



Original Research

Clinical Outcomes of Percutaneous Coronary Intervention in Amyloidosis, Sarcoidosis, and Hemochromatosis



Bilal Hussain, MD^a, Hamza Malik, MD^b, Mamas A. Mamas, MD^c, Rupak Desai, MBBS^d, Vikas Aggarwal, MD^e, Gautam Kumar, MD^f, M. Chadi Alraies, MD^g, Ankur Kalra, MD^h, Timir K. Paul, MD, PhD^{i,*}

^a Department of Internal Medicine, The Brooklyn Hospital Center, Brooklyn, New York; ^b Department of Internal Medicine, Central Michigan University, Saginaw, Michigan; ^c Cardiovascular Research Group, Keele University, Stoke-on-Trent, United Kingdom; ^d Division of Cardiology, Atlanta VA Medical Center, Decatur, Georgia; ^e Division of Cardiology, University of Michigan, Ann Arbor, Michigan; ^f Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia; ^g Division of Cardiology, Wayne State University/Detroit Medical Center, Detroit, Michigan; ^h Division of Cardiology, Indiana University School of Medicine, Indianapolis, Indiana; ⁱ Division of Cardiology, University of Tennessee Health Sciences Center at Nashville, Ascension St. Thomas Hospital, Nashville, Tennessee

ABSTRACT

Background: Infiltrative diseases (IDs), including amyloidosis, sarcoidosis, and hemochromatosis, are characterized by abnormal cellular infiltration in multiple organs, including the heart. The prognosis of percutaneous coronary intervention (PCI) patients with underlying IDs has not been well-studied. We evaluated the prevalence of IDs in patients undergoing PCI and their association with post-PCI outcomes.

Methods: The National Inpatient Sample (NIS) 2016-2020 database was used to identify PCI patients with ICD-10 codes for a retrospective analysis. PCI patients were then divided into those with and without underlying IDs, which included amyloidosis, sarcoidosis, and hemochromatosis. Multivariable logistic regression was performed for composite post-PCI outcomes analyses.

Results: Among 2,360,860 patients admitted to undergo PCI, 7855 patients had underlying IDs. The highest prevalence was observed for sarcoidosis (0.2%) followed by hemochromatosis (0.07%) and amyloidosis (0.04%). Underlying amyloidosis was associated with worse composite post-PCI outcomes (odds ratio [OR], 1.6; 95% CI, 1.1-2.44; $P = .02$), including higher in-hospital mortality (OR, 1.9; 95% CI, 1.1-3.4; $P = .04$), higher risk of intra/post-PCI stroke (OR, 4.0; 95% CI, 1.1-16.0; $P = .04$), but not major bleeding (OR, 2.2; 95% CI, 0.97-5.03; $P = .058$). In contrast, underlying sarcoidosis (OR, 1.1; 95% CI, 0.87-1.41; $P = .4$), and hemochromatosis (OR, 1.18; 95% CI, 0.77-1.8; $P = .44$) were not associated with composite post-PCI outcomes. Amyloidosis patients undergoing PCI also had higher hospitalization charges (\$212,123 vs \$141,137; $P = .03$) and longer length of stay (8.2 vs 3.9 days; $P < .001$).

Conclusions: Underlying amyloidosis was associated with worse post-PCI outcomes including higher in-hospital mortality, intra/post-PCI stroke, and socioeconomic burden. A multidisciplinary approach and future studies are needed to investigate the screening and treatment strategies in these patients.

Introduction

Infiltrative diseases (ID) are a heterogeneous group of genetic and acquired disorders that involve cell infiltration and extracellular deposition of abnormal materials leading to organ dysfunction.¹ ID cause cardiomyopathy due to the extracellular deposition of infiltrative substances in the myocardium, which can result in systolic or diastolic dysfunction. Common types of infiltrative cardiomyopathies are caused by the deposition of amyloid, iron, or granulomas.² Cardiac amyloidosis involves extracellular deposition of proteins, including transthyretin and

immunoglobulin light chains in the heart, which in turn can lead to heart failure.³ Sarcoidosis is a granulomatous condition that can induce cardiac inflammation and fibrosis, causing heart block, arrhythmias, and sudden cardiac death.⁴ Hemochromatosis is an autosomal recessive condition characterized by the deposition of excessive iron in the body tissues. Excessive iron accumulation can lead to the formation of reactive oxygen species, which can cause lipid peroxidation, alteration of membrane permeability, and myocyte death.⁵ The most common manifestations of hemochromatosis in the heart include restrictive as well as dilated cardiomyopathy. These ID can compromise heart

Abbreviations: CAD, coronary artery disease; ID, infiltrative diseases; PCI, percutaneous coronary intervention.

Keywords: amyloidosis; hemochromatosis; infiltrative diseases; mortality; percutaneous coronary intervention; sarcoidosis; stroke.

* Corresponding author: timirpaul@gmail.com (T.K. Paul).

