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Cohort Study

The Effects of Body Mass Index on In-hospital mortality following first ischemic or hemorrhagic stroke events: Does the "obesity paradox" apply?

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ABSTRACT

Background: While it is widely held that obesity is a risk factor for stroke, its role in mortality after stroke is less understood. We aim to examine effects of Body Mass Index (BMI) on in-hospital mortality after non-subarachnoid, subarachnoid, and ischemic stroke.

Methods: Retrospective cohort study. Patients aged ≥18 years, who were hospitalized in Florida hospitals between 2008 and 2012 with a diagnosis of first-time stroke as reported by the Agency for Health Care Administration (AHCA). The main independent variable was BMI category, which was divided into non-overweight/non-obese, obese, and morbidly obese. The primary outcome was the adjusted odds ratio (aOR) for in-hospital mortality for subarachnoid and non-subarachnoid hemorrhagic stroke, and ischemic stroke. Logistic regression modeling was utilized to examine the association between each BMI category and in-hospital mortality, while controlling for several potential confounders. This study was reported in line with the STROCSS criteria.

Results: Of the 333,367 patients included in the database, 150,153 (45.0%) patients met inclusion criteria. After adjusting for age, gender, ethnicity and other possible confounders, obese patients were 21% less likely to die during their hospitalization following a first ischemic stroke (0.79 aOR, 0.69–0.92, 95% CI, $p = 0.002$), and 32% less likely following a first non-subarachnoid hemorrhage (0.68 aOR, 0.57–0.82, 95% CI, $p = 0.0001$) compared to non-overweight/non-obese counterparts.

Conclusion: Obese patients are less likely to die during hospitalization following first-time non-subarachnoid hemorrhage and ischemic stroke than non-overweight/non-obese patients. These findings support the "obesity paradox" concept, though more research is needed for recurrent stroke patients.

1. Background

Stroke is the leading cause of long-term disability in the United States (US), and costs nearly $50 billion in medical bills and missed wages annually [1]. Over recent decades, the number people with risk factors for stroke has increased with the obesity epidemic [2–5]. Obesity has many maladaptive effects on the cardiovascular system, particularly in patients with the metabolic syndrome [6]. Obesity also is linked to a pro-inflammatory state which causes endothelial dysfunction and increased risk of thrombosis [7]. While there is an increased risk of stroke among obese patients, the rate of in-hospital mortality has trended downwards [8]. There are several factors at play (medications, treatments, improved risk factor management, and guideline advancements) but evaluation of the impact of obesity on stroke outcomes is warranted.

An increased BMI is thought to augment the chances of stroke because it is interconnected to well-established stroke risk factors such as type-2 diabetes and hypertension [6]. Abdominal obesity is an independent, and potent risk factor for ischemic stroke in all race-ethnic groups and among younger persons [9]. Despite this, there is evidence that a paradox exists in the prognosis of obese patients who have suffered from an acute stroke. This "obesity paradox" is the observation that obesity acts as a protective factor for acute stressors to the body. Other conditions found to be associated with improved survival among obese patients include myocardial infarction, heart failure, chronic kidney disease, and chronic obstructive pulmonary disease [10–12]. For stroke specifically, study findings show improved survival rates in patients hospitalized with a stroke who are overweight and obese as

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compared to patients with normal BMI [13–15]. A meta-analysis by Oesch et al. showed that, in 10 of 12 studies, obese patients had reduced mortality rates after stroke [16]. These effects have been further replicated in meta-analyses of large US datasets. Some of which point to the interesting finding that overweight and class I obesity are not significantly correlated with years of life lost, whereas classes II and III significantly increase mortality [17–19]. This outcome has been attributed to better management of the conditions that are associated with obesity, such as hypertension, hypercholesterolemia, and diabetes [19].

Given the large number of annual cases of stroke in the US, studying mortality from stroke is of significant epidemiological importance. A better understanding of this can guide further research aimed at identifying causes of varying mortality among different populations. Our research aims to determine if the obesity paradox exists in this population, and to compare such trends among a variety of patient demographics.

2. Methods

This study is a secondary analysis of data collected by the Agency for Health Care administration (AHCA) Florida Hospital Discharge Database for Stroke from 2008 to 2012. The dataset revealed 333,367 patients who were admitted in Florida for stroke. The database has information for patients based on their demographics, diagnosis and procedures codes, attending physician, operating or procedure performing physician, and total gross charges. All inclusion and exclusion criteria were based on ICD-9 coding provided by the physicians caring for the patients. Adults (≥18 years old) who were admitted for first-time stroke were included. We excluded patients who had missing data for secondary characteristics of ethnicity and race. We also chose not to include the related cerebrovascular insult of transient ischemia.

The independent variables were individual BMI categories defined as non-overweight/non-obese (BMI<25 kg/m^2), overweight (BMI 25–29.99 kg/m^2), obese (BMI 30–39.99 kg/m^2), and morbidly obese (BMI>40 kg/m^2). The primary outcome was in-hospital mortality. Possible confounders analyzed were age which was divided categorically into 3 groups; 18–44 years of age, 45–64, and ≥65 years of age, gender (male, female), race (Black, White, Asian, other), ethnicity (Hispanic, non-Hispanic), health insurance status (insured, not insured), alcoholism, tobacco use, hyperlipidemia, type 2 diabetes mellitus, hypertension, renal disease, atrial fibrillation, and administration of thrombolytic infusion.

We conducted a descriptive analysis. A bivariate analysis utilizing chi-square tests for categorical variables was used to compare these values. Finally, a multivariate analysis using logistic regression was used to adjust for the potential confounders mentioned previously and reported as an adjusted odds ratio (aOR). Statistical significance level was defined at p-value <0.05 for two-sided tests. This study was conducted in compliance with ethical standards, reviewed by our Institutional Review Board, and was deemed exempt. This study was registered with the research registry under UIN # researchregistry7020 and reported in line with the STROCSS guidelines [20].

