PCI	319 (49.2)	449 (57.5)	<0.01
Previous CABG	118 (18.2)	198 (25.3)	<0.01
Estimated GFR, MDRD, mL/min/1.73m^2, mean (SD)	66 (29)	65 (29)	0.32
eGFR<30 mL/min/1.73m^2	23 (4.0)	35 (6.0)	0.28
eGFR 30–59 mL/min/1.73m^2	246 (42.7)	244 (42.1)	
Procedural characteristics			
ACS as indication for PCI	272 (41.9)	336 (43.0)	0.69
Angiographic findings			
Single vessel (not LM)	184 (28.4)	229 (29.3)	0.93
Multivessel disease	465 (71.7)	553 (70.7)	
Left main disease	121 (18.6)	140 (18.0)	0.74
Intra-aortic balloon pump	1 (0.2)	22 (2.8)	<0.01
Temporary pacemaker	7 (1.1)	96 (12.3)	<0.01
Number of treated segments per procedure			
1 segment	192 (29.6)	289 (37.0)	<0.01
2 segments	211 (32.5)	276 (35.3)	
≥ 3 segments	246 (37.9)	217 (27.7)	
Procedure with at least one stent	614 (94.6)	695 (88.9)	<0.01
Procedure with at least one DES≠	584 (95.1)	578 (83.2)	<0.01
Number of stents per procedure≠			
1 stent	183 (29.8)	273 (39.3)	<0.01
2 stents	186 (30.3)	214 (30.8)	
≥ 3stents	245 (39.9)	208 (29.9)	
At least one CTO was treated during the procedure	51 (7.9)	78 (10.0)	0.16
Complete revascularization	413 (63.6)	391 (50.0)	<0.01
Intravascular imaging	76 (11.7)	58 (7.4)	0.01
Active Vascular closure devices †	n/a	588 (75.2)	n/a
Fluoroscopy time, minutes, median (25th-75th percentile)	30 (21–44)	28 (21–40)	0.17
Successful procedure	624 (96.1)	745 (95.2)	0.47
Procedural medication**			
Acetylsalicylic acid	626 (96.5)	758 (96.9)	0.62
P2Y12 receptor inhibitors	630 (97.1)	772 (98.7)	0.03
Clopidogrel/ticlopidine	408 (62.9)	596 (76.2)	<0.01
Ticagrelor/prasugrel	222 (34.2)	176 (22.5)	
Fondaparinux	84 (12.9)	91 (11.6)	0.45
Low molecular weight heparin	46 (7.1))	200 (25.6)	<0.01
Unfractionated heparin	592 (91.2)	500 (63.9)	<0.01
Bivalirudin	60 (9.2)	139 (17.8)	<0.01
Glycoprotein IIb/IIIa inhibitors	143 (22.0)	151 (19.3)	0.20

Figures presented as number (percentage) if not otherwise notified. SD, standard deviation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal Disease; ACS, acute coronary syndrome; LM, left main; DES, drug eluting stent; CTO, chronic total occlusion;. *In patients with diabetes, †Active vascular closure devices included Angioseal, Perclose, Starclose, Femoseal. ≠Between patients treated with at least one stent. **Drugs administrated the last 24 h or during the procedure.

Table 2
Outcomes.

	Radial access	Femoral access	
Patients, n	649	782	
In-hospital outcomes			
	Events, n (%)		OR (95% CI)
Major in-hospital bleeding			
Crude	5 (0.8)	29 (3.7)	0.20 (0.08–0.52)
Adjusted			0.16 (0.05–0.47)
Any in-hospital bleeding			
Crude	17 (2.6)	51 (6.5)	0.39 (0.22–0.67)
Adjusted			0.32 (0.13–0.78)
Other in-hospital complications			
Crude	39 (6.0)	38 (4.9)	1.25 (0.79–1.98)
Adjusted			1.06 (0.74–1.52)
1-year clinical outcomes			
	Events, n (%)		HR (95% CI)
MACE			
Crude	97 (15.3)	156 (20.2)	0.74 (0.58–0.96)
Adjusted			0.87 (0.64–1.19)
All-cause mortality			
Crude	47 (7.4)	67 (8.6)	0.85 (0.59–1.24)
Adjusted			1.02 (0.68–1.52)
Myocardial infarction			
Crude	34 (5.7)	66 (9.0)	0.62 (0.41–0.94)
Adjusted			0.84 (0.61–1.16)
TVR			
Crude	34 (5.7)	48 (6.6)	0.85 (0.55–1.33)
Adjusted			1.01 (0.59–1.74)
Lesions, n	988	1160	
Restenosis			
Crude	28 (3.1)	52 (5.0)	0.62 (0.39–0.98)
Adjusted			0.95 (0.47–1.91)
Target lesion thrombosis			
Crude	7 (0.8)	8 (0.8)	1.01 (0.37–2.79)
Adjusted			1.32 (0.43–4.04)

