

Original Article

Obesity paradox in atrial fibrillation and flutter: a multivariate nationwide inpatient analysis

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Abstract: Objectives: Atrial Fibrillation and atrial flutter (Afib/Aflut) are the most common arrhythmias that present in the emergency department. This study aimed to evaluate in-hospital mortality based on weight categories in patients with Afib/flut. Methods: Using ICD-10 codes from the large Nationwide Inpatient Sample (NIS) database in the years 2016-2020, we evaluated any association between the presence of Afib/Aflut and mortality in different weight categories in adults over the age of 18. Results: A total of 23,037,013 Afib/flut patients were found in the NIS database. Total mortality in patients with Afib/Aflut was 5.03%. Mortality in patients with normal weight was 5.26%. Mortality was lowest in overweight (2.3%) followed by Obesity (2.97%) and morbid obesity (2.97%). It was highest in cachectic patients (15.89%), all *p*-values were *P*<0.001. These associations persisted after multivariate adjustment for demographics and co-morbid conditions. Furthermore, Mortality was highest during the COVID-19 year of 2020, regardless of weight categories. Conclusions: The obesity paradox is present in patients admitted to the hospital with Afib/Aflut. Regardless of comorbid conditions or demographics, the lowest mortality was seen in overweight patients. Furthermore, the COVID-19 pandemic year independently increased inpatient mortality from Afib/Aflut.

Keywords: Obesity paradox, obesity, atrial fibrillation, atrial flutter, morbid obesity, risk factors, arrhythmia, mortality

Introduction

Atrial fibrillation (Afib) and atrial flutter (Aflut) are common arrhythmias that contribute to considerable morbidity and mortality worldwide. Deaths in patients with Afib and Aflut are primarily attributed to cardiovascular-related conditions, including sudden cardiac death, heart failure, and myocardial infarctions [1, 2]. Moreover, the increased risk of embolic events secondary to blood stasis in the atria presents another major contributor to mortality in patients with Afib and Aflut [3, 4]. Similarly, in patients with obesity, cardiovascular diseases, most notably myocardial infarctions, are among the leading causes of mortality [5-7]. Obesity can also increase one's risk of stroke and other thrombotic events, largely due to the hypercoagulable state induced by chronic inflammation [8]. The excess adipose tissue contributes to pro-inflammatory cytokine release, enhancing coagulation and impairing fibrinolysis [8]. As the risk of mortality increases with both Afib/Aflut and obesity independently, it is essential

to understand the interplay of these conditions to develop more effective strategies to reduce mortality in these populations [1, 2, 6, 7].

Notably, obesity is a risk factor for the development of Afib and Aflut, with over 20% of patients diagnosed with Afib/Aflut also being affected by obesity [9]. Therefore, it would appear logical that increasing weight in patients with these arrhythmias would correlate with an elevated risk of mortality. However, prior research has shown that this is not necessarily the case, with what is termed the 'obesity paradox' applying to patients with Afib and Aflut [10, 11]. This 'obesity paradox' describes the phenomenon in which individuals with a higher body mass index (BMI) display better survival rates, even though obesity is a known health risk. A prior study evaluating the relationship between Afib and BMI found that patients with Afib categorized as obese had a lower risk of stroke and all-cause mortality compared to their normal-weight counterparts [10]. Notably, there have also been studies reporting contrasting find-

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Table 1. The international classification of diseases, 10th revision (ICD-10) codes for the variables evaluated in this study

Variable	ICD-10 Code (s)
Atrial Fibrillation & Flutter	I48
Cachexia	R64
Overweight	E66.3
Obesity	E66.9, E66.8, E66.0
Morbid Obesity	E66.01, E66.2
Smoking	F17.20, Z72.0, Z87.891
Diabetes	E08-E13
Hypertension	I10, I11.0, I11.9, I120, I129, I13.0, I13.10, I13.11, I13.2, I15.0, I15.1, I15.2, I15.9, I16.0, I16.1, I16.9
Chronic Obstructive Pulmonary Disease	J41.0, J41.1, J41.8, J42., J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9, J47.0, J47.1, J47.9, J684
Chronic Kidney Disease	I13.11, I13.2, N289, Q613, N181, N182, N183, N1830, N1831, N1832, N184, N185, N186, N189, R880, N19
Old Myocardial Infarction	I25.2
ST-Elevation Myocardial Infarction	I21.01, I21.02, I21.09, I21.11, I21.19, I21.21, I21.29, I21.3, I21.9, I21.A1, I21.A9, I22.0, I22.1, I22.5, I22.9
Non-ST-Elevation Myocardial Infarction	I21.4, I22.2

ings, showing that a high BMI is associated with increased mortality [12]. Interestingly, patients with Afib who have undergone bariatric surgery are shown to be more likely to experience mortality than those who are obese and have not undergone the procedure [11]. These findings highlight the complex relationship between weight and mortality in patients with Afib/Aflut, suggesting additional factors may contribute to this trend. As the literature has limited information regarding the role outside factors play in mortality for patients with Afib and Aflut across weight categories, further investigation is needed to further elucidate this complex relationship.