<https://doi.org/10.1016/j.jscai.2023.101267>

Received 24 September 2023; Received in revised form 20 November 2023; Accepted 11 December 2023

Available online 30 December 2023

2772-9303/© 2024 The Author(s). Published by Elsevier Inc. on behalf of the Society for Cardiovascular Angiography and Interventions Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

function and increase susceptibility to cardiac arrhythmias and heart failures.^{2,6}

Percutaneous coronary intervention (PCI) is the most commonly performed invasive treatment of coronary artery disease (CAD). ID may potentially increase the risk of PCI through mechanisms, such as the development of a cardiomyopathy, as left ventricular function is an important determinant of PCI outcomes. ID, such as amyloidosis increase both hemorrhagic and thromboembolic risks.⁷ Perivascular amyloid deposition results in amyloid angiopathy, which leads to the fragility of the vascular wall increasing the vulnerability to mucosal bleeding.⁸ Amyloidosis can cause cerebral bleeding, gastrointestinal bleeding, and bleeding after diagnostic procedures.⁹ Furthermore, amyloidosis increases the risk of cardiac thrombi and subsequent embolic strokes due to arrhythmias and atrial amyloid myopathy.³ There are limited data studying the outcomes of PCI in patients with ID. A study reported that ST-elevation myocardial infarction is associated with an increased risk of mortality and complications in amyloidosis and coronary revascularization does not have mortality benefits.¹⁰ Whether performing PCI in these patients with ID worsens the outcomes or ensures a good long-term recovery requires further analysis. We studied outcomes of patients with ID undergoing PCI using a national administrative data set.

Methods

Study data and population

A retrospective study was conducted using the National Inpatient Sample (NIS) from January 1, 2016, to December 31, 2020. NIS is part of the Healthcare Cost and Utilization Project and it undergoes annual assessments to verify its internal validity and has access to patient discharges from 48 states plus the District of Columbia.¹¹ Weighted, NIS represents up to 35 million hospitalizations annually. It has been used extensively for national estimates of inpatient costs, trends, disparities, and outcomes. Because, NIS is publicly available and contains de-identified data, informed consent and institutional review board approval were not required. Patients hospitalized for PCI in the United States during 2016-2020 were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) procedure codes (Supplemental Table S1). We then divided these patients into 3 ID cohorts: amyloidosis, sarcoidosis, and hemochromatosis. PCI outcomes in patients with these underlying ID were compared with those without ID.

Patient characteristics and study end points

We compared the baseline characteristics of patients who underwent PCI with and without underlying ID in terms of age, sex, ethnicity, comorbidities, socioeconomic, and hospital characteristics. Additionally, we recorded the prevalence of amyloidosis, sarcoidosis, and hemochromatosis in patients with PCI and their trends from the year 2016-2020. The primary outcome was composite post-PCI outcomes, including in-hospital mortality, intra/postprocedure stroke, and major bleeding in patients with underlying amyloidosis, sarcoidosis, and hemochromatosis. Secondary outcomes were (1) mortality rate trends in PCI with underlying amyloidosis, sarcoidosis, and hemochromatosis; (2) hospitalization costs (adjusted for inflation according to 2022), length of stay; and (3) independent predictors of mortality in this patient population.

Statistical analysis

Categorical variables were documented as numbers and proportions, which were compared with Pearson χ^2 and Fisher exact tests.

Continuous variables were reviewed as weighted means and compared with t test. Univariable logistic regression model was used to report the unadjusted effect of underlying amyloidosis, sarcoidosis, and hemochromatosis on PCI. Multivariable logistic regression was performed to calculate adjusted effect accounting for age, sex, ethnicity, median household income, insurance, hospital bed size, teaching status, and location. Yearly trends for crude and adjusted mortality rates to account for covariates were tabulated using marginal standardization following logistic regression analyses. A linear regression model was used to compare continuous outcomes. All analyses were performed using Healthcare Cost and Utilization Project-recommended stratifying, clustering, and weighting samples with Stata Statistical Software version 17 (StataCorp LLC).

Results

From 2016 to 2020, 2,360,860 patients underwent PCI, of which 7855 patients (0.33%) had underlying ID. Patients undergoing PCI with amyloidosis had higher mean age than those with sarcoidosis (70.8% vs 64%, respectively) (Table 1). PCI patients with underlying sarcoidosis had the highest proportion of females (48.7%), and those with hemochromatosis had the highest White population (91.1%), compared with other ID. Patients with amyloidosis undergoing PCI had the highest comorbidity burden ie, 85.4% of patients had a Charlson comorbidity index of ≥ 3 (Table 1). Among the ID studied, sarcoidosis was most prevalent (0.2%) followed by hemochromatosis (0.07%) and amyloidosis (0.04%) (Figure 1, Supplemental Table S2). Figure 2 illustrates the trends for the prevalence of ID in patients with PCI. The prevalence of amyloidosis in patients undergoing PCI slightly increased from 2016 to 2020 (0.03%-0.06%; $P < .01$) (Figure 2, Supplemental Table S3), whereas the prevalence of sarcoidosis and hemochromatosis in patients undergoing PCI did not significantly change ($P > .05$).

Figure 3 and Table 2 outline the univariable and multivariable logistic regression for the effect of underlying ID in patients with PCI. Patients who underwent PCI with underlying amyloidosis had worse composite post-PCI outcomes (OR, 1.6; 95% CI, 1.1-2.44; $P = .02$). Upon further analysis, the composite outcomes were driven by higher mortality (OR, 1.9; 95% CI, 1.1-3.4; $P = .04$), and higher risk of intra/postprocedure stroke (OR, 4.0; 95% CI, 1.1-16.0; $P = .04$) in patients with amyloidosis undergoing PCI. Although, the risk of major bleeding was higher but did not reach statistical significance on multivariable analysis (OR, 2.2; 95% CI, 0.97-5.03; $P = .058$) (Central Illustration). Furthermore, PCI in patients with underlying sarcoidosis and hemochromatosis was not associated with an increased risk of mortality, intra/postprocedure stroke, or major bleeding (Table 2). Mortality rates did not significantly change from 2016-2020 for patients with amyloidosis, sarcoidosis, and hemochromatosis undergoing PCI ($P > .5$; Figure 4, Supplemental Tables S4-S6). Patients with underlying amyloidosis hospitalized for PCI had higher adjusted total charges (\$212,123 vs \$141,137; $P = .03$) and longer length of stay (8.2 vs 3.9 days; $P < .001$) than those without amyloidosis. However, patients with PCI with underlying sarcoidosis and hemochromatosis did not have significantly higher charges or length of stay ($P > .05$; Table 3).

