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The Association Between Chronic Kidney Disease and Rates of Transfusion and Progression to End–Stage Renal Disease in Patients Undergoing Transradial Versus Transfemoral Cardiac Catheterization – An Analysis from the Veterans Affairs CART Program

Running title: *Vora et al.; Transradial access and CKD*

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ABSTRACT:

Background: Patients with chronic kidney disease (CKD) are at increased risk for bleeding, transfusion, and dialysis after cardiac catheterization. Whether rates of these complications are increased in this high–risk population undergoing transradial (TR) access compared to transfemoral (TF) access is unknown.

Methods and Results: From the Veterans Affairs CART Program, we identified 229,108 patients undergoing cardiac catheterization between 2007-2014, of which 48,155 (21.0%) had baseline glomerular filtration rate (GFR) between 15–59 ml/min. We used multivariable Cox modeling to determine the independent association between TR access and post–procedure transfusion as well as progression to new dialysis by degree of renal dysfunction. Overall, 35,979 (15.7%) of patients underwent TR access. TR patients tended to be slightly younger but overall had similar rates of CKD compared with TF patients (24.3% vs. 27.1%). TR patients had longer fluoroscopy times (7.2 vs 6.0 minutes, p<0.001) but lower contrast use (85.0 vs 100.0 ml, p<0.001). The estimated rate of blood transfusion within 48 hours was lower among TR patients (0.85% vs. 1.01%) as were rates of new dialysis at one year (0.58% vs. 0.71%). After multivariable adjustment, TR access was associated with lower rates of progression to dialysis at one year overall (HR 0.83, 95% CI 0.70-0.98) with no trend of increased risk for dialysis by degree of CKD compared with TF access. TR access was associated with greater reduction in transfusion rates with increasing degree of CKD (p-value for trend=0.04: non-CKD: HR 0.99, 95% CI 0.73-1.34; GFR 45–59 ml/min: HR 0.93, 95% CI 0.70-1.23; GFR 30–44 ml/min: HR 0.73, 95% CI 0.51-1.03; GFR 15–29 ml/min: HR 0.43 95% CI 0.20-0.90).

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Conclusions: Among patients undergoing cardiac catheterization in the VA health system, TR access was associated with lower risk for post–procedure transfusion within 48 hours among patients with more severe CKD, and with lower risk of progression to ESRD at one year compared with TF access. These data provide additional evidence that TR access may provide significant benefit in this high-risk population.

Key words: radial artery catheter; chronic kidney disease; dialysis; blood transfusion

INTRODUCTION

Chronic kidney disease (CKD) is common among patients with coronary artery disease (CAD) and is independently associated with increased risk for adverse cardiovascular and renal outcomes.[1-3] Clinical trials often exclude patients with CKD because of their likelihood of suffering bleeding complications with antithrombotic therapy and progression to dialysis after cardiac catheterization.[4] As such, evidence–based approaches to patients with coexisting CKD and CAD are lacking.

The risk for dialysis after cardiac catheterization can be due to atheroemboli from aortic atherosclerosis,[5-7] direct renal injury from iodinated contrast,[8] or a combination of these factors. The only accepted strategies to reduce the incidence of renal injury are volume expansion and minimization of contrast load.[9] Similarly, the increased risk for bleeding in patients with CKD may be due to reduced clearance of antithrombotic agents, increased vascular calcification and stiffness leading to vascular complications, or both.[10] In this context, the use of radial artery access for cardiac catheterization and PCI is an attractive strategy to reduce both the risk for bleeding and dialysis because the catheter avoids the abdominal aorta and the radial artery is superficial and lends itself more easily to hemostasis. On the other hand, it may be prudent to avoid radial arterial access because the attendant damage to the artery can increase the risk for radial artery occlusion and complicate the placement of permanent dialysis access. Thus, the role of a radial approach in patients with CKD remains unclear.

Accordingly, we used data from the Veterans Affairs Clinical Assessment Reporting and Tracking (CART) program to compare procedural characteristics, rates of blood transfusion within 48 hours of cardiac catheterization, and progression to new dialysis within one year in

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patients undergoing cardiac catheterization via the TR and TF approach, stratified by degree of renal dysfunction. We hypothesized that patients undergoing transradial access would have lower rates of transfusion within 48 hours but similar rates of progression to new dialysis by one year, with greatest potential benefit observed in patients with more severe renal disease.