Therefore, this study aimed to investigate the in-hospital mortality rate in patients diagnosed with Afib or Aflut based on weight category. Moreover, as various confounding variables, including comorbidities or treatment variations, may impact the relationship, it also sought to assess the correlational impact of risk factors and demographics on mortality in patients with Afib or Aflut by weight category. As prior studies have been limited by smaller sample sizes and/or inadequate adjustment for confounders, this study expands on prior work by employing a large, national dataset while accounting for a range of risk factors to better evaluate the impact of weight on Afib and Aflut mortality [9-12].

Methods

Data source

This analysis utilized data from the National Inpatient Sample (NIS) database, which includes about 20% of all hospital discharges throughout America. The Agency for Healthcare Research and Quality offers this publicly accessible dataset, which includes over 8 million patient records [13-15]. As there was no direct patient contact or access to identifying information, this study did not require institutional review board approval.

Study population

The NIS dataset was evaluated for patients with Afib and Aflut using the International Classification of Diseases, 10th revision (ICD-10) codes (**Table 1**). Weight categories were assigned based on ICD-10 codes related to BMI classifications, as direct BMI values were not available in the dataset (**Table 1**). Inclusion criteria included patients of any gender, sex, or ethnicity who were aged 18 or older at the visit, with a documented diagnosis of Afib or Aflut, and hospitalization between 2016 and 2020. Exclusion criteria include those who were younger than 18 years old and those without a diagnosis of Afib or Aflut.

Mortality in atrial fibrillation and flutter across weight categories

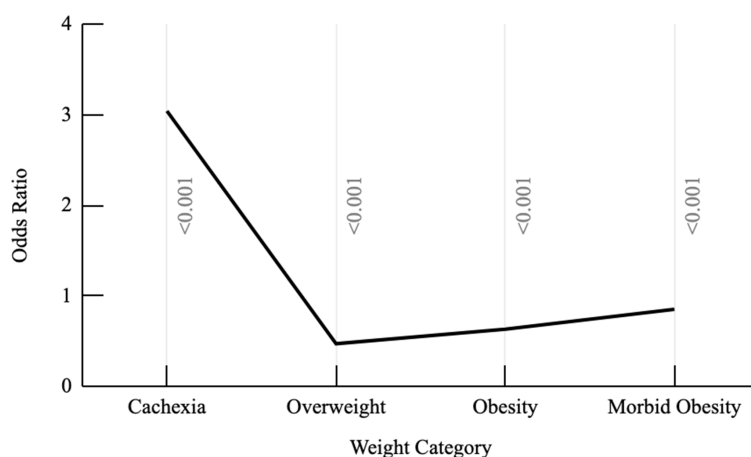


Figure 1. Odds ratios for mortality in hospitalized patients with atrial fibrillation and atrial flutter between 2016 and 2020 by weight category after multivariate adjustment for demographics, comorbidities, and lifestyle factors.

logistic regression was employed to explore the odds of binary clinical outcomes concerning both patient and hospital attributes, as well as the odds of these outcomes over time. The statistical models were adjusted for confounding factors and variables. Additionally, population discharge weights were applied throughout the analysis. Statistical significance was evaluated using two-sided *p*-values, with $P < 0.05$ considered statistically significant. STATA 17 (Stata Corporation, College Station, TX) was employed to analyze the data.

Study outcome and statistical analysis

This study aimed to assess the relationship between weight categories and mortality in adult patients diagnosed with Afib or Aflut. Specifically, in-hospital mortality was selected as the primary outcome as the database employed most reliably captures this information and minimizes confounding factors affecting mortality outside of the hospital, allowing for a better assessment of the study's objective. Further, it incorporated various risk factors and demographics, including sex and race, associated with Afib and Aflut to conduct a multivariate logistic regression analysis to determine how these variables interact to influence patient outcomes. Risk factors were selected for multivariate logistic regression based on availability within the dataset from known risk factors of mortality in obesity and Afib/Aflut. These included lifestyle characteristics, such as smoking history, and comorbidities, such as diabetes mellitus (DM), hypertension (HTN), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), ST-elevation myocardial infarction (STEMI), non-STEMI, as well as myocardial infarction (MI). These variables were extracted from the NIS database utilizing their associated ICD-10 codes (**Table 1**).