Various comorbidities were studied to identify independent predictors of mortality due to multisystem involvement in ID (Supplemental Tables S7-S9). In patients with PCI with underlying amyloidosis, independent predictors of mortality were ventricular arrhythmias (OR, 6.5; 95% CI, 1.8-23; $P < .01$), and pericardial effusion (OR, 5.4; 95% CI, 1.1-27.3; $P = .04$). Although for patients with sarcoidosis undergoing PCI, independent predictors of mortality were ventricular arrhythmias (OR, 3.3; 95% CI, 1.27-8.8; $P = .01$), pulmonary embolism (OR, 12; 95% CI, 2.5-59; $P < .01$), kidney disease (OR, 4; 95% CI, 1.5-11.4; $P < .01$), hypercalcemia/hypercalciuria (OR, 7; 95% CI, 1.3-37; $P = .02$), and adrenal insufficiency (OR, 8.4; 95% CI, 1.76-39.7; $P < .01$).

Table 1. Baseline characteristics for percutaneous coronary intervention (PCI) patients with amyloidosis, sarcoidosis, and hemochromatosis.

Baseline characteristic	PCI patients (N = 2,360,860)					
	Amyloidosis (n = 990)		Sarcoidosis (n = 5260)		Hemochromatosis (n = 1625)	
Age, y	70.8 ± 0.78	<.001	64 ± 0.35	<.001	64.7 ± 0.64	>.05
Sex						
Male	700 (70.8)	>.05	2700 (51.3)	<.001	1270 (78)	<.001
Female	290 (29.2)		2560 (48.7)		355 (21.8)	
Race/ethnicity						
White	555 (57.5)	<.001	3215 (62)	<.001	1430 (91.1)	<.001
African American	220 (22.8)		1560 (30)		40 (2.6)	
Hispanic	105 (10.9)		150 (2.9)		55 (3.5)	
Other ethnicity	85 (8.8)		255 (5.1)		45 (2.8)	
Comorbidities						
Coronary artery disease	975 (98.5)	<.01	5215 (99)	.01	1620 (99.7)	>.05
Congestive heart failure	655 (66.2)	<.001	1780 (33.8)	<.001	390 (24)	>.05
Arrhythmia	535 (54)	<.001	1940 (36.9)	.02	585 (36)	>.05
Hypertension	895 (90.4)	<.01	4585 (87.2)	<.001	1305 (80.3)	>.05
Diabetes	475 (48)	>.05	2765 (52.3)	<.001	560 (34.5)	.01
Hyperlipidemia	695 (70.2)	>.05	3855 (73.3)	>.05	1175 (72.3)	>.05
Peripheral artery disease	40 (40.4)	>.05	175 (3.3)	>.05	30 (18.5)	>.05
Chronic pulmonary disease	200 (20.2)	>.05	1625 (30.9)	<.001	370 (22.8)	>.05
Liver disease	65 (65.7)	<.01	275 (5.2)	<.001	190 (11.7)	<.001
Kidney disease	665 (67.2)	<.001	1970 (37.5)	<.001	390 (24)	>.05
Anemia	390 (39.4)	<.001	1175 (22.3)	<.001	240 (14.7)	>.05
Obesity	160 (16.2)	>.05	1455 (27.7)	<.001	335 (20.6)	>.05
Smoking	145 (14.7)	<.001	695 (13.2)	<.001	440 (27.1)	>.05
Charlson comorbidity index						
0	–	<.001	32 (3.8)	<.001	100 (61.5)	>.05
1	60 (6.6)		71 (183)		440 (27.1)	
2	85 (8.6)		75 (20.9)		420 (25.9)	
≥3	845 (85.4)		128 (56.9)		665 (40.9)	
Median household income						
\$1-\$49,999	275 (28.2)	≥.05	1665 (32)	<.001	365 (23)	<.001
\$50,000-\$85,999	460 (47.2)		2370 (45.5)		780 (49.2)	
>\$86,000	240 (24.6)		1170 (22.5)		440 (27.8)	
Insurance						
Medicare	755 (76.7)	<.001	3135 (59.7)	<.001	840 (51.7)	.04
Medicaid	50 (5.1)		410 (7.8)		120 (7.4)	
Private insurance	120 (12.2)		1485 (28.3)		550 (33.9)	
Others	60 (6)		225 (4.2)		115 (7)	
Hospital characteristics						
Hospital bedsize						
Small	155 (15.7)	.01	705 (13.4)	>.05	210 (12.9)	>.05
Medium	200 (20.2)		1505 (28.6)		490 (30.1)	
Large	635 (64.1)		3050 (58)		925 (57)	
Location/teaching status						
Rural	25 (2.5)	<.001	225 (4.3)	<.001	115 (70.1)	>.05
Urban nonteaching	90 (9.1)		875 (16.6)		365 (22.5)	
Urban teaching	875 (88.4)		4160 (79.1)		1145 (70.4)	
Region						
Northeast	215 (21.7)	.04	1280 (24.2)	<.001	420 (25.9)	<.001
Midwest	260 (26.3)		1305 (24.8)		310 (19.1)	
South	315 (31.8)		2100 (40)		565 (34.8)	
West	200 (20.2)		575 (11)		330 (20.2)	
Ownership						
Government	115 (11.6)	<.01	445 (8.5)	<.01	100 (6.2)	.04
Private	875 (88.4)		660 (91.5)		1525 (93.8)	

Values are n (%) or mean ± SD.