3. Results

After inclusion/exclusion criteria, our study included 150,153 stroke patients. Tables 1A, 1B, and 1C display the distribution of demographic characteristics and comorbidities of included patients, based on BMI and stroke type. Overweight category was excluded from analyses due to the relatively small sample size compared to other BMI groups. Therefore, the main BMI categories going through final analysis were non-overweight/non-obese, obese, and morbidly obese.

Within the subarachnoid hemorrhage group, there was a larger proportion of younger patients (18–44 years) for all BMI categories compared to other stroke types. Among the subarachnoid hemorrhage group, there was also a larger portion of female patients for all BMI categories. In both the non-subarachnoid and ischemic stroke groups, gender was evenly distributed. When examining race, the percentages of Black patients increased as BMI increased within each type of stroke. This differed from White, Asian, and Other Race patients. The highest rates of tobacco users were found among the subarachnoid hemorrhage patients. Among the ischemic stroke patients, there was a significantly larger proportion of patients who had hyperlipidemia compared to other stroke types. Additionally, among ischemic stroke patients, there were higher rates of atrial fibrillation compared to the other stroke categories.

Tables 2A, 2B, and 2C show the distribution of patient demographic characteristics and comorbidities, based on stroke type and survival status at hospital discharge.

Table 1A
Baseline characteristics of non-subarachnoid hemorrhage patients.

Characteristics	Non-overweight/ Non-Obese (%)n = 17,093	Obese (%)n = 964	Morbidly Obese (%) n = 533	χ2	P-value
Age				426.2614	0.0001
18–44 years	5.99	9.23	12.38		
45–64 years	27.64	45.54	55.53		
≥65 years	66.37	45.23	32.08		
Gender				4.0613	0.131
Male	51.78	49.90	48.03		
Female	48.22	50.10	51.97		
Race				143.3688	0.0001
White	74.78	68.73	57.06		
Black	18.14	24.97	36.53		
Asian	1.37	0.63	0.38		
Other	5.71	5.67	6.03		
Ethnicity				7.8383	0.020
Non-Hispanic	86.54	83.58	88.10		
Hispanic	13.46	16.42	11.90		
Insurance Status				6.6515	0.036
Insured	93.57	91.91	91.74		
Uninsured	6.43	8.09	8.26		
Tobacco Use				2.3759	0.305
No	88.95	87.34	88.93		
Yes	11.05	12.66	11.07		
Alcoholism				3.1382	0.208
No	95.85	96.47	97.19		
Yes	4.15	3.53	2.81		
Hypertension				5.9347	0.051
No	29.96	27.28	26.45		
Yes	70.04	72.72	73.55		
Hyperlipidemia				54.9578	0.000
No	66.67	55.91	60.23		
Yes	33.33	44.09	39.77		
Diabetes				271.4195	0.000
No	77.21	61.10	53.85		
Yes	22.79	38.90	46.15		
Atrial Fibrillation				7.4707	0.024
No	81.04	84.13	83.49		
Yes	18.96	15.87	16.51		
Renal Disease				44.6822	0.000
No	88.67	83.40	81.99		
Yes	11.33	16.60	18.01		
Thrombolytic use				0.8202	0.664
No	99.06	98.96	98.69		
Yes	0.94	1.04	1.31		

*Overweight category excluded from table due to small number of patients (n = 46).

3.1. Non-subarachnoid hemorrhage patients classified by in-hospital mortality

In this group of stroke patients, non-overweight/non-obese patients had the highest rates of in-hospital mortality (22.25%), followed by

Table 1B
- Baseline characteristics of subarachnoid hemorrhage patients.

Characteristics	Non-overweight/ Non-Obese (%)n = 6,726	Obese (%)n = 349	Morbidly Obese (%) n = 196	χ2	P-value
Age				36.2924	0.0001
18–44 years	16.67	11.17	22.45		
45–64 years	45.90	57.88	54.08		
≥65 years	37.44	30.95	23.47		
Gender				6.7885	0.034
Male	38.12	31.23	36.73		
Female	61.88	68.77	63.27		
Race				25.4234	0.0001
White	75.08	74.56	65.63		
Black	16.33	18.71	28.65		
Asian	1.48	0.29	0.52		
Other	7.11	6.43	5.21		
Ethnicity				3.3756	0.185
Non-Hispanic	82.89	86.19	85.71		
Hispanic	17.11	13.81	14.29		
Insurance Status				7.2593	0.027
Insured	10.76	8.31	5.61		
Uninsured	89.24	91.69	94.39		
Tobacco Use				0.6944	0.707
No	77.24	75.64	78.57		
Yes	22.76	24.36	21.43		
Alcoholism				7.0468	0.029
No	96.27	98.85	97.45		
Yes	3.73	1.15	2.55		
Hypertension				30.4450	0.0001
No	37.70	26.36	25.00		
Yes	62.30	73.64	75.00		
Hyperlipidemia				35.7069	0.0001
No	75.54	61.32	73.98		
Yes	24.46	38.68	26.02		
Diabetes				122.0290	0.0001
No	85.22	70.20	62.76		
Yes	14.78	29.80	37.24		
Atrial Fibrillation				2.9925	0.224
No	90.77	89.11	87.76		
Yes	9.23	10.89	12.24		
Renal Disease				7.1367	0.028
No	94.47	91.40	92.35		
Yes	5.53	8.60	7.65		
Thrombolytic Use				2.4545	0.293
No	98.05	98.85	96.94		
Yes	1.95	1.15	3.06		

*Overweight category excluded from table due to small number of patients (n = 22).

Table 1C
- Baseline characteristics of ischemic stroke patients.