Patient demographic, clinical, and hospital characteristics were expressed as medians with interquartile ranges (IQR) for continuous variables and proportions with 95% confidence intervals for categorical variables. Multivariate

Results

The NIS database was analyzed for patients with Afib and Aflut hospitalized from 2016 to 2020, with a total of 23,037,013 patients identified. The median age of patients was 77 years, with 53% being male and 78% identifying as White. In terms of comorbidities, approximately 30% of patients were smokers, 34% had DM, 83% had HTN, 28% had COPD, 34% had CKD, 3% had suffered a STEMI, 4% had a non-STEMI, and 11% had a history of MI.

The mortality rates of patients diagnosed with Afib and Aflut across weight categories were assessed. The overall all-cause mortality rate for patients with Afib and Aflut was 5.03%. Similarly, the mortality rate of patients classified as normal weight was 5.26%. In contrast, patients who were overweight displayed a significantly lower mortality rate of 2.34% with an odds ratio (OR) of 0.43 (95% CI: 0.39-0.48). Mortality rates were higher in patients with obesity (2.97%; OR: 0.55 (95% CI: 0.54-0.56)) and morbid obesity (3.80%; OR: 0.71 (95% CI: 0.70-0.72)), although these rates remained significantly lower than those seen in patients identified with normal weight. On the other hand, cachectic patients demonstrated a significantly higher mortality rate of 15.89% with an odds ratio of 3.40 (95% CI: 3.32-3.49). These associations persisted in significance even after multivariate adjustment for demographics, comorbidities, and other risk factors (**Figure 1**).

Mortality in atrial fibrillation and flutter across weight categories

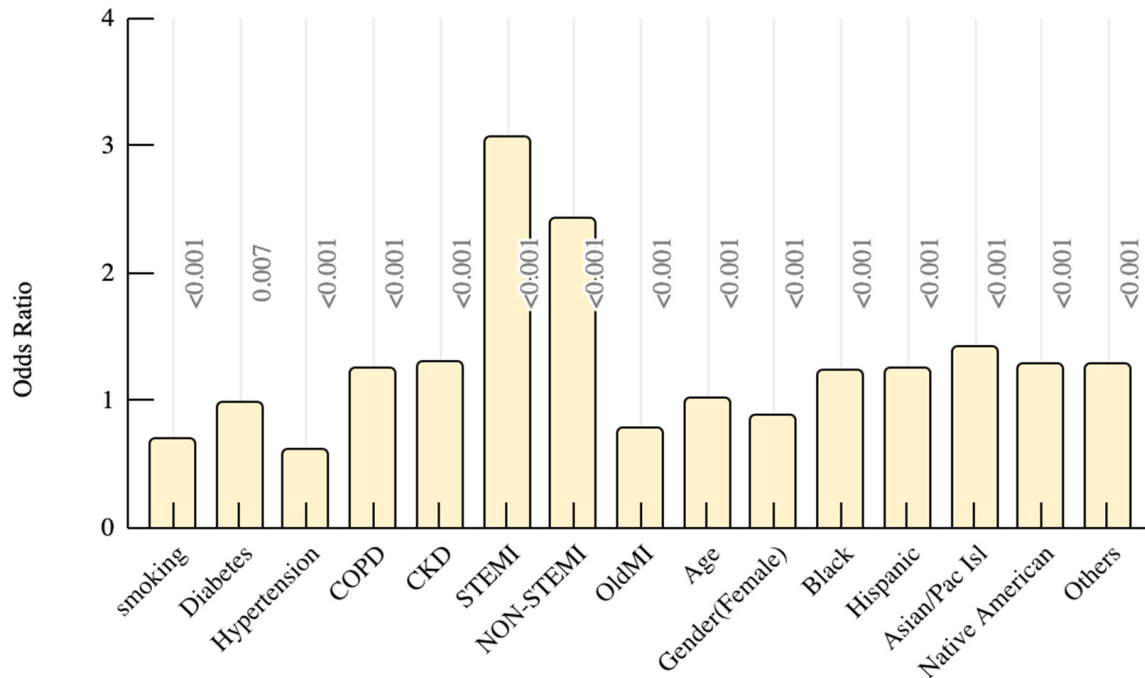


Figure 2. Odds ratio of mortality in hospitalized patients with atrial fibrillation and atrial flutter (2016-2020) by co-morbidity and demographic factor in those classified as cachexic.

