

Lower likelihood of cardiac procedures after acute coronary syndrome in patients with human immunodeficiency virus/acquired immunodeficiency syndrome

Meredith E. Clement, MD^{a,b,*}, Li Lin, MS^b, Ann Marie Navar, MD, PhD^{b,c}, Nwora Lance Okeke, MD, MPH^a, Susanna Naggie, MD, MHS^{a,b}, Pamela S. Douglas, MD^{b,c}

Abstract

Cardiovascular disease (CVD) is an increasing cause of morbidity and mortality in human immunodeficiency virus (HIV)-infected adults; however, this population may be less likely to receive interventions during hospitalization for acute coronary syndrome (ACS). The degree to which this disparity can be attributed to poorly controlled HIV infection is unknown.

In this large cohort study, we used the National Inpatient Sample (NIS) to compare rates of cardiac procedures among patients with asymptomatic HIV-infection, symptomatic acquired immunodeficiency syndrome (AIDS), and uninfected adults hospitalized with ACS from 2009 to 2012. Multivariable analysis was used to compare procedure rates by HIV status, with appropriate weighting to account for NIS sampling design including stratification and hospital clustering.

The dataset included 1,091,759 ACS hospitalizations, 0.35% of which (n=3783) were in HIV-infected patients. Patients with symptomatic AIDS, asymptomatic HIV, and uninfected patients differed by sex, race, and income status. Overall rates of cardiac catheterization and revascularization were 53.3% and 37.4%, respectively. In multivariable regression, we found that relative to uninfected patients, those with symptomatic AIDS were less likely to undergo catheterization (odds ratio [OR] 0.48, confidence interval [CI] 0.43–0.55), percutaneous coronary intervention (OR 0.69, CI 0.59–0.79), and coronary artery bypass grafting (0.75, CI 0.61–0.93). No difference was seen for those with asymptomatic HIV relative to uninfected patients (OR 0.93, CI 0.81–1.07; OR 1.06, CI 0.93–1.21; OR 0.88, CI 0.72–1.06, respectively).

We found that lower rates of cardiovascular procedures in HIV-infected patients were primarily driven by less frequent procedures in those with AIDS.

Abbreviations: ACS = acute coronary syndrome, AIDS = acquired immunodeficiency syndrome, BMS = bare metal stent, CABG = coronary artery bypass grafting, CVD = cardiovascular disease, DES = drug-eluting stent, HCUP = healthcare cost and utilization project, HIV = human immunodeficiency virus, ICD-9 = International Classifications of Disease, Ninth Edition, LOS = length-of-stay, NIS = National Inpatient Sample, NSTEMI = non-ST-elevation myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction, UA = unstable angina.

Keywords: acquired immunodeficiency syndrome, acute coronary syndrome, catheterization, coronary artery bypass, HIV infections, inequalities, percutaneous coronary intervention

1. Introduction

In the United States, non-AIDS-defining illnesses including cardiovascular disease have become the leading cause of death in HIV-infected patients. HIV infection is associated with a 50%

increased risk of acute myocardial infarction (MI).^[1] Given high rates of acute coronary syndromes (ACS) in this population, adequate access to standard-of-care interventions and revascularization procedures for HIV-infected patients with ACS is critical.

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^a Division of Infectious Diseases, ^b Duke Clinical Research Institute, ^c Division of Cardiology, Duke University, Durham, NC.

* Correspondence: Meredith E. Clement, Duke Clinical Research Institute, 2400 Pratt St, Durham, NC 27705 (e-mail: meredith.edwards@duke.edu).

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Unfortunately, there is evidence that disparities may exist in management of ACS by HIV status. A recent study demonstrated that in patients presenting with ACS, HIV-infected patients were less likely to receive percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), and drug-eluting stents (DES), and had higher in-hospital mortality as compared with patients without HIV.^[2] It is not clear to what extent these differences can be attributed to poorly controlled HIV-infection, that is, acquired immunodeficiency syndrome (AIDS). We used the National Inpatient Sample (NIS), a component of the Healthcare Cost and Utilization Project (HCUP), to compare rates of cardiac catheterization and revascularization (PCI and CABG) among patients with asymptomatic HIV-infection, AIDS, and uninfected adults hospitalized with ACS to determine whether inequalities with respect to HIV status are attributable to symptomatic HIV/AIDS.

2. Methods

2.1. Data source

The National Inpatient Sample (NIS) is a systematic random sample of discharges stratified by hospital characteristics (<https://www.hcup-us.ahrq.gov/db/nation/nis/nisdbdocumentation.jsp>). However, unified sampling weighting has been provided for HCUP so that all the annual NIS data can be analyzed together and weighted survey analysis results apply to all US community hospital discharges. We used 2009 as our initial analysis year to allow for stabilization in usage rates of drug eluting stents.^[3] This study was granted exemption by the Duke Institutional Review Board due to the lack of identifiable patient health information.

2.2. Study population

The study population was patients aged 18 years and older hospitalized with acute coronary syndromes (ACS) diagnosis (including ST-elevation myocardial infarction [STEMI], non-STEMI [NSTEMI], and unstable angina [UA]), grouped by HIV status. International Classifications of Disease, Ninth Edition (ICD-9) codes were used to identify hospitalizations for ACS diagnoses and related procedures (Supplementary Table 1, <http://links.lww.com/MD/C117>). HIV status was determined based on presence of ICD-9 code of 042 (symptomatic HIV infection/AIDS) or V08 (asymptomatic HIV infection) included in the hospitalization claim. This procedure has been used in prior analyses of HCUP data to distinguish between those who have documented diagnoses that reflect current or prior severe HIV-related immunosuppression and those who do not.^[4,5] Medical comorbidities and drug, alcohol, and substance use/abuse were defined based on the NIS Clinical Classifications Software tool, a methods of condensing patient diagnoses into clinically meaningful categories.

We investigated rates of catheterization as well as time to catheterization for all patients presenting with ACS. Specifically, we determined whether a patient with STEMI as admitting diagnosis underwent catheterization within 24 hours and whether a patient with NSTEMI underwent catheterization within 48 hours. Time thresholds are based upon guidelines^[6] and findings from prior studies.^[7,8] We additionally examined revascularization rates including PCI and CABG procedures and stent type for all patients undergoing PCI, and evaluated outcomes including length-of-stay (LOS) and in-hospital mortality for the index admission.

2.3. Statistical analysis

The eligible hospitalizations were categorized into 3 groups by patients' HIV status—symptomatic HIV/AIDS, asymptomatic HIV, and uninfected. Unweighted descriptive statistics were used to describe baseline characteristics of the sample groups. Intervention rates and postprocedure short-term outcomes were based on survey data analysis, with weight and hospital clustering effect adjusted. Rao-Scott chi-squared tests or analysis of variance were used to test significance of the differences among the three groups, and 95% CIs of proportions or means were constructed for direct comparisons. To examine adjusted effects of HIV status on the outcomes, weighted multilevel logistic or linear regression^[9] was used. We controlled for the following variables in our model: age, sex, race/ethnicity, income, year of hospitalization, tobacco use, alcohol use, substance abuse, ACS event type, comorbidities (congestive heart failure, renal disease, malignancy, cerebrovascular disease, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease, diabetes, obesity, and liver failure), hospital type/ownership, and insurance status. Race was evaluated by NIS categories including Black, White, Hispanic, Asian/Pacific Islander, Native American, or Other. Insurance Status was evaluated by NIS categories including Private, Medicaid, Medicare, Self-Pay, No Charge, or Other. Model estimated odds ratios (OR) or difference in least square means with 95% CIs were reported. *P*-value <.05 was considered statistically significant. All analyses were performed using SAS statistical software SAS 9.4 (SAS Institute, Cary, NC).

3. Results

We analyzed 1,093,849 hospitalizations for ACS, including 3792 (0.35%) in HIV-infected patients. Baseline characteristics of the study population are provided in Table 1. HIV-infected patients (including those with asymptomatic HIV and symptomatic HIV/AIDS) were younger and more often male, Black or Hispanic, and of lower income status relative to uninfected patients. HIV-uninfected patients had greater rates of traditional CVD risk factors and equivalents compared with those with HIV infection. Patients with symptomatic HIV/AIDS had higher rates of malignancy, liver disease, and kidney disease relative to both uninfected patients and those with asymptomatic HIV infection. Smoking, substance abuse, and alcohol abuse were higher among those with HIV infection (both symptomatic HIV/AIDS and asymptomatic disease) as compared with uninfected patients. Among ACS events, unstable angina occurred less frequently and NSTEMI more frequently in those with symptomatic HIV/AIDS, relative to those with asymptomatic HIV or without HIV infection.

3.1. Catheterization after ACS event and timing to catheterization

Overall rate of cardiac catheterization was 53.3%, including 62.6% of patients with asymptomatic HIV infection, 43.0% of those with symptomatic HIV/AIDS, and 53.4% of patients without HIV infection (Table 2). After adjustment for patient and hospital characteristics, we found that relative to uninfected patients, those with symptomatic HIV/AIDS were less likely to undergo catheterization (OR 0.48, confidence interval [CI] 0.43–0.55), while patients with asymptomatic HIV were not (OR 0.93, CI 0.81–1.07).

Table 1**Baseline characteristics.**

	No HIV n = 1,090,057	Asymptomatic HIV n = 1810	History of AIDS n = 1982
Age, median	69	54	54
Male sex, %	631,637 (57.9%)	1397 (77.2%)	1510 (76.2%)
Race			
Black	104,630 (10.8%)	746 (43.5%)	841 (45.3%)
White	734,307 (75.8%)	726 (42.4%)	734 (39.5%)
Hispanic	69,848 (7.2%)	153 (8.9%)	191 (10.3%)
Asian/Pacific Islander	22,106 (2.3%)	4 (0.2%)	4 (0.2%)
Native American	6094 (0.6%)	8 (0.5%)	4 (0.2%)
Other	31,182 (3.2%)	76 (4.5%)	84 (4.5%)
Income			
First quartile	321,145 (30.2%)	673 (44.1%)	770 (46.3%)
Second quartile	283,607 (26.6%)	351 (23.0%)	423 (25.5%)
Third quartile	2,523,523 (23.8%)	333 (21.8%)	275 (16.5%)
Fourth quartile	206,290 (19.4%)	169 (11.1%)	194 (11.7%)
Weekend admission day	254,399 (23.3%)	416 (23.0%)	498 (25.1%)
Facility size (No. of beds)			
Small	119,471 (11.1%)	146 (8.2%)	148 (7.6%)
Medium	250,820 (23.3%)	439 (24.6%)	444 (22.7%)
Large	707,891 (65.7%)	1198 (67.2%)	1363 (69.7%)
Geographic region			
Northeast	214,189 (19.6%)	533 (29.4%)	582 (29.4%)
Midwest	252,659 (23.2%)	289 (16.0%)	287 (14.5%)
South	428,535 (39.3%)	866 (47.8%)	781 (39.4%)
West	194,674 (17.9%)	122 (6.7%)	332 (16.8%)
Hospital type			
Rural	123,487 (11.5%)	66 (3.7%)	57 (2.9%)
Urban non-teaching	4,545,187 (42.2%)	513 (28.8%)	561 (28.7%)
Urban teaching	499,508 (46.3%)	1204 (67.5%)	1337 (68.4%)
Hospital ownership			
Government	108,248 (10.0%)	268 (15.0%)	377 (19.3%)
Private, not-for-profit	814,158 (75.5%)	1301 (73.0%)	1369 (70.0%)
Private, invest-owned	155,776 (14.4%)	214 (12.0%)	209 (10.7%)
Insurance			
Private	257,123 (23.6%)	427 (23.4%)	298 (15.1%)
Medicaid	72,646 (6.7%)	423 (23.4%)	533 (26.9%)
Medicare	669,248 (61.5%)	746 (41.4%)	961 (48.6%)
Self-pay	55,159 (5.1%)	139 (7.7%)	116 (5.9%)
No charge	4834 (0.4%)	14 (0.8%)	8 (0.4%)
Other	28,466 (2.6%)	55 (3.0%)	63 (3.2%)
Year			
2009	284,495 (26.1%)	415 (22.9%)	499 (25.2%)
2010	266,518 (24.4%)	432 (23.9%)	496 (25.0%)
2011	278,330 (25.5%)	468 (25.9%)	513 (25.9%)
2012	260,714 (23.9%)	495 (27.3%)	474 (23.9%)
Comorbidities			
CHF	348,348 (32.0%)	403 (22.3%)	584 (29.5%)
Renal disease	236,436 (21.7%)	374 (20.7%)	568 (28.7%)
Malignancy	44,011 (4.0%)	51 (2.8%)	129 (6.5%)
Hypertension	568,410 (52.1%)	866 (47.8%)	698 (35.2%)
COPD	254,826 (23.4%)	392 (21.7%)	440 (22.2%)
Diabetes	386,925 (35.5%)	491 (27.1%)	513 (25.9%)
Obesity	137,208 (12.6%)	146 (8.1%)	96 (4.8%)
Liver failure	4507 (0.4%)	9 (0.5%)	24 (1.2%)
Peripheral vascular disease	96,809 (8.9%)	97 (5.4%)	94 (4.7%)
Cerebrovascular disease	91,453 (8.4%)	75 (4.1%)	136 (6.9%)
Hyperlipidemia	616,889 (56.6%)	936 (51.7%)	708 (35.7%)
Alcohol abuse	18,343 (1.7%)	56 (3.1%)	78 (3.9%)
Substance abuse	3309 (0.3%)	45 (2.5%)	49 (2.5%)
Current smoker	207,754 (19.1%)	676 (37.3%)	572 (28.9%)
Former smoker	149,304 (13.7%)	224 (12.4%)	183 (9.2%)
Type of event			
Unstable angina	313,680 (28.8%)	537 (29.7%)	427 (21.5%)
NSTEMI	550,414 (50.5%)	845 (46.7%)	1134 (57.2%)
STEMI	225,963 (20.7%)	428 (23.6%)	421 (21.2%)

CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, CVD = cerebrovascular disease, NSTEMI = non-ST-elevation myocardial infarction, PVD = peripheral vascular disease, STEMI = ST-elevation myocardial infarction.

Table 2**Rates and multivariable analysis for catheterization and revascularization procedures.**

		Direct estimates			Model estimates	
		Not infected	HIV+	AIDS	OR (HIV vs not infected)	OR (AIDS vs not infected)
		% (n=1,090,057)	% (n=1810)	% (n=1982)		
Catheterization	Any	53.4 (52.3, 54.4)	62.6 (59.9, 65.3)	43.0 (40.1, 46.0)	0.93 (0.81, 1.07)	0.48 (0.43, 0.55)
	If yes, w/in 24 h STEMI	81.9 (81.4, 82.4)	84.8 (81.1, 88.5)	78.2 (73.0, 83.4)	0.99 (0.85, 1.15)	0.73 (0.60, 0.89)
	If yes, w/in 48 h NSTEMI	66.6 (65.8, 67.3)	72.8 (68.6, 76.9)	61.1 (56.2, 66.0)	1.12 (0.93, 1.36)	0.77 (0.63, 0.93)
Revascularization	Any	37.4 (36.4, 38.4)	43.5 (40.8, 46.2)	28.4 (25.7, 31.0)	0.99 (0.87, 1.14)	0.61 (0.53, 0.70)
	PCI	29.2 (28.4, 30.0)	36.8 (34.4, 39.3)	23.9 (21.4, 26.4)	1.06 (0.93, 1.21)	0.69 (0.59, 0.79)
	If PCI, DES	73.0 (72.1, 73.9)	66.8 (62.6, 70.9)	60.1 (55.3, 64.9)	0.78 (0.63, 0.95)	0.68 (0.50, 0.93)
	CABG	8.4 (8.0, 8.7)	6.9 (5.7, 8.0)	4.9 (3.9, 5.9)	0.88 (0.72, 1.06)	0.75 (0.61, 0.93)
Outcomes	Mortality	6.9 (6.8, 7.0)	3.4 (2.6, 4.2)	11.4 (9.9, 12.8)	0.76 (0.57, 1.01)	2.23 (1.85, 2.69)
	Length of stay	5.5 (5.4, 5.5)*	4.5 (4.1, 5.0)*	8.3 (7.7, 8.8)*	-1.13 (-1.39, -0.87) [†]	1.57 (0.94, 2.20) [†]

AIDS=acquired immunodeficiency syndrome, CABG=coronary artery bypass grafting, DES=drug-eluting stent, HIV=human immunodeficiency virus, NSTEMI=non-ST-elevation myocardial infarction, OR=odds ratio, PCI=percutaneous coronary intervention, STEMI=ST-elevation myocardial infarction.

* Direct estimates for length of stay is in days.

[†] Model estimates for length of stay is difference in least square means with 95% confidence interval.

Cardiac catheterization after STEMI was performed within 24 hours of hospital admission for 84.8% of patients with asymptomatic HIV infection, 78.2% of patients with symptomatic AIDS, and 81.9% of uninfected patients. In adjusted analyses, STEMI patients with symptomatic HIV/AIDS were less likely to have a timely procedure relative to uninfected patients (OR 0.73, CI 0.60–0.89); there was no difference for patients with asymptomatic HIV (OR 0.99, CI 0.85–1.15). For patients presenting with NSTEMI, cardiac catheterization was performed within 48 hours of hospital admission for 72.8% of patients with asymptomatic HIV infection, 61.1% of those with symptomatic HIV/AIDS, and 66.6% of uninfected patients. In adjusted analyses, patients with symptomatic HIV/AIDS were less likely to have a timely procedure relative to uninfected patients (OR 0.77, CI 0.63–0.93), while there was no difference for patients with asymptomatic HIV infection (1.12, CI 0.93–1.36).

3.2. Revascularization after ACS event

Overall rate of revascularization (PCI or CABG) was 37.4%. In unadjusted analysis, revascularization was performed in 43.5% of those with asymptomatic HIV infection, 28.4% of those with symptomatic HIV/AIDS, and 37.4% of uninfected patients. In multivariable regression, we found that relative to uninfected patients, those with symptomatic HIV/AIDS were less likely to undergo PCI (OR 0.69, CI 0.59–0.79) and CABG (0.75, CI 0.61–0.93), while patients with asymptomatic HIV were not (OR 1.06, CI 0.93–1.21; OR 0.88, CI 0.72–1.06, respectively). The proportion of those receiving DES was 66.8% in those with asymptomatic HIV, 60.1% for those with symptomatic HIV/AIDS, and 73.0% for uninfected patients. In adjusted analyses, placement of DES was less likely in both asymptomatic HIV-infected patients (OR 0.78, CI 0.63–0.95) and those with symptomatic HIV/AIDS (0.68, CI 0.50–0.93) relative to uninfected patients.

3.3. Short-term outcomes

Length of stay was longest for those with symptomatic HIV/AIDS (mean 8.3 days for those with HIV/AIDS, 4.5 for those with asymptomatic HIV, and 5.5 days for uninfected patients). Unadjusted mortality was highest in those with symptomatic HIV/AIDS (11.4% vs 3.4% for those with asymptomatic HIV

infection and 6.9% for uninfected patients). In adjusted analysis, patients with symptomatic HIV/AIDS had higher risk of in-hospital mortality relative to uninfected patients (OR 2.23, CI 1.85–2.69), although those with asymptomatic HIV did not (OR 0.76, CI 0.57–1.01).

4. Discussion

In this analysis of ACS hospitalizations from a large national dataset, we found lower likelihood of cardiac procedures after ACS for HIV-infected patients with symptomatic HIV/AIDS, but not for those with asymptomatic disease. Compared with uninfected patients, patients with symptomatic HIV/AIDS were less likely to undergo cardiac catheterization, PCI, and CABG, whereas those with asymptomatic HIV were not. These findings are meaningful in light of a recent study by Smilowitz et al.^[2] Using the same NIS dataset, the authors documented disparities in cardiac procedures for HIV-infected patients across the board.^[2] Our contemporary data demonstrate that the primary driver behind lower rates of procedures for these patients is presence of symptomatic HIV/AIDS, and suggest less prevalent disparities for asymptomatic HIV-infected persons with CVD.

Other prior studies have explored the likelihood or frequency of cardiac procedures in HIV-infected persons, although with mixed results and not accounting for the contribution of HIV/AIDS. One study matched 44 HIV-infected patients with ACS by age and race to uninfected patients with ACS.^[10] The authors found that after matching, the rate of catheterization was lower in the HIV-infected group versus uninfected group (75% vs 86%) despite higher rates of STEMI in the infected group, although the results were not statistically significant ($P=.10$). Another study investigated rates of PCI after positive stress and catheterization. Interestingly, those with HIV infection were more likely to undergo PCI than those without HIV infection.^[11] However, this study did not look at rates of CABG, which may have impacted PCI rates.

Our study's finding of lower rates of procedures in those with symptomatic HIV/AIDS is notable and deserves further exploration in future studies. Higher rates of sepsis or bacteremia in this group may lead to a higher proportion of type II MI that would not necessarily require intervention. In fact, a recent study by Crane et al^[12] incorporating data from the pre-ART period (1996–2014) showed a high rate of type II MI in patients with

HIV infection, and in this study, those with type II MIs had a low median cluster of differentiation 4 (CD4) count (230 cells/mm³). Early studies demonstrated increased postoperative complications and mortality for patients with HIV/AIDS undergoing surgery^[13,14]; these studies contributed to the historic use of a CD4 count threshold of 200 cells/mL to guide eligibility for surgery or procedures.

However, these early studies and the aforementioned CD4 threshold predate the era of effective anti-retroviral therapy (ART) for HIV infection. Since the introduction of combination ART, there have been vast improvements in interventional complications, including mortality.^[15] Additionally, earlier studies did not account for suppression of HIV viral load, which is also associated with postsurgical outcomes and may be more important than CD4 count in predicting mortality.^[15,16] Further studies are warranted regarding contribution of CD4 count and HIV viral load; clarification would allow surgeons and interventionalists to better risk-stratify their HIV-infected patients and may relieve hesitation in taking them for surgical or interventional procedures.

Our findings on DES use were consistent with those of Smilowitz et al—all patients with HIV (asymptomatic and end-stage disease) were less likely to receive DES placement.^[2] This finding is more problematic when considering that HIV-infected patients have high rates of severe diffuse in-stent restenosis after PCI with bare metal stent,^[17] although data about stent use and complications are limited in the HIV-infected population. However, in the general population, studies as of 2008 have demonstrated improvement in long-term risks after DES as compared with bare metal stents (BMS),^[18] quelling controversy regarding late stent thrombosis and allowing rates of DES usage to stabilize.^[3] More recently, a large clinical trial with long-term follow-up confirmed lower rates of repeat revascularization in patients receiving DES.^[19]

Reasons for lower rates of DES among HIV-infected patients are unclear.

Placement of drug-eluting stent material requires that the patient strictly adhere to a dual antiplatelet regimen, and providers may feel this is not feasible for some patients with HIV-infection. Additionally, concern about drug interactions may play a role, although the interaction between ART and anti-platelet agents remains theoretical.^[20] Clopidogrel, the anti-platelet drug that would have been used during our study period, is a prodrug requiring transformation to an active metabolite, a process mediated by numerous CYP450 isoenzymes. Because of the involvement of multiple isoenzymes, it is difficult to interpret the pharmacodynamics, and more formal data are needed.

A strength of the NIS dataset is its size, as we were able to analyze over one million hospitalizations using contemporary data for this study. However, there are also limitations. As an administrative database, there is potential for misclassification based on administrative code-related definitions of HIV and other variables. That is, we had no way of knowing if correct codes were entered for all patients. Additionally, we were unable to determine why catheterization, revascularization, or placement of DES was deferred in some settings. Acute illness may have contributed to the decision not to pursue procedures or surgery, but we were unable to determine degree of clinical acuity; however, we did control for chronic comorbidities and high-risk behaviors such as drug abuse. We did not have information on severity of coronary disease so were unable to evaluate indication for CABG. NIS also does not provide access to medication data or laboratory information such as CD4 count

or viral load; however, we believe that diagnosis of symptomatic AIDS by ICD-9 code is a useful proxy for low CD4 count. Lastly, because this database includes deidentified data, we were unable to assess readmission rates and long-term outcomes for these patients. As with all observational studies, there is the possibility of residual confounding, although we performed extensive adjustment in this study. Despite these limitations with using the NIS, multiple studies have used this database to effectively evaluate procedure utilization and outcomes.^[4,5,21] In our setting, NIS had particular value in allowing us to look broadly and beyond a single institution at healthcare utilization for HIV infected and uninfected persons after ACS.

5. Conclusion

We provide an assessment of care delivery for HIV-infected patients presenting with acute coronary syndrome, an event that generally should be acted upon in a timely and standardized fashion. HIV-infected patients with symptomatic HIV/AIDS were less likely to undergo catheterization and revascularization relative to uninfected patients, although the same was not true for those with asymptomatic HIV. Further research should be done to understand the contribution of CD4 count and viral load to care delivery, complication rates, and outcomes for these patients. Additionally, the lower rate of DES use in the HIV-infected population, regardless of AIDS diagnosis, requires further attention. Our study highlights the need for further work in this area, to allow for improved quality of care for this population with a high burden of cardiovascular disease.

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