THE TEXAS HEART INSTITUTE® JOURNAL

Clinical Investigation

Takotsubo Syndrome in Black Americans: Insights From the National Inpatient Sample

Olga Vriz, MD[1,2]; Ali Hassan Mushtaq, MD[3]; Ahmed Nahid Elshaer, MD[3]; Abdullah Shaik, MD[3]; Irene Landi, MD[4]; Talal Alzahrani, MD, MPH[5]

[1]Heart Centre, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia
[2]Department of Cardiology and Sport Medicine, San Antonio Hospital, San Daniele del Friuli, Udine, Italy
[3]School of Medicine, College of Medicine, Alfaisal University, Riyadh, Saudi Arabia
[4]Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy
[5]Department of Medicine, College of Medicine, Taibah University, Medina, Saudi Arabia

Abstract

Background: Data on race-related differences in the clinical outcomes of Takotsubo syndrome are limited, particularly for Black patients. This study aimed to assess whether race and sex may have an additional impact on the inpatient mortality of patients with Takotsubo syndrome.

Methods: A total of 4,628 patients from the United States' National Inpatient Sample from 2012 to 2016 were identified; propensity score analysis revealed a similar propensity score between Black patients (n = 2,314) and White patients (n = 2,314), which was used to balance observed covariates. Sex and age distributions were identical between the 2 groups. The groups were also similar in baseline characteristics, including cardiovascular risk factors. White patients were compared with Black patients on in-hospital outcomes and inpatient mortality. A logistic regression analysis was conducted to measure the difference in mortality based on race and sex.

Results: Compared with White patients, Black patients had a higher percentage of in-hospital complications, including cerebrovascular accidents (4.9% vs 2.5%, $P \leq .01$), acute kidney injury (25% vs 19%, $P \leq .01$); longer lengths of stay (8 vs 7 days, $P \leq .01$); and higher inpatient mortality (6.1% vs 4.5%, $P < .01$). When analysis was conducted with race and sex combined, inpatient mortality was higher among Black men than among White women (odds ratio, 2.7 [95% CI, 1.80-3.95]; $P \leq .01$).

Conclusion: This study showed that Black patients with Takotsubo syndrome have higher in-hospital complications and inpatient mortality rates. When race and sex were combined, inpatient mortality was significantly higher among Black men than among either White men and women or Black women.

Keywords: Black people; cardiomyopathies; mortality; postoperative complications

Introduction

Racial disparities are associated with increased risk of cardiovascular disease (CVD) and poor outcomes, including mortality.[1-5] In this regard, Black patients appear to have a more substantial burden of CV risk factors (in particular, hypertension and diabetes), lower adherence to therapeutic interventions, and a higher rate of CV complications and mortality than their White counterparts.[6-10] One CVD with limited race-related data is Takotsubo syndrome (TTS), a disorder characterized by a temporary left ventricle wall motion abnormality and that shares common clinical characteristics with acute coronary syndrome.[11,12] Accumulating data suggest that patients with TTS may have worse short-term[13] and long-term[14,15] prognoses than an age- and sex-matched population without TTS.

Citation: Vriz O, Mushtaq AH, Elshaer AN, Shaik A, Landi I, Alzahrani T. Takotsubo syndrome in Black Americans: insights from the National Inpatient Sample. *Tex Heart Inst J*. 2023;50(5):e228055. doi:10.14503/THIJ-22-8055
Corresponding author: Olga Vriz, MD, Heart Centre, King Faisal Specialist Hospital and Research Centre, Zahrawi St, Al Maather, Al Maazer, Riyadh 12713, Saudi Arabia (olgavriz@yahoo.com)

This study explored National Inpatient Sample (NIS) data from the Healthcare Cost and Utilization Project to investigate differences in in-hospital outcomes, including mortality, between Black and White patients with TTS.