For hemochromatosis patients undergoing PCI, independent predictors of mortality were diabetes mellitus (OR, 28.3; 95% CI, 1.8-441; *P* = .01), pneumonia (OR, 29.8; 95% CI, 4.5-195; *P* < .001), and hepatocellular carcinoma (OR, 24.7; 95% CI, 1.3-471; *P* = .03)

Discussion

The main findings of our study include (1) patients with amyloidosis undergoing PCI had a higher comorbidity burden due to multisystem involvement; (2) sarcoidosis was the predominant ID in patients hospitalized for PCI; (3) underlying amyloidosis was associated with a higher risk of mortality, intra/postprocedure stroke, hospitalization charges,

and length of stay in patients undergoing PCI; and (4) sarcoidosis and hemochromatosis were not associated with mortality, intra/post-procedure stroke, and major bleeding in patients with PCI.

ID may impact different organ systems and our analysis suggests that baseline comorbidity burden was higher in patients with PCI with underlying ID. Patients with amyloidosis undergoing PCI were generally older than those with sarcoidosis and hemochromatosis subgroups. This could be attributed to late presentation of patients with amyloidosis due to indolent disease progression with nonspecific symptoms. Studies have shown that the average age of diagnosis of patients with amyloid light-chain (AL) amyloidosis is 65 years¹² while it is 73 years for transthyretin (ATTR) amyloidosis.¹³ Moreover, there has been a gradual increase in amyloidosis patients undergoing PCI from 2016 to 2020.

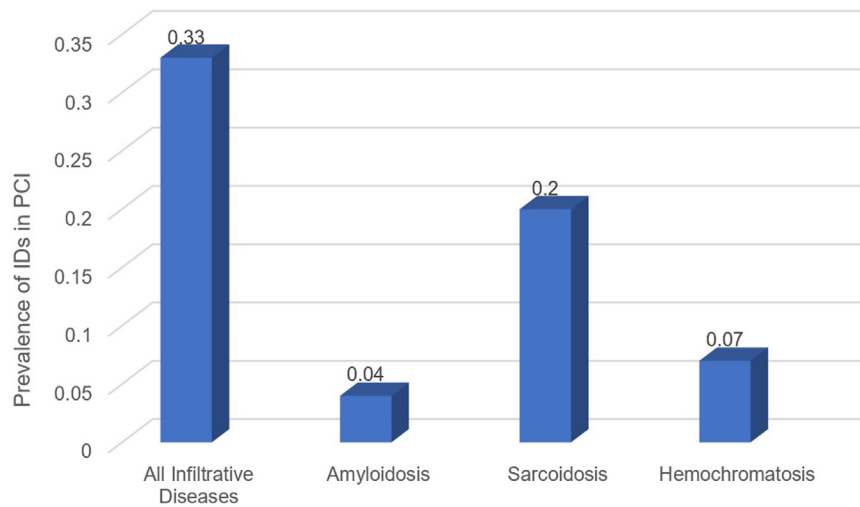


Figure 1.

Prevalence of infiltrative diseases (ID) in percutaneous coronary intervention (PCI) patients. In patients undergoing PCI, sarcoidosis is the most prevalent ID followed by hemochromatosis and amyloidosis.

Recent studies have documented that hospitalizations from amyloidosis have increased over recent times and at the same time, cardiac amyloidosis is associated with increasing in-hospital mortality prompting management and hospitalization.¹⁴

Amyloidosis primarily leads to restrictive heart failure with preserved ejection fraction.¹⁵ However, over time, continuous deterioration causes reduced ejection fraction and overt heart failure with thickened left ventricular walls.¹⁶ Cardiac amyloid proteins, such as ATTR and AL are highly unstable proteins that damage the myofibrils in the myocardium. Among the ID studied, amyloidosis was associated with worse composite post-PCI outcomes including higher mortality in patients undergoing PCI. However, no association with mortality was observed for patients with sarcoidosis and hemochromatosis hospitalized for PCI. This difference could be due to increased severity of CAD in patients with amyloidosis as well as more compromised cardiac function in such patients. This fact is supported by the study of Bosah et al¹⁷ who found that cardiac amyloidosis can manifest in patients who have underlying ischemic cardiomyopathy. Furthermore, Mueller et al¹⁸ studied that besides affecting the myocardium, amyloidosis can also infiltrate the lumen of the coronary arteries, thus increasing the risk of ACS.

Simultaneously, there is a very high likelihood of amyloid infiltration in organs besides the heart, which could compromise their functionality and increase the risk of death following PCI.¹⁹

Amyloidosis in patients undergoing PCI was also associated with increased risk of intra/postprocedure stroke. Amyloidosis causes both ischemic²⁰ and hemorrhagic stroke.²¹ Amyloidosis increases the risk of thromboembolic events due to cardiac causes including left ventricular diastolic dysfunction, atrial fibrillation, and atrial amyloid myopathy.^{8,22} Furthermore, it is also associated with noncardiac causes, such as nephrotic syndrome leading to renal anticoagulant loss and increased procoagulant synthesis which predisposes to thromboembolic events.²² Feng et al²³ reported intracardiac thrombosis in amyloidosis due to reduced atrial contractility, atrial enlargement, and blood stasis, which can subsequently lead to ischemic stroke, which is sometimes observed to be the presenting complication of amyloidosis.²⁴ Additionally, cerebral amyloid angiopathy is known to cause hemorrhagic strokes due to amyloid fibril deposition in cerebral vessels increasing vascular fragility and impairing vasoconstriction.²⁵ Other mechanisms of increased bleeding risk in amyloidosis are acquired deficiency of coagulation factors, such as factor X, abnormal fibrin polymerization,

