




Association between atrial fibrillation and bundle branch block

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Abstract

Background: The association between atrial fibrillation (Afib) and sinus and AV nodal dysfunction has previously been reported. However, no data are available regarding the association between Afib and bundle branch block (BBB).

Methods: Patient data were obtained from the Nationwide Inpatient Sample (NIS) database between years 2009 and 2015. Patients with a diagnosis of Afib and BBB were identified using validated International Classification of Diseases, 9th revision, and Clinical Modification (ICD-9-CM) codes. Statistical analysis using the chi-square test and multivariate linear regression analysis were performed to determine the association between Afib and BBB.

Results: The total number of patients with BBB was 3,116,204 (1.5%). Patients with BBB had a mean age of 73.5 ± 13.5 years, 53.6% were males, 39.1% belonged to the age group ≥ 80 years, and 72.9% were Caucasians. The prevalence of Afib was higher in the BBB group, as compared to the non-BBB group (29% vs 11.8%, p value $< .001$). This association remained significant in multivariate regression analysis with an odds ratio of 1.25 (CI: 1.24-1.25, $P < .001$). Among the subtypes of BBB, Afib was comparatively more associated with RBBB (1.32, CI 1.31-1.33, p value $< .0001$) than LBBB (1.17, CI 1.16-1.18, p value $< .0001$). The mean cost was higher among Afib with BBB, compared with Afib patients without BBB (\$15 795 vs \$14 391, p value $< .0001$). There was no significant difference in the mean length of stay (5.6 vs 5.9 days, p value $< .0001$) or inpatient mortality (4.9% vs 4.8%).

Conclusion: This study demonstrates that prevalence of Afib is higher in patients with BBB than without BBB. Cost are higher for Afib patients with BBB, compared to those without BBB, with no significant increase in mortality or length of stay.

KEYWORDS

arrhythmias, atrial fibrillation, bundle branch block, conduction abnormalities

1 | INTRODUCTION

Bundle branch block (BBB) usually develops as a consequence of degenerative changes.¹ BBB can lead to ventricular dyssynchrony and an increased risk of developing heart failure.² The presence of BBB is associated with increased morbidity and mortality in patients with coronary artery disease and congestive heart failure.^{3–8}

Atrial fibrillation (Afib) is the most common arrhythmia in clinical practice.⁹ Afib is associated with increased risk of developing conduction abnormalities like sinus node and atrioventricular (AV) nodal dysfunction.^{10–13} However, data regarding the association between Afib and BBB are lacking. We conducted a retrospective cohort study utilizing the National Inpatient Sample (NIS) database to assess the association between Afib and BBB, and determine the impact of the presence of BBB on clinical outcomes in Afib patients.

2 | METHODS

The study was conducted using the National Inpatient Sample (NIS) database, the largest inpatient database in the United States. Data included in this study were obtained between 2009 and 2015. NIS is a part of the Healthcare Cost and Utilization Project (HCUP) developed by the Agency for Healthcare Research and Quality. NIS comprises data from 48 states and represents more than 97% of the United States population, with an average of 7–8 million discharges yearly. It excludes data from long-term acute care facilities and rehabilitation centers. Its utilization has been described in further detail in previous studies.^{14,15}

NIS provides de-identified data that protect the confidentiality of the patients. Therefore, IRB approval was not required. Afib and BBB cases were identified using International Classification of Disease, Nine Edition, Clinical Modification (ICD-9-CM) codes. All ICD codes included in the study for Bundle Branch Blocks and Afib are listed in Table 1. Exclusion criteria included patients less than 18 years. Baseline characteristics including age, gender, race, body mass index (BMI), socioeconomic status, type of insurance, comorbidities, geographic distribution, and hospital-level characteristics (teaching status, outcomes, and disposition were obtained; Table 2). The primary outcome of our study was to determine the association between Afib and BBB. Secondary outcomes were to compare the

mean hospitalization cost, in-hospital mortality, and length of stay between Afib patients with and without BBB.