Characteristics	Non-overweight/ Non-Obese (%)n = 112,066	Obese (%)n = 8,046	Morbidly Obese (%) n = 3,719	χ2	P-value
Age				3.0e+03	0.0001
18–44 years	3.62	7.01	10.43		
45–64 years	25.41	42.61	48.27		
≥65 years	70.97	50.39	41.30		
Gender				169.2383	0.0001
Male	49.51	46.51	39.63		
Female	50.49	53.49	60.37		
Race				617.4665	0.0001
White	76.87	70.25	65.65		
Black	17.26	23.96	29.95		
Asian	0.83	0.48	0.24		
Other	5.04	5.31	4.16		
Ethnicity				63.7058	0.0001
Non-Hispanic	88.14	86.90	89.84		
Hispanic	11.86	13.10	10.16		
Insurance Status				149.6865	0.0001
Insured	94.66	81.88	92.47		
Uninsured	5.34	8.12	7.53		
Tobacco Use				18.4768	0.0001
No	83.88	82.14	83.49		
Yes	16.12	17.86	16.51		
Alcoholism				18.6756	0.0001
No	97.54	98.07	98.36		
Yes	2.46	1.93	1.64		
Hypertension				92.1443	0.0001
No	31.42	26.58	31.11		
Yes	68.58	73.42	68.89		
Hyperlipidemia				842.8880	0.0001
No	47.23	32.20	36.92		
Yes	52.77	67.80	63.08		
Atrial Fibrillation				191.8522	0.0001
No	76.01	81.98	80.83		
Yes	23.99	18.02	19.17		
Renal Disease				187.7616	0.000
No	87.40	85.10	80.37		
Yes	12.60	14.90	19.63		
Thrombolytic Infusion				2.5825	0.461
No	94.26	93.98	93.82		
Yes	5.74	6.02	6.18		

*Overweight category excluded from table due to small number of patients (n = 393).

morbidly obese (21.80%), and finally, obese patients (20.26%) (Table 2A). When evaluating unadjusted in-hospital mortality (Table 3A), compared to non-obese/non-overweight patients, obese patients had an approximately 40% decreased risk of death (0.60 OR, 0.499–0.718, 95%CI). Findings for morbidly obese patients were not significant.

For adjusted in-hospital mortality values in non-subarachnoid hemorrhagic stroke patients, the aOR for in-hospital mortality was significantly reduced in several categories. When compared to non-overweight/non-obese patients, obese patients had a 32% (0.68 aOR, 0.565–0.824, 95%CI) decreased odds. Patients in the age groups of 18–44 and 45–64 faced in-hospital mortality at 30% (0.70 aOR, 0.587–0.822, 95%CI) and 15% (0.85 aOR, 0.769–0.928, 95%CI) lower odds compared to patients aged 65 years and older. In comparison to White patients, Black patients and patients of Other Race had a 10% (0.90 aOR, 0.815–0.998, 95%CI) and a 28% (0.72 aOR, 0.567–0.909, 95%CI) decreased odds of in-hospital mortality and Hispanics had a 17% (0.83 aOR, 0.742–0.936, 95%CI) decrease compared to non-Hispanics. Tobacco users experienced in-hospital mortality decreases of 26% (0.74 aOR, 0.647–0.839, 95%CI) compared to non-smokers. Patients with a diagnosis of hypertension had a 23% (0.77 aOR, 0.700–0.843, 95%CI) decreased odds while patients with a diagnosis of hyperlipidemia had a 40% (0.60 aOR, 0.554–0.65, 95%CI) decreased odds compared to counterparts without such diagnosis.

In adjusted values, female patients had a 9% (1.09 aOR, 1.011–1.171, 95%CI) increased risk of in-hospital mortality when compared to men. Those without insurance died in the hospital at a 47% higher rate (1.47 aOR, 1.269–1.711, 95%CI) than those with insurance. Atrial fibrillation patients showed a 27% (1.27 aOR, 1.162–1.397, 95% CI) increased in-hospital mortality when compared to those without atrial fibrillation. Morbid obesity, Asian race, alcoholism, type 2 diabetes, use of thrombolytic therapy, and renal disease did not show significant associations against baseline controls. This is graphically represented in Table 4A and Fig. 1.

3.2. Subarachnoid hemorrhage patients classified by in-hospital mortality

Among patients with subarachnoid hemorrhage, differences in BMI were not found to be significant ($\chi2 = 3.1467$, Pr = 0.207) (Table 2B).

When comparing unadjusted in-hospital mortality outcomes

Table 2A
Baseline characteristics of non-subarachnoid hemorrhage patients classified by in-hospital mortality.

Characteristics	In-hospital Mortality (%) = 21.79 n = 4,060	χ2	P-value
Obesity status		31.9084	0.0001
Non-overweight/Non-obese	22.25		
Obese	20.26		
Morbidly obese	21.80		
Age		33.3962	0.0001
18–44 years	18.15		
45–64 years	19.80		
≥65 years	23.08		
Gender		10.0925	0.001
Male	20.87		
Female	22.79		
Race		15.3688	0.002
White	22.36		
Black	20.10		
Asian	24.27		
Other	18.67		
Ethnicity		13.0497	0.0001
Non-Hispanic	22.16		
Hispanic	18.91		
Insurance Status		7.3453	0.007
Insured	21.58		
Uninsured	24.90		
Tobacco Use		33.3716	0.0001
No	22.42		
Yes	16.86		
Alcoholism		3.6461	0.056
No	21.92		
Yes	21.80		
Hypertension		43.3673	0.0001
No	24.87		
Yes	20.51		
Hyperlipidemia		142.8835	0.0001
No	24.40		
Yes	16.77		
Diabetes		2.0515	0.152
No	22.05		
Yes	21.04		
Atrial Fibrillation		38.3864	0.0001
No	20.90		
Yes	25.71		
Renal Disease		1.3222	0.250
No	21.67		
Yes	22.75		
Thrombolytic Use		0.0217	0.883
No	21.81		
Yes	21.35		

Table 2B
- Baseline characteristics of subarachnoid hemorrhage patients classified by in-hospital mortality.