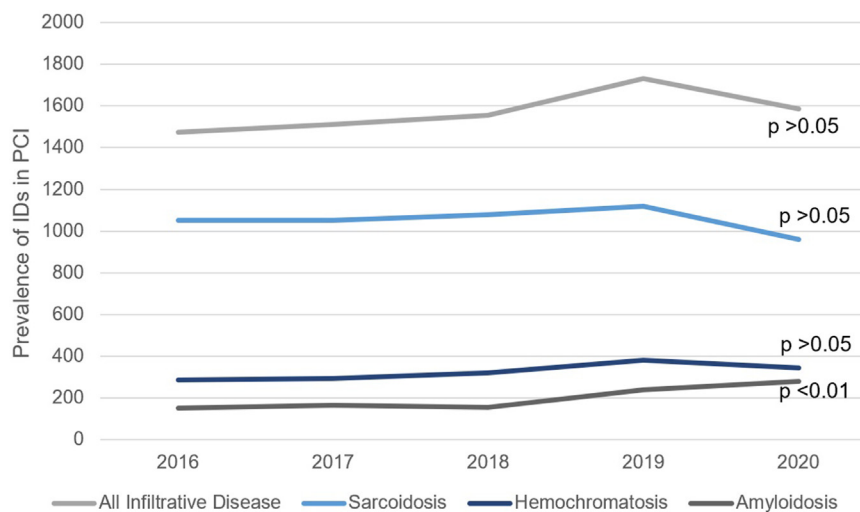


Figure 2.

Trends for prevalence of infiltrative diseases (ID) in percutaneous coronary intervention (PCI) patients. The prevalence of amyloidosis in patients undergoing PCI has slightly increased from 2016-2020, while the prevalence of sarcoidosis and hemochromatosis has not significantly changed.

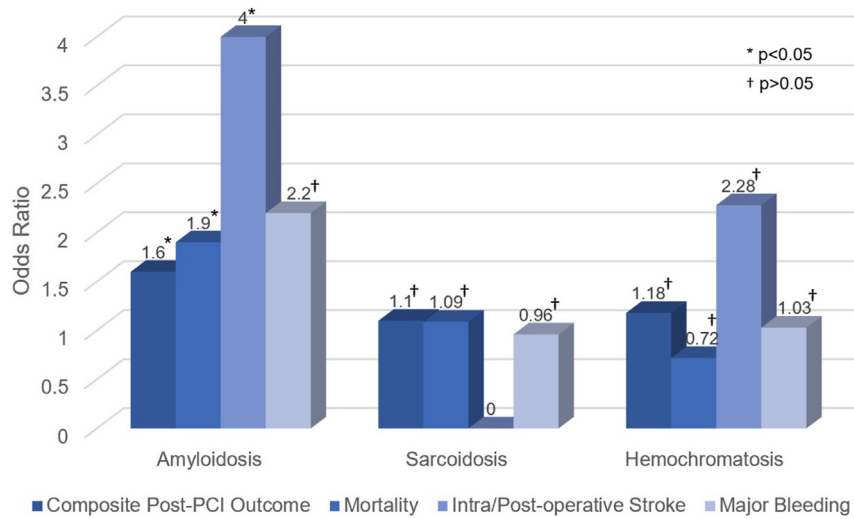


Figure 3.

Post-PCI outcomes in patients with amyloidosis, sarcoidosis, and hemochromatosis. In patients undergoing percutaneous coronary intervention (PCI), underlying amyloidosis is associated with worse composite post-PCI outcomes including higher in-hospital mortality and higher risk of intra/post-PCI stroke with no increased risk of major bleeding, whereas underlying sarcoidosis and hemochromatosis are not associated with worse post-PCI outcomes.

hyperfibrinolysis, and platelet dysfunction.⁹ Besides cerebral bleeding, amyloidosis manifests as gastrointestinal bleeding, diagnostic procedure-related bleeding, genitourinary bleeding, skin hematomas, and spontaneous spleen rupture.⁹ It is plausible that amyloidosis may increase bleeding complications in patients with PCI. However, major bleeding was not significantly increased in patients with amyloidosis in our study, although it showed a trend toward increased bleeding tendency.

Amyloidosis was also associated with higher hospitalization costs and longer length of stay in patients undergoing PCI. Increased risk of complications intraprocedure or post-PCI may account for this observation. Additionally, amyloidosis may have necessitated preprocedure optimization requiring higher cost of drugs and management strategies.²⁶ As mentioned above, amyloidosis is a multisystemic disease; therefore, its management necessitates a multidisciplinary approach with medical care from numerous subspecialties, which can contribute to higher costs of care and longer duration of in-hospital stay. It was

found that various disorders contributed to increasing mortality in patients with ID undergoing PCI in the 3 subgroups. It has been reported that amyloid fibril deposition causes inflammation, oxidative stress, myocyte separation, remodeling, and left ventricular fibrosis, all of which contribute to the development of arrhythmogenic potential in these patients²⁷ as well as pericardial effusion.²⁸ Our findings that ventricular arrhythmias and pericardial effusion in patients with amyloidosis undergoing PCI were associated with increased mortality risk are consistent with such mechanisms.

Overall, the prevalence of ID in patients undergoing PCI was approximately 0.33% with patients predominantly having sarcoidosis followed by hemochromatosis and amyloidosis. This could be explained by the increased inflammatory state in sarcoidosis which simultaneously predisposes patients to have CAD.²⁹ The trends for the prevalence of sarcoidosis and hemochromatosis in PCI have been nonsignificant. Sex distribution was approximately similar in sarcoidosis patients undergoing PCI, but patients with hemochromatosis were predominantly males. In hemochromatosis, the sex differences are mostly related to females losing iron in blood during menstruation³⁰ and therefore, having less likelihood of developing iron-mediated organ damage.