The data were entered and analyzed in SAS statistical software version 9.4. Categorical data were calculated as frequency and percentages. The continuous variables were presented as mean and standard deviation or median. Categorical variables were analyzed using the Pearson Chi-square test. Continuous variables were analyzed using the independent Student's t-test. Differences in the mean of continuous variables were analyzed using the Pearson Chi-square test. Logistic regression analysis was further performed to identify the association between Afib and BBB in multivariate analysis. Logistic regression data were reported as odds ratios with 95% confidence interval. A p value of < .05 was considered as statistically significant.

3 | RESULTS

NIS database included a sample of 246 379 065 hospital admissions between the years 2009–2015. After excluding <18 years, we obtained a sample size of 207 421 616 admissions for our study. Hospitalizations were divided into two groups—hospitalizations with and without the presence of BBB based on ICD-9 codes; 3 116 204 hospitalizations had a diagnosis of BBB (1.5% of total sample size) and 204 438 167 (98.5%) did not have BBB (Figure S1). A comparison of baseline patient-level characteristics between the two groups of BBB and no BBB is shown in Table 2. Hospitalizations with bundle branch block were older with a mean age of 73.5 ± 13.5 years, and more likely to be male (53.6% vs. 40.5%, p value < .001). The hospitalizations in BBB group were more likely to be Caucasian (72.9% vs. 62.6%, p value < .001). The prevalence of Afib was significantly higher in the BBB group (29% vs. 11.8%, p value < .001). The prevalence of other comorbidities such as hypertension, diabetes mellitus, hypothyroidism, myocarditis, obstructive sleep apnea (OSA), congestive heart failure (CHF), cardiomyopathy, coronary artery disease, renal failure, and collagen vascular disease were also significantly higher in the BBB group (Table 2). The patient-level characteristics were further extended toward the major subtypes, that is, left bundle branch block (LBBB), and right bundle branch block (RBBB) (Table S1). LBBB was present in 44.2% of males, comparatively lower than RBBB with 62.1%. It showed that LBBB was more prevalent in females while RBBB is the otherwise (Table S1).

The association between Afib and BBB was further assessed using multiple regression analysis (Table 3). Despite adjusting for all other comorbidities significant in univariate analysis, Afib remained statistically significantly associated with the presence of BBB (odds ratio 1.25, CI 1.24–1.25, p value < .0001). Among the subtypes of BBB, Afib was comparatively more associated with RBBB (odds ratio of 1.32, CI 1.31–1.33, p value < .0001) than LBBB (odds ratio 1.17, CI 1.16–1.18, p value < .0001) (Table 4).

We divided all hospitalizations with a diagnosis of Afib two groups—with BBB and without BBB, to assess the clinical impact of the presence of BBB in Afib. Secondary clinical outcomes are shown

TABLE 1 ICD 9 codes used for the identification of bundle branch blocks

ICD codes used	
Left bundle branch block (LBBB)	426.3
Right bundle branch block (RBBB)	426.4
Bilateral BBB	426.53
Bifascicular BBB	426.51, 426.52
Atrial fibrillation	I48.0, I48.1, I48.2, I48.91
Coronary arterial disease	I20, I21, I22, I24.0, I24.8, I24.9, I25.1
Obstructive sleep apnea	G47.33

TABLE 2 Patient-level characteristics of BBB versus without BBB in 2009-2015 patients

