

SUPPLEMENTAL MATERIAL

USE OF RENIN-ANGIOTENSIN INHIBITORS IN PEOPLE WITH RENAL ARTERY STENOSIS

Kaleigh L. Evans, M.D.¹, Katherine R. Tuttle, M.D.², David A. Folt, M.D.¹, Taylor Dawson, M.S.B.S.¹, Steven T. Haller, Ph.D.¹, Pamela S. Brewster, M.A.¹, Wencan He, M.S.¹, Kenneth Jamerson, M.D.³, Lance Dworkin, M.D.⁴, Donald Cutlip, M.D.⁵, Timothy P. Murphy, M.D.⁴, Ralph B. D'Agostino, Sr., Ph.D.⁵, William Henrich, M.D.⁶, and Christopher J. Cooper, M.D.¹

Author Affiliations:

¹University of Toledo, Toledo, OH

²University of Washington School of Medicine, Providence Sacred Heart Medical Center, Spokane, WA

³University of Michigan, Ann Arbor, MI

⁴Alpert Medical School of Brown University, Providence, RI

⁵Harvard Clinical Research Institute, Boston, MA

⁶University of Texas Health Science Center, San Antonio, TX

Running Title: Angiotensin inhibitor use in renal artery stenosis

Address for correspondence:

Kaleigh L. Evans, M.D.

Department of Medicine

University of Toledo College of Medicine

3000 Arlington Ave., MS 1025

Toledo, OH 43614

Phone 419-383-3923

Fax 419-383-3172

Kaleigh.Evans@utoledo.edu

Table S1. Baseline characteristics and medical management associated with renin-angiotensin inhibition of participants enrolled in the CORAL clinical trial controlled for age, gender and location.

Variable	Category	OR	95% LL	95%UL	P-Value
Demographic / Physical Exam					
Age		1.00	0.98	1.02	0.96
Gender	Male	1.28	0.97	1.67	0.08
Race	White	1.15	0.70	1.90	0.57
Hispanic/Latino		1.48	0.82	2.66	0.20
Location	US	0.52	0.36	0.76	0.001
Height (ins)		0.98	0.94	1.03	0.40
Weight(lbs)		1.00	1.00	1.01	0.06
Body Mass Index		1.03	1.01	1.06	0.01
SBP (mmHg)		0.99	0.98	1.00	0.002
DBP (mmHg)		0.99	0.98	1.00	0.01
SBP at Goal		1.53	1.11	2.09	0.009
Laboratory Values					
Creatinine (mg/dl)		0.54	0.39	0.75	<0.001
MDRD-eGFR (ml/min/1.73m ²)		1.01	1.00	1.02	1.016
Cystatin C (mg/L)		0.72	0.53	0.97	0.03
Urine Protein (dipstick)	Trace	1.00	0.73	1.35	0.98
	30 mg/dl	0.92	0.54	1.57	0.76
	100 mg/dl	0.35	0.16	0.80	0.01
	300 mg/dl	0.41	0.10	1.64	0.21
	≥2000 mg/dl	1.17	0.16	8.40	0.88
Risk Factors / Indications					
PAD*		1.07	0.78	1.47	0.68
Smoking (past year)		0.98	0.70	1.37	0.91
Hyperlipidemia		1.11	0.71	1.75	0.65
MI		1.15	0.85	1.57	0.36
TIA		0.83	0.59	1.17	0.28
Angina		1.54	1.00	2.37	0.05
CVD		0.95	0.71	1.28	0.73
PVD		0.86	0.65	1.13	0.27
Diabetes		1.98	1.47	2.65	<0.001
CHF		1.42	0.96	2.12	0.08
CKD		0.68	0.50	0.91	0.009
Bilateral disease		0.88	0.62	1.26	0.50
Medication Use					
Diuretic		3.80	2.81	5.14	<0.001
Aldosterone antagonist		1.29	0.57	2.89	0.54
Beta blocker		2.16	1.62	2.88	<0.001

Alpha blocker	1.11	0.76	1.61	0.59
Alpha-beta blocker	0.91	0.59	1.41	0.67
Calcium channel blocker	2.55	1.88	3.47	<0.001
Renin inhibitor	1.25	0.25	6.28	0.78
Vasodilator	0.63	0.33	1.20	0.16
Nitrate	1.38	0.97	1.95	0.07
Anti-platelet	1.93	1.40	2.65	<0.001
Lipid lowering	4.81	3.40	6.79	<0.001
Total HTN medications	3.25	2.77	3.81	<0.001
Total all medications	2.03	1.83	2.25	<0.001

US, United States; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MDRD-eGFR, Modified Diet in Renal Disease Glomerular Filtration Rate; MI, Myocardial Infarction; TIA, Transient Ischemic Attack; CVD, Cerebrovascular disease; PVD, Peripheral Vascular Disease; CHF, Congestive Heart Failure; CKD, Chronic Kidney Disease; and HTN, Hypertension.

*PAD, Premature atherosclerotic disease: CAD, CVD or PVD in male relatives < 55 and/or female relatives < 65 years old.

Table S2. Model for ACEI/ARB use obtained from stepwise logistic regression

	OR	95% LL	95% UL	P-Value
Body Mass Index	1.027	0.999	1.055	0.06
Creatinine	0.521	0.372	0.731	<0.001
Diabetes	1.96	1.43	2.685	<0.001
Age	1.009	0.993	1.026	0.26
Gender: Male	1.559	1.158	2.098	0.003
Location: US	0.486	0.326	0.724	<0.001
CHF	1.396	0.913	2.135	0.12

US, United States; CHF, Congestive Heart Failure; Std., Standard; OR Odds Ratio; LL, Lower Limit; UL, Upper Limit.

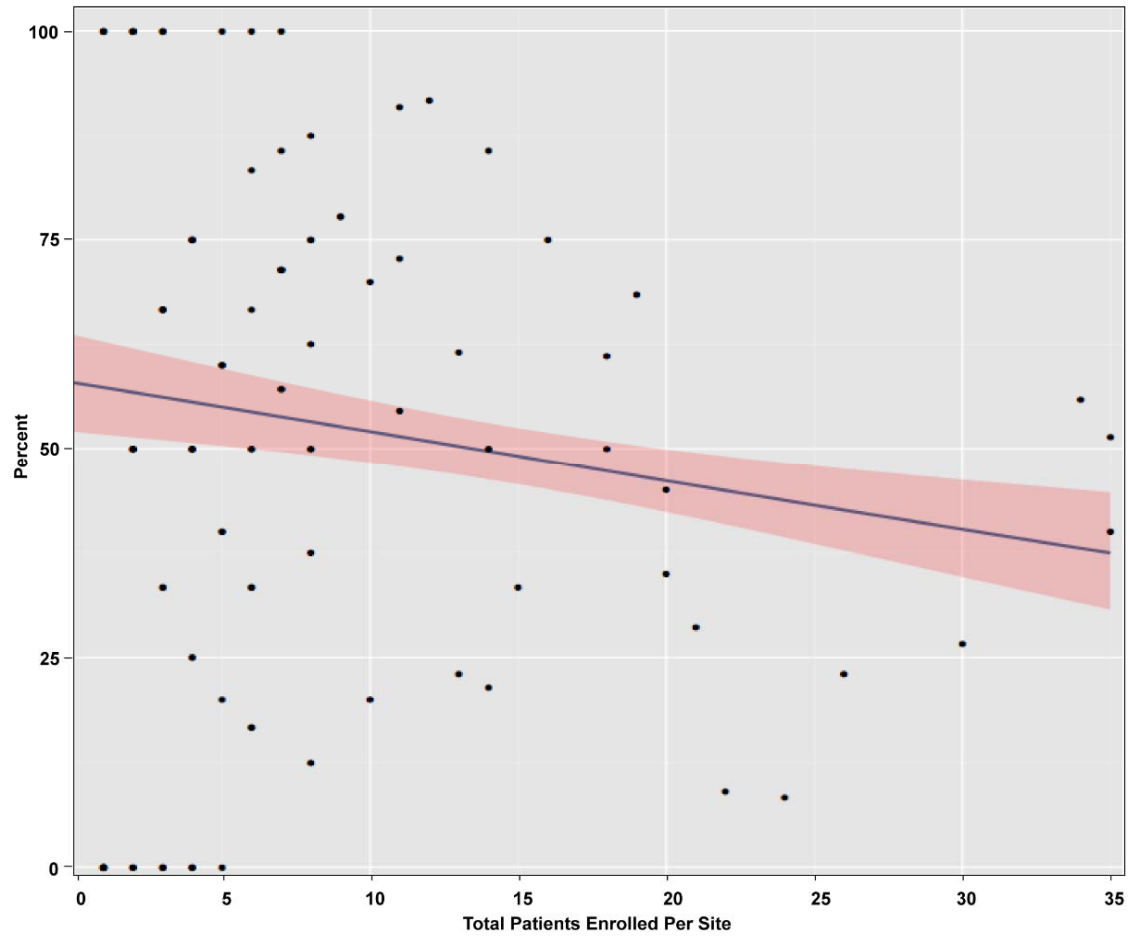


Figure S1. Funnel plot of the total number of patients enrolled at each site by the percent use of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers (ACEI/ARB) for the site. The fitted logistic regression line with 95% confidence intervals indicated by light red shading demonstrates the inverse relationship between the number of enrolled patients and rate of ACEI/ARB use with higher volume sites using ACEI/ARB at a lower rate.

Table S3a. Model for ACEI/ARB use obtained from logistic regression on data aggregated by site.

	OR	95% LL	95% UL	P- Value
Total patients	0.980	0.966	0.995	0.008
PI: IC	1.126	0.771	1.646	0.54
PI: IR	0.917	0.586	1.433	0.70
PI: VS	1.084	0.529	2.237	0.82
Location: US	0.397	0.256	0.609	<0.001
Gender: Male	2.018	0.912	4.495	0.08
Age (years)	1.013	0.974	1.055	0.52
Creatinine (mg/dl)	0.553	0.252	1.201	0.14
Diabetes:	3.772	1.536	9.501	0.004
BMI	1.133	1.053	1.222	<0.001

PI, Principal Investigator; IC, Interventional Cardiologist; IR, Interventional Radiologist; VS, Vascular Surgeon; US, United States; BMI, Body Mass Index; Std., Standard; OR, Odds Ratio; LL, Lower Limit; UL, Upper Limit.

Table S3b. Model for ACEI/ARB use obtained from stepwise logistic regression on data aggregated by site without principal investigators.

	OR	95% LL	95% UL	P- Value
Total patients	0.980	0.967	0.994	0.007
Location: US	0.409	0.267	0.620	<0.001
Gender: Male	2.006	0.963	4.208	0.06
Age (years)	1.015	0.976	1.057	0.44
Creatinine (mg/dl)	0.504	0.237	1.059	0.07
Diabetes:	4.205	1.756	10.343	<0.001
BMI	1.140	1.060	1.228	<0.001

US, United States; BMI, Body Mass Index; Std., Standard; OR, Odds Ratio; LL, Lower Limit; UL, Upper Limit.

Table S3c. Model for ACEI/ARB use for only the significant variables

	OR	95% LL	95% UL	P-Value
Total patients	0.982	0.968	0.995	0.009
Location: US	0.405	0.266	0.609	<0.001
Diabetes	3.371	1.449	8.009	0.005
BMI	1.136	1.058	1.222	<0.001

US, United States; BMI, Body Mass Index; Std., Standard; OR, Odds Ratio; LL, Lower Limit; UL, Upper Limit.