For sarcoidosis patients with PCI, kidney disease, ventricular arrhythmias, hypercalcemia, and pulmonary embolism were associated with increased mortality. Hypercalcemia is commonly observed in sarcoidosis due to increased activation of 1-alpha-hydroxylase enzyme.³¹ Increased levels of calcium can cause kidney damage and increase the probability of arrhythmias.³² Sarcoidosis is also associated with increased inflammatory response in the body, which can predispose patients to venous thromboembolism³³ and adrenal insufficiency.³⁴ Granulomas are areas of inflammation and a hallmark of sarcoidosis, and these granulomas can induce organ damage. Similarly, some of the factors increasing mortality in patients with hemochromatosis undergoing PCI included diabetes mellitus secondary to beta cell damage³⁵ in the pancreas and insulin resistance, liver cancer,³⁶ and pneumonia. Iron deposition leads to free radical production and oxidative stress, especially in the liver which predisposes the hepatocytes to proliferate into cancerous cells.³⁷ Moreover, it is believed that pathogens require iron to proliferate and because iron is excessive in hemochromatosis, bacteria can proliferate easily and cause serious infections.³⁸ These comorbidities raise the importance of medically stabilizing the patients before performing PCI to improve the outcomes and reduce mortality.

Table 2. Post-PCI outcomes of mortality, intra/postprocedure stroke, and major bleeding in amyloidosis, sarcoidosis, and hemochromatosis.

Outcomes	Univariable logistic regression		Multivariable logistic regression	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Composite post-PCI outcomes				
Amyloidosis	2.56 (1.7-3.82)	<.001	1.6 (1.1-2.44)	.02
Sarcoidosis	1.1 (0.87-1.41)	.4	-	-
Hemochromatosis	1.18 (0.77-1.8)	.44	-	-
Mortality				
Amyloidosis	2.11 (1.18-3.8)	.01	1.9 (1.1-3.4)	.04
Sarcoidosis	1.09 (0.77-1.56)	.6	-	-
Hemochromatosis	0.72 (0.34-1.53)	.39	-	-
Intra/postprocedure stroke				
Amyloidosis	7.56 (1.88-30.47)	.004	4.0 (1.1-16.0)	.04
Sarcoidosis	-	-	-	-
Hemochromatosis	2.28 (0.32-16.3)	.4	-	-
Major bleeding				
Amyloidosis	2.59 (1.15-5.85)	.02	2.2 (0.97-5.03)	.058
Sarcoidosis	0.96 (0.54-1.69)	.88	-	-
Hemochromatosis	1.03 (0.39-2.77)	.95	-	-

PCI, percutaneous coronary intervention.

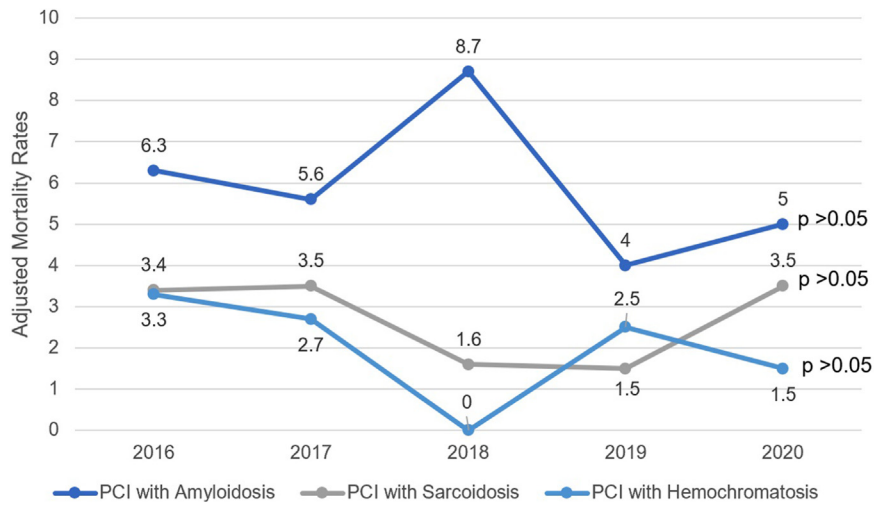


Figure 4. Trends for mortality rates in percutaneous coronary intervention (PCI) and infiltrative diseases. Mortality rates have not significantly changed from 2016-2020 for patients with amyloidosis, sarcoidosis, and hemochromatosis undergoing PCI.

There are some limitations of this study as it is retrospective in nature and relies on ICD-10 codes. Therefore, we are not able to confirm how the diagnosis of ID was made and the duration of diagnosis before PCI. Furthermore, we had limited data on the severity of symptoms of ID at hospital presentation and there was lack of medication records and imaging findings that could have provided more insight. Despite these limitations, we used a reliable database with a very large sample of patients which has been used extensively in observational studies.

Conclusion

Among the ID, amyloidosis was associated with higher mortality, intra/postprocedure stroke risk, and socioeconomic burden in patients undergoing PCI. There was no association with mortality or hospital costs in patients with sarcoidosis and hemochromatosis undergoing PCI. A multidisciplinary approach is essential to provide optimal medical care in patients hospitalized for PCI due to multisystemic

Worse Composite Post-PCI Outcomes in Amyloidosis
(OR 1.6, CI 1.1-2.44, p=0.02)

(A) Higher In-hospital Mortality
OR 1.9, CI 1.1-3.4, p=0.04

(B) Higher Intra/Post-Procedure Stroke
OR 4.0, CI 1.1-16.0, p=0.04

(C) No increased Major Bleeding
OR 2.2, CI 0.97-5.03, p=0.058

Outcomes of PCI in Amyloidosis Patients: Underlying amyloidosis is associated with higher in-hospital mortality and higher risk of intra/post-procedure stroke in patients undergoing PCI with no increased risk of major bleeding

Central Illustration. Outcomes of percutaneous coronary intervention (PCI) in amyloidosis patients.

Table 3. Adjusted total charges and length of stay for percutaneous coronary intervention (PCI) with and without infiltrative disease.

Parameter	Adjusted total charges (\$)			Mean length of stay (d)		
	Value	Standard error	P value	Value	Standard error	P value
Amyloidosis						
PCI with amyloidosis	212,123	20,201	.03	8.2	0.6	<.001
PCI without amyloidosis	141,137	895		3.9	0.01	
Sarcoidosis						
PCI with sarcoidosis	142,718	3742	.5	4.7	0.15	.06
PCI without sarcoidosis	14,164	896		3.9	0.01	
Hemochromatosis						
PCI with hemochromatosis	133,046	5414	.3	3.8	0.2	.7
PCI without hemochromatosis	141,173	896		3.9	0.01	

involvement in amyloidosis. Further prospective studies are required to establish screening and management guidelines and improve outcomes in this patient population.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding sources

This work was not supported by funding agencies in the public, commercial, or not-for-profit sectors.

Ethics statement and patient consent

The National Inpatient Sample which is a deidentified database was used for the analysis, so patient consent was not required.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at [10.1016/j.jscai.2023.101267](https://doi.org/10.1016/j.jscai.2023.101267).

References

- Li G, Han D, Wei S, Wang H, Chen L. Multiorgan involvement by amyloid light chain amyloidosis. *J Int Med Res.* 2019;47(4):1778–1786. <https://doi.org/10.1177/0300060518814337>
- Bejar D, Colombo PC, Latif F, Yuzepolskaya M. Infiltrative cardiomyopathies. *Clin Med Insights Cardiol.* 2015;9(suppl 2):29–38. <https://doi.org/10.4137/CMC.S19706>
- Siddiqi OK, Ruberg FL. Cardiac amyloidosis: an update on pathophysiology, diagnosis, and treatment. *Trends Cardiovasc Med.* 2018;28(1):10–21. <https://doi.org/10.1016/j.tcm.2017.07.004>
- Doughan AR, Williams BR. Cardiac sarcoidosis. *Heart.* 2006;92(2):282–288. <https://doi.org/10.1136/hrt.2005.080481>
- Hornitz LD, Rosenthal EA. Iron-mediated cardiovascular injury. *Vasc Med.* 1999;4(2):93–99. <https://doi.org/10.1177/1358836X9900400207>
- Kichloo A, Jamal S, Albosta M, et al. Increased inpatient mortality in patients hospitalized for atrial fibrillation and atrial flutter with concomitant amyloidosis: insight from National Inpatient Sample (NIS) 2016–2017. *Indian Pacing Electrophysiol J.* 2021;21(6):344–348. <https://doi.org/10.1016/j.ipej.2021.06.005>
- Bever KM, Masha LI, Sun F, et al. Risk factors for venous thromboembolism in immunoglobulin light chain amyloidosis. *Haematologica.* 2016;101(1):86–90. <https://doi.org/10.3324/haematol.2015.133900>
- Nicol M, Siguret V, Vergaro G, et al. Thromboembolism and bleeding in systemic amyloidosis: a review. *ESC Heart Fail.* 2022;9(1):11–20. <https://doi.org/10.1002/ehf2.13701>
- Sucker C, Hetzel GR, Grabensee B, Stockschlaeder M, Scharf RE. Amyloidosis and bleeding: pathophysiology, diagnosis, and therapy. *Am J Kidney Dis.* 2006;47(6):947–955. <https://doi.org/10.1053/j.ajkd.2006.03.036>
- Uddin MM, Mir T, Kaur J, Pervaiz E, Babu MA, Sheikh M. ST-elevation myocardial infarction among cardiac amyloidosis patients: a national readmission database study. *Heart Fail Rev.* 2022;27(5):1579–1586. <https://doi.org/10.1007/s10741-021-10210-w>