Key Points

- Compared with their White counterparts, Black patients with TTS had more CV risk factors and in-hospital adverse outcomes, including longer hospital stays and higher mortality.
- Compared with their White counterparts, Black patients with TTS showed a higher rate of in-hospital complications, including mortality, even after matching the groups for confounders by propensity score matching.
- When race was combined with sex, Black men with TTS showed higher mortality rates, suggesting that sex could unmask the CV predisposition for the worst outcome.

Abbreviations and Acronyms

CABG	coronary artery bypass graft
CV	cardiovascular
CVD	cardiovascular disease
ICD-9	*International Classification of Diseases, Ninth Revision*
ICD-10	*International Statistical Classification of Diseases, Tenth Revision*
MI	myocardial infarction
NIS	National Inpatient Sample
PCI	percutaneous coronary intervention
TTS	Takotsubo syndrome

Patients and Methods

Study Population

From the NIS data,[16] 27,135 adult patients at least 18 years of age, identified by *International Classification of Diseases, Ninth Revision (ICD-9)* and *International Statistical Classification of Diseases, Tenth Revision (ICD-10)* codes for TTS (*ICD-9* 429.83; *ICD-10* I51. 81) and admitted to hospital between 2012 and 2016, were included in this study. The final sample consisted of 2,317 Black patients and 24,817 White patients.

Baseline demographic characteristics—such as age, sex, body mass index, and year of hospital admission—and clinical characteristics—such as smoking status; presence of diabetes, hypertension, or hyperlipidemia; and a history of myocardial infarction (MI), percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG), atrial fibrillation or flutter, peripheral artery disease, and sepsis—,were identified based on *ICD-9* and *ICD-10* codes. In-hospital outcomes such as length of stay, cardiogenic shock, cardiac arrest, cerebrovascular accidents, invasive mechanical ventilation, mechanical circulation support, acute kidney injury, and mortality were registered using the *ICD-9-Clinical Modification* codes.[17]

Statistical Analysis

Given the observed baseline covariates, a logistic regression model was constructed to calculate the predicted probability and propensity score of being Black for each patient at the time of admission. The propensity score represented the relationship between prespecified baseline characteristics (ie, sex; age; smoking status; presence of diabetes, hypertension, or hyperlipidemia; and history of MI, PCI, CABG, atrial fibrillation or flutter, peripheral artery disease, or sepsis) and being Black as a single characteristic. A matching approach was then used to obtain a matched cohort with a similar propensity score between Black patients and White patients to balance observed covariates.

The propensity score distribution between the 2 groups in the original sample and the matching sample was compared to assess the balance in the matched cohort that the propensity model produced. The standardized difference was calculated as the mean difference between the 2 groups divided by a measure of the SD of each covariate.

Baseline demographic and clinical characteristics were reported as a medians for continuous variables and percentages for categorical variables. A Wilcoxon rank sum test and a χ^2 test were conducted for continuous and binary variables, respectively, to compare the proposed groups (Black patients and White patients) before and after matching. In-hospital complications and inpatient mortality were compared between the matched groups to determine differences in clinically significant outcomes between Black and White patients.

The logistic regression model was used to calculate the odds ratio of in-hospital mortality for the combined race-sex effect, using a group of White women as the reference in the matched group after adjusting for baseline characteristics (sex; age; smoking status; presence of diabetes, hypertension, or hyperlipidemia; and history of MI, PCI, CABG, atrial fibrillation or flutter, peripheral artery disease, or sepsis). Statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc) and Stata, version 16 (StataCorp LLC) statistical

software. All tests used $\alpha = .05$ as the probability for a type I error.