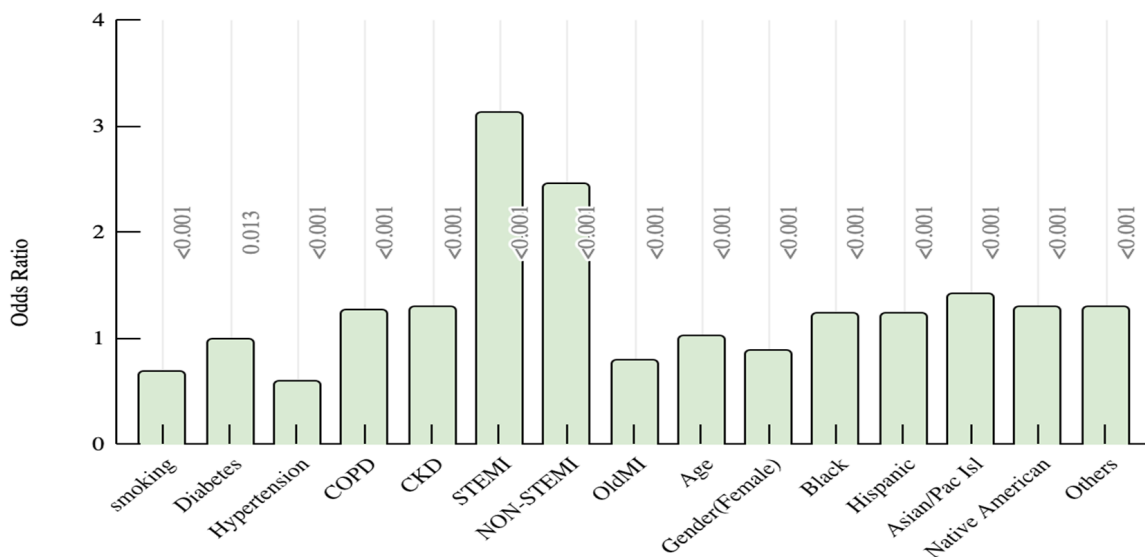


Figure 3. Odds ratio of mortality in hospitalized patients with atrial fibrillation and atrial flutter (2016-2020) by co-morbidity and demographic factor in those classified as overweight.

The mortality rates of patients diagnosed with Afib and Aflut across weight categories were evaluated concerning various demographic factors and comorbid conditions. Across all weight categories, smoking, HTN, and a history of MI were associated with significantly lower odds of

mortality in patients with Afib and Aflut (**Figures 2-5; Table 2**). Conversely, STEMI, Non-STEMI, CKD, and COPD were associated with significantly higher odds of mortality (**Figures 2-5; Table 2**). A diagnosis of DM did not reveal a significant correlation with altering the odds of

Mortality in atrial fibrillation and flutter across weight categories

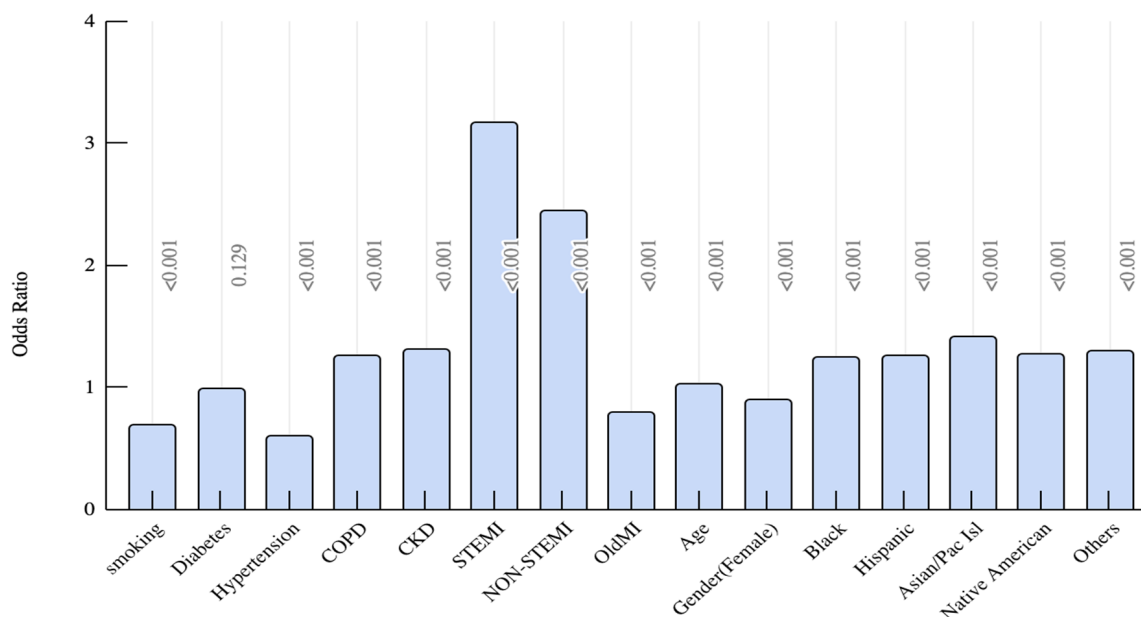


Figure 4. Odds ratio of mortality in hospitalized patients with atrial fibrillation and atrial flutter (2016-2020) by co-morbidity and demographic factor in those classified as obese.