Characteristics	BBB	No BBB	P value
N = 207 421 616	N = 2 983 449 (1.4%)	N = 204 438 167 (98.6%)	
Age			<.0001
Mean years (SD)	73.5 ± 13.5	57.1 ± 20.6	
Gender			<.0001
Male	1 598 183 (53.6%)	82 780 406 (40.5%)	
Female	1 385 129 (46.4%)	121 541 222 (59.5%)	
*missing-116 676			
Age groups			<.0001
18-34	38 299 (1.3%)	40 690 620 (19.9%)	
35-49	128 729 (4.3%)	32 034 321 (15.7%)	
50-64	524 255 (17.6%)	48 278 764 (23.6%)	
65-79	1 124 714 (37.7%)	49 395 133 (24.2%)	
≥80	1 167 452 (39.1%)	34 039 329 (16.6%)	
Race			<.0001
Caucasians	2 174 726 (72.9%)	128 004 387 (62.6%)	
African-Americans	262 090 (8.8%)	27 980 390 (13.7%)	
Others	546 579 (18.3%)	48 445 642 (23.7%)	
*missing-7802			
AHRQ comorbidities			
Coronary arterial disease	1 519 774 (50.9%)	41 392 468 (20.2%)	<.0001
Afib	866 245 (29%)	24 173 315 (11.8%)	<.0001
Cardiomyopathy	419 304 (14%)	5 981 638 (2.9%)	<.0001
Myocarditis	1 290 (0.04%)	27 053 (0.01%)	<.0001
Obstructive sleep apnea	232 663 (7.8%)	9 543 528 (4.7%)	<.0001
Congestive heart failure	490 472 (16.4%)	16 788 751 (8.2%)	<.0001
Valvular disease	272 665 (9.1%)	6 911 392 (3.4%)	<.0001
Chronic pulmonary disease	756 427 (25.3%)	36 613 892 (17.9%)	<.0001
Hypertension	2 138 993 (71.7%)	98 635 340 (48.2%)	<.0001
Diabetes mellitus	1 015 931 (34%)	46 882 161 (22.9%)	<.0001
Hypothyroidism	490 210 (16.4%)	22 603 619 (11.1%)	.0001
Renal failure	667 557 (22.4%)	23 384 757 (11.4%)	<.0001
Alcohol abuse	96 917 (3.2%)	9 546 051 (4.7%)	<.0001
RA/Collagen vascular disease	96 449 (3.2%)	5 359 058 (2.6%)	<.0001

Abbreviations: Afib, atrial fibrillation; BBB, bundle branch bundle; IQR, interquartile range; SD, standard deviation.

in Table 5. The mean hospitalization cost was significantly higher in the BBB group (\$15 795 vs. \$14 391, p value < .001). Similarly, the hospitalization cost was higher in Afib with RBBB (15 011 vs 14 429) and Afib with LBBB (16 589 vs. 14 402) (Tables S2, S3).

There was no significant difference in inpatient mortality and the length of stay between the two groups, Afib with BBB vs Afib without BBB, that is (4.9% vs. 4.8%) and (5.6% vs. 5.9%), respectively. Similarly, Afib with RBBB and LBBB also do not have a significant difference in inpatient mortality and the length of stay (Table S3).

The annual trends of mean hospitalization cost, length of stay in the hospital, and inpatient mortality were compared between Afib and BBB and Afib without BBB, as shown in Figures 1, 2 and 3, respectively. The

mean cost of the hospital stays gradually increased in both groups over the study period and was found the maximum in the year 2015. The cost was consistently higher in Afib with BBB over all the years (Figure 1). The hospital length of stay was maximum in the Afib without BBB group compared to Afib with BB. The length of stay was maximum in the years 2009 and 2010 in the group of without BBB (Figure 2). The inpatient mortality remained fairly consistent in the non-BBB group, but varied significantly in the BBB group over the years with the highest mortality rate in the year 2012 (Figure 3). Similar trends were observed in terms of mortality among the groups of LBBB and RBBB with Afib. Highest mortality rate was observed in LBBB with Afib in the year 2015 (Figure S2), while in the Afib with RBBB group, it was observed in the year 2011.

TABLE 3 Odds ratio of the bundle branch blocks after adjusting with other independent variables

	ODDS ratio	95% Wald confidence limits	P value
Atrial fibrillation	1.25	1.24-1.26	<.0001
Coronary artery disease	2.13	2.12-2.17	<.0001
Cardiomyopathy	3.50	3.48-3.51	<.0001
Myocarditis	3.66	3.45-3.87	<.0001
Obstructive sleep apnea	1.42	1.41-1.45	<.0001
Hypothyroidism	0.99	0.98-1.00	.06
Renal failure	1.03	1.02-1.04	<.0001
Valvular disease	1.45	1.43-1.46	<.0001
Hypertension	1.25	1.24-1.26	<.0001
Diabetes mellitus	1.08	1.07-1.09	<.0001
Congestive heart failure	1.44	1.42-1.47	<.0001
Collagen vascular disease	1.02	1.01-1.03	.0006
Alcohol abuse	1.14	1.13-1.15	<.0001
Age	1.03	1.02-1.05	<.0001

4 | DISCUSSION

Our study utilized the NIS database study to identify the association between Afib and the presence of BBB. There was an association between Afib and BBB in a very large sample size in both univariate and multivariate analyses (odds ratio 1.25, CI 1.24-1.25 p value < .0001). To the best of our knowledge, there are no data available regarding the association between Afib and presence of BBB. Furthermore, our study showed that the presence of BBB with Afib is associated with increased mean hospitalization cost, but no significant difference in inpatient mortality or mean length of stay. The mean hospitalization cost in Afib with BBB remained consistently higher over the study period.