Results

Unmatched Population

The total number of patients admitted with TTS between 2012 and 2016 was 27,135 (median age, 68 years; 86% women). There were 2,317 (8.54%) Black patients and 24,817 (91.46%) White patients. The group of Black patients was younger (63 vs 68 years of age, $P < .01$) and had a lower percentage of women (81% vs 86%, $P < .01$). Black patients were also more likely to have diabetes (31.46% vs 20.81%, $P < .01$) and hypertension (54.9% vs 54.5%, $P = .01$) than their White counterparts. Conversely, hyperlipidemia (39.7% vs 45.4%, $P = .01$) and atrial fibrillation (13.5% vs 21%, $P < .01$) were more frequent in White patients (Table I). Black patients had more in-hospital complications; this finding did not change after adjustment for age and sex (Supplementary Table I).

Matched Population

Propensity score distribution between the 2 groups in the original sample and the matched sample was used to assess the balance between baseline confounding factors before and after matching. The propensity score distribution differed between the 2 groups in the original sample (Fig. 1) but was similar in the matched sample (Fig. 2). Figure 3 shows that the 2 groups' age distribution at admission was similar after matching. Figure 4 shows a reduction in the standardized differences in propensity score in the matched sample compared with the original sample. The standardized differences in the matched sample were less than 5%.

TABLE I. Differences in Demographic Characteristics Between Black and White Patients With TTS Before Matching

	White patients (n = 24,817)	Black patients (n = 2,317)	*P* value[a]
Demographic characteristics			
Female sex, No. (%)	21,431 (86.4)	1,873 (80.9)	<.01
Age, median, y	68	63	<.01
Clinical characteristics, No. (%)			
Smoker	7,146 (28.8)	704 (30.4)	.11
Diabetes	5165 (20.8)	729 (31.5)	<.01
Hypertension	13,568 (54.5)	1,271 (54.9)	.01
Hyperlipidemia	11,400 (45.9)	919 (39.7)	<.01
History of MI related to coronary artery disease	2,896 (11.7)	261 (11.3)	.56
History of PCI	1,319 (5.3)	96 (4.1)	.02
History of CABG	466 (1.9)	33 (1.4)	.12
Atrial fibrillation or flutter	5,203 (21.0)	313 (13.5)	<.01
Peripheral artery disease	1,173 (4.7)	109 (4.7)	.96
Sepsis	2,546 (10.3)	278 (12.0)	.01

CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention; TTS, Takotsubo syndrome.

[a]$P < .05$ was considered statistically significant.

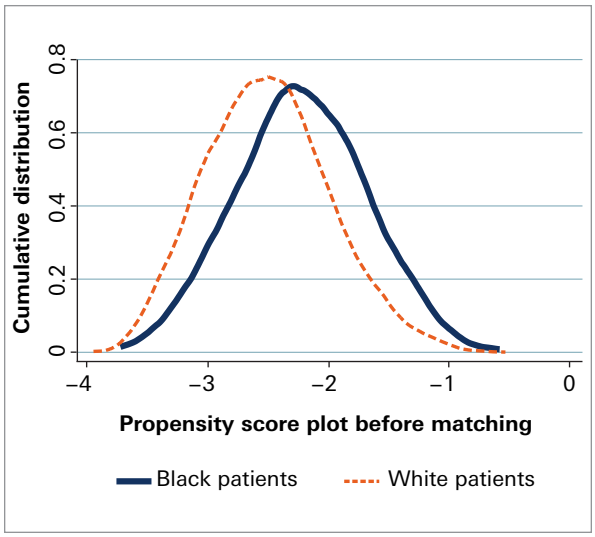

Fig. 1 Propensity score distribution differs between the Black and White patient groups in the original sample