METHODS

Data Sources

The Veterans Affairs (VA) Clinical Assessment Reporting and Tracking (CART) program is a national clinical quality program for all VA cardiac catheterization laboratories. It collects data about catheterization procedures performed in all 78 VA cardiac catheterization laboratories using a software application that is embedded within the VA electronic medical record (EMR), which then allows for data linkage in order to assess short– and long–term longitudinal outcomes. Institutional review board and VA research and development approvals were obtained for the creation of the dataset and for this particular study. This study was approved by the Colorado Multiple Institutional Review Board (COMIRB) with waiver of informed consent, given the retrospective nature of the study.

The data elements included within the CART program are standardized by the American College of Cardiology's National Cardiovascular Data Registry (NCDR)[11] and include information on procedural indications, demographic and clinical characteristics, presentation details, procedures performed, access site, peri–procedural complications, and pre–procedure and intra–procedure medications. Continuous monitoring, maintenance, and updating of the CART application are performed by a dedicated staff, and the quality and integrity of the data are maintained through the use of standardized data definitions, uniform data transmission protocols, and routine data quality checks and audits. Additional details of the design and conduct of this registry have been previously described.[12-15]

Study Population and Data Definitions

We studied all veterans undergoing cardiac catheterization for any indication in the VA Health System between October 1, 2007 and September 30, 2014. Among the 261,274 patients in the initial sample, we excluded patients with no information about access site (N= 2,863), access site crossover (N=2,134), no administrative data for follow–up (N=41), prior cardiac transplant

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(N=1,552), treated at sites with no TR access patients (N=1,102), with eGFR<15 ml/min (N=7,477), those on dialysis at the time of the catheterization (N=2,877), and those with eGFR >59ml/min but a documented history of chronic kidney disease (N=14,120). Estimated GFR was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) equation[16] based on the most recent measured creatinine prior to catheterization, which was ≤ 30 days prior to the date of catheterization. We identified patients undergoing cardiac catheterization via a TR or TF route. Patients were stratified by degree of CKD into four categories based the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI): ≥59 ml/min (no CKD), 45–59 ml/min (Stage 3A), 30–44ml/min (Stage 3B), and 15–29 ml/min (Stage 4).

Outcomes of Interest

The primary clinical events of interest were the occurrence of blood transfusion within 48 hours and progression to dialysis within one year of the index catheterization. Blood transfusion was used as a surrogate for bleeding complications since bleeding events in CART are not adjudicated. Progression to new dialysis was assessed by dialysis procedures recorded in VA administrative and fee-based data sources after the date of the catheterization through September 2014. Since the outcomes were censored for some patients, we used survival methods that account for censoring in the analysis, as described below.

Statistical Methods

We compared baseline demographic, clinical, and presentation characteristics between patients undergoing cardiac catheterization via a TR versus a TF approach. Continuous variables are expressed as median values with 25^{th} and 75^{th} percentiles whereas categorical values are presented as percentages. We used Pearson $\chi 2$ tests for categorical variables and Wilcoxon rank sum tests for continuous variables.

We compared the unadjusted rates of each outcome of interest using cumulative incidence plots, estimated event rates and Gray's test, accounting for both censoring and death as a competing risk. We then used Cox proportional hazards modeling with a robust covariance estimator to account for correlation by hospital in order to determine the independent association between TR access and post–procedure transfusion as well as progression to new dialysis, using TF as the reference. We modeled this relationship between access site and the outcomes with

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and without an interaction term between access site and degree of CKD, and evaluated the trend across degree of CKD using type 3 tests in the SAS Phreg procedure. The outcomes were adjusted for the following variables: demographics [age, sex, race, Hispanic ethnicity, obesity], medical history [hypertension, hyperlipidemia, diabetes, tobacco use, chronic obstructive pulmonary disease (COPD), peripheral artery disease (PAD), prior MI, prior cardiac transplant, prior coronary artery bypass surgery (CABG), congestive heart failure (CHF), cerebrovascular disease (CVD), post–traumatic stress disorder (PTSD), depression, obstructive sleep apnea (OSA)], anemia, and presence of cardiogenic shock or heart failure on admission.

We performed a sensitivity analysis in which we repeated the Cox models comparing the risk of the outcomes for TR access relative to TF access in the subset of patients with both ad hoc PCI and non-missing contrast volume (N= 47,412). We performed another sensitivity analysis restricting the study population to sites performing TR access in at least 5% of patients. Additionally, we sought to explore whether the association between access site and progression to dialysis was mediated by the decrease in transfusion among patients undergoing TR access.[17] We performed the four-step mediation analysis developed by Baron and Kenney using similar Cox proportional hazards models to those described above.[18]

A P–value of 0.05 was considered statistically significant. All statistical analyses were performed by the CART Coordinating Center at the Denver VA Medical Center using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina) and R version 3.2.2. The study was approved by the Colorado Multiple Institutional Review Board.

RESULTS

Between 2007-2014, 261,274 patients underwent cardiac catheterization. After applying exclusions, the final study sample consisted of 229,108 patients at 78 cardiac catheterization facilities across the VA Health System, of which 35,979 (15.7%) underwent catheterization via TR access (Figure 1). Baseline characteristics for the two groups are listed in Table 1. TR access patients were younger, more likely African–American, and more likely obese, but had lower rates of prior cardiac events and procedures compared with TF access patients; most differences were statistically significant but clinically modest. Patients with prior cardiac procedures were less likely to undergo catheterization via a TR route. TR patients had longer fluoroscopy times

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(7.2 vs 6.0 minutes, p<0.001) but lower contrast use (85.0 vs 100.0 ml, p<0.001).When stratified by degree of CKD, TR access patients were less likely to have Stage 3B or Stage 4 CKD than TF patients: No CKD: 80.5% vs 78.7%; GFR 45–59 ml/min: 14.8%vs. 15.5%; GFR 30–44 ml/min: 4.1% vs. 4.9%; GFR 15–29 ml/min: 0.6% vs. 0.9% (p<0.001); however, overall differences were modest. Rates of TR versus TF access are described in Table S1.

Rates of Blood Transfusion within 48 Hours and Progression to New Dialysis during Follow-up

The cumulative incidence curve for the rate of blood transfusion within 48 hours is shown in Figure 2. The estimated rate of blood transfusion within 48 hours of cardiac catheterization was 0.99% (95% CI: 0.94-1.02); it was 0.85% (95% CI: 0.75-0.94) among those who underwent catheterization via TR access and 1.01% (95% CI: 0.96-1.05) via TF access (p=0.004). Within each access category, transfusion rates were higher among patients with more advanced CKD (Table 2).

The cumulative incidence curve for the progression to dialysis at one year is shown in Figure 2. An estimated 0.69% (95% CI 0.65-0.72) of patients progressed to new dialysis during the follow–up period. Unadjusted rates of progression to dialysis were slightly lower among TR patients (0.58%; 95% CI: 0.50-0.65 vs. 0.71%; 95% CI: 0.67-0.75; p=0.005) and increased with increasing severity of CKD for both groups.

Multivariable Analyses

We performed Cox proportional hazards modeling to compare risks of blood transfusion and progression to new dialysis between patients undergoing catheterization via each access strategy. For each outcome, we tested the interaction between TR access and degree of CKD, and the trend in association of TR with outcomes by degree of CKD. After multivariable adjustment, TR access was associated with decreasing rates of blood transfusion within 48 hours with increasing severity of CKD, with significant association only for patients with most severe CKD (p-value for trend=0.04; No CKD: HR=0.99, 95% CI: 0.73-1.34; GFR 45–59 ml/min: HR=0.93; 95% CI: 0.70-1.23; GFR 30–44 ml/min: HR=0.73; 95% CI: 0.51-1.03; GFR 15–29 ml/min: HR=0.43; 95% CI: 0.20-0.90) (Figure 3). Combining all patients, the risk of transfusion did not differ significantly by access site (HR 0.91, 95% CI 0.72-1.15, p=0.44), but among CKD patients only, risk for transfusion was lower among TR patients (HR 0.79, 95% CI 0.64-0.98, p=0.03).

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Among all patients undergoing cardiac catheterization the risk of progression to ESRD within one year was lower among patients undergoing TR access (HR 0.83, 95% CI 0.70-0.98, p=0.03) and was similar when restricted only to patients with CKD (HR 0.80, 95%CI 0.68-0.94, p=0.008). The benefit of TR access did not vary significantly with degree of CKD, nor was there a significant trend by degree of CKD (p-value for interaction=0.15; p-value for trend=0.08), although the hazard ratios were lowest among those with the most severe CKD (No CKD: HR=0.89, 95% CI: 0.69-1.15; GFR 45–59 ml/min: HR=1.1; 95% CI: 0.83-1.48; GFR 30–44 ml/min: HR=0.78; 95% CI: 0.58-1.05; GFR 15–29 ml/min: HR= 0.69, 95% CI 0.51-0.94) (Figure 3).

In sensitivity analysis, after adjusting for contrast volume and excluding patients who did not undergo ad hoc PCI, similar trends were observed with respect to blood transfusion and progression to dialysis (Table S2). After repeating the analysis excluding 28 sites performing TR access in <5% of patients, results similar to those in the primary analysis were observed (Table S3). We also excluded patients with a history of prior CABG (Table S4) and demonstrated results similar to those in the primary analysis. To explore the mediating effect of lower transfusion rates among TR access patients in progression to dialysis, we adjusted for transfusions as a potential intermediary mechanism in the model of progression to dialysis. After adjustment, the HR for access site (TR versus TF) was 0.81 (95% CI 0.67 – 0.96, p=0.01), with the occurrence of transfusion within 48 hours being independently associated with dialysis (HR 2.97, 95% CI 2.26-3.92, p<0.001), suggesting that although bleeding was associated with higher risk for dialysis, the reduction in bleeding with TR access did not seem to be the mediator of the decreased risk for dialysis with TR access.

DISCUSSION

In this large, national sample of veterans undergoing cardiac catheterization, we observed that TR access was associated with: 1) Slightly increased fluoroscopy times yet no increased used in contrast; 2) Significantly lower rates of blood transfusion within 48 hours among patients with CKD, with increasing observed benefit with increasing severity of renal dysfunction; 3) Lower rates of progression to dialysis at one year, particularly among patients with severe CKD, compared with TF access; this effect was not mediated by the decreased bleeding with TR

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access. Therefore, the results of this study suggest that TR access is associated with lower risk of peri-procedural bleeding in CKD patients with greatest benefit in patients with severe CKD. Additionally, rates of progression to ESRD appear to be lower among TR patients. These data suggest that TR may be safer in patients with CKD; however, prospective randomized trials in this population are needed to confirm our observational findings

Acute kidney injury (AKI) due to contrast induced nephropathy is a known complication of cardiac catheterization, and the risk of AKI is directly related to the degree of CKD prior to catheterization, the amount of contrast used during the procedure, and the prior burden of atheroemboli in the aorta. We found slightly lower overall usage of contrast in patients undergoing catheterization via TR access. While the overall difference in contrast usage between the TR and TF patients is modest and clinically similar, prior studies have reported varying levels of contrast use during TR procedures.[19,20] Importantly, patients undergoing TR access were less likely to have prior CABG (and thus require coronary bypass angiography) and also less likely to undergo left ventriculography. Nevertheless, our data provide some reassurance that TR catheterization may not worsen CKD due to a higher volume of contrast during the procedure.

Clinically significant bleeding events are among the most common complications after PCI and have significant downstream consequences, including increased rates of stroke, nonfatal myocardial infarction, and short– and long–term mortality. Although estimates of major bleeding complications vary widely in the literature, depending on the specific population and the precise definition,[21-24] more recent estimates have placed the rate of major bleeding events at less than 5%, a decrease that has been attributed to better periprocedural anticoagulation and TR access. CKD has consistently been shown to be a major risk factor for bleeding across clinical trials and registries.[25,26] Indeed, rates of bleeding among patients with CKD undergoing PCI have been reported to be even higher compared with patients without CKD. Saltzman, et. al. noted an almost 3–fold higher rate of major bleeding (19.3% vs. 6.7%, $p<0.001$) among patients presenting with STEMI undergoing PCI in the HORIZONS–AMI trial.[27] In the NSTEMI population, an analysis using the ACTION Registry – Get With the Guidelines noted that patients with stage 3–5 CKD had 2–6 fold increased unadjusted risk of major bleeding compared with patients with an estimated GFR $\geq$ 60 ml/min/1.73m^2, a difference that was attenuated but persisted after multivariable adjustment.[27] Randomized trial data [19, 28] as well as large–scale

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registry data[29] have described the significant reduction in major bleeding with TR access compared with TF access. Our study confirms and extends those findings in a number of ways. We report significantly lower bleeding rates among patients with CKD. Additionally, we demonstrate lower bleeding with a directional trend toward increased benefit in patients with the most severe CKD, a population that is at highest baseline risk of significant bleeding. These results suggest that the benefit of TR access may be greatest in patients at highest risk of bleeding, which is a novel finding. Nevertheless, the benefits in major bleeding with TR access need to be weighed against the overall risk of progression to ESRD, a situation in which preservation of potential access sites for dialysis is of primary importance. We report that an estimated 0.69% of patients progressed to new dialysis within 1 year, with lower rates among TR versus TF patients (0.58% vs 0.71%, p-value=0.005). There was a clear relationship between degree of renal insufficiency and progression to new dialysis, with 19.6% of patients with Stage 4 CKD (GFR 15–29 ml/min) progressing to new dialysis but only 1.0% of patients with Stage 3A CKD (GFR 45–59 ml/min). There is concern that TR access may damage the radial artery, making it potentially unusable for subsequent AVF creation. Previous studies have noted increased inflammation by the introducer sheath[30] and thrombus formation, and optical coherence tomography (OCT) of accessed vessels have demonstrated intimal tears, medial dissections, and the formation of microthrombi.[31] Although our data do not describe rates of access site complications that may complicate radio–cephalic AVF creation, prior studies have underscored the risk of radial artery occlusion (RAO). The risk for RAO can be minimized with low profile equipment, adequate anticoagulation, prevention of radial artery spasm, and use of non-occlusive hemostasis after transradial procedures. These strategies have been shown to reduce RAO rates to 0.1 – 1.5%.[32] Additionally, difficulty with radio–cephalic AVF creation typically is due to complications with the cephalic vein, not the radial artery.[33] These data, as well as our findings, should be taken into account when selecting an access site in CKD patients undergoing cardiac catheterization or PCI.

Our study must be considered in the context of several important limitations. First, our data only captured rates of transfusion within 48 hours after cardiac catheterization and does not capture actual rates of major or minor bleeding. It is possible that there is heterogeneity in individual providers' threshold for administering a transfusion.[34] Nevertheless, large studies have described worse outcomes after PCI in patients that have required transfusion.[35] Next, our data

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only describe progression to new dialysis at one year; it is likely that the risk of developing worsening renal disease increases over time. Nevertheless, given the safety profile of TR access with respect to bleeding, it would seem reasonable to consider a strategy that minimizes a known complication given the theoretical risk of challenging AVF creation further into the future. Third, we do not have systematic data on access site complications with either TF or TR access. We also do not have data regarding possible increased difficulty with creating a radiocephalic AVF after TR access. Fourth, we did not capture right radial versus left radial access, which may have affected the total amount of fluoroscopy time and contrast usage among TR patients. We also did not collect operator experience, which also may have affected our findings. Additionally, access site selection was not random, and there is the possibility that the observed benefit associated with TR access was due to patient selection factors and not access route. Specifically, we do not have information on whether the patient present with ST-segment elevation myocardial infarction, the patient population for which strong evidence exists regarding the superiority of TR access. Because patients undergoing TR access were less likely to have a prior history of CABG and also less likely to undergo left ventriculography, lower use of contrast during the procedure may be affected by these factors more than the actual access site. Our sensitivity analyses adjusted for contrast use and did not demonstrate a significant change in the overall results. Finally, as this is an observational analysis, we cannot draw causal inferences from these results, and we cannot exclude the possibility of unmeasured confounding.

CONCLUSIONS

Among patients undergoing cardiac catheterization in the VA health system, TR access was associated with greater reduction in post–procedure transfusion within 48 hours with increasing severity of CKD and less progression to ESRD at one year. These data provide additional evidence that TR access may provide significant benefit in this high-risk population and may be considered when selecting an access site for CKD patients undergoing PCI; however, prospective randomized trials in this population are needed to confirm our observational findings

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Table 1. Baseline characteristics*

	Overall (N=229,108)	***Transradial access (n=35,979)***	***Transfemoral access (n=193,129)***
Demographics			
Age in years (median, IQR)	64 (59-70)	64 (59-68)	64 (60-70)
Male	97.0	96.8	97.0

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	Overall (N=229,108)	*Transradial access (n=35,979)*	*Transfemoral access (n=193,129)*
Race			
White	79.2	74.8	80.0
Black	13.9	18.1	13.1
Other	6.9	7.1	6.9
Hispanic	4.7	3.6	4.9
BMI (median, IQR)	29.9 (26.4-34.0)	30.3 (26.7-35.1)	29.8 (26.4-33.9)
Past Medical History			
Prior MI	32.7	30.2	33.1
Prior CHF	26.4	25.0	26.6
Prior CVA	16.1	15.6	16.2
Prior PCI	32.4	30.0	32.8
Prior CABG	21.8	11.7	23.7
Hypertension	88.2	89.4	88.0
Diabetes	45.2	46.3	45.0
Dyslipidemia	86.5	86.7	86.5
Peripheral Artery Disease	18.4	20.4	18.1
COPD	22.2	21.4	22.4
PTSD	17.4	20.8	16.7
Depression	31.5	33.2	31.1
Sleep apnea	20.8	25.1	20.0
Presenting features:			
Acute coronary syndrome	20.3	18.6	20.6

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	Overall (N=229,108)	*Transradial access (n=35,979)*	*Transfemoral access (n=193,129)*
Heart failure	6.0	5.6	6.1
Cardiogenic shock within 24 hours			
Systolic BP on presentation	132 (123-141)	133 (124-142)	132 (123-141)
Heart rate on presentation	69 (61–80)	70 (62-80)	69 (61-79)
Hemoglobin (g/dL)	13.7 (12.5-14.7)	13.7 (12.5-14.7)	13.8 (12.6-14.8)
Creatinine	1.0 (0.9-1.2)	1.0 (0.9-1.2)	1.0 (0.9-1.2)
Procedural features:			
Fluoroscopy time	6.1 (3.5-11.2)	7.2 (4.4-12.3)	6.0 (3.3-11.0)
Contrast volume (ml)	100 (70-136)	85.0 (60.0-125.0)	100 (70-140)
LV Ventriculography	38.7	33.8	39.6

Abbreviations: BP, blood pressure; BMI, body mass index; CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; MI, myocardial infarction; PCI, percutaneous coronary intervention; PTSD, post–traumatic stress disorder

*Data are expressed as percentage of patients for categorical variables, median (interquartile range) for continuous variables.

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Table 2. Estimated Cumulative Incidence of Outcomes (%; 95% CI)

		Femoral				Radial			
	Total (N=229,108)	**GFR>59 ml/min**	**GFR: 45–59 ml/min**	**GFR: 30–44 ml/min**	**GFR: 15–29 ml/min**	**GFR>59 ml/min**	**GFR: 45–59 ml/min**	**GFR: 30–44 ml/min**	**GFR: 15–29 ml/min (**
		N=152,006 (66.3%)	N=29,892 (13.0%)	N=9,491 (4.1%)	N=1,740 (0.8%)	N=28,947 (12.6%)	N=5,315 (2.3%)	N=1,485 (0.6%)	N=232 (0.1%)
New Dialysis	0.69 (0.65,0.72)	0.31 (0.28,0.34)	0.95 (0.84,1.06)	3.21 (2.81,3.51)	19.26 (16.49,20.13)	0.28 (0.22,0.34)	1.08 (0.8,1.35)	2.59 (1.75,3.36)	14.36 (8.87,17.63)
Transfusion within 48 hours	0.99 (0.94,1.02)	0.79 (0.74,0.83)	1.3 (1.16,1.42)	2.72 (2.37,3.02)	6.41 (5.12,7.42)	0.72 (0.62,0.82)	1.13 (0.84,1.41)	1.9 (1.19,2.58)	3.05 (0.79,5.2)

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Figure Legends:

Figure 1. Study Population Characteristics. This figure displays the study population characteristics, including exclusions. Abbreviations: eGFR, estimated glomerular filtration rate.

Figure 2. Cumulative Incidence of Reported Outcomes. This figure displays the cumulative incidence of (**A**) blood transfusion within 48 hours, (**B**) progression to dialysis at 1 year.

Figure 3. Hazard Ratios for Reported Outcomes, Stratified by Degree of Chronic Kidney Disease. This figure displays the adjusted hazard ratio for (**A**) blood transfusion within 48 hours, (**B**) progression to dialysis at 1 year, stratified by degree of chronic kidney disease.

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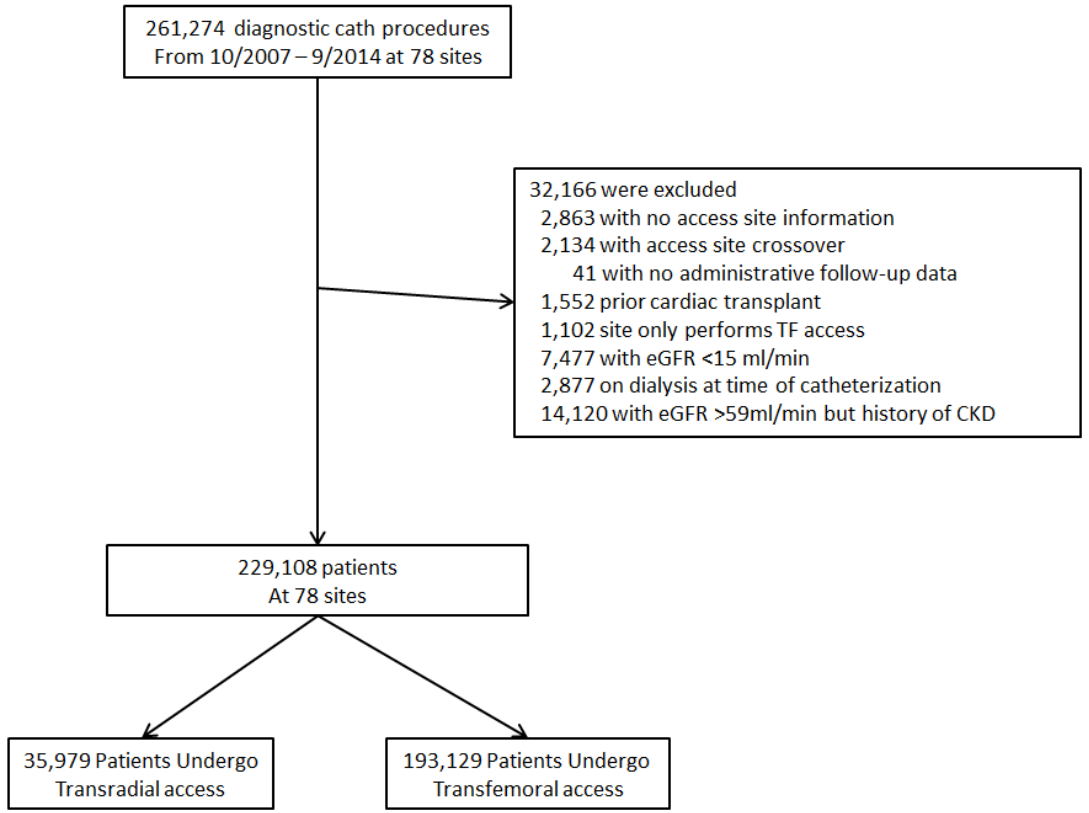

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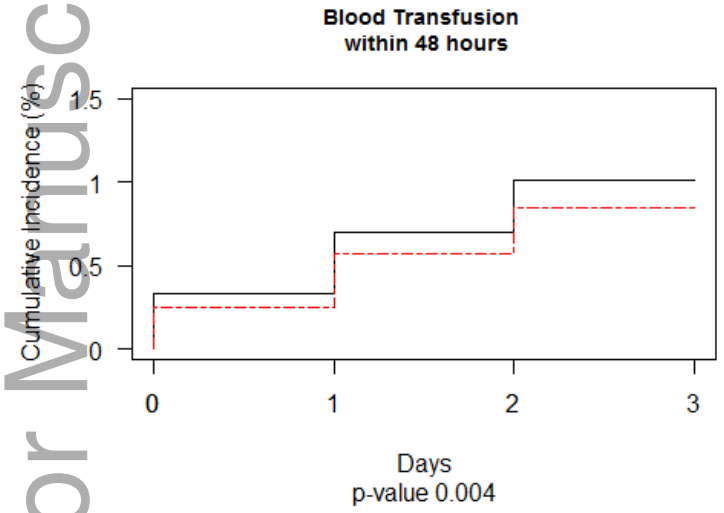