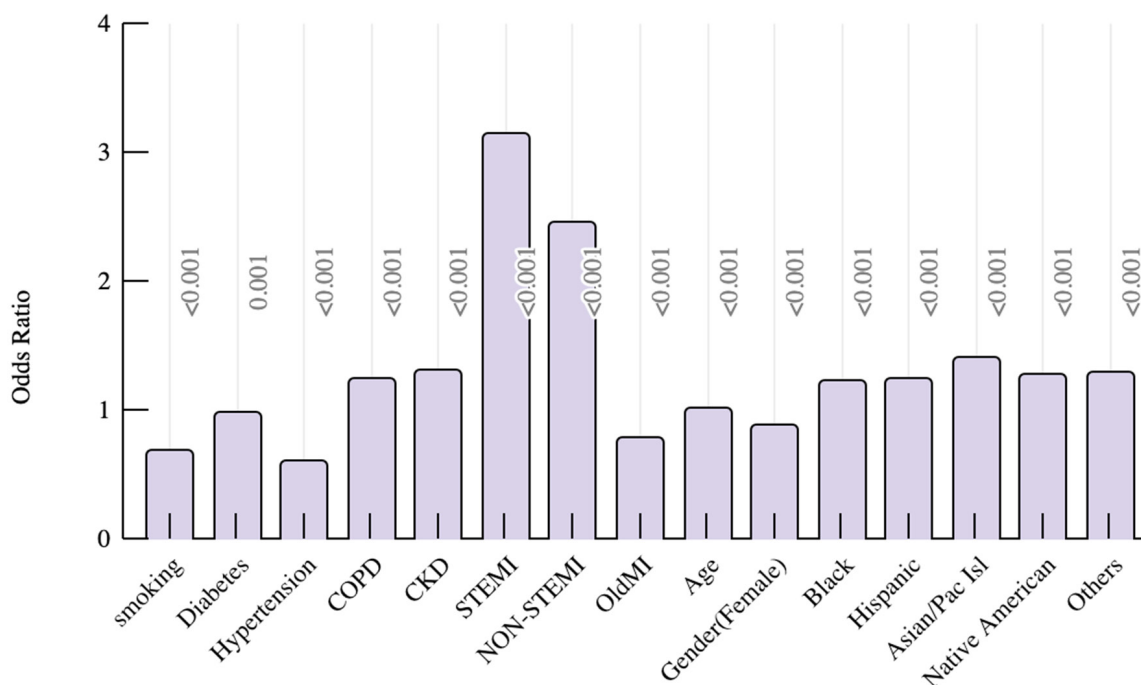


Figure 5. Odds ratio of mortality in hospitalized patients with atrial fibrillation and atrial flutter (2016-2020) by co-morbidity and demographic factor in those classified as morbidly obese.

mortality in patients with Afib or Aflut in any weight category (**Figures 2-5; Table 2**). Female patients with Afib or Aflut were less likely to experience mortality, with an odds ratio of 0.89

(95% CI: 0.88-0.9) for obese and morbidly obese patients. Furthermore, patients identifying as non-white, including black, Hispanic, Asian/Pacific islanders, and native American,

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Table 2. Odds ratios with 95% confidence intervals (CI) of hospitalized patients with atrial fibrillation and atrial flutter in each weight category stratified by traditional risk factors, including smoking, diabetes mellitus (DM), hypertension (HTN), chronic obstructive pulmonary disease (COPD) chronic kidney disease (CKD), old myocardial infarction (MI) ST-Elevation Myocardial Infarction (STEMI), and Non-ST-Elevation Myocardial Infarction (non-STEMI), as well as demographic characteristics across weight categories