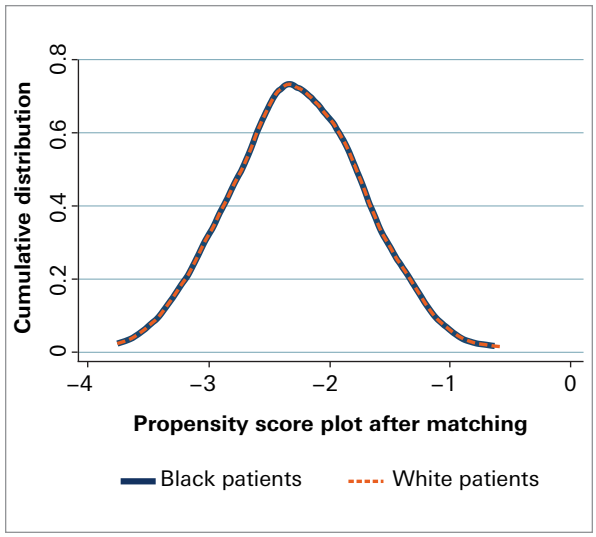

Fig. 2 Propensity score distribution is similar between the 2 matched groups

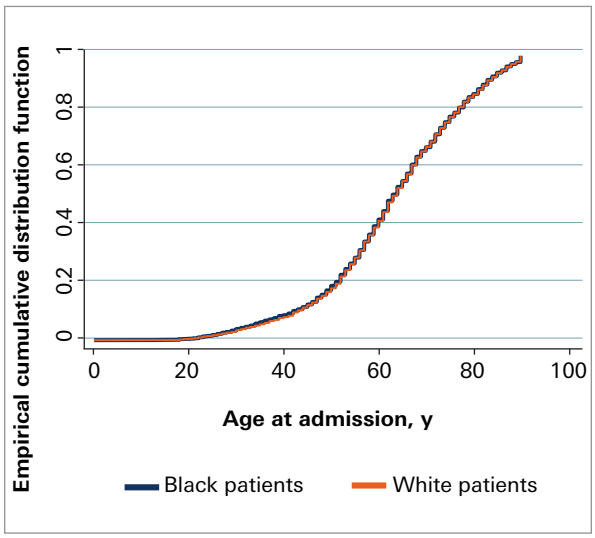

Fig. 3 Age distribution in the 2 matched groups is similar

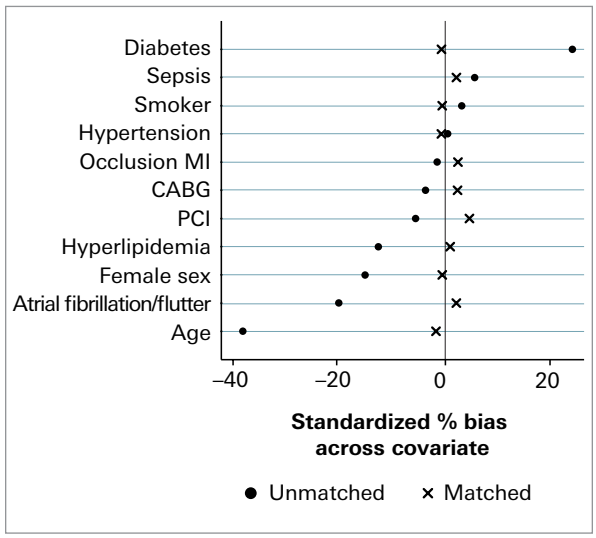

Fig. 4 Graph shows a reduction in the standardized differences in propensity score in the matched sample compared with the original sample. The standardized differences in the matched sample were less than 5%.

CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; MI, myocardial infarction.

After matching, 4,628 patients were identified with a similar propensity score between Black patients (n = 2,314) and White patients (n = 2,314). Sex and age distributions were identical between the 2 groups. The 2 groups also had similar baseline characteristics, including CV risk factors (Table II). The difference in in-hospital complications between Black patients and White patients is reported in Table III. The prevalence rates of cerebrovascular accidents ($P < .01$), length of stay ($P < .01$), and acute kidney injury ($P < .01$) were significantly higher in Black patients. The rate of in-hospital mortality was still significantly higher

TABLE II. Differences in Demographic Characteristics Between Black and White Patients With TTS After Matching