Hazard ratio (HR) and odds ratio (OR) with 95% confidence interval was derived from cox proportional hazard models and logistic regression models, respectively. MACE, major adverse cardiac events; TVR, target vessel revascularization.

the course of the study period, it remained considerably lower than that reported in the general PCI population.

Bleeding after PCI has been recognized as strong predictor of adverse outcomes [14–16]. Although access site bleeding has traditionally been considered less important than non-access site bleeding, femoral access site bleeding has also been associated with worse short and long-term survival [17,18]. Apart from life threatening bleeding that increases the risk for death, bleeding may lead to early discontinuation of antiplatelet therapy, activation of coagulation cascade and blood transfusion that increase the risk for adverse events [14,16]. In large, randomized control trials, TRA significantly reduced the risk for bleeding and improved survival compared to TFA [6–8] with the greatest benefit observed in patients with STEMI or cardiogenic shock [7,19,20]. Thus, our finding of a substantially reduced bleeding incidence in patients undergoing TRA HSRA-PCI underlines the importance of the access site choice in this setting and demonstrates the clinical importance of TRA. Lower risk for bleeding with TRA has previously been associated with less overall patient discomfort, earlier ambulation, shorter hospital stay [21,22] and significantly lower healthcare cost

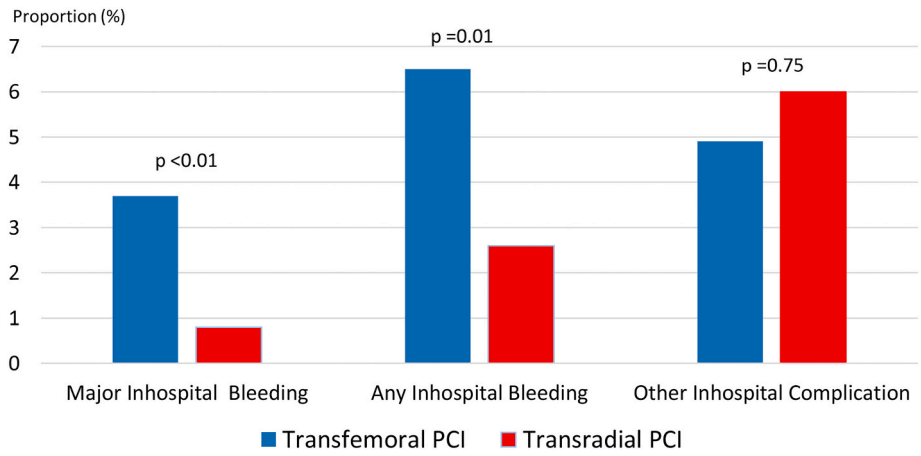

Fig. 1. In-hospital complications stratified by access site. The adjusted *p* value was calculated using inverse probability of treatment weights logistic regression.