Variable	Cachexia		Overweight		Obesity		Morbid Obesity	
	OR	CI	OR	CI	OR	CI	OR	CI
Smoking	0.7	0.69-0.71	0.69	0.42-0.53	0.69	0.68-0.7	0.69	0.68-0.70
DM	0.98	0.97-1	0.99	0.68-0.7	0.99	0.98-1	0.98	0.97-0.99
HTN	0.61	0.6-0.62	0.6	0.97-1	0.6	0.59-0.61	0.6	0.59-0.61
COPD	1.24	1.23-1.26	1.26	0.6-0.61	1.26	1.25-1.27	1.25	1.24-1.26
CKD	1.3	1.28-1.31	1.3	1.25-1.27	1.31	1.30-1.33	1.31	1.3-1.33
STEMI	3.07	3.01-3.14	3.13	1.29-1.32	3.16	3.09-3.23	3.15	3.09-3.22
Non-STEMI	2.42	2.38-2.47	2.45	3.06-3.2	2.44	2.40-2.49	2.45	2.41-2.49
Old MI	0.78	0.77-0.8	0.79	2.4-2.49	0.79	0.77-0.8	0.78	0.77-0.79
Age	1.02	1.02-1.02	1.02	0.77-0.80	1.02	1.02-1.02	1.02	1.02-1.02
Gender (female)	0.88	0.88-0.89	0.89	1.02-1.02	0.89	0.88-0.9	0.89	0.88-0.9
Race (Black)	1.23	1.21-1.25	1.24	0.88-0.89	1.24	1.21-1.26	1.23	1.2-1.25
Race (Hispanic)	1.24	1.21-1.27	1.24	1.22-1.27	1.25	1.22-1.29	1.24	1.21-1.27
Race (Asian/Pacific Islander)	1.41	1.37-1.45	1.42	1.21-1.28	1.41	1.37-1.46	1.41	1.37-1.46
Race (Native American)	1.28	1.19-1.38	1.29	1.19-1.39	1.27	1.18-1.38	1.27	1.18-1.37
Race (Other)	1.29	1.25-1.34	1.3	1.25-1.35	1.3	1.25-1.35	1.3	1.25-1.35

were more likely to experience mortality, with the highest odds ratio in those identifying as Asian/Pacific islanders (**Figures 2-5**).

Furthermore, mortality rates in patients diagnosed with Afib and Aflut varied depending on the year evaluated. Across all weight categories, the mortality rates were highest during the coronavirus disease of 2019 (COVID-19) year of 2020 (**Figure 6**). On the other hand, the years with the lowest mortality rates varied by weight category: 2018 for cachectic patients (15.19%), 2019 for normal weight patients (4.80%), 2017 for overweight patients (1.74%), 2019 for obese patients (2.41%), and 2019 for morbidly obese patients (3.19%) (**Table 3**). The hierarchy of mortality odds ratios in patients with Afib and Aflut remained consistent across all five years, with cachexia associated with the highest risk, followed by normal weight, morbid obesity, obesity, and overweight, in that order (**Figure 6**).

Discussion

This study aimed to evaluate the mortality rate of hospitalized patients with Afib and Aflut based on weight category. This investigation

revealed that Afib and Aflut patients classified as cachexia were the most likely to experience mortality, while those classified as overweight were the least likely. These correlational findings reinforce the notion of the 'obesity paradox', highlighting how Afib/Aflut patients with elevated BMIs may have a more favorable prognosis than those of normal weight [16-18]. Moreover, they underscore the influence diminished physiologic resources and resiliency may have in cachectic patients in the context of Afib and Aflut [19, 20]. These findings align with prior literature, which has suggested factors such as a greater metabolic reserve, aggressive early interventions for those of higher BMIs, and inherent limitations of the BMI classification system may explain this phenomenon [21-25]. As obesity is a well-established risk factor for the development of Afib/Aflut and associated comorbidities, it remains unclear exactly how weight should factor into one's clinical risk profile [26]. Nonetheless, this study highlights the importance of considering one's BMI category when prioritizing management targets in patients with Afib or Aflut.

Interestingly, not all studies regarding mortality in Afib/Aflut patients have come to the same