Characteristics	In-hospital Mortality (%) = 19.74 n = 1,440	χ2	P-value
Obesity status		3.1467	0.207
Non-overweight/non-obese	20.00		
Obese	16.33		
Morbidly obese	19.76		
Age		80.9431	0.0001
18–44 years	14.12		
45–64 years	17.61		
≥65 years	25.04		
Gender		6.0555	0.014
Male	18.29		
Female	20.66		
Race		10.8846	0.012
White	20.12		
Black	17.10		
Asian	28.28		
Other	18.31		
Ethnicity		5.1993	0.023
Non-Hispanic	20.14		
Hispanic	17.21		
Insurance Status		2.6678	0.102
Insured	19.50		
Uninsured	21.99		
Tobacco Use		32.0693	0.0001
No	21.20		
Yes	14.90		
Alcoholism		2.7128	0.100
No	19.91		
Yes	15.77		
Hypertension		14.3007	0.0001
No	22.08		
Yes	18.42		
Hyperlipidemia		20.5834	0.0001
No	20.99		
Yes	16.11		
Diabetes		3.8751	0.049
No	19.36		
Yes	21.86		
Atrial Fibrillation		3.6848	0.055
No	19.47		
Yes	22.55		
Renal Disease		8.9249	0.003
No	19.42		
Yes	25.42		
Thrombolytic Use		0.0008	0.977
No	19.76		
Yes	19.86		

(Table 3B) to non-obese/non-overweight patients, obese patients had an approximately 17% decreased risk of death (0.83 OR, 0.625–1.104, 95% CI) and morbidly obese patients had a 22% decreased risk of death (0.78 OR, 0.532–1.145 95%CI), which were not significant (p = 0.201, p = 0.206, respectively).

When evaluating the adjusted odds ratio of in-hospital mortality for subarachnoid hemorrhage patients, those aged 18–44 and those aged 45–64 had a 59% (0.41 aOR, 0.333–0.513, 95%CI) and 40% (0.60 aOR, 0.517–0.690, 95%CI) decrease compared to patients aged 65 years and older, respectively. Black patients had a 17% decrease (0.83 aOR, 0.696–0.993, 95%CI) and Hispanic patients had a 20% decrease (0.80 aOR, 0.669–0.956, 95%CI) in odds of in-hospital mortality in comparison to Whites and non-Hispanic, respectively. When evaluated against non-smokers, tobacco users showed a 24% (0.76 aOR, 0.646–0.895, 95%CI) lower odds of in-hospital mortality. Hypertensive patients experienced in-hospital mortality at a 22% lower rate (0.78 aOR, 0.680–0.896, 95%CI) than non-hypertensives. Hyperlipidemic patients had a 39% decrease (0.61 aOR, 0.519–0.707, 95%CI) in mortality compared to patients without such a diagnosis.

The odds for in-hospital mortality were increased in uninsured patients by 47% (1.47 aOR, 1.201–1.803, 95%CI) and Type 2 diabetes patients by 18% (1.18 aOR, 1.0004–1.398, 95%CI) compared to insured patients and non-diabetics, respectively. Obesity and morbid obesity, gender, race classified as Asian or Other, alcoholism, atrial fibrillation, thrombolytic infusion, and renal disease did not show significant associations compared to baseline controls. This is graphically represented in Table 4B and Fig. 2.

3.3. Ischemic stroke patients classified by in-hospital mortality

When examining in-hospital mortality in patients who experienced ischemic strokes, the non-overweight/non-obese BMI group was found to have the highest rates of in-hospital mortality at 4.21%. This was followed by the morbidly obese (3.44%) and obese (2.60%) (Table 2C).

When comparing unadjusted odds of in-hospital mortality for patients experiencing ischemic stroke (Table 3C), patients classified as obese and morbidly obese patients had a 39% (0.61 OR, 0.527–0.698, 95%CI), and 19% (0.81 OR, 0.678–0.969, 95%CI) decreased risk compared to non-overweight/non-obese patients, respectively.

When analyzing the adjusted values for ischemic stroke patients, the

Table 2C
- Baseline characteristics of ischemic stroke patients classified by in-hospital mortality.

Characteristics	In-hospital Mortality (%) = 4.08 n = 5,063	χ2	P-value
Obesity status		60.6290	0.0001
Non-overweight/non-obese	4.21		
Obese	2.60		
Morbidly obese	3.44		
Age		364.9255	0.0001
18–44 years	2.06		
45–64 years	4.80		
≥65 years	4.08		
Gender		12.2384	0.0001
Male	3.88		
Female	4.27		
Race		64.3680	0.0001
White	4.29		
Black	3.11		
Asian	4.02		
Other	4.03		
Ethnicity		8.1001	0.004
Non-Hispanic	4.00		
Hispanic	4.50		
Insurance Status		29.7083	0.0001
Insured	4.15		
Uninsured	2.82		
Tobacco Use		233.4245	0.0001
No	4.45		
Yes	2.13		
Alcoholism		7.1210	0.008
No	4.10		
Yes	3.12		
Hypertension		370.3191	0.0001
No	5.68		
Yes	3.35		
Hyperlipidemia		731.0997	0.0001
No	5.72		
Yes	2.68		
Diabetes		25.5572	0.0001
No	4.26		
Yes	3.64		
Atrial Fibrillation		969.0912	0.0001
No	3.11		
Yes	7.23		
Renal Disease		106.9788	0.0001
No	3.85		
Yes	5.58		
Thrombolytic Use		329.3615	0.0001
No	3.82		
Yes	8.19		

aOR for in-hospital mortality was significantly decreased in obese patients by 21% (0.79 aOR, 0.686–0.918, 95%CI) compared to non-overweight/non-obese patients. Patients between the ages of 18–44 had decreased odds of in-hospital mortality of 53% (0.47 aOR, 0.381–0.575, 95%CI) while patients aged 45–64 had decreased odds of 30% (0.70 aOR, 0.637–0.759, 95%CI) compared to those ≥65 years old. Users of tobacco experienced in-hospital mortality at a 37% lower rate (0.63 aOR, 0.562–0.699, 95%CI) in comparison to non-smokers. When evaluating risks of mortality with hypertension, hypertensive patients had 38% lower odds (0.62 aOR, 0.573–0.659, 95%CI) compared to those without hypertension. In patients with hyperlipidemia, in-hospital mortality was seen at a 51% lower rate (0.49 aOR, 0.458–0.518, 95% CI) than those without hyperlipidemia.