	White patients (n = 2,314)	Black patients (n = 2,314)	*P* value[a]
Demographic characteristics			
Female sex, No. (%)	1,877 (81.1)	1,873 (80.9)	.88
Age, median, y	63	63	.75
Clinical characteristics, No. (%)			
Smoker	708 (30.6)	704 (30.38)	.87
Diabetes	734 (31.7)	728 (31.5)	.85
Hypertension	1,277 (55.2)	1,270 (54.9)	.84
Hyperlipidemia	909 (39.3)	918 (39.7)	.79
History of MI related to coronary artery disease	243 (10.5)	261 (11.3)	.40
History of PCI	72 (3.1)	95 (4.1)	.07
History of CABG	26 (1.1)	33 (1.4)	.36
Atrial fibrillation or flutter	292 (12.6)	311 (13.4)	.41
Peripheral artery disease	84 (3.6)	108 (4.7)	.08
Sepsis	262 (11.3)	278 (12.0)	.46

CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention; TTS, Takotsubo syndrome.

[a] $P < .05$ was considered statistically significant.

TABLE III. Differences Between Black and White Patients With TTS for In-Hospital Complications After Matching

Characteristic	White patients (n = 2,314)	Black patients (n = 2,314)	*P* value[a]
Cardiogenic shock, No. (%)	129 (5.6)	138 (6.0)	.57
Cardiac arrest, No. (%)	84 (3.6)	103 (4.5)	.16
Cerebrovascular accident, No. (%)	57 (2.5)	113 (4.9)	<.01
Mechanical ventilation, No. (%)	454 (19.6)	496 (21.4)	.13
Mechanical support, No. (%)	40 (1.7)	43 (1.9)	.74
Length of stay, median, d	7	8	<.01
Acute kidney injury, No. (%)	448 (19.4)	584 (25.2)	<.01
Inpatient death, No. (%)	104 (4.5)	142 (6.1)	<.01

TTS, Takotsubo syndrome.

[a] $P < .05$ was considered statistically significant.

in Black patients than in White patients (6.1 vs. 4.5, $P < .01$) (Table III).

Logistic Regression Analysis

A logistic regression analysis in the unmatched groups, adjusted for baseline characteristics, showed a 25% increased mortality rate in Black patients vs White patients (odds ratio, 1.25 [95% CI, 1.03-1.51]; $P = .02$). When sex and race were combined and adjusted for CV risk factors, Black men had the highest mortality rates, followed by White men and Black women (Supplementary Table II). The matched groups showed the same results when sex and race were combined: Black men had the highest mortality rates, followed by White men and Black women (Table IV).

Discussion

Few studies have illustrated the impact of race on patients with TTS, particularly Black patients.[8-24] Brinjikji et al,[19] using data from the 2008-2009 NIS hospital database, reported that race and age were not independently associated with mortality but being male was. Zaghlol et al,[18] using data from the 2006-2014 NIS hospital database, compared Black patients (8.2%) and White patients (91.8%) with respect to outcomes and complications. In this case, the authors found that after fully adjusting the data, being Black was not independently associated with worse in-hospital complications and that mortality rates were similar between Black and White patients.

TABLE IV. Risk of Inpatient Mortality Among Matched Groups for Combined Sex and Race[a]

Characteristic	Odds ratio	95% CI	*P* value[b]
White woman	[Reference]	–	–
Black women	1.4	1.01-1.88	.04
White men	1.9	1.22-2.91	<.01
Black men	2.7	1.80-3.95	<.01

[a] A logistic regression model was used to calculate the odds ratio for inpatient death in the matched groups.
[b] $P < .05$ was considered statistically significant.

The Uniqueness of the Present Study

The present study represents one of the most extensive reports on Black patients admitted to US hospitals with TTS. Key features to be highlighted are (1) Black patients had an overall greater occurrence of CV risk factors and in-hospital outcomes, including length of hospital stay and mortality rates; (2) Black patients had higher in-hospital mortality rates after balancing the study groups by propensity score matching, although CV risk factors were similar between the 2 groups; and (3) when race and sex were combined, sex likely masked the higher susceptibility to mortality in Black men.