Mortality in atrial fibrillation and flutter across weight categories

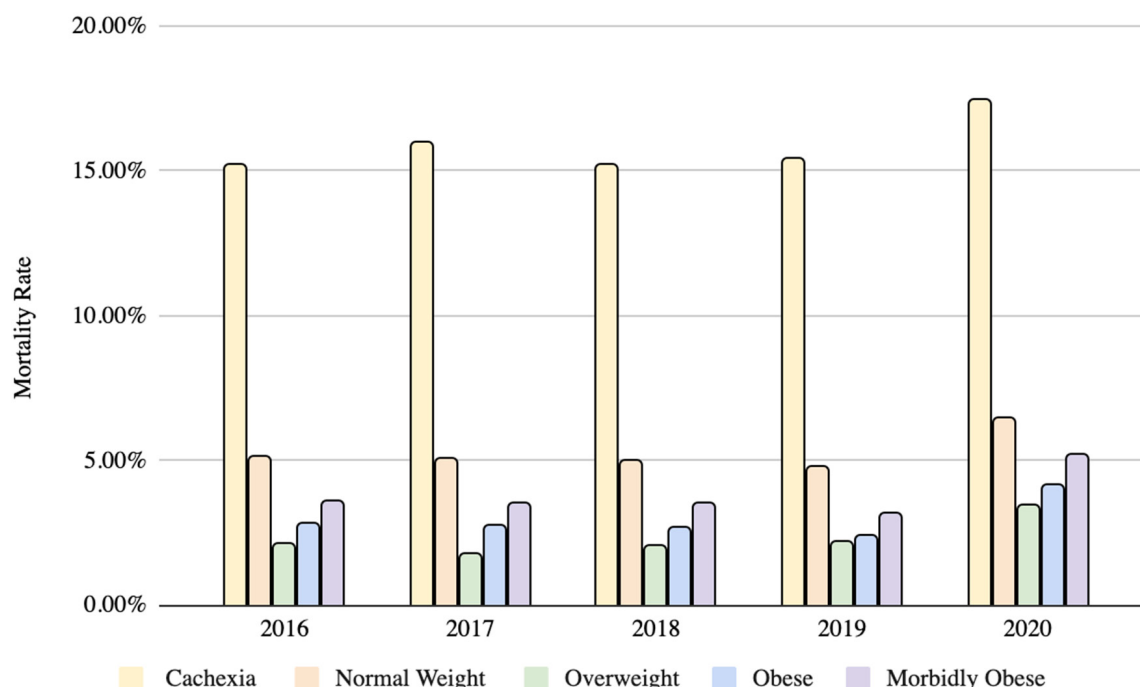


Figure 6. Mortality rate of hospitalized patients with atrial fibrillation and atrial flutter in each weight category across the years 2016 to 2020.

Table 3. Odds ratios with 95% confidence intervals (CI) of hospitalized patients with atrial fibrillation and atrial flutter in each weight category across the years 2016 to 2020

Year	Odds Ratio (95% CI) of Mortality			
	Cachexia	Overweight	Obese	Morbidly Obese
2016	3.35 (3.16-3.56)	0.40 (0.30-0.52)	0.54 (0.51-0.57)	0.69 (0.66-0.72)
2017	3.58 (3.37-3.80)	0.33 (0.26-0.43)	0.53 (0.51-0.56)	0.68 (0.65-0.71)
2018	3.42 (3.24-3.62)	0.40 (0.31-0.50)	0.52 (0.50-0.54)	0.69 (0.67-0.72)
2019	3.62 (3.41-3.83)	0.44 (0.35-0.56)	0.49 (0.46-0.51)	0.65 (0.63-0.68)
2020	3.05 (2.90-3.21)	0.51 (0.42-0.63)	0.63 (0.60-0.65)	0.79 (0.76-0.81)

conclusion [12, 27]. In fact, some research has found that increased weight worsens outcomes and leads to higher mortality rates [23]. Additionally, it has been found that obesity accelerates the progression of Afib, while weight loss through calorie restriction and exercise can lead to a reversal of this progression [28]. Unfortunately, this trend does not hold up with patients who have undergone bariatric surgery, suggesting that other factors beyond the numbers on the scale are at play [11]. As differences in metabolic profile, hormone levels, and other physiological factors may be to blame for this discrepancy, the relationship between obesity, weight loss, and clinical outcomes in those with Afib or Aflut is increasingly complex and

poorly understood [17, 29]. This underscores the need for further research to better clarify these dynamics to provide patients with better guidance and improve health outcomes.

Moreover, there may be additional explanations for why patients with Afib/Aflut and elevated BMIs appear to have better outcomes than those with normal weight. One possible rationale may be selection and lead-time bias, where patients with higher BMIs may receive more frequent medical attention and thus earlier management. However, the literature has also exhibited conflicting thoughts on this, with weight bias and stigmatization shown to negatively influence healthcare quality and out-

comes [30]. Another explanation may be the limitations of BMI as a metric for assessing the impact of obesity on Afib/Aflut. For example, prior studies have employed other measures, including weight-to-height ratio, body composition, or biochemical markers such as leptin, to evaluate this relationship [22]. Although our study's database lacked information on these additional metrics, further research with a similarly large, diverse sample size should compare these measures.