The prevalence of BBB increases with age, with an estimated prevalence of 3.2% in patients >52 years old.^{2,16} The average age for occurrence of BBB has been reported to be 70 ± 10 years.^{17,18} Afib has been reported to cause electrophysiological remodeling of the atrial tissue, sinus nodal tissue, and AV nodal tissue.¹⁰⁻¹² The high atrial firing rate of Afib is believed to cause structural and electrophysiological remodeling of the atrial and sinoatrial nodal tissue. AV node plays a vital role in Afib by slowing down the conduction of impulses to the ventricles. However, constant bombarding of the AV nodal tissue by rapid atrial depolarizations has been shown to cause electrophysiological remodeling of the AV node as well.¹¹ Afib may have the same mechanism for causing remodeling in bundle branches as well. Our retrospective study only shows an association and does not prove causation. Further studies are required to provide a better understanding of the underlying mechanisms and nature of the relationship between the two entities.

TABLE 4 Multiple regression analysis of Types of BBB with all of below risk factors in the table

	LBBB ODDS ratio, 95% CI, P value	RBBB ODDS ratio, 95% CI, P value
Atrial fibrillation	1.17, 1.16-1.18, <.0001	1.32, 1.31-1.33, <.0001
Coronary artery disease	2.39, 2.38-2.40, <.0001	1.87, 1.86-1.88, <.0001
Cardiomyopathy	6.09, 6.06-6.12, <.0001	1.39, 1.38-1.41, <.0001
Myocarditis	3.69, 3.42-3.97, <.0001	3.49, 3.19-3.82, <.0001
Obstructive sleep apnea	1.19, 1.18-1.20, <.0001	1.63, 1.62-1.65, <.0001
Hypothyroidism	1.08, 1.07-1.09, .0001	0.92, 0.91-0.93, <.0001
Renal failure	1.02, 1.01-1.03, <.0001	1.05, 1.04-1.06, <.0001
Valvular disease	1.32, 1.31-1.34, <.0001	1.54, 1.53-1.56, <.0001
Hypertension	1.29, 1.28-1.30, <.0001	1.21, 1.20-1.22, <.0001
Diabetes mellitus	1.04, 1.03-1.05, <.0001	1.13, 1.12-1.14, <.0001
Congestive heart failure	1.82, 1.89-1.91, <.0001	1.80, 1.79-1.81, <.0001
Collagen vascular disease	1.00, 0.99-1.01, .73	1.02, 1.01-1.03, <.0001
Alcohol abuse	0.98, 0.96-9.99, <.68	1.28, 1.27-1.30, <.0001
AGE	1.04, 1.03-1.05, <.0001	1.03, 1.02-1.04, <.0001

The secondary outcomes of the study assessed the effect of BBB on inpatient mortality, length of stay, and total cost of treatment in patients with Afib. The presence of BBB in patients with Afib can affect clinical management, such as misdiagnosing Afib with a rapid ventricular rate in the presence of BBB as ventricular tachycardia, and challenges with the use of QTc prolonging anti-arrhythmic agents such as sotalol or dofetilide. Our study showed that the mean cost of hospitalization was significantly higher in Afib patients with BBB, compared with Afib patients without BBB (Table 5). This difference was consistent over the duration of the study period, years 2009-2015 (Figure 1). This may be related to reduced use of anti-arrhythmic drugs in BBB patients due to fear of QTc prolongation and increased utilization of advanced procedures.

The mean length of stay was not different between the two groups, with a median length of stay of 4 days in both groups. However, there was a difference in length of stay in the year 2009. But the curves gradually converged with no difference in the year 2015 (Figure 2). There was a gradual decrease in length of stay in Afib with BBB and a gradual increase in length of stay in Afib

TABLE 5 Clinical outcomes of patients with Afib with BBB versus Afib without BBB from years 2009 to 2015

Characteristics	Afib with BBB	Afib without BBB	P value
N = 25 039 561	N = 866 246 (3.5%)	N = 24 173 315 (96.5%)	
Age			<.0001
Mean \pm SD, in y	77.6 \pm 10.9	75.5 \pm 12	
Gender			<.0001
Male	480 695 (55.5%)	12 121 042 (50.1%)	
Female	385 516 (44.5%)	12 050 541 (49.8%)	
*missing-1767			
Age groups			<.0001
18-34	2 409 (0.3%)	121 866 (0.5%)	
35-49	12 846 (1.5%)	633 330 (2.6%)	
50-64	91 082 (10.5%)	3 554 336 (14.7%)	
65-79	319 979 (36.90%)	9 288 551 (38.4%)	
\geq 80	439 930 (50.8%)	10 575 232 (43.7%)	
Race			<.0001
Caucasians	686 958 (79.3%)	18 369 496 (75.9%)	
African-Americans	49 002 (5.7%)	1 832 557 (7.6%)	
Others	130 261 (15%)	3 970 554 (16.4%)	
*missing-733			
Elixhauser comorbidities			
Coronary arterial disease	486 041 (56.1%)	10 387 062 (42.9%)	<.0001
Cardiomyopathy	151 212 (17.5%)	2 159 378 (8.9%)	<.0001
Myocarditis	142 (0.02%)	2 566 (0.01%)	<.0001
Obstructive sleep apnea	79 619 (9.2%)	20 597 103 (8.5%)	<.0001
Congestive heart failure	196 287 (22.7%)	5 803 492 (24%)	<.0001
Valvular disease	107 569 (12.4%)	2 388 952 (9.9%)	<.0001
Chronic pulmonary disease	248 271 (28.7%)	6 748 841 (27.9%)	<.0001
Hypertension	637 113 (73.5%)	17 128 392 (70.9%)	<.0001
Diabetes mellitus	294 125 (33.9%)	7 964 849 (32.9%)	<.0001
Hypothyroidism	165 850 (19.1%)	4 474 350 (18.5%)	<.0001
Renal failure	246 447 (28.4%)	5 872 465 (24.3%)	<.0001
Alcohol abuse	22 300 (2.6%)	711 225 (2.9%)	<.0001
Collagen vascular disease	28 163 (3.2%)	826 955 (3.4%)	<.0001
Outcomes			
In-hospital mortality	43 025 (4.9%)	1 169 403 (4.8%)	<.0001
*missing-14 460			
Length of stay, mean \pm SD, in days	5.6 \pm 5.5	5.9 \pm 6.7	<.0001
Total hospitalization cost, \$, mean \pm SD, in days	15 795 \pm 18 632	1 4391 \pm 19 937	<.0001

Abbreviations: Afib, atrial fibrillation; BBB, bundle branch bundle; IQR, interquartile range; SD, standard deviation.

patients without BBB. These findings may be again attributable to increased use of Afib ablation in patients with BBB (usually overnight stay in an uncomplicated procedure) and increased use of drugs such as sotalol or dofetilide in non-BBB patients (usually require 3 days hospital stay for loading).

Afib and BBB have both been previously shown as independent predictors of all-cause mortality.^{3,19} However, our study of a very large sample size showed no significant effect of presence of BBB

on overall inpatient mortality in Afib patients (4.9% in Afib with BBB vs. 4.8% in Afib without BBB). Our study evaluated the incidence of mortality, hospital length of stay, and hospitalization costs in Afib with LBBB and RBBB groups as compared to no BBB groups. Hospitalization cost was higher in Afib group having LBBB and RBBB as compare to no BBB block. There was no huge difference in term of mortality and length of stay in Afib having LBBB and RBBB group as compare to the Afib without LBBB and RBBB groups.



FIGURE 1 Compares trends of mean hospitalization costs in Afib patients with and without BBB. The hