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U.S. Department
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Evaluation of the Impact of Chronic Kidney Disease on Occurrence of Major Adverse Cardiovascular Events in Patients on Dual Antiplatelet Therapy Post-Acute Coronary Syndrome Resulting in Percutaneous Coronary Intervention

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DISCLAIMER

- This material is the result of work supported with resources and the use of facilities at the VA St. Louis Health Care System.
- The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.
- This study was approved by the Institutional Review Board (IRB) at the VA St. Louis Health Care System.



Chronic Kidney Disease (CKD)

35-40% patients with ACS also have renal dysfunction

↑ risk of cardiovascular disease

↑ risk of thrombosis and bleeding

Clopidogrel in CKD

Reduced or no benefit?

Insufficient active metabolite generation

Enhanced platelet turnover & low platelet count

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2. Gurm HS. *JACC Cardiovasc Interv*. 2017;10(20):2026-28.
3. Morel, et al. *Nephro Dial Transplant*. 2013;28:1994-2002.
4. Best PJ, et al. *Am Heart J*. 2008;155(4):687-93.
5. Keltai M, et al. *Eur J Cardiovasc Prev Rehabil*. 2007;14(2):312-8.
6. James, S et al. *Circulation*. 2010;122(11):1056-67.
7. Gremmel T, et al. *Nephro Dial Transplant*. 2013;28(8):2116-22.



CLINICAL QUESTION

Utility of DAPT with clopidogrel in the CKD population?



OBJECTIVE & HYPOTHESIS

Objective

- To evaluate if CKD (GFR < 60 mL/min/1.73m²) affects MACE outcomes in patients on DAPT with clopidogrel post-ACS resulting in PCI

Hypothesis

- Higher incidence of MACE outcomes associated with GFR < 60 mL/min/1.73m² than GFR ≥ 60 mL/min/1.73m²



METHODS

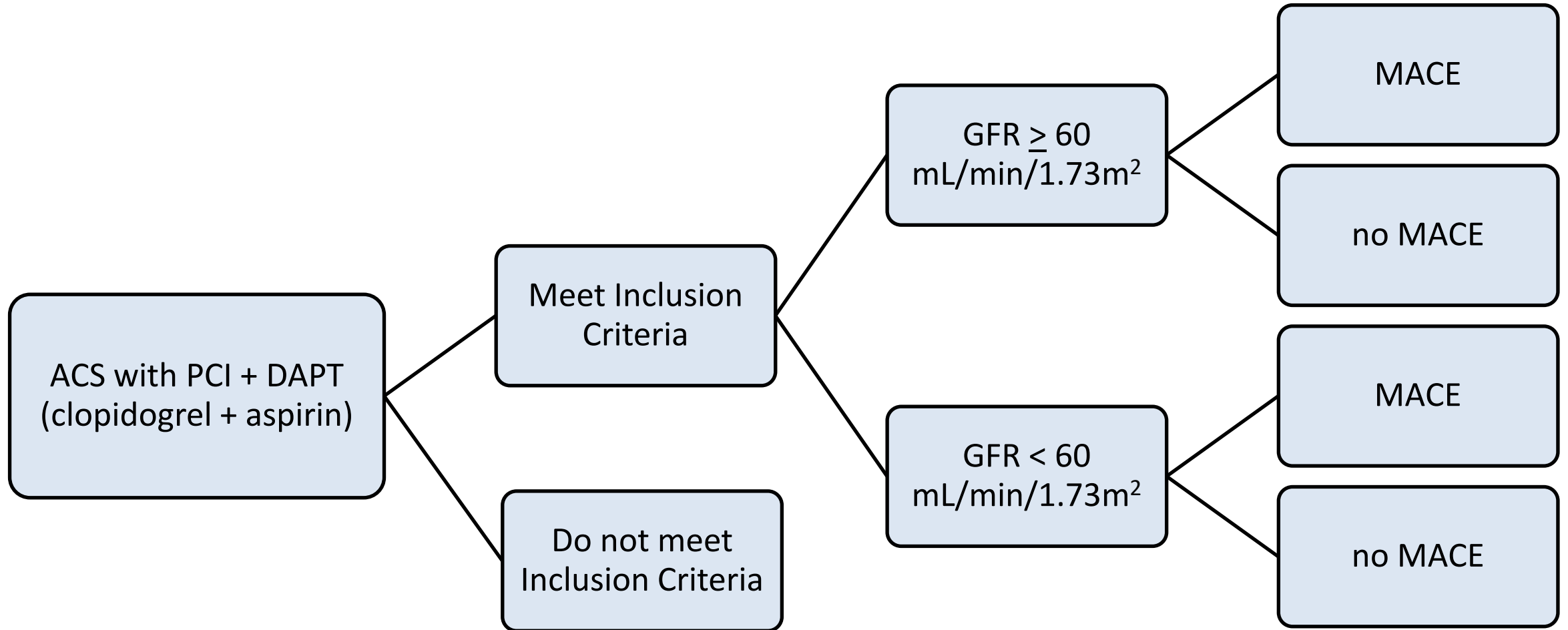
Retrospective
Cohort

Single VA
Medical
Center

Time Frame:
1/1/2013 – 1/1/2019



STUDY DESIGN

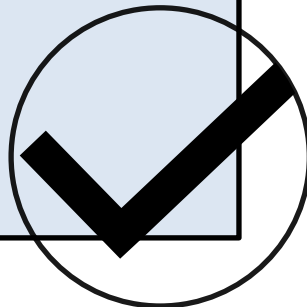




INCLUSION & EXCLUSION CRITERIA

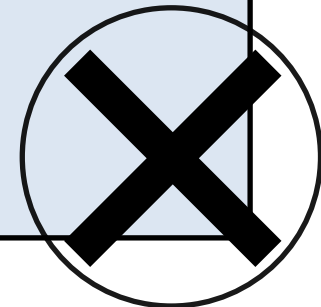
- Age ≥ 18 to ≤ 89 years old
- Admitted with an ACS event and underwent urgent/emergent PCI with stent placement
- Initiated on clopidogrel + aspirin within 3 days
- Prescription for clopidogrel + aspirin (or aspirin listed as non-VA medication) at hospital discharge

Inclusion



- Other antiplatelets initiated
- Bypass surgery performed
- Overlapping stents placed
- Previously on DAPT with in-stent thrombosis
- Not initiated on DAPT within 3 days
- Lost to follow-up
- Medication possession ratio $< 80\%$

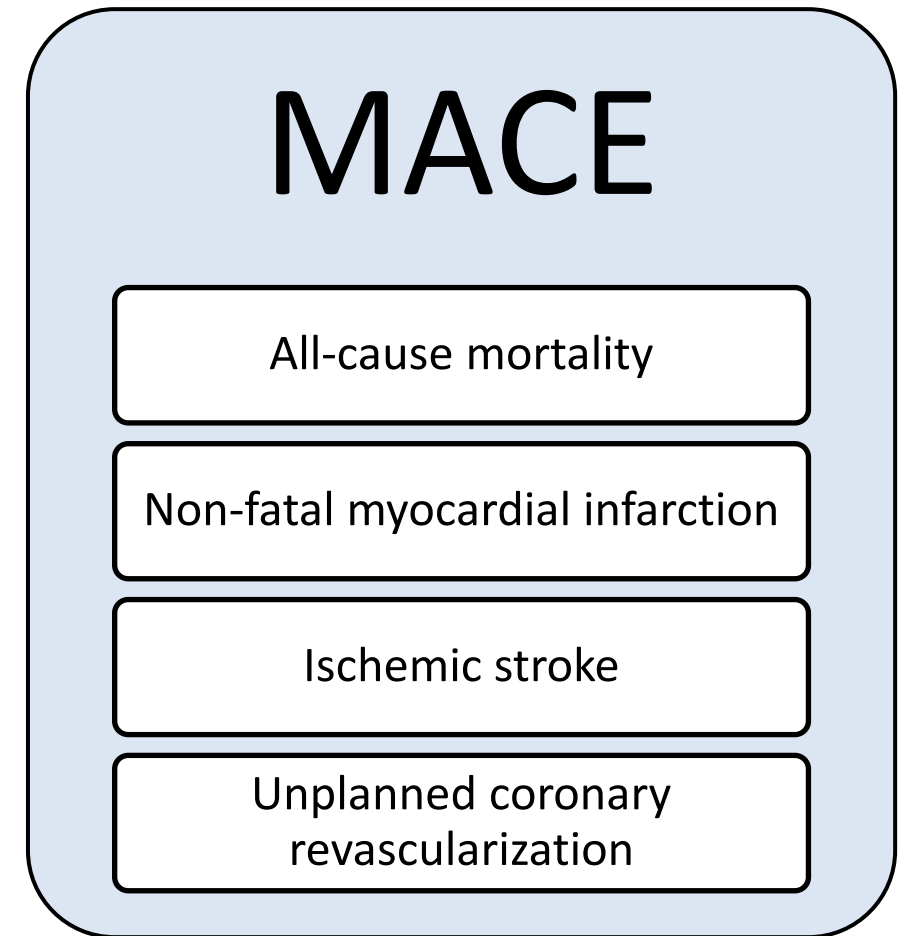
Exclusion





OUTCOMES

- **Primary (at 12 months):**
 - Composite of major adverse cardiovascular events (MACE)
- **Secondary (at 12 months):**
 - All-cause mortality
 - Non-fatal myocardial infarction
 - Ischemic stroke
 - Unplanned coronary revascularization
 - Stent thrombosis
 - Cardiovascular mortality





STATISTICAL ANALYSIS

Baseline Characteristics

- Descriptive statistics
- Chi-square/Fisher's exact for categorical variables
- Independent t-test for continuous variables

Primary & Secondary Outcomes

- One-sided alpha of 0.05
- 175 patients per group needed to give 80% power to detect a 10% difference
- Fisher's exact

Sub-analysis

- Univariate analysis
- Multivariate analysis including variables with $p < 0.2$ in univariate analysis



BASELINE CHARACTERISTICS

Baseline Characteristics	GFR < 60 (n=16)	GFR ≥ 60 (n=91)	P-value
Age, yr (mean ± SD)	72.3 ± 10.5	63.8 ± 11.6	0.007
Gender— Male, n (%)	16 (100)	90 (98.9)	1.00
Race, n (%)			
Caucasian	14 (87.5)	60 (65.9)	0.140
African American	2 (12.5)	30 (33.0)	
Other	0 (0)	1 (1.1)	
Serum creatinine, mg/dL (mean ± SD)	2.04 ± 0.97	0.93 ± 0.15	<0.001
eGFR, mL/min/1.73m ² (mean ± SD)	39.3 ± 14.8	85.1 ± 16.9	<0.001
CKD Stage			
Stage 3a	7 (43.8)	n/a	n/a
Stage 3b	5 (31.3)		
Stage 4	3 (18.8)		
Stage 5	1 (6.3)		



BASELINE CHARACTERISTICS

Comorbidities	GFR < 60 (n=16)	GFR ≥ 60 (n=91)	P-value
Diabetes, n (%)	12 (75)	41 (45)	0.032
Hypertension, n (%)	15 (93.4)	76 (83.5)	0.457
Hyperlipidemia, n (%)	16 (100)	70 (76.9)	0.038
Coronary Artery Disease, n (%)	11 (68.8)	41 (45.1)	0.106
Prior Acute Coronary Syndrome, n (%)	8 (50)	24 (26.4)	0.057
Prior Revascularization, n (%)	11 (68.8)	38 (41.8)	0.059
Peripheral Artery Disease, n (%)	4 (16.7)	11 (13.3)	0.741
Tobacco Use, n (%)			
Current	3 (18.8)	45 (49.5)	0.095
Former	9 (56.3)	38 (41.8)	
Never	4 (25)	8 (8.8)	



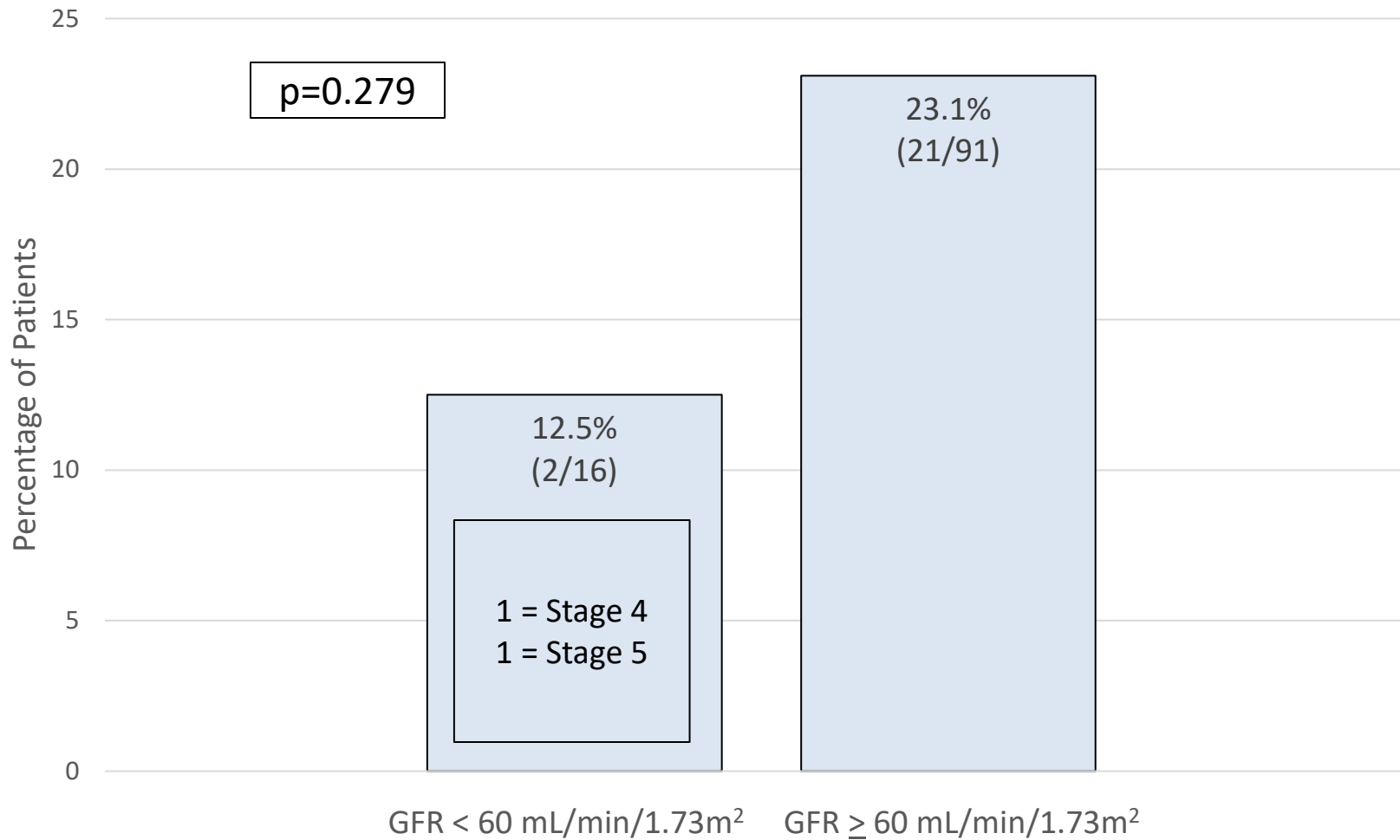
BASELINE CHARACTERISTICS

Medications	GFR < 60 (n=16)	GFR ≥ 60 (n=91)	P-value
Statin Use, n (%)	16 (100)	84 (92.3)	0.591
ACE-inhibitor/ARB Use, n (%)	11 (68.8)	67 (73.6)	0.686
Beta Blocker Use, n (%)	15 (94)	83 (91.2)	1.00
Proton Pump Inhibitor, n (%)	5 (31.3)	27 (30)	1.00



RESULTS—PRIMARY OUTCOME

Major Adverse Cardiovascular Events





RESULTS—SECONDARY OUTCOMES

Outcome	GFR < 60 (n=16)	GFR ≥ 60 (n=91)	P-value
All-cause mortality, n (%)	1 (6.3)	9 (9.9)	0.279
Non-fatal myocardial infarction, n (%)	1 (6.3)	5 (5.5)	0.540
Ischemic stroke, n (%)	0 (0)	4 (4.4)	0.518
Unplanned coronary revascularization, n (%)	1 (6.3)	10 (11)	0.485
Stent thrombosis, n (%)	0 (0)	1 (1.1)	0.851
Cardiovascular mortality, n (%)	0 (0)	0 (0)	n/a



UNIVARIATE ANALYSIS

Risk Factor	MACE (n=24)	No MACE (n=83)	P-value
Gender—Male, n (%)	24 (100)	82 (98.8)	1.00
Race, n (%)			
Caucasian	17 (70.8)	57 (68.7)	1.00
African American	7 (29.2)	25 (30.1)	
Other	0 (0)	1 (1.2)	
Age (mean \pm SD)	65.9 \pm 11.2	64.5 \pm 12	0.585
GFR, mL/min/1.73m ² (mean \pm SD)	75 \pm 21.5	79.2 \pm 23.8	0.89
CKD – GFR < 60 mL/min/1.73m ² , n (%)	2 (8.3)	14 (16.9)	0.516
Diabetes, n (%)	15 (62.5)	38 (45.8)	0.149
Hypertension, n (%)	23 (95.8)	68 (81.9)	0.114
Hyperlipidemia, n (%)	19 (79.2)	67 (80.7)	1.00
Coronary artery disease, n (%)	14 (58.3)	38 (45.8)	0.279



UNIVARIATE ANALYSIS

Risk Factor	MACE (n=24)	No MACE (n=83)	P-value
Prior Acute Coronary Syndrome, n (%)	7 (29.2)	25 (30.1)	1.00
Prior Revascularization, n (%)	12 (50)	37 (44.6)	0.639
Peripheral Artery Disease, n (%)	4 (16.7)	11 (13.3)	0.740
Tobacco Use, n (%)			
Current	9 (37.5)	39 (47)	0.410
Former	14 (58.3)	33 (39.8)	0.106
Never	1 (4.2)	11 (13.3)	0.292
Statin Use, n (%)	20 (83.3)	80 (96.4)	0.043
Type of stent– Drug-eluting, n (%)	21 (87.5)	71 (85.5)	1.00
Multiple stents, n (%)	10 (41.7)	24 (28.9)	0.237



LOGISTIC REGRESSION

Multivariate analysis for independent risk factors associated with MACE

Risk Factor	OR (95% CI)	P-value
Chronic Kidney Disease	0.335 (0.066-1.71)	0.188
Diabetes	2.24 (0.796-6.32)	0.126
Hypertension	4.38 (0.514-37.33)	0.176
Former Tobacco Use	0.479 (0.18-1.280)	0.142
Statin Use	0.210 (0.039-1.13)	0.069



DISCUSSION

- MACE numerically higher in patients with $GFR \geq 60 \text{ mL/min/1.73m}^2$
- Majority of CKD population included with Stage 3 CKD
- No statin: potential predictor of MACE?

Inconsistent with previous findings

Two composite events: CKD Stage 4 & 5

100% patients with CKD received statin therapy

**CKD Stage?
Role of statin therapy?**



STRENGTHS & LIMITATIONS

Strengths

- Medication possession ratio \geq 80% for inclusion
- Inclusion of all types of ACS
- Use of MDRD over CrCl
- Serum creatinine measurement used reflective of baseline

Limitations

- Single center, retrospective study design
- Inability to verify non-VA aspirin adherence
- Drug-eluting stent changes
- Unbalanced baseline characteristics
- Underpowered (risk for type II error)
- Generalizability



CONCLUSIONS

- No difference seen in MACE in patients on DAPT with clopidogrel despite renal function
- Larger studies are needed to further investigate outcomes in patients with $\text{GFR} < 60 \text{ mL/min/1.73m}^2$
 - Consider focusing on $\text{GFR} < 30 \text{ mL/min/1.73m}^2$

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UNIVARIATE ANALYSIS

Risk Factor	MACE (n=24)	No MACE (n=83)	P-value
ACE-inhibitor, n (%)	15 (62.5)	52 (62.7)	0.989
ARB, n (%)	2 (8.3)	9 (10.8)	1.00
Beta Blocker, n (%)	21 (87.5)	77 (92.8)	0.416
Proton Pump Inhibitor, n (%)	6 (25)	26 (31.3)	0.551



CHRONIC KIDNEY DISEASE STAGES DEFINED

Stage	Definition	GFR mL/min/1.73m²
Stage 3a	Mild-moderate CKD	45-59
Stage 3b	Moderate-severe CKD	30-44
Stage 4	Severe CKD	15-29
Stage 5	Kidney Failure	< 15