- Healthcare Cost and Utilization Project. Overview of the National (Nationwide) Inpatient Sample (NIS). Accessed October 16, 2023. <http://www.hcup-us.ahrq.gov/nisoverview.jsp>; 2023.
- Desport E, Bridoux F, Sirac C, et al. AL amyloidosis. *Orphanet J Rare Dis.* 2012;7:54. <https://doi.org/10.1186/1750-1172-7-54>
- Pinney JH, Whelan CJ, Petrie A, et al. Senile systemic amyloidosis: clinical features at presentation and outcome. *J Am Heart Assoc.* 2013;2(2), e000098. <https://doi.org/10.1161/JAHA.113.000098>
- Oladiran OD, Oladunjoye AO, Dhital R, Oladunjoye OO, Nwosu I, Licata A. Hospitalization rates, prevalence of cardiovascular manifestations and outcomes associated with amyloidosis in the United States. *Cureus.* 2021;13(3), e14177. <https://doi.org/10.7759/cureus.14177>
- Brown KN, Pendela VS, Ahmed I, Diaz RR. Restrictive cardiomyopathy. In: *StatPearls.* StatPearls Publishing; 2023.
- Oerlemans MIFJ, Rutten KHG, Minnema MC, Raymakers RAP, Asselbergs FW, de Jonge N. Cardiac amyloidosis: the need for early diagnosis. *Neth Heart J.* 2019; 27(11):525–536. <https://doi.org/10.1007/s12471-019-1299-1>
- Bosah AN, Tobaa A, Gajjar K, Kashyap K, Alpert C. Acute decompensated heart failure due to combined ischemic cardiomyopathy and cardiac amyloidosis. *Cureus.* 2022;14(12), e32281. <https://doi.org/10.7759/cureus.32281>
- Mueller PS, Edwards WD, Gertz MA. Symptomatic ischemic heart disease resulting from obstructive intramural coronary amyloidosis. *Am J Med.* 2000;109(3):181–188. [https://doi.org/10.1016/s0002-9343\(00\)00471-x](https://doi.org/10.1016/s0002-9343(00)00471-x)
- McFarlane M, Bashford A, Sah S, Disney BR. Multisystem amyloidosis as the unifying diagnosis for constipation, collapse and cardiomyopathy. *BMJ Case Rep.* 2018; 2018. <https://doi.org/10.1136/bcr-2018-225301>
- Zubkov AY, Rabinstein AA, Dispenzieri A, Wijdicks EF. Primary systemic amyloidosis with ischemic stroke as a presenting complication. *Neurology.* 2007;69(11):1136–1141. <https://doi.org/10.1212/01.wnl.0000276951.39112.2b>
- Chen D, Zhang C, Parikh N, et al. Association between systemic amyloidosis and intracranial hemorrhage. *Stroke.* 2022;53(3):e92–e93. <https://doi.org/10.1161/STROKEAHA.121.038451>
- Cappelli F, Tini G, Russo D, et al. Arterial thrombo-embolic events in cardiac amyloidosis: a look beyond atrial fibrillation. *Amyloid.* 2021;28(1):12–18. <https://doi.org/10.1080/13506129.2020.1798922>
- Feng D, Syed IS, Martinez M, et al. Intracardiac thrombosis and anticoagulation therapy in cardiac amyloidosis. *Circulation.* 2009;119:2490–2497.
- Marques P, Beato-Coelho J, Durães J, Geraldo A. Ischaemic stroke as the initial manifestation of systemic amyloidosis. *BMJ Case Rep.* 2019;12(6). <https://doi.org/10.1136/bcr-2018-228979>
- Kuhn J, Sharan T. Cerebral amyloid angiopathy. In: *StatPearls.* StatPearls Publishing; 2020.
- Kazi DS, Bellows BK, Baron SJ, et al. Cost-effectiveness of tafamidis therapy for transthyretin amyloid cardiomyopathy. *Circulation.* 2020;141(15):1214–1224. <https://doi.org/10.1161/CIRCULATIONAHA.119.045093>
- Khanna S, Lo P, Cho K, Subbiah R. Ventricular arrhythmias in cardiac amyloidosis: a review of current literature. *Clin Med Insights Cardiol.* 2020;14, 1179546820963055. <https://doi.org/10.1177/1179546820963055>
- Binder C, Duca F, Binder T, et al. Prognostic implications of pericardial and pleural effusion in patients with cardiac amyloidosis. *Clin Res Cardiol.* 2021;110(4):532–543. <https://doi.org/10.1007/s00392-020-01698-7>
- Hansen JC, Patel AR, Nayak HN, Moss JD, Sweiss N, Beshai JF. Cardiac sarcoidosis and coronary artery disease: a two-hit mechanism to left ventricular dysfunction (or is it)? *Sarcoidosis Vasc Diffuse Lung Dis.* 2013;30(3):237–240.
- Harrison-Findik DD. Gender-related variations in iron metabolism and liver diseases. *World J Hepatol.* 2010;2(8):302–310. <https://doi.org/10.4254/wjh.v2.i8.302>
- Ackermann D. [Hypercalcemia in sarcoidosis—case report, prevalence, pathophysiology and therapeutic options]. *Ther Umsch.* 2007;64(5):281–286. <https://doi.org/10.1024/0040-5930.64.5.281>
- El-Sherif N, Turitto G. Electrolyte disorders and arrhythmogenesis. *Cardiol J.* 2011; 18(3):233–245.
- Geremek AG, Tomkowski W, Geremek M, et al. Sarcoidosis as a risk factor for venous thromboembolism. *Sarcoidosis Vasc Diffuse Lung Dis.* 2017;34(2):170–178. <https://doi.org/10.36141/svld.v34i2.4911>
- Malakooti SK, Simon LV. A sarcoidosis patient presents with adrenal insufficiency: A standardized patient scenario for medical students and residents. *Cureus.* 2018; 10(6), e28333. <https://doi.org/10.7759/cureus.28333>

35. Raju K, Venkataramappa SM. Primary hemochromatosis presenting as type 2 diabetes mellitus: a case report with review of literature. *Int J Appl Basic Med Res.* 2018;8(1):57–60. https://doi.org/10.4103/ijabmr.IJABMR_402_16
36. Fracanzani AL, Conte D, Fraquelli M, et al. Increased cancer risk in a cohort of 230 patients with hereditary hemochromatosis in comparison to matched control patients with non-iron-related chronic liver disease. *Hepatology.* 2001;33(3):647–651. <https://doi.org/10.1053/jhep.2001.22506>
37. Kew MC. Hepatic iron overload and hepatocellular carcinoma. *Liver Cancer.* 2014;3(1):31–40. <https://doi.org/10.1159/000343856>
38. Nairz M, Weiss G. Iron in infection and immunity. *Mol Aspects Med.* 2020;75, 100864. <https://doi.org/10.1016/j.mam.2020.100864>