Increased odds of mortality of 13% (1.13 aOR, 1.026–1.236, 95%CI) was seen in Hispanics when evaluated against non-Hispanics. Atrial fibrillation patients died in the hospital at a 95% higher rate (1.95 aOR, 1.829–2.072, 95%CI) than patients without atrial fibrillation. In cases involving the use of thrombolytic infusion, patients experienced in-hospital mortality at a roughly 110% higher rate (2.10 aOR, 1.910–2.302, 95%CI) than in those without. Morbid obesity, gender, race, insurance status, alcoholism, type 2 diabetes, and renal disease did not show significant associations compared to baseline controls. This is graphically represented in Table 4C and Fig. 3.

Table 3A
Unadjusted odds ratio (OR): Non-subarachnoid hemorrhage.

Characteristics	Odds Ratio	95% CI	P-value
Obese	0.60	0.499–0.718	0.000
Morbidly Obese	0.89	0.716–1.010	0.276
Age 18-44	0.74	0.634–0.862	0.000
Age 45-64	0.82	0.761–0.891	0.000
Female	1.12	1.044–1.200	0.001
Black	0.87	0.796–0.957	0.004
Asian	1.11	0.825–1.499	0.484
Other Race	0.80	0.679–0.935	0.005
Hispanic	0.82	0.735–0.913	0.000
Uninsured	1.20	1.053–1.378	0.007
Tobacco User	0.70	0.622–0.729	0.000
Alcoholic	0.84	0.694–1.005	0.057
Hypertensive	0.78	0.723–0.839	0.000
Type 2 Diabetes	0.94	0.868–1.022	0.152
Hyperlipidemic	0.62	0.577–0.674	0.000
Atrial Fibrillation	1.31	1.202–1.427	0.000
Renal Disease	1.06	0.957–1.184	0.250

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No Renal Disease.

Table 3B
Unadjusted odds ratio (OR)- subarachnoid hemorrhage.

Characteristics	Odds Ratio	95% CI	P-value
Obese	0.83	0.625–1.104	0.201
Morbidly Obese	0.78	0.532–1.145	0.206
Age 18-44	0.49	0.409–0.592	0.000
Age 45-64	0.64	0.565–0.725	0.000
Female	1.16	1.031–1.312	0.014
Black	0.82	0.694–0.966	0.018
Asian	1.57	1.006–2.436	0.047
Other Race	0.89	0.702–1.128	0.333
Hispanic	0.83	0.699–0.973	0.023
Uninsured	1.16	0.970–1.396	0.103
Tobacco User	0.65	0.560–0.756	0.0001
Alcoholic	0.75	0.537–1.056	0.101
Hypertensive	0.80	0.708–0.896	0.0001
Type 2 Diabetes	1.17	1.001–1.357	0.049
Hyperlipidemic	0.72	0.628–0.832	0.0001
Atrial Fibrillation	1.20	0.996–1.455	0.055
Renal Disease	1.41	1.125–1.777	0.003

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No Renal Disease.

4. Discussion

Our analysis of the AHCA Florida Hospital Discharge Database for Stroke supports the finding that obesity was significantly associated with higher rates of survival during hospitalization after first incident of non-subarachnoid hemorrhagic and ischemic stroke compared to non-obese/non-overweight patients. Our data did not show a significant decrease in aOR for in-hospital mortality following subarachnoid hemorrhage in obese patients. The odds of mortality between obesity vs non-overweight/non-obese status after ischemic stroke and non-subarachnoid hemorrhage did not change greatly after adjustment for potential confounders. Morbid obesity was found to have non-significant associations with in-hospital mortality across all stroke types after adjustment of confounders. When further analyzing the data, it is apparent that among the different stroke types, obese patients had the

Table 3C
Unadjusted odds ratio (OR)- ischemic stroke.

Characteristics	Odds Ratio	95% CI	P value
Obese	0.61	0.527–0.698	0.0001
Morbidly Obese	0.81	0.678–0.969	0.021
Age 18-44	0.42	0.344–0.509	0.0001
Age 45-64	0.52	0.484–0.561	0.0001
Female	1.11	1.045–1.170	0.0001
Black	0.72	0.660–0.777	0.0001
Asian	0.94	0.678–1.291	0.684
Other Race	0.94	0.823–1.069	0.335
Hispanic	1.13	1.039–1.230	0.004
Uninsured	0.67	0.580–0.775	0.0001
Tobacco User	0.47	0.423–0.516	0.0001
Alcoholic	0.75	0.612–0.928	0.008
Hypertensive	0.57	0.543–0.609	0.0001
Type 2 Diabetes	0.85	0.797–0.905	0.0001
Hyperlipidemic	0.45	0.428–0.481	0.0001
Atrial Fibrillation	2.43	2.293–2.573	0.0001
Renal Disease	1.48	1.370–1.589	0.0001

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No Renal Disease.

Table 4A
Adjusted odds ratio (aOR): Non-subarachnoid hemorrhage.

Characteristics	Odds Ratio	95% CI	P-value
Obese	0.68	0.565–0.824	0.0001
Morbidly Obese	0.99	0.793–1.241	0.944
Age 18-44	0.70	0.587–0.822	0.0001
Age 45-64	0.85	0.769–0.928	0.0001
Female	1.09	1.011–1.171	0.025
Black	0.90	0.815–0.998	0.046
Asian	1.10	0.810–1.490	0.544
Other Race	0.72	0.567–0.909	0.006
Hispanic	0.83	0.742–0.936	0.002
Uninsured	1.47	1.269–1.711	0.0001
Tobacco User	0.74	0.647–0.839	0.0001
Alcoholic	0.94	0.772–1.142	0.531
Hypertensive	0.77	0.700–0.843	0.0001
Type 2 Diabetes	1.03	0.948–1.129	0.447
Hyperlipidemic	0.60	0.554–0.653	0.0001
Atrial Fibrillation	1.27	1.162–1.397	0.0001
Thrombolytic Infusion	1.06	0.728–1.536	0.771
Renal Disease	0.91	0.796–1.039	0.162

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

Table 4B
Adjusted odds ratio (aOR): Subarachnoid hemorrhage.

Characteristics	Adjusted Odds Ratio	95% CI	P-value
Obese	0.89	0.660–1.210	0.468
Morbidly Obese	0.89	0.594–1.318	0.548
Age 18-44	0.41	0.333–0.513	0.0001
Age 45-64	0.60	0.517–0.690	0.0001
Female	1.10	0.964–1.246	0.163
Black	0.83	0.696–0.993	0.042
Asian	1.56	0.992–2.455	0.054
Other Race	1.00	0.728–1.381	0.987
Hispanic	0.80	0.669–0.956	0.014
Uninsured	1.47	1.201–1.803	0.0001
Tobacco User	0.76	0.646–0.895	0.001
Alcoholic	0.82	0.576–1.171	0.277
Hypertensive	0.78	0.680–0.896	0.0001
Type 2 Diabetes	1.18	1.0004–1.398	0.049
Hyperlipidemic	0.61	0.519–0.707	0.0001
Atrial Fibrillation	0.95	0.775–1.169	0.639
Thrombolytic Infusion	1.21	0.786–1.850	0.391
Renal Disease	1.15	0.888–1.501	0.284

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

Table 4C
Adjusted odds ratio (aOR): Ischemic stroke.

Characteristics	Odds Ratio	95% CI	P-value
Obese	0.79	0.686–0.918	0.002
Morbidly Obese	1.04	0.860–1.245	0.714
Age 18-44	0.47	0.381–0.575	0.0001
Age 45-64	0.70	0.637–0.759	0.0001
Female	0.99	0.937–1.055	0.852
Black	0.92	0.846–1.007	0.073
Asian	1.14	0.820–1.588	0.423
Other Race	0.96	0.811–1.144	0.668
Hispanic	1.13	1.026–1.236	0.013
Uninsured	1.14	0.973–1.341	0.104
Tobacco User	0.63	0.562–0.699	0.0001
Alcoholic	0.97	0.778–1.206	0.776
Hypertensive	0.62	0.573–0.659	0.0001
Type 2 Diabetes	0.98	0.915–1.046	0.520
Hyperlipidemic	0.49	0.458–0.518	0.0001
Atrial Fibrillation	1.95	1.829–2.072	0.0001
Thrombolytic Infusion	2.10	1.910–2.302	0.0001
Renal Disease	0.99	0.897–1.077	0.707

Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

greatest decrease in in-hospital mortality in the non-subarachnoid hemorrhage group compared to that of the ischemic group.

This result is consistent with findings in the literature that focus on the obesity paradox noted in other medical conditions. The literature has shown significantly lower mortality and readmission rates for obese patients who suffered strokes when adjusting for age, hypertension, diabetes, and marital status over both the long and short term [13–15,21–24]. Among these studies that are consistent with our findings, are the retrospective cohort studies by Andersen at al. and Olsen et al. In these, 29,326 patients and 21,884 patients with 10 and 5 years follow up, respectively. Also included in these, were Vemmos et al. and Dangayach et al., who conducted prospective cohort studies and followed 2,785 patients with 10-year follow-up and 202 patients with 1-year follow up, respectively. Nevertheless, our review of the literature also identified two studies that contradict this association between obesity and short-term mortality after stroke [25,26]. Dehlendorff et al., in a retrospective cohort study involving over 70,000 stroke patients from the years 2001–2011, did not find obesity to be associated with a decrease in mortality, whereas Andersen et al. reported strong support for the obesity paradox. However, the key difference between the two studies was that Dehlendorff et al. used multiple imputation to account for the nearly 20,000 patients with missing data [25]. It is likely that this technique minimized the protective effect of obesity on mortality. Jiang et al., in a prospective study involving approximately 86,000 patients, followed over 13 years, also did not find a protective effect of obesity among the US patients who suffered from stroke [26]. This study, however was not able to evaluate and, therefore, analyze differences in ischemic versus hemorrhagic stroke, which did yield different results in our analysis across several categories. Furthermore, data from the Prospective Studies Collaboration, involving approximately 900,000 adult patients with a mean follow up of 13 years, reveal that, for every 5 kg/m^2 increase in BMI over 25 kg/m^2, there is an approximately 40% higher risk of mortality. But, this study grouped overweight BMI between 25 and 50 kg/m^2 together and compared findings to lower BMI groups between 15 and 25 kg/m^2 [27].

In addition to obesity's protective effect in the presented data, a similar effect was also found in those aged 18–44 and 45–64 in all stroke

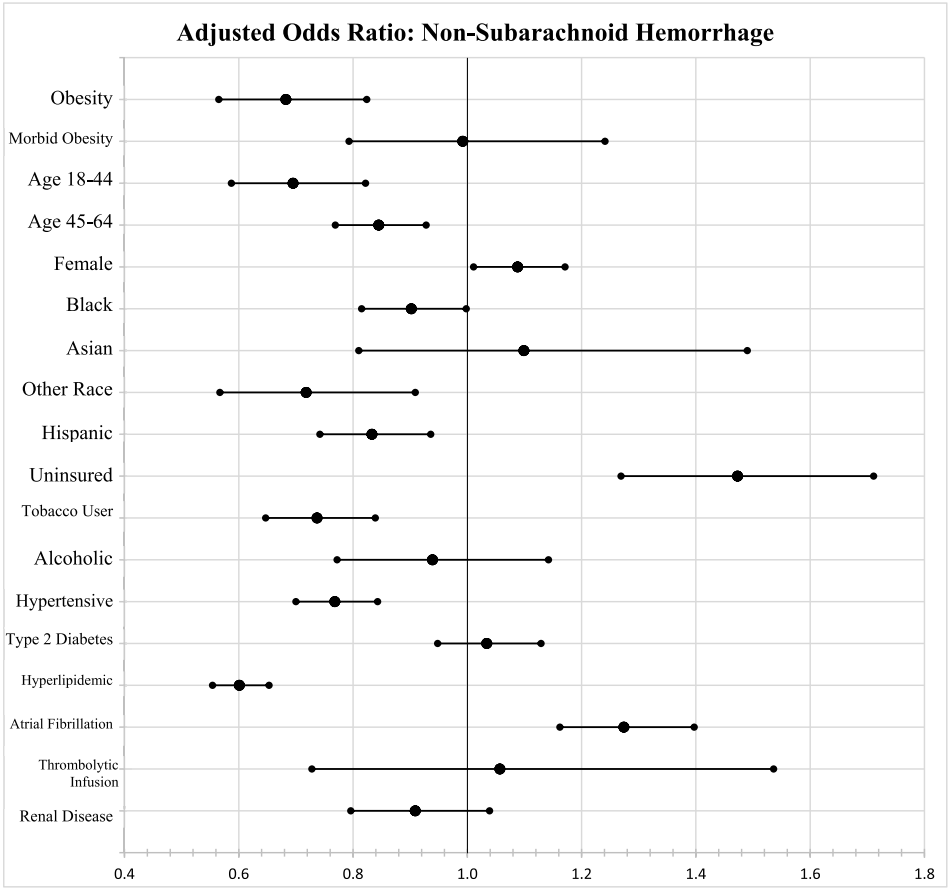

Fig. 1. - Adjusted odds ratios (aOR) between Obesity and in-hospital mortality among non-subarachnoid hemorrhage patients compared to baseline controls. Odds ratio of 1 is graphically represented to display statistical significance. Error bars show 95% CI.
Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

types studied. Previous evidence has shown a clear association between case fatality and increasing age in stroke patients among various populations [28,29]. Many factors may attribute to this association, including declines in functional reserve with age and that older patients may be less likely to receive aggressive interventional care when presenting with stroke [30].

Having health insurance was protective in non-subarachnoid and subarachnoid stroke types but this association was not significant for ischemic stroke outcomes. Other studies, such as the retrospective cohort studies by James et al. with 95,986 patients, and Medford-Davis et al. with 589,320 patients, have elucidated a similar association between uninsured status and increased mortality, such that uninsured patients had higher rates of death compared to private insurance patients and Medicaid/Medicare patients [31,32].

Other factors that were associated with decreased mortality were Black race relative to White race and Hispanic ethnicity relative to non-Hispanic ethnicity in non-ischemic stroke. There are other studies that show similar trends in mortality among racial and ethnic groups, but some show results that conflict with this, showing Black race and Hispanic ethnicity as risk factors for mortality in stroke [1,33–38]. Among the studies we compared, the discrepancy could lie differences in sample populations examined.

Interestingly, it was noted that across the 3 stroke types evaluated, tobacco use, hyperlipidemia and hypertensive disease were associated with significant decreases in in-hospital mortality. Hyperlipidemia and hypertension are potentially protective because these put patients at risk for medical diseases that necessitate chronic medical care. It is possible that the increased contact with medical providers, as well as the medications that these patients take regularly for these conditions are protecting them at the time of their stroke. By taking anti-hypertensives and cholesterol lowering drugs, it is possible that the cerebral vasculature is healthier at the time of stroke and better prepared to limit the damage at the time of vascular insult. Smoking, however, has been linked to increased mortality rates for strokes [39]. It is possible, though, that some of the known risk factors for increased stroke, such as the comorbid conditions noted in this study, limit the severity of stroke and improve the ability to manage care. In other words, disease in the presence of known risk factors can open the door to studied efficacious treatments with better protocols, whereas disease in the absence of risk factors may have a more insidious underlying mechanism that is less easily treated with standard practices.

Another possibility is that patients with these known comorbid conditions, along with those who are obese and have health insurance, have greater access to healthcare and are more aware of sequelae they can be affected by because of their contact with medical professionals and may be quicker to respond to the symptoms of stroke. Timing is an important factor in stroke outcomes and the sooner these patients are treated, the better their chances are of surviving and decreasing sequelae [40–42]. In addition, those who are obese, hypertensive, hyperlipidemic, and have renal disease are all more likely to have a stroke and, therefore, may have a higher index of suspicion when presenting with symptoms, necessitating more rapid workup and treatment. In contrast, it can be postulated that patients without known risk factors who develop stroke may have more extensive disease with irreversible or non-modifiable processes and which may confer a greater risk of failure of treatment and subsequent mortality.

Our study has several limitations. First, we focused on different stroke types but could not assess the severity of the strokes that affected patients as this information was not available in the database. It is possible that the strokes that affected the patients in the groups with lower mortality were less severe than those in the greater mortality arm. This is particularly important given that neurologic evaluation of stroke