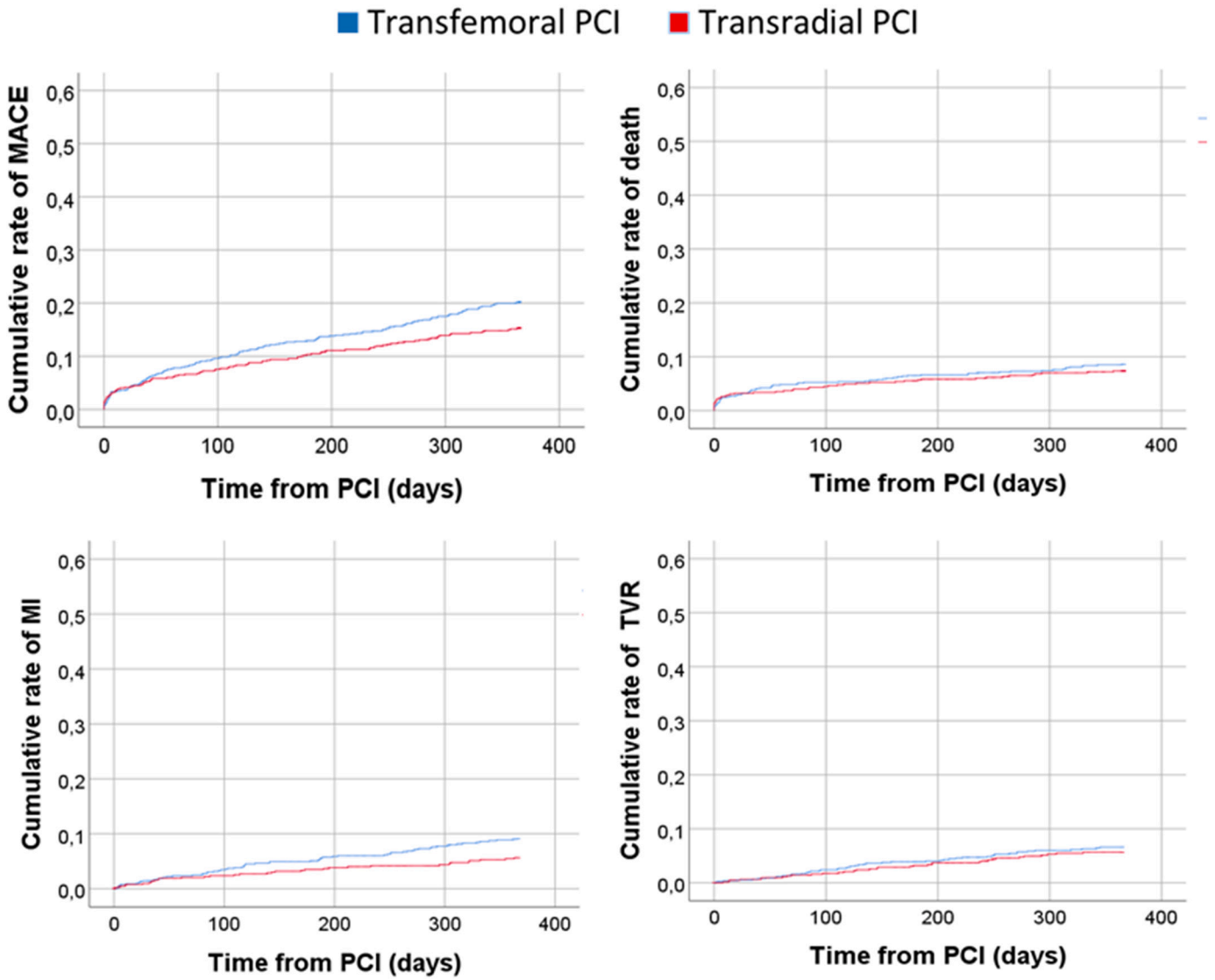

Fig. 2. Kaplan-Meier curves for efficacy outcomes, stratified by access site. MACE, major adverse cardiac events, included death, myocardial infarction (MI) or target vessel revascularisation (TVR).

[23]. Similar results have been obtained in patients undergoing HSRA-PCI [24,25]. The lack of mortality benefit with TRA in our study may be explained by the very low proportion of STEMI patients and the fact that HSRA-PCI is often performed as a staged procedure that may increase adherence to best practice for TFA and decrease the overall risk for TFA related complications.

To our knowledge, this is the first study comparing long-term efficacy (TVR, MI or clinically driven restenosis) for TRA vs TFA in subjects undergoing HSRA-PCI. We found that TRA was associated with equivalent long-term efficacy compared to TFA. HSRA technique has over the years evolved from aggressive plaque debulking to plaque modification which allows subsequent balloon expansion and stent deployment [2,26]. The latter can be accomplished with small burrs (1.25 to 1.75 mm) accommodated in a 6F guide catheter. Large burr sizes ($\geq$2.00 mm) has not improved outcomes in small observational studies [27] and are associated with higher risk of coronary artery perforation or slow flow [2,26]. Furthermore, recent advances in PCI technique, such as sheathless guide catheters and balloon- or pigtail-assisted tracking allows the use of 7 or 7.5 Fr guide catheter through the radial artery if more extensive rotablation with up to 2.0 mm burr size is needed [28].

Our findings are in line with that of previous studies, including small single-center observational studies [24,25], two registry-based studies [11,29] and one meta-analysis [30] which showed that HSRA by TRA was associated with similar angiographic success but lower risk for in-hospital bleeding and vascular complications compared to TFA. Our study expands these findings in a large nationwide all-comer population and for the first time provides long-term efficacy outcomes that may reveal long-term complications from suboptimal PCI due to access site related issues.

In line with previous reports from other countries [11], the use of TRA in HSRA-PCI remained considerably lower than that in the overall PCI population in Sweden [12]. Although patient and anatomical characteristics may have defined the access site choice in selected cases, we found no significant interaction between baseline characteristics and temporal changes in TRA use. The large difference regarding access site choice between the 10 highest HSRA-PCI procedure volume operators indicates that operators' preference may be the main reason for the lower utilization of TRA in HSRA-PCI. Nevertheless, avoidance of bleeding complications by TRA is crucial to further improve outcomes, quality of care and reduce cost in patients undergoing HSRA-PCI.

4.1. Limitation

The main limitation of the present study is the non-randomized selection of the access site. Despite adequate statistical methods to adjust for observed confounders we cannot exclude residual confounders that may have affected our findings. However, our results are in line with randomized control trials comparing TRA and TFA in a general PCI population. Information about sheath, guide catheter and burr sizes were not collected in the registry. However, the influence of burr size in access site choice should be modest and overuse of large sheaths and guiding catheters to deliver small burr sizes have previously been described. In current practice there is rarely a need to use Burr sizes $>$1.75 mm thus obviating even the need for frequently using guide catheters larger than 6 Fr and based on our experience, burr sizes $\geq$2.00 mm have scarcely been used in patients undergoing HSRA-PCI in Sweden. Information about bilateral femoral or bilateral radial access were not collected in the registry. However, exclusion of patients undergoing CTO-PCI did not significantly change our findings. The reported incidence of periprocedural MI was low, indicating that only clinically relevant periprocedural MI were collected in the registry.

5. Conclusion

In patients undergoing HSRA-PCI, TRA as compared to TFA, was associated with significantly lower risk for bleeding complications without any difference in angiographic success and long-term efficacy. Our study supports the adoption of TRA as the default access site choice to improve HSRA-PCI-related outcomes.

Contribution of authors

L. Desta and D. Venetsanos were responsible for the conception and design of the study, statistical analysis and interpretation of the data and drafted the manuscript. J. Jurga, S. Völz, E. Omerovic, A. Ulvenstam, S. Zwackman, C. Pagonis, F. Calle, G. Olivecrona, J. Persson have participated in the interpretation of the data and have critically revised the manuscript and added important intellectual content. All authors have read and approved the manuscript.

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CRediT authorship contribution statement

Liyew Desta: Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Visualization, Project administration. **Juliane Jurga:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Sebastian Völz:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Elmir Omerovic:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Anders Ulvenstam:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Sammy Zwackman:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Christos Pagonis:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Fredrik Calle:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Göran K. Olivecrona:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Jonas Persson:** Conceptualization, Methodology, Validation, Writing – review & editing, Visualization. **Dimitrios Venetsanos:** Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Visualization, Project administration.

Declaration of Competing Interest

L. Desta has nothing to declare, J. Jurga has nothing to declare, S. Völz has nothing to declare, E. Omerovic reports institutional research grant from Astra Zeneca and consulting fees from Novartis, MSD, Astra Zeneca and Bayer, outside the submitted work, A. Ulvenstam has nothing to declare, S. Zwackman has nothing to declare, C. Pagonis has nothing to declare, F. Calle has nothing to declare, G K Olivecrona has nothing to declare, J. Persson reports unrestricted research grant and lecture fee from Abbott Vascular, outside the submitted work, D. Venetsanos received an unrestricted institutional research grant from Boston Scientific International S.A for the submitted work.

Appendix A. Supplementary data

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