In the unmatched groups, the higher prevalence of CV risk factors in Black patients could be considered the predisposing factor for the worst outcome.[25-27] In particular, Black men tend to develop hypertension earlier in life than Black women and White individuals, with the onset of related complications starting at a younger age.[6,26] Diabetes is common in patients with TTS, particularly men, and is frequently associated with hypertension.[28] Diabetes is also 1 of the main predictors of short-term and long-term mortality in the InterTAK Prognostic Score[15] and in other studies[28,29] for patients with TTS. The 2 racial groups were similar, however, in their rates of prior MI and history of PCI and CABG, as reported by others.[13,30] In terms of in-hospital complications, Black patients presented with higher rates of cerebrovascular accident, acute kidney injury, and inpatient mortality and had longer hospital stays than their White counterparts,[18,21] suggesting that race may play a role in the outcomes of Black patients with TTS; this finding is in contrast with those of previous studies.[18,19,31]

Propensity score matching was used to create 2 balanced groups and overcome the confounding baseline factors between them. The 2 groups were similar in age, sex, CV risk factors, and incidence of CVD, but Black patients still had higher rates of in-hospital complications. When sex and race were combined, mortality rates were significantly higher in Black men, followed by White men and Black women. It is likely that male sex masks a baseline predisposition among Black individuals for the worst outcome. The mechanisms underlying racial differences in TTS outcomes remains to be clarified. Differences in genes that control sympathetic activity, however, and differences in endothelium homeostasis have been identified in Black patients. These distinctive

characteristics are associated with increased sympathetic tone, leading to an aggravated CV response to physiologic and psychological stimuli in Black patients compared with White patients.[32] Acetylcholine testing could be applied in this setting to highlight the endothelial dysfunction hypothesized to be particularly reactive in Black patients.[33] This information, however, is not part of the NIS registry. Male sex characteristics, such as hormone status,[34] different gene expressions related to estrogens,[35] a higher inflammatory state, whether a physical stressor was involved,[36] and higher susceptibility to develop CVD and complications at a younger age[37] could explain the poorer outcomes in Black men.

Limitations

Study limitations intrinsic to the NIS data set must be addressed. The NIS data set is a retrospective report based on administrative data using *ICD-10* and *ICD-9* coding. Consequently, the accuracy of diagnosis relies entirely on proper coding. The NIS database also captures hospitalizations rather than individual patients. The actual prevalence of TTS in Black patients may therefore need to be considered. Laboratory data (including cardiac biomarkers), electrocardiographic data, and echocardiographic data were also unavailable. Predischarge evaluations for echocardiographic recovery, long-term prognosis information, and prehospital admission events were not provided and could not be considered in the study. Specific diagnostic tests, such as acetylcholine testing for endothelial dysfunction, were not reported and likely not performed in general hospitals. The NIS database registers only in-hospital events, so no prehospital admission data on complications and mortality in general and in events related to TTS in particular were available.

Conclusion

The analysis of NIS data highlighted that compared with their White counterparts, Black patients with TTS have distinct clinical characteristics of more frequent, higher CV risk factors. Black patients also showed a higher rate of in-hospital complications, including mortality, even after propensity score matching. When race was combined with sex, Black men showed the highest rate of mortality, suggesting that sex-related factors could unmask the CV predisposition for the worst outcome. There is therefore a rising need to investigate the actual prevalence of TTS among Black patients and develop race-specific prognostic score models and tailored therapeutic interventions.

Article Information

Published: 19 October 2023

Author Contributions: All authors have read and approved the final version of the manuscript. O.V. contributed to article design, study planning, statistical analysis, and critical article revision. A.H.M, A.N.E., A.S., and T.A. participated in the acquisition of data, data analysis, and manuscript writing. I.L. contributed to the drafting of the article and reviewed the manuscript text.

Conflict of Interest/Disclosure: None.

Funding/Support: None.

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