JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
MAY 30, 2017
VOLUME 69
NUMBER 21

■ www.onlinejacc.org
ELSEVIER
ISSN 0735-1097

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2017 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 69, NO. 21, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.02.070

Acute Kidney Injury After Radial or Femoral Access for Invasive Acute Coronary Syndrome Management

AKI-MATRIX

Giuseppe Andò, MD, PhD,[a] Bernardo Cortese, MD,[b] Filippo Russo, MD,[c] Martina Rothenbühler, MSc,[d] Enrico Frigoli, MD,[e] Giuseppe Gargiulo, MD,[f,aa] Carlo Briguori, MD,[g] Pascal Vranckx, MD, PhD,[h] Sergio Leonardi, MD, MHS,[i] Vincenzo Guiducci, MD,[j] Flavia Belloni, MD,[k] Fabio Ferrari, MD,[l] Jose Maria de la Torre Hernandez, MD,[m] Salvatore Curello, MD,[n] Francesco Liistro, MD,[o] Andrea Perkan, MD,[p] Stefano De Servi, MD,[q] Gavino Casu, MD,[r] Antonio Dellavalle, MD,[s] Dionigi Fischetti, MD,[t] Antonio Micari, MD,[u] Bruno Loi, MD,[v] Fabio Mangiacapra, MD,[w] Nunzio Russo, MD,[x] Fabio Tarantino, MD,[y] Francesco Saia, MD, PhD,[z] Dik Heg, PhD,[d] Stephan Windecker, MD,[aa] Peter Jüni, MD,[aa,bb] Marco Valgimigli, MD, PhD,[aa]
for the MATRIX Investigators

ABSTRACT

BACKGROUND It remains unclear whether radial access (RA), compared with femoral access (FA), mitigates the risk of acute kidney injury (AKI).

OBJECTIVES The authors assessed the incidence of AKI in patients with acute coronary syndrome (ACS) enrolled in the MATRIX-Access (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox) trial.

METHODS Among 8,404 patients, 194 (2.3%) were excluded due to missing creatinine values, no or an incomplete coronary angiogram, or previous dialysis. The primary AKI-MATRIX endpoint was AKI, defined as an absolute (>0.5 mg/dl) or a relative (>25%) increase in serum creatinine (sCr).

RESULTS AKI occurred in 634 patients (15.4%) with RA and 712 patients (17.4%) with FA (odds ratio [OR]: 0.87; 95% confidence interval [CI]: 0.77 to 0.98; p = 0.0181). A >25% sCr increase was noted in 633 patients (15.4%) with RA and 710 patients (17.3%) with FA (OR: 0.87; 95% CI: 0.77 to 0.98; p = 0.0195), whereas a >0.5 mg/dl absolute sCr increase occurred in 175 patients (4.3%) with RA versus 223 patients (5.4%) with FA (OR: 0.77; 95% CI: 0.63 to 0.95; p = 0.0131). By implementing the Kidney Disease Improving Global Outcomes criteria, AKI was 3-fold less prevalent and trended lower with RA (OR: 0.85; 95% CI: 0.70 to 1.03; p = 0.090), with stage 3 AKI occurring in 28 patients (0.68%) with RA versus 46 patients (1.12%) with FA (p = 0.0367). Post-intervention dialysis was needed in 6 patients (0.15%) with RA and 14 patients (0.34%) with FA (p = 0.0814). Stratified analyses suggested greater benefit with RA than FA in patients at greater risk for AKI.

CONCLUSIONS In ACS patients who underwent invasive management, RA was associated with a reduced risk of AKI compared with FA. (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX [MATRIX]; NCT01433627) (J Am Coll Cardiol 2017;69:2592-603) © 2017 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Azienda Ospedaliera Universitaria Policlinico "Gaetano Martino," University of Messina, Messina, Italy; [b]Department of Medicine, Ospedale Fate bene Fratelli, Milano, Italy; [c]Azienda Ospedaliera Sant'Anna, Como, Italy; [d]CTU Bern, and Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland; [e]EUSTRATEGY Association, Forli (FC), Italy; [f]Department of Advanced Biomedical Science, University of Naples Federico II, Naples, Italy; [g]Clinica Mediterranea, Napoli, Italy; [h]Department of Cardiology and Critical Care Medicine, Hartcentrum Hasselt, Jessa Ziekenhuis, Hasselt, Belgium; [i]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [j]A.O. Santa Maria Nuova, Reggio Emilia, Italy; [k]Ospedale Santo Spirito in Saxia, Roma,

Acute kidney injury (AKI) occurs in 10% to 27% of patients with acute coronary syndrome (ACS) who undergo percutaneous coronary intervention (PCI) and is associated with greater morbidity and mortality (1,2). Pathophysiology of AKI in these patients is multifactorial, involving contrast volume, impaired systemic and renal hemodynamic conditions, imbalance of endogenous vasodilating and vasoconstrictive factors, and direct cholesterol embolization (1). Although the risk of AKI can be predicted (3), and contrast media volume plays a central role in its pathogenesis (4), the possibility of implementing prophylactic interventions is limited (5). This is especially relevant for patients who require urgent PCI, such as those undergoing intervention for ACS. Observational data with propensity matching (6,7) and a meta-analysis (8) have suggested an association between the use of radial access (RA) and a lower incidence of AKI. Putative explanations for this effect are a reduction of bleeding events (7) and/or a lower risk of cholesterol embolization in the renal circulation (9,10) offered by RA (11). However, no prospective assessment of the incidence of AKI has been carried out in randomized studies of patients receiving RA compared with femoral access (FA). In the largest randomized comparison between RA and FA to date, the MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of Angiox) trial, RA was associated with a reduced incidence of net adverse clinical events because of a reduction of bleeding and fatalities compared with FA (12).

SEE PAGE 2604

We pre-specified (11) a prospective assessment of whether RA compared with FA reduced the incidence of AKI in patients with ACS, including analysis of patients with ST-segment elevation myocardial infarction (STEMI) or non–ST-segment elevation myocardial infarction (NSTEMI) who underwent invasive management.

METHODS

MATRIX-Access was designed as a randomized, multicenter, superiority trial comparing RA with FA in patients with myocardial infarction with or without ST-segment elevation who underwent coronary angiography, and, if clinically indicated, PCI (12,13). This was the first of 3 randomized comparisons of the MATRIX program and was performed in all consenting patients. The trial was approved by the institutional review board at each center, and all patients gave written