Additionally, this study sought to evaluate the correlational impact of risk factors and patient demographics on mortality in patients with Afib or Aflut. It found that STEMI, Non-STEMI, CKD, and COPD were associated with significantly higher mortality rates in patients with Afib or Aflut across weight categories. This can be explained by the role these conditions play in cardiac remodeling, which can exacerbate the severity and progression of Afib and Aflut [31-34]. On the other hand, smoking, HTN, and old MIs were associated with lower mortality rates across all weight categories. One possible explanation for this decreased risk in those with a past history of MIs could be the aggressive management they receive post-infarction, including pharmacologic therapy as well as cardiac rehabilitation [35]. However, prior studies have shown that a history of MI increases one's likelihood of all-cause mortality, complicating the interpretation of the observations in this study [36, 37]. Similarly, the rationale behind the findings for smoking and HTN is unclear, as prior studies have revealed that both smoking and HTN are also associated with increased all-cause mortality, heightened cardiovascular risk, and higher rates of ischemic events [23, 38]. Although study limitations may contribute to these findings, previous research has also supported similar associations, suggesting factors such as medication use, improved risk factor management, and more frequent screening may play a role [39]. Additionally, the presence of a diagnostic code, which served as our measure in this study, may reflect more vigilant clinical oversight and formally recognized disease. While additional factors including healthcare access and frequency of monitoring may influence these patients' outcomes, further research is essential to better elucidate these complex relationships.

Furthermore, our findings suggest that non-white patients experience higher mortality rates, despite this demographic having a lower risk of developing Afib and Aflut in the first place [40, 41]. These findings are supported by prior studies that revealed similar trends [40, 42-44]. Interestingly, however, a study conducted with Medicare data found that, after adjusting for comorbid conditions, patients who identified as Black no longer displayed an elevated all-cause mortality ratio [42]. Given that our study also adjusted for similar comorbidities, this discrepancy may be explained by our differences in the patient population. Their focus was on older adults with Medicare, while this study evaluated a database containing hospitalized patients of all ages [42]. These differences in findings may be explained by racial and ethnic inequities in healthcare access. For example, patients who identified as Black were disproportionately less likely to utilize outpatient services and more likely to rely on emergency department care when compared to white patients [45-47]. This lower proportion of outpatient visits may limit preventative care and ultimately contribute to worse outcomes for this demographic. Moreover, a large portion of Medicare beneficiaries have an annual income that classifies them as low-income, which can further exacerbate health disparities [48]. In fact, a prior study highlighted how patients with Afib of lower socioeconomic status face higher mortality rates, potentially explaining the findings in the aforementioned study [49]. Nonetheless, our findings highlight the need for better measures to ensure more equitable healthcare and improved outcomes for all patients with Afib and Aflut regardless of demographic factors. Furthermore, as this study lacked detailed social data beyond race and gender, the large, diverse sample size supports broad generalizability and highlights the need for further research on additional, specific socioeconomic indicators in Afib/Aflut outcomes.

Lastly, this study showed that mortality in patients with Afib and Aflut was highest during the year 2020. Notably, this was also the year that the coronavirus disease-19 (COVID-19) pandemic began [32]. Prior studies have shown that COVID-19 and Afib share a bidirectional relationship, as COVID-19 can increase one's risk of developing Afib and Afib can increase mortality in patients with COVID-19 [50-53].

These findings highlight the dangerous interplay of this viral disease and these arrhythmias, emphasizing the need for heightened vigilance in patients who develop both conditions.

Conclusion

Overall, this study reinforces the 'obesity paradox' and highlights how Afib and Aflut patients with elevated BMIs are less likely to experience mortality than those of normal weights. Additionally, those who are cachexic face the highest mortality rates, emphasizing the importance of considering one's BMI in the risk stratification for patients with these arrhythmias. Other independent factors for increased mortality in Afib and Aflut to consider include identifying as non-white and presenting with STEMI, non-STEMI, CKD, and COPD. On the other hand, smoking, HTN, and prior MIs were independently associated with decreased mortality in patients with Afib and Aflut. As the relationship between these factors and Afib/Aflut patient outcomes across weight categories remains complex and poorly understood, continued investigation is required to further elucidate the interaction of these variables. Moreover, as mortality rates were highest during the year the COVID-19 pandemic began, further evaluation of how this viral infection influences Afib and Aflut across varying weights is needed.

Limitations

There are various limitations of this study, including possible reduced generalizability and causality. As the NIS database represents about 20% of hospital discharges in the United States, there is an inherent possibility of reduced generalizability as this dataset does not cover all possible discharges nor address the outpatient setting. However, the large sample size aids in mitigating this issue and permits useful information to still be extracted. Furthermore, as the highest incidence of COVID-19 was in 2021 and our study could only extract data up to the year 2020, this study may not fully capture the role the COVID-19 pandemic played in mortality for patients with Afib and Aflut [54]. Additionally, as this was a retrospective investigation, a direct causal relationship between the evaluated variables and weight categories cannot be explicitly made. Moreover, the use of a database may result in

missing data, and reliance on ICD-10 codes could introduce misclassification bias due to insufficient or inaccurate diagnosing of weight categories or other variables, potentially reducing the reliability of our findings. However, the extremely large sample size aims to mitigate these limitations by enhancing statistical power and overall generalizability.

Disclosure of conflict of interest

None.

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