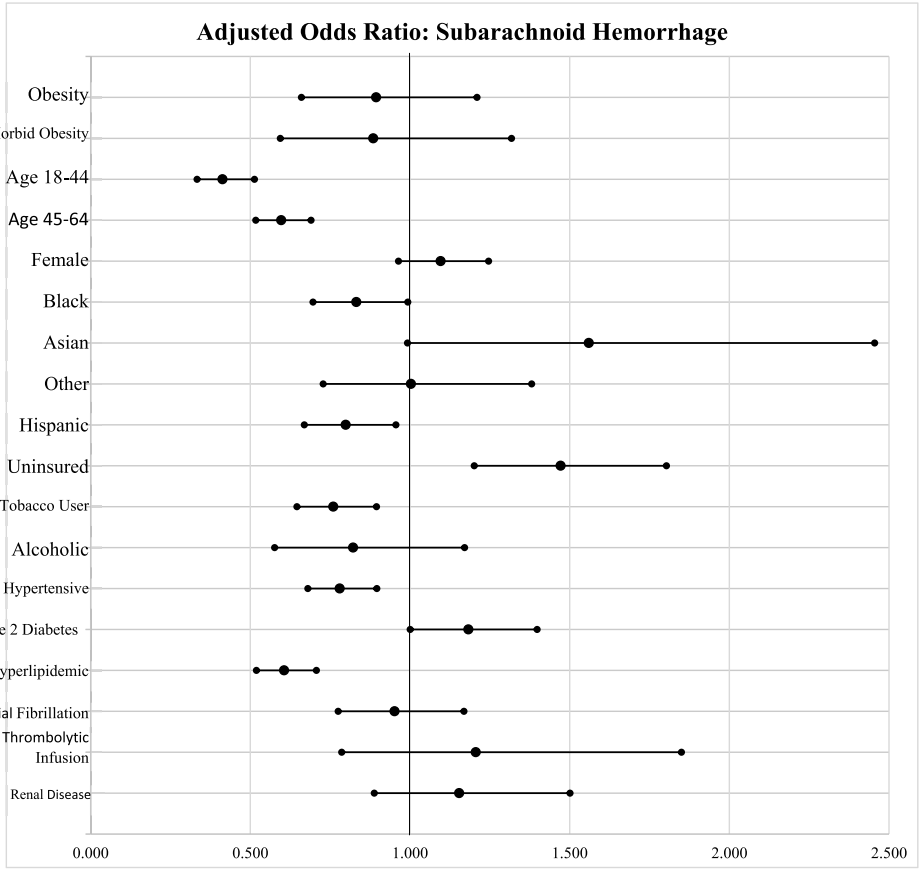

Fig. 2. - Adjusted odds ratios (aOR) between Obesity and in-hospital mortality among subarachnoid hemorrhage patients compared to baseline controls. Odds ratio of 1 is graphically represented to display statistical significance. Error bars show 95% CI.
Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

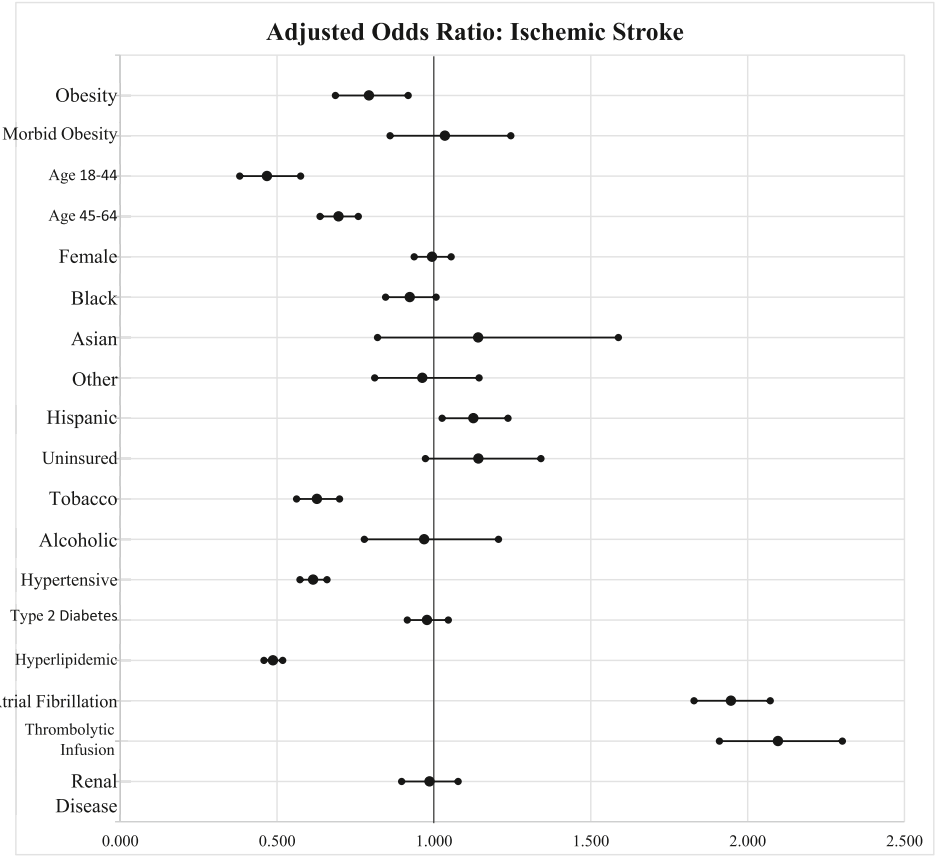

Fig. 3. - Adjusted odds ratios (aOR) between Obesity and in-hospital mortality among ischemic stroke patients compared to baseline controls. Odds ratio of 1 is graphically represented to display statistical significance. Error bars show 95% CI.
Baseline comparison for characteristic categories: Non-overweight/Non-obese, Age ≥65, Male, White, Non-Hispanic, Insured, Non-Tobacco user, Non-Alcoholic, Non-Hypertensive, No Type 2 Diabetes, Non-Hyperlipidemic, No Atrial Fibrillation, No use of thrombolytic infusion, No Renal Disease.

severity is one of the most important prognostic factors for outcomes [43–45]. Second, data used to conduct our analyses were not very recent and involved data from the years 2008–2012. This was the most recent data available to us from this dataset at the time of collection. Although more recent data would be preferred, this dataset captured a significant number of patients and trends are unlikely to have changed significantly over the past few years. Lastly, there was a very small sample size concerning the number of overweight patients in certain groups, thus excluded from our analysis. This limited our ability to perform an adjusted model analysis among all BMI groups. Future research, possibly with more directed prospective cohort studies, should be aimed at following patients after stroke and hospitalization with more expansive patient demographic and prognostic data collection and may focus on mortality and other important secondary outcomes such as neurologic sequelae and post-hospitalization mortality.

5. Conclusion

Obese patients are less likely to die during hospitalization for first-time non-subarachnoid hemorrhage and ischemic stroke than non-overweight/non-obese patients. These findings support the "obesity paradox". Future research is needed to further investigate and understand the effects of obesity and other related risk factors on outcomes in patients with first-time or recurrent ischemic or hemorrhagic stroke.

Ethical approval

This study was conducted in compliance with ethical standards, reviewed by our institutional review board and deemed exempt.

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None.

Authors' contribution

KK, RA, PR, JR, JZ, AE: Study design and conception; KK, RA, CK, LF, LS, ZD, PR, JR, JJZ, AE: Data collection, interpretation and analysis; KK, RA, CK, LF, LS, ZD, PR, JR, JZ, AE: Manuscript preparation; KK, RA, PR, AE: Critical revision of manuscript, All authors read and approved the final manuscript.

Research registration unique identifying number (UIN)

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Declaration of competing interest

Authors declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102839.

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