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

AKI = acute kidney injury

BARC = Bleeding Academic Research Consortium

CES = cholesterol embolization syndrome

CI = confidence interval

CIN = contrast-induced nephropathy

eGFR = estimated glomerular filtration rate

FA = femoral access

KDIGO = Kidney Disease Improving Global Outcomes

NSTEMI = non–ST-segment elevation myocardial infarction

OR = odds ratio

PCI = percutaneous coronary intervention

RA = radial access

RRR = relative risk ratio

sCR = serum creatinine

STEMI = ST-segment elevation myocardial infarction

Italy; [l]A.O. Universitaria San Luigi Gonzaga di Orbassano Turin, Italy; [m]Hospital Marques de Valdecilla, Santander, Spain; [n]A.O. Spedali Civili, Brescia, Italy; [o]Ospedale San Donato, Arezzo, Italy; [p]A.S.U.I, Trieste, Italy; [q]Ospedale Civile di Legnano, Legnano, Italy; [r]Ospedale San Francesco, Nuoro, Italy; [s]Ospedali Riuniti ASL 17, Savigliano (CN), Italy; [t]Ospedale Vito Fazzi, Lecce, Italy; [u]GVM Care and Research Maria Eleonora Hospital, Palermo, Italy; [v]A.O. Brotzu, Cagliari, Italy; [w]Campus Biomedico, Roma, Italy; [x]P.O. San Vincenzo, Taormina (ME), Italy; [y]Ospedale G.B. Morgagni, Forlì, Italy; [z]University Hospital of Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy; [aa]Swiss Cardiovascular Center Bern, Bern University Hospital, Bern, Switzerland; and the [bb]Institute of Primary Health Care, University of Bern, Bern, Switzerland. The MATRIX trial was funded by The Medicines Company and Terumo. This substudy did not receive any direct or indirect funding. The program was designed by the principal investigator (Dr. Valgimigli); sponsored by the Italian Society of Interventional Cardiology (GISE), a nonprofit organization; and received grant support from The Medicines Company and TERUMO (Online Appendix). Sponsor and companies had no role in study design, data collection, data monitoring, analysis, interpretation, or writing of the report. Dr. Andò has received nonfinancial support from Terumo, Abbott Vascular, Biotronik, AstraZeneca, and Menarini; personal fees and nonfinancial support from St. Jude Medical; and personal fees from Bayer Healthcare Pharmaceuticals and Daiichi-Sankyo. Dr. Cortese has received institutional research grant support from AB Medica; honorarium from Hexacath, Amgen, Stentys; and is a consultant for Aachen Resonance, Abbott Vascular, AstraZeneca, Kardia, Innova, and Stentys. Dr. Gargiulo has received a research grant from Cardiopath. Dr. Vranckx has received nonfinancial support from AstraZeneca, Bayer Health Care, Boehringer Ingelheim, Daiichi-Sankyo, and The Medicines Co. Dr. Leonardi has received grants and personal fees from AstraZeneca; and personal fees from The Medicines Company and Daiichi-Sankyo. Dr. Guiducci has received speaker fees from Abbott. Dr. Liistro has received personal fees from Cook Medical. Dr. Tarantino has received personal fees from Abbott Vascular. Dr. Saia has received personal fees from The Medicine Company, AstraZeneca, Daiichi-Sankyo, Terumo, St. Jude, Abbott Vascular, Menarini, Sanofi, Boston Scientific, Livanova, Medtronic, Eli Lilly, and Servier. Dr. Jüni has received research grants to the institution from AstraZeneca, Biotronik, Biosensors International, Eli Lilly, and The Medicines Company; and serves as an unpaid member of the steering group of trials funded by AstraZeneca, Biotronik, Biosensors, St. Jude Medical, and The Medicines Company. Dr. Windecker has received research grants to the institution from Bracco, Boston Scientific, and Terumo. Dr. Valgimigli has received grants from Terumo and The Medicines Company; grants and personal fees from AstraZeneca, and personal fees from Terumo, Bayer, and Biosensors. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 28, 2016; revised manuscript received January 31, 2017, accepted February 2, 2017.

TABLE 1 Baseline Clinical and Procedural Characteristics

	Radial Access (n = 4,109)	Femoral Access (n = 4,101)	p Value
Clinical characteristics			
Age, yrs	65.5 ± 11.8	65.9 ± 11.8	0.17
≥75 yrs	1,040 (25.3)	1,076 (26.2)	0.34
Male	3,063 (74.5)	2,977 (72.6)	0.045
Hypotension*	26 (0.6)	33 (0.8)	0.36
Anemia†	796 (19.4)	810 (19.8)	0.66
Diabetes	936 (22.8)	917 (22.4)	0.65
Creatinine >1.5 mg/dl	4,003 (97.4)	4,003 (97.6)	0.58
Killip class III or IV	129 (3.1)	101 (2.5)	0.063
STEMI	1,977 (48.1)	1,975 (48.2)	0.97
NSTEMI	2,132 (51.9)	2,126 (51.8)	0.97
Troponin negative	233 (5.7)	255 (6.2)	0.29
Troponin positive	1,899 (46.2)	1,871 (45.6)	0.59
With ST-segment deviation	983 (23.9)	956 (23.3)	0.51
With T-wave inversion	637 (15.5)	656 (16.0)	0.54
Ejection fraction ≤35%	339 (8.6)	362 (9.2)	0.33
Systolic arterial pressure, mm Hg	138.6 ± 25.5	139.0 ± 25.7	0.50
Hemoglobin at baseline, g/dl	13.9 ± 1.9	13.9 ± 1.9	0.26
Glucose at baseline, mg/dl	138.3 ± 66.8	138.9 ± 63.9	0.67
Medications administered before catheterization laboratory			
Statins	1,766 (43.0)	1,815 (44.3)	0.24
ACE inhibitors	1,227 (29.9)	1,266 (30.9)	0.32
Angiotensin II receptor antagonist	441 (10.7)	456 (11.1)	0.57
Loop diuretics	463 (11.3)	471 (11.5)	0.76
Potassium-sparing diuretics	85 (2.1)	95 (2.3)	0.44
Other diuretics	114 (2.8)	94 (2.3)	0.16
Procedural characteristics			
Any crossover during index hospitalization	329 (8.0)	231 (5.6)	0.00012
Total amount of contrast used during index hospitalization	183.3 ± 104.5	183.9 ± 110.1	0.83
No PCI attempted after coronary angiography during index hospitalization	742 (18.1)	747 (18.2)	0.85
CABG	144 (3.5)	146 (3.6)	0.89
Patients with significant lesion and medical treatment	472 (11.5)	474 (11.6)	0.92
Patients without significant lesion	129 (3.1)	128 (3.1)	0.96
≥1 PCI attempted	3,367 (81.9)	3,354 (81.8)	0.85
Died during PCI	1 (0.0)	0 (0.0)	1.00
≥1 PCI completed during index hospitalization	3,366 (81.9)	3,354 (81.8)	0.88
Medications administered in and after the catheterization laboratory			
Aspirin	228 (5.5)	274 (6.7)	0.032
Clopidogrel	270 (6.6)	257 (6.3)	0.57
Prasugrel	331 (8.1)	291 (7.1)	0.10
Ticagrelor	376 (9.2)	391 (9.5)	0.55
GPIs	582 (14.2)	522 (12.7)	0.057
Planned GPI	420 (10.2)	369 (9.0)	0.060
Bailout GPI	165 (4.0)	154 (3.8)	0.54
Unfractionated heparin	2,071 (50.4)	1,908 (46.5)	0.00044
Total unfractionated heparin, U/kg	41.0 ± 51.3	37.9 ± 48.8	0.0066
At least 1 subtherapeutic regimen, <50 U/kg	465 (11.3)	337 (8.2)	<0.0001
At least 1 therapeutic regimen, ≥50 U/kg	1,643 (40.0)	1,597 (38.9)	0.33
Bivalirudin	1,697 (41.3)	1,719 (41.9)	0.57
Prolonged infusion post-PCI	863 (21.0)	868 (21.2)	0.86
Average of total duration of post-PCI bivalirudin infusion, min	82.2 ± 201.8	87.5 ± 223.8	0.26
Patients receiving full bivalirudin regimen post-PCI	320 (7.8)	301 (7.3)	0.44
Average of total duration of full bivalirudin regimen, min	21.7 ± 86.9	21.1 ± 104.6	0.78
Patients receiving low bivalirudin regimen post-PCI	552 (13.4)	580 (14.1)	0.35
Average of total duration of low bivalirudin regimen, min	60.4 ± 187.8	66.4 ± 203.8	0.17
≥1 intra-aortic balloon pump	80 (1.9)	96 (2.3)	0.22