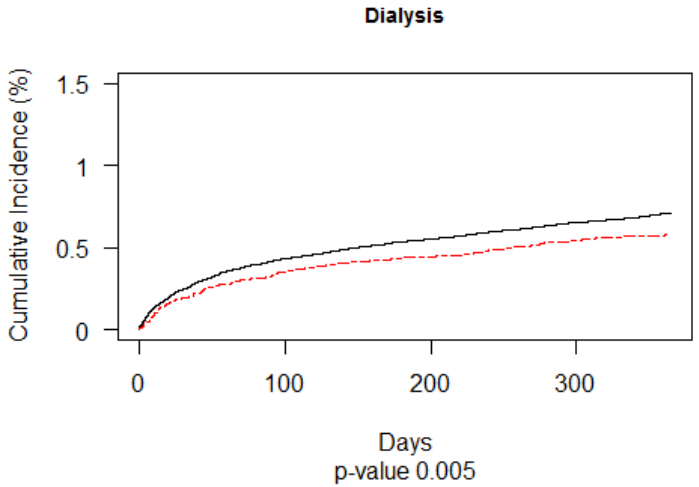

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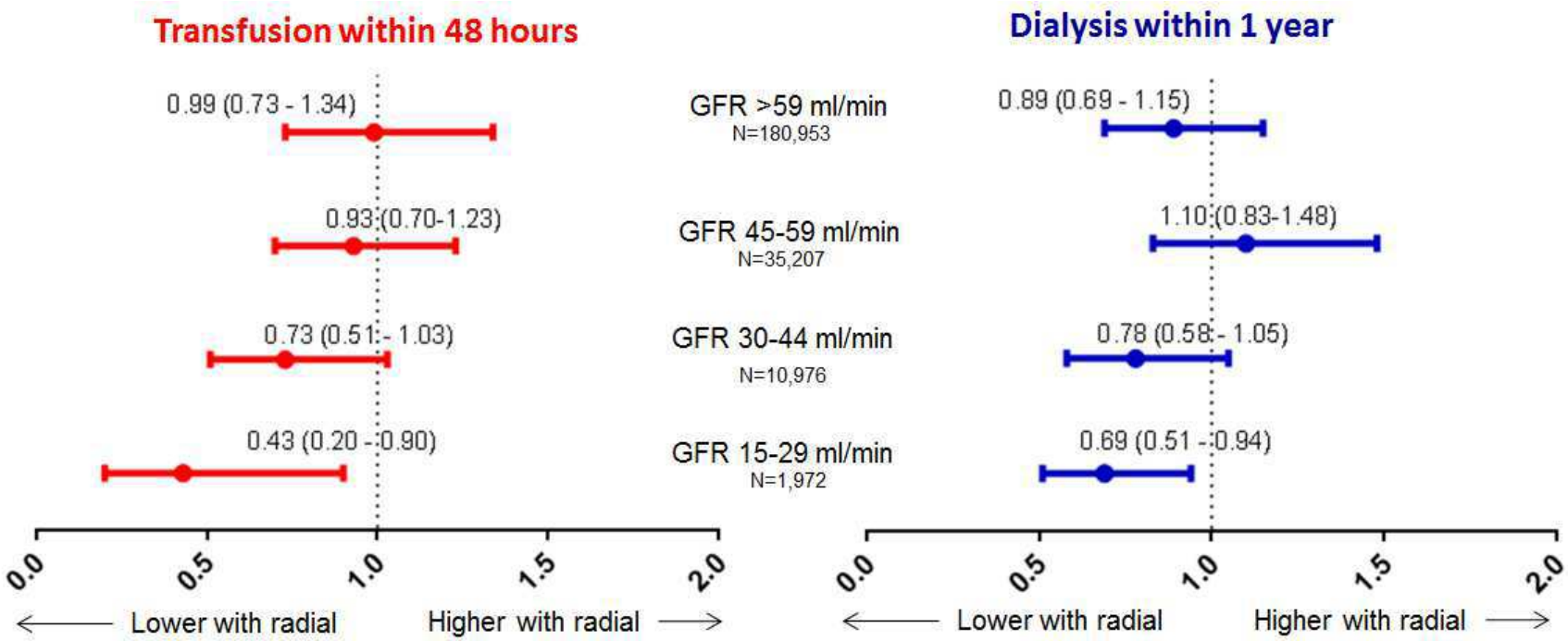

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