Continued on the next page

TABLE 1 Continued

	Radial Access (n = 4,109)	Femoral Access (n = 4,101)	p Value
≥1 PCI completed	3,366	3,354	
TIMI flow grade 3 in all treated lesions during whole index hospitalization	3,193 (94.9)	3,189 (95.1)	0.68
Coronary stenosis <30% in all treated lesions	3,206 (95.2)	3,185 (95.0)	0.59
Procedural success in all treated lesions	3,109 (92.4)	3,098 (92.4)	1.00
Duration of procedure	61.2 ± 36.6	60.1 ± 37.4	0.22
Amount of contrast used	202.8 ± 103.1	204.2 ± 109.6	0.61
Treated vessel(s) per patient			
Left main coronary artery	175 (5.2)	156 (4.7)	0.30
Left anterior descending artery	1,846 (54.9)	1,813 (54.1)	0.51
Left circumflex artery	1,055 (31.4)	1,044 (31.1)	0.84
Right coronary artery	1,241 (36.9)	1,232 (36.7)	0.90
Bypass graft	21 (0.6)	37 (1.1)	0.034
At least 2 vessels treated	806 (24.0)	793 (23.7)	0.77
Lesions treated per patient, n	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.74
1	2,314 (68.8)	2,313 (69.0)	
2	738 (21.9)	754 (22.5)	
≥3	312 (9.3)	286 (8.5)	
≥1 complex lesion	1,856 (55.2)	1,789 (53.4)	0.13
Stents per patient, n	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.26
Overall stent length per patient, mm	58.1 ± 54.6	57.3 ± 55.0	0.50
Lesions			
Number of lesions with PCI	4,843	4,768	
Lesions stented	4,437 (91.6)	4,324 (90.7)	0.13
≥1 drug-eluting stent	3,281 (67.7)	3,240 (68.0)	0.79
≥1 bare-metal stent	1,156 (23.9)	1,084 (22.7)	0.26
Lesions not stented	406 (8.4)	444 (9.3)	0.13
TIMI flow grade pre-procedure			0.88
0 or 1	1,657 (34.2)	1,645 (34.5)	0.87
2	565 (11.7)	562 (11.8)	0.87
3	2,619 (54.1)	2,559 (53.7)	0.99
TIMI flow grade post-procedure			0.76
0 or 1	79 (1.6)	73 (1.5)	0.73
2	106 (2.2)	103 (2.2)	0.98
3	4,656 (96.2)	4,590 (96.3)	0.78
Coronary stenosis <30%	4,661 (96.3)	4,582 (96.1)	0.67
Procedural success	4,554 (94.0)	4,489 (94.1)	0.82
Number of lesions stented	4,437	4,324	
Total stent length per lesion, mm	26.2 ± 14.7	26.5 ± 14.9	0.61
Average stent diameter per lesion, mm	3.0 ± 0.5	3.0 ± 0.5	0.25
≥1 direct stenting	978 (22.0)	922 (21.3)	0.77
Post-dilation	2,034 (45.8)	2,016 (46.6)	0.48

Values are mean ± SD, n (%), n, or median (interquartile range). *Systolic blood pressure <80 mm Hg. †<12 g/dl for women, <13 g/dl for men.

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass graft surgery; GPI = glycoprotein IIb/IIIa inhibitor; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction.

informed consent. Patients were eligible if they had ACS and planned coronary angiography, and the interventional cardiologist was willing to proceed with either RA or FA. That meant cardiologists were required to have expertise in both, including at least 75 coronary interventions performed and at least 50% of interventions in ACS via the radial route during the previous year. The main inclusion and exclusion criteria of the MATRIX-Access trial were previously reported (Online Appendix) (12,14). All patients enrolled in MATRIX-Access were eligible for the AKI-MATRIX substudy, except those with incomplete creatinine data who did not receive a complete angiogram or those who had end-stage renal disease that required dialysis.

STUDY PROTOCOL AND RANDOMIZATION. Before angiography, patients were centrally allocated 1:1 to

RA or FA 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 NSTEMI, and in the latter case, whether troponin-positive or not), and anticipated use of immediate PCI. Patients proceeding to PCI were further randomized to bivalirudin, administered according to product labeling, or to unfractionated heparin, dosed at 70 to 100 U/kg in patients who did not receive glycoprotein IIb/IIIa inhibitors or at 50 to 70 U/kg in patients who received planned glycoprotein IIb/IIIa inhibitors. Use of other anticoagulants was not allowed, whereas other antithrombotic medications, including oral antiplatelet agents and non-antithrombotic medications, were allowed as per guidelines (15).

STUDY OUTCOMES. The endpoints of the MATRIX-Access study have been previously reported (12,13). The primary endpoint of the AKI-MATRIX substudy was the incidence of AKI, defined as either an absolute (>0.5 mg/dl) or a relative (>25%) increase from baseline in serum creatinine (sCr) levels during hospitalization in the intention-to-treat population (16). The incidence of AKI was also assessed using either defining criterion, as well as the Kidney Disease Improving Global Outcomes (KDIGO) criteria and staged for severity (17). Sensitivity analyses were also performed in patients who had the randomly allocated access site (i.e., excluding patients with access site crossover) or in those proceeding to PCI after diagnostic coronary angiography (i.e., excluding patients who received only an angiogram and no further PCI). Bleeding complications were defined per the Bleeding Academic Research Consortium (BARC) scale (Online Appendix).

STATISTICAL ANALYSIS. Details related to the sample size calculation and the statistical analyses have been described previously (12). No a priori sample size considerations were performed to assess AKI-MATRIX study power (11). However, for explorative purposes, power analyses were previously computed assuming a 5% absolute increase in sCr of >0.5 mg/dl in the FA group and 50%, 35%, and 25% relative risk reductions (RRRs) in the RA group. We conservatively assumed a 5% incidence of AKI in the FA group, although the incidence of AKI in contemporary studies of PCI in ACS could be 3-fold higher. Available data suggested a possible 25% RRR in AKI incidence with the RA approach across unselected populations who underwent PCI. Hypothesizing a 33% RRR of AKI with RA in the MATRIX study, with 3,400 patients per group who underwent PCI, we would have >93% power of detecting a reduction in the incidence of AKI to 3.3% in the RA group at the 5% alpha level.

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 differences at lesion level considered the nested structure of lesions within individuals, and then were analyzed using multilevel general or generalized mixed models, as appropriate. We applied both univariate and multivariable logistic regression models to evaluate the association of AKI during index hospitalization with Mehran's score, bleeding, and measures of bleeding severity. Furthermore, we performed stratified logistic regressions by subgroups, including the center's proportion of radial PCI, diabetes at baseline, estimated glomerular filtration rate (eGFR), age, clinical presentation, Killip class, left ventricular ejection fraction, and Mehran's score. The analyses were done using Stata release 14.1 (StataCorp LLC, College Station, Texas) and R 3.3.0 (R Foundation, Vienna, Austria).

RESULTS

Among 8,404 patients enrolled in the MATRIX-Access trial from 78 centers in Italy, the Netherlands, Spain, and Sweden between October 2011 and July 2014, 194 patients (2.3%) were excluded due to an incomplete sCr dataset (96 FA and 82 RA patients), no or an incomplete coronary angiogram (6 FA and 2 RA patients), or previous dialysis at randomization (4 patients in each group) (Online Figure 1). Among the 8,210 patients included in the analysis, one-half (n = 4,109) were allocated to RA and the other 4,101 participating patients were allocated to FA. Baseline demographics and procedural characteristics were similar for the 2 groups (**Table 1**).

AKI occurred in 1,345 patients (16.4%), per the primary endpoint as defined by a relative (>25%) increase in sCr and in 387 patients (4.7%) according to an absolute increase in sCr of >0.5 mg/dl. Patients with AKI were older and more frequently women, and had a higher prevalence of diabetes and anemia (Online Table 1). Study participants who developed AKI were more likely to have presented with STEMI and advanced Killip class; plus, their access site crossover rate was twice as frequent. Patients with AKI more commonly underwent PCI or received treatment for complex or multiple lesions, including

left main or left anterior coronary arteries (Online Table 1). Patients who had AKI had lower rates of statin therapy but higher rates of angiotensin II receptor blocker and diuretic use before presentation to the catheterization laboratory. The amount of contrast used and procedural failure rate were higher in patients with AKI compared with those without AKI (Online Table 1).

ENDPOINTS ACCORDING TO ACCESS SITE. Before randomization, sCr and eGFR were similar between the RA and FA groups (Table 2). Peak sCr after intervention or at discharge did not differ in the RA group versus the FA group, whereas nadir eGFR was lower in the FA group during hospitalization (79.6 ± 25.9 ml/min/1.73 m^2 vs. 78.2 ± 25.7 ml/min/1.73 m^2; p = 0.0099) and at discharge (84.6 ± 26.5 ml/min/1.73 m^2 vs. 83.4 ± 26.1 ml/min/1.73 m^2; p = 0.030) (Table 2).

The primary outcome of AKI occurred in significantly fewer patients with RA than in those with FA (15.4% vs. 17.4%; p = 0.0181) (Central Illustration, Table 3). Both components of the AKI primary endpoint definition were significantly lower in patients with RA. Specifically, a >25% increase in sCr was observed in 633 patients (15.4%) with RA and 710 patients (17.3%) with FA (odds ratio [OR]: 0.87; 95% confidence interval [CI]: 0.77 to 0.98; p = 0.0195), and a >0.5 mg/dl absolute increase in sCr occurred in 175 patients (4.3%) with RA and 223 patients (5.4%) with FA (relative risk: 0.77; 95% CI: 0.63 to 0.95; p = 0.0131). Post-intervention dialysis occurred in fewer patients with RA than in those with FA (0.15% vs. 0.34%; p = 0.0814) (Table 3).

After excluding patients who did not receive the randomly allocated access site (n = 605), either because it failed or it was not attempted, AKI occurred in significantly fewer patients with RA compared with FA (14.3% vs. 16.7%; p = 0.0038) because of significant reductions of both components of the primary endpoint. The need for dialysis was also lower with RA access compared with FA (OR: 0.16; 95% CI: 0.04 to 0.69; p = 0.0146) (Table 3).

Among patients who received PCI after coronary angiography during the index hospitalization (n = 6,616; 80.5% of the AKI-MATRIX population), RA was associated with a 14% risk reduction of AKI compared with FA (OR: 0.86; 95% CI: 0.76 to 0.98; p = 0.0202). Three (0.09%) patients in the RA group and 10 (0.3%) patients in the FA group underwent dialysis therapy (p = 0.0659) (Table 3).

By implementing the KDIGO criteria, AKI occurred in 213 patients (5.2%) with RA and 248 patients (6.1%) with FA (p = 0.090). Stage 1 or 2 AKI were not reduced in the RA group (Table 2), but stage 3 was lower with RA (0.7% vs. 1.1%; p = 0.037) (Central Illustration, Table 3).

TABLE 2 Renal Function

	Randomized to Radial Access (n = 4,109)	Randomized to Femoral Access (n = 4,101)	p Value
Creatinine, mg/dl			
Pre-PCI	0.97 ± 0.36	0.98 ± 0.32	0.7434
Post-PCI	1.06 ± 0.55	1.08 ± 0.54	0.1271
At hospital discharge	0.99 ± 0.44	1.00 ± 0.43	0.2361
eGFR, ml/min/1.73 m^2 (MDRD formula)			
Pre-PCI	84.22 ± 25.36	83.46 ± 25.51	0.1786
Post-PCI	79.63 ± 25.87	78.16 ± 25.65	0.0099
At hospital discharge	84.62 ± 26.50	83.35 ± 26.10	0.0300

Values are mean ± SD.

eGFR = estimated glomerular filtration rate; MDRD = Modification of Diet in Renal Disease; PCI = percutaneous coronary intervention.

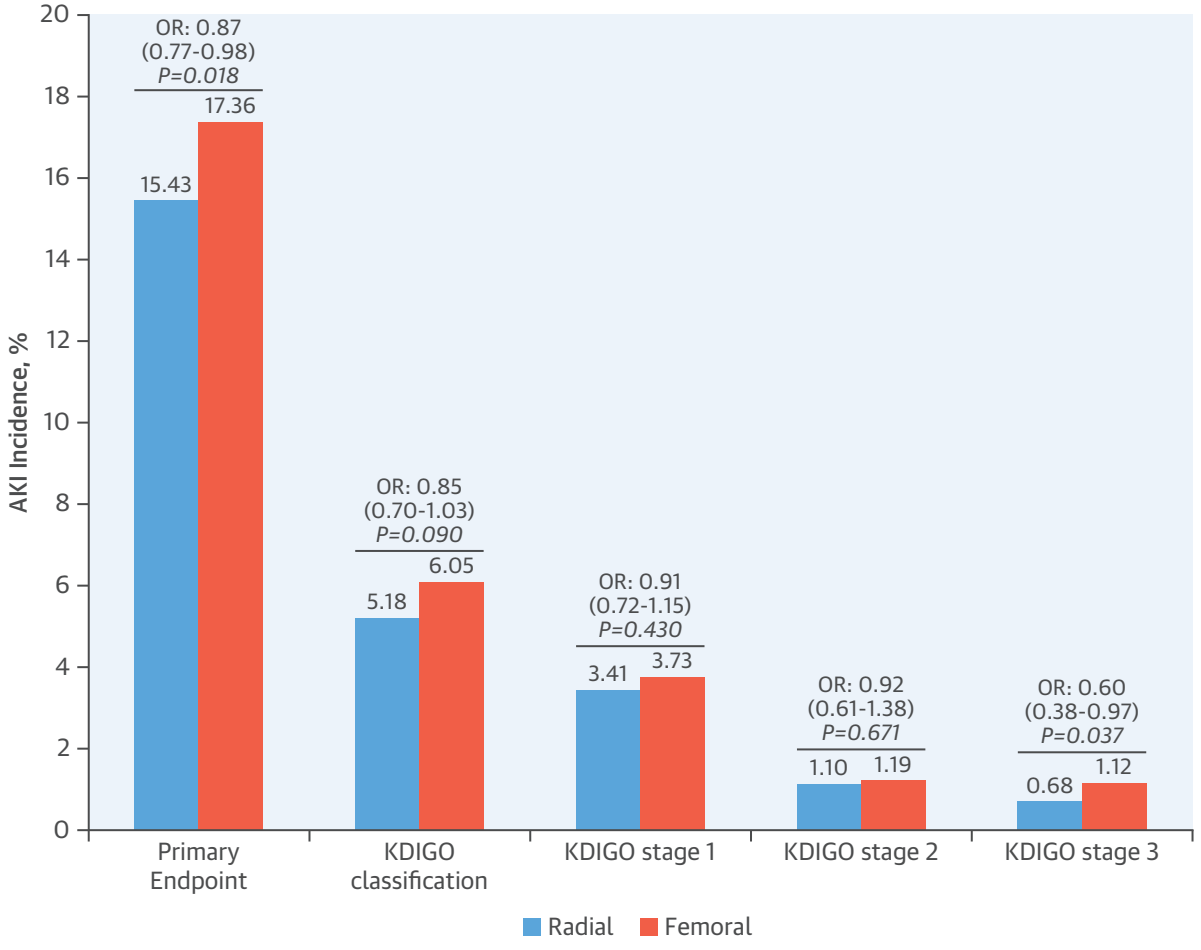
SUBGROUP ANALYSIS AND MULTIVARIATE MODELING. The effects of RA versus the effects of FA in reducing the incidence of AKI was largely consistent across subgroups, including the participating center's proportion of radial PCI, diabetes, age, and clinical presentation (Figure 1). Positive quantitative interaction testing was noted between the randomized access site and the pre-procedural renal function, Killip class, and Mehran score, which suggested relatively greater benefit with RA compared with FA in patients at higher baseline risk for AKI. There was significant interaction also between the access site and antithrombotic therapy, with RA showing benefit in patients who received unfractionated heparin, but apparently no benefit was seen in those allocated to bivalirudin. Online Figure 2 shows subgroup analysis according to the components of the Mehran risk score.

At multivariable modeling, random allocation to RA remained associated with a significantly lower risk of AKI (OR: 0.87; 95% CI: 0.77 to 0.98; p = 0.0217) when the covariates included in the Mehran score were entered (Table 4). When access site bleeding was entered into the logistic model (model 2), random allocation to RA was associated with a nonsignificant 11% RRR (p = 0.0647), whereas an access-related BARC score of ≥2 complications showed a 2-fold significantly increased risk (OR: 2.19; 95% CI: 1.66 to 2.89; p < 0.0001) (Table 4). Hemoglobin drop after randomization (model 3) and blood red transfusion (model 4) were also associated with AKI (Table 4).

DISCUSSION

Among patients with ACS (with or without ST-segment elevation) who were managed invasively,

CENTRAL ILLUSTRATION **Radial Versus Femoral Approach in AKI Patients Undergoing Invasive Management**



Andò, G. et al. J Am Coll Cardiol. 2017;69(21):2592–603.

We assessed whether use of radial versus femoral access mitigated incidence of acute kidney injury (AKI) in patients with acute coronary syndrome who underwent invasive management. Radial access significantly reduced AKI incidence in terms of the primary endpoint (defined as either a 25% relative increase or a 0.5 mg/dl absolute increase of serum creatinine). Reductions also were seen by Kidney Disease Improving Global Outcomes (KDIGO) classification, but only significantly so in stage 3. OR = odds ratio.

the use of RA was significantly associated with a reduced occurrence of AKI compared with FA. Both components of the primary endpoint (i.e., an absolute >0.5 mg/dl or a relative >25% increase in sCR) were reduced with RA, and fewer patients in the RA group underwent dialysis, even if this difference did not reach statistical significance. These findings were consistent across pre-defined patient subgroups. However, there was quantitative positive interaction testing in patients at the highest risk for AKI, such as those with reduced eGFR, advanced Killip class, or high Mehran score, in whom a greater benefit of RA versus FA was observed. In the subpopulation of patients who entered the antithrombin portion of the study, we also noted a significant interaction with the type of allocated anticoagulant at the time of PCI. A greater than average treatment effect was observed in patients who received unfractionated heparin, but no apparent effect was seen in those allocated to bivalirudin.

Sensitivity analyses showed consistent results among patients in whom access was made as randomly allocated and in patients who underwent PCI during their index hospitalization. The

TABLE 3 Acute Kidney Injury

	Randomized to Radial Access	Randomized to Femoral Access	Odds Ratio (95% CI)	p Value
All patients receiving an angiography and/or PCI	4,109	4,101		
AKI according to primary endpoint definition	634 (15.43)	712 (17.36)	0.87 (0.77–0.98)	0.0181
AKI 25% relative increase	633 (15.41)	710 (17.31)	0.87 (0.77–0.98)	0.0195
AKI 0.5 absolute increase	175 (4.26)	223 (5.44)	0.77 (0.63–0.95)	0.0131
After index procedure only	605 (14.72)	670 (16.34)	0.88 (0.78–1.00)	0.0436
AKI 25% relative increase	603 (14.68)	668 (16.29)	0.88 (0.78–1.00)	0.0434
AKI 0.5 absolute increase	170 (4.14)	217 (5.29)	0.77 (0.63–0.95)	0.0138
After staged procedure only	75 (1.83)	95 (2.32)	0.78 (0.58–1.06)	0.1189
AKI 25% relative increase	72 (1.75)	95 (2.32)	0.75 (0.55–1.02)	0.0711
AKI 0.5 absolute increase	19 (0.46)	25 (0.61)	0.76 (0.42–1.38)	0.3625
AKI according to the KDIGO classification	213 (5.18)	248 (6.05)	0.85 (0.70–1.03)	0.0900
Stage 1	140 (3.41)	153 (3.73)	0.91 (0.72–1.15)	0.4295
Stage 2	45 (1.10)	49 (1.19)	0.92 (0.61–1.38)	0.6713
Stage 3	28 (0.68)	46 (1.12)	0.60 (0.38–0.97)	0.0367
Dialysis during hospitalization	6 (0.15)	14 (0.34)	0.43 (0.16–1.11)	0.0814
Patients without crossover during PCI	3,765	3,840		
AKI according to primary endpoint definition	538 (14.29)	641 (16.69)	0.83 (0.73–0.94)	0.0038
AKI 25% relative increase	538 (14.29)	639 (16.64)	0.84 (0.74–0.95)	0.0046
AKI 0.5 absolute increase	140 (3.72)	198 (5.16)	0.71 (0.57–0.89)	0.0025
Dialysis during hospitalization	2 (0.05)	13 (0.34)	0.16 (0.04–0.69)	0.0146
Only patients who underwent index PCI*	3,317	3,299		
AKI according to primary endpoint definition	530 (15.98)	598 (18.13)	0.86 (0.76–0.98)	0.0202
AKI 25% relative increase	529 (15.95)	596 (18.07)	0.86 (0.76–0.98)	0.0219
AKI 0.5 absolute increase	145 (4.37)	184 (5.58)	0.77 (0.62–0.97)	0.0244
Dialysis during hospitalization	3 (0.09)	10 (0.30)	0.30 (0.08–1.08)	0.0659

Values are n or n (%) unless otherwise indicated. *Excluding patients who underwent angiography only.

AKI = acute kidney injury; CI = confidence interval; KDIGO = Kidney Disease Improving Global Outcomes; PCI = percutaneous coronary intervention.

occurrence of AKI was further assessed according to KDIGO criteria (17), which revealed a much lower prevalence of AKI and a consistent 15% risk reduction in favor of RA, even if the treatment effect did not reach statistical significance. Notably, when analyzed by AKI severity, rates of stage 1 or 2 AKI were similar regardless of access site, but stage 3 AKI was reduced by 40% with RA compared with FA.

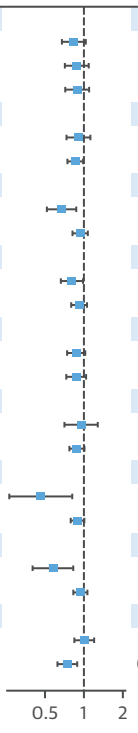
No randomized controlled trial of RA versus FA has assessed whether the access site might affect the risk of AKI. Therefore, AKI-MATRIX was the first prespecified analysis of a large randomized controlled trial that prospectively analyzed the occurrence of AKI in relation to RA or FA.

The British Columbia Cardiac and Renal Registries reported a reduced risk for chronic kidney disease within 6 months after catheterization among patients who underwent RA (18). However, the occurrence of AKI during hospitalization was not collected. A propensity-matched analysis of 17,714 patients who received urgent or elective PCI from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium database showed a 24% reduction in the risk of AKI, defined as an absolute increase in sCr of >0.5 mg/dl in patients who underwent RA (7). A single-center registry also showed a reduced risk of AKI (defined as sCr >0.5 mg/dl or a 50% increase of sCr) with RA compared with FA, but the access site was no longer associated with increased risk of AKI after propensity matching (OR: 1.48; 95% CI: 0.72 to 3.04; p = 0.286) (19). Finally, in a STEMI population that underwent primary PCI at high-volume urban centers, FA compared with RA was associated with a 56% greater adjusted risk of AKI, which occurred in 12.7% of the patients based on an increase in sCr >0.5 mg/dl or >25% (6).

The prevalence of AKI varies largely across studies based on the definition and the population investigated (1,2). However, there is accumulating evidence indicating that small increments in sCR are associated, in a variety of settings, with adverse outcomes that manifest in short-term morbidity and mortality as well as in longer term outcomes, including 1-year mortality (1,2,20). Because no effective therapeutic

FIGURE 1 Primary Endpoint: Subgroup Analysis

AKI during index hospitalization	Randomized to Radial Access	Randomized to Femoral Access	Odds Ratio (95% CI)	p Value	p Value for interaction	Numbers needed to treat to prevent 1 AKI
Center's proportion of radial PCI					0.70*	
Low (14.9-64.4%)	181/1391	225/1473	0.83 (0.67-1.02)	0.083		45 (21 to ∞)
Intermediate (65.4-79.0%)	230/1433	251/1400	0.88 (0.72-1.07)	0.18		54 (22 to ∞)
High (80.0-98.0%)	223/1285	236/1228	0.88 (0.72-1.08)	0.23		54 (21 to ∞)
Diabetes					0.68	
Yes	191/936	203/917	0.90 (0.72-1.13)	0.36		58 (19 to ∞)
No	443/3173	509/3184	0.85 (0.74-0.98)	0.024		50 (27 to 369)
Estimated glomerular filtration rate (eGFR)					0.027	
<60 ml/min/1.73 m^2	126/688	174/695	0.67 (0.52-0.87)	0.0025		15 (10 to 42)
≥60 ml/min/1.73 m^2	508/3406	538/3396	0.93 (0.82-1.06)	0.29		108 (38 to ∞)
Age					0.31	
≥75 years	239/1040	291/1076	0.80 (0.66-0.98)	0.031		25 (13 to 265)
<75 years	395/3069	421/3025	0.91 (0.79-1.06)	0.23		96 (37 to ∞)
Clinical presentation					0.98	
STEMI	354/1977	397/1975	0.87 (0.74-1.02)	0.079		46 (22 to ∞)
NSTEACS	280/2132	315/2126	0.87 (0.73-1.03)	0.11		60 (27 to ∞)
LVEF under 40%					0.65	
<40%	122/397	135/423	0.95 (0.70-1.27)	0.71		85 (14 to ∞)
≥40%	500/3566	552/3522	0.88 (0.77-1.00)	0.051		61 (31 to ∞)
Killip class					0.026	
Killip class III or IV	34/129	44/101	0.46 (0.27-0.81)	0.0066		6 (4 to 21)
Killip class I or II	600/3980	668/4000	0.89 (0.79-1.00)	0.047		62 (31 to 4767)
Mehran score					0.013	
>10 points	79/274	111/269	0.58 (0.40-0.82)	0.0025		9 (5 to 23)
≤10 points	550/3754	587/3774	0.93 (0.82-1.06)	0.27		111 (40 to ∞)
Randomization to bivalirudin					0.018	
Bivalirudin	300/1770	301/1780	1.00 (0.84-1.20)	0.98		-2561 (42 to ∞)
UFH	271/1771	345/1764	0.74 (0.62-0.89)	0.00087		24 (15 to 57)



*P value for trend across ordered groups

Radial access reduced incidence of acute kidney injury (AKI) across analyzed subgroups. CI = confidence interval; LVEF = left ventricular ejection fraction; NSTEACS = non–ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin.

measure, apart from renal replacement therapy, exists in patients with AKI, there is a growing awareness in the medical community of the need to implement preventive measures in patients at greater risk.

Hydration with isotonic saline remains the only Class I recommended intervention in patients at medium to high risk who are undergoing invasive management (15). Yet, many patients with ACS, especially those with ongoing myocardial ischemia, are not eligible for this preventive treatment due to the need to expedite catheterization. Therefore, contrast minimization during intervention remains the most important preventive intervention in these patients. Importantly, we also confirmed that some drug categories might help prevent (statins) or increase the risk of AKI (renin-angiotensin inhibitors and diuretics) (Online Table 1), as previously shown (21,22).

In a seminal paper, Nikolsky et al. (23) were the first to investigate the association between baseline hematocrit and AKI, which occurred in 13.9% of 6,773 consecutive patients treated with PCI, based on an increase of ≥25% or ≥0.5 mg/dl in pre-procedure sCr. By multivariate analysis, lower baseline hematocrit was associated with contrast-induced nephropathy (CIN); each 3% decrease in baseline hematocrit resulted in a significant increase in the odds of CIN in patients with and without chronic kidney disease (11% and 23%, respectively) (23). When introduced into the multivariate model, change in hematocrit also showed a significant association with CIN after coronary intervention. Interestingly, a procedure-related drop in hematocrit was an independent prognostic determinant of CIN, regardless of baseline hematocrit (23). More recently, Ohno et al. (24) confirmed that patients who experienced

peri-procedural bleeding had a higher incidence of AKI, the severity of which, in turn, correlated closely with the severity of bleeding. The mechanism by which the drop in hemoglobin causes AKI is likely the impairment in renal perfusion due to significant blood loss, regardless of changes in systemic blood pressure (23,24). Blood transfusion was also identified as a risk factor for AKI in cardiac surgery (25) and in transcatheter aortic valve replacement. Moreover, in patients with ACS who underwent PCI within the CathPCI Registry (n = 1,756,864), blood transfusion was strongly associated with AKI, which was defined as an increase in sCr post-PCI of ≥0.5 mg/dl or ≥25% during hospitalization compared with baseline values (26).

Our present findings expanded on previous observations by showing that a bleeding minimization strategy, such as RA as opposed to FA, reduced the risk of AKI, with a greater effect observed in patients at higher risk for AKI. The mechanisms by which RA reduced the incidence of AKI might be due to a reduction of bleeding events (7), by a reduction in embolization in the renal circulation (9,10), or by a combination of both (11). When access site bleeding, hemoglobin drop, need for transfusion, and/or randomly allocated access site were simultaneously entered into the model, bleeding complications per se and their possible consequences (i.e., hemoglobin drop and blood transfusion) remained strongly associated with AKI. However, only a trend remained for the association between RA and AKI. Hence, our results confirmed previous observations that access site bleeding is associated with AKI, and suggested that RA, by minimizing those, mitigated the risk of AKI.

Unlike in the parent trial (12), the proportion of PCI undertaken with RA among participating centers did not emerge as an effect modifier for the study endpoint. This finding suggested that kidney protection was conferred by RA at any stage of the learning curve for transradial procedures. This observation indirectly confirmed the importance of bleeding prevention as a possible mechanism through which RA reduces the risk of AKI; operator proficiency significantly affected the occurrence of major adverse cardiovascular events, but failed to affect bleeding endpoints in our study (12). Conversely, RA provided greater benefits for AKI prevention in patients at higher risk of AKI and in those randomly assigned to unfractionated heparin compared with bivalirudin. This latter finding should be interpreted with caution because it was based on the subpopulation randomized to receive the 2 tested parenteral anticoagulants, and no interaction was observed between access site and type of antithrombin in the MATRIX-Access or antithrombin type programs with respect to both co-primary endpoints or bleeding events.

TABLE 4 Associations of AKI During Index Hospitalization*

	Odds Ratio (95% CI)	p Value
Model 1		
Randomized to radial access	0.87 (0.77–0.98)	0.0217
Components of the Mehran score†		
Hypotension‡	0.87 (0.44–1.72)	0.6957
Use of intra-aortic balloon pump	2.96 (2.13–4.11)	<0.0001
Killip class III or IV	1.83 (1.35–2.50)	0.0001
Age >75 yrs	1.99 (1.75–2.27)	<0.0001
Anemia§	1.20 (1.04–1.39)	0.0135
Diabetes	1.33 (1.16–1.52)	<0.0001
Contrast media volume, per 100 ml	1.34 (1.26–1.43)	<0.0001
Creatinine >1.5 mg/dl	1.15 (0.76–1.72)	0.5108
Model 2		
Randomized to radial access	0.89 (0.80–1.01)	0.0647
Bleeding BARC 2, 3, or 5 related to access site	2.19 (1.66–2.89)	<0.0001
Model 3		
Randomized to radial access	0.90 (0.80–1.01)	0.0758
Bleeding BARC 2, 3, or 5 related to access site	1.81 (1.36–2.40)	<0.0001
Hemoglobin nadir <9 g/dl	3.35 (2.71–4.13)	<0.0001
Model 4		
Randomized to radial access	0.90 (0.80–1.02)	0.0868
Bleeding BARC 2, 3, or 5 related to access site	1.68 (1.25–2.25)	0.0005
Hemoglobin nadir <9 g/dl	2.81 (2.23–3.53)	<0.0001
Blood transfusion	2.57 (1.63–4.03)	<0.0001

Number of included patients = 8,210. *With Mehran score, bleeding, and measures of bleeding severity. †Range 0 to 30. ‡Systolic blood pressure <80 mm Hg. §<12 g/dl for women and <13 g/dl for men.
BARC = Bleeding Academic Research Consortium; CI = confidence interval.

It remains unclear as to whether RA, by avoiding direct passage of catheters in proximity to renal arteries, might also contribute to lower risk of AKI through a reduction and/or avoidance of direct embolization into the renal circulation. Coronary angiography is the most common procedure to cause embolisms (27). Estimates of the incidence of cholesterol embolization syndrome (CES) after vascular procedures ranged from 0.15% in clinical studies to 25% to 30% in pathological series (27). Clinical studies probably underestimated the incidence because only a minority of patients could be clinically recognized. Therefore, despite the importance of CES as a complication of percutaneous diagnostic and interventional procedures, its relative contribution remains uncertain to the overall occurrence of AKI in patients who have undergone vascular cardiac catheterization and who received contrast media.

In light of our findings, future studies should evaluate whether the use of RA in patients with

advanced chronic kidney disease affects or prevents a conduit for fistula for dialysis.

STUDY LIMITATIONS. Most centers participating in the MATRIX program were highly experienced in RA; similar outcomes might not be applicable in centers that perform lower volumes of RA. Although reported subgroups were pre-specified in the statistical analysis plan, we did not adjust for multiple comparisons, increasing the risk of a type I error. We were not able to adjust the results for the intensity of either periprocedural hydration or type of contrast media used, because these 2 variables were not collected in the data set. However, the unrestricted use of hydration to expand intravascular fluid in clinical practice is the simplest and cheapest intervention aimed at preventing AKI and is unlikely to have influenced the effect of RA (28). Patients with STEMI, who are routinely referred to emergent intervention without hydration, derived consistent benefit in terms of lower AKI from RA. Time and date of sCr peak during hospitalization and sCr values after discharge were not collected. Although blood loss minimization, also based on our multivariable model, appeared to be the most likely explanation for our findings, it remains possible that use of RA as opposed to FA decreased the occurrence of CES. Although with low sensitivity, presence of eosinophilia could raise the level of suspicion for CES or occurrence of extrarenal emboli, this was not systematically collected in the study case report form. Hence, the mechanisms through which RA mitigated the risk of AKI remain unclear.

CONCLUSIONS

Our results showed that in a broad population of patients with ACS who underwent invasive management, the use of RA versus FA was associated with a reduced incidence of post-procedural AKI. This analysis lent further support to the concept that RA should be prioritized over FA in ACS patients undergoing invasive management.

ADDRESS FOR CORRESPONDENCE: Prof. Marco Valgimigli, Swiss Cardiovascular Center Bern, Bern University Hospital, Freiburgstrasse 4, CH- 3010 Bern, Switzerland. E-mail: marco.valgimigli@insel.ch.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with acute coronary syndromes undergoing invasive management, radial arterial access is associated with a lower risk of acute kidney injury than femoral access.

TRANSLATIONAL OUTLOOK: Additional research is needed to assess whether this advantage of radial over femoral access applies across specific subsets of patients, such as the elderly or those with cardiogenic shock, coronary bypass grafts, or chronic kidney disease, and whether concurrent medication therapies modify the difference in renal outcomes.

REFERENCES

1. Marenzi G, Cosentino N, Bartorelli AL. Acute kidney injury in patients with acute coronary syndromes. Heart 2015;101:1778–85.

2. McCullough PA, Choi JP, Feghali GA, et al. Contrast-induced acute kidney injury. J Am Coll Cardiol 2016;68:1465–73.

3. Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;44:1393–9.

4. Gurm HS, Dixon SR, Smith DE, et al. Renal function-based contrast dosing to define safe limits of radiographic contrast media in patients undergoing percutaneous coronary interventions. J Am Coll Cardiol 2011;58:907–14.

5. Marenzi G, Ferrari C, Marana I, et al. Prevention of contrast nephropathy by furosemide with matched hydration: the MYTHOS (Induced Diuresis With Matched Hydration Compared to Standard Hydration for Contrast Induced Nephropathy Prevention) trial. J Am Coll Cardiol Intv 2012;5:90–7.

6. Cortese B, Sciahbasi A, Sebik R, et al. Comparison of risk of acute kidney injury after primary percutaneous coronary interventions with the transradial approach versus the transfemoral approach (from the PRIPITENA urban registry). Am J Cardiol 2014;114:820–5.

7. Kooiman J, Seth M, Dixon S, et al. Risk of acute kidney injury after percutaneous coronary interventions using radial versus femoral vascular access: insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium. Circ Cardiovasc Interv 2014;7:190–8.

8. Ando G, Costa F, Trio O, Oreto G, Valgimigli M. Impact of vascular access on acute kidney injury after percutaneous coronary intervention. Cardiovasc Revasc Med 2016;17:333–8.

9. Fukumoto Y, Tsutsui H, Tsuchihashi M, Masumoto A, Takeshita A. Cholesterol Embolism Study I. The incidence and risk factors of cholesterol embolization syndrome, a complication of cardiac catheterization: a prospective study. J Am Coll Cardiol 2003;42:211–6.

10. Scolari F, Ravani P, Gaggi R, et al. The challenge of diagnosing atheroembolic renal disease: clinical features and prognostic factors. Circulation 2007;116:298–304.

11. Ando G, Cortese B, Frigoli E, et al. Acute kidney injury after percutaneous coronary intervention: rationale of the AKI-MATRIX (Acute Kidney Injury-Minimizing Adverse Hemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) sub-study. Catheter Cardiovasc Interv 2015;86:950–7.

12. Valgimigli M, Gagnor A, Calabro P, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015;385:2465–76.

13. Valgimigli M, Gagnor A, Calabrò P, et al., MATRIX investigators. Design and rationale for the Minimizing Adverse haemorrhagic events by TRansradial access site and systemic Implementation of angioX program. Am Heart J 2014;168:838–45.e6.

14. Valgimigli M, Calabro P, Cortese B, et al. Scientific Foundation and Possible Implications for

Practice of the Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX (MATRIX) Trial. J Cardiovasc Transl Res 2014;7:101–11.

15. Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, et al. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012;33:2569–619.

16. Slocum NK, Grossman PM, Moscucci M, et al. The changing definition of contrast-induced nephropathy and its clinical implications: insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). Am Heart J 2012; 163:829–34.

17. Summary of recommendation statements. Kidney Int Suppl 2012;2:8–12.

18. Vuurmans T, Byrne J, Fretz E, et al. Chronic kidney injury in patients after cardiac catheterisation or percutaneous coronary intervention: a comparison of radial and femoral approaches (from the British Columbia Cardiac and Renal Registries). Heart 2010;96:1538–42.

19. Damluji A, Cohen MG, Smairat R, Steckbeck R, Moscucci M, Gilchrist IC. The incidence of acute kidney injury after cardiac catheterization or PCI: a comparison of radial vs. femoral approach. Int J Cardiol 2014;173:595–7.

20. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.

21. Giacoppo D, Capodanno D, Capranzano P, Aruta P, Tamburino C. Meta-analysis of randomized controlled trials of preprocedural statin administration for reducing contrast-induced acute kidney injury in patients undergoing coronary catheterization. Am J Cardiol 2014;114:541–8.

22. Bainey KR, Rahim S, Etherington K, et al. Effects of withdrawing vs continuing renin-angiotensin blockers on incidence of acute kidney injury in patients with renal insufficiency undergoing cardiac catheterization: results from the Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker and Contrast Induced Nephropathy in Patients Receiving Cardiac Catheterization (CAPTAIN) trial. Am Heart J 2015;170:110–6.

23. Nikolsky E, Mehran R, Lasic Z, et al. Low hematocrit predicts contrast-induced nephropathy after percutaneous coronary interventions. Kidney Int 2005;67:706–13.

24. Ohno Y, Maekawa Y, Miyata H, et al. Impact of periprocedural bleeding on incidence of contrast-induced acute kidney injury in patients treated with percutaneous coronary intervention. J Am Coll Cardiol 2013;62: 1260–6.

25. Karkouti K, Grocott HP, Hall R, et al. Interrelationship of preoperative anemia, intraoperative anemia, and red blood cell transfusion as potentially modifiable risk factors for acute kidney injury in cardiac surgery: a historical multicentre cohort study. Can J Anaesth 2015;62: 377–84.

26. Karrowni W, Vora AN, Dai D, Wojdyla D, Dakik H, Rao SV. Blood transfusion and the risk of acute kidney injury among patients with acute coronary syndrome undergoing percutaneous coronary intervention. Circ Cardiovasc Interv 2016; 9:e003279.

27. Scolari F, Ravani P. Atheroembolic renal disease. Lancet 2010;375:1650–60.

28. Pannu N, Wiebe N, Tonelli M. Alberta Kidney Disease Network. Prophylaxis strategies for contrast-induced nephropathy. JAMA 2006;295: 2765–79.

KEY WORDS bleeding, coronary intervention, creatinine, estimated glomerular filtration rate, ST-segment elevation

APPENDIX For supplemental information regarding the MATRIX trial as well as supplemental figures and table, please see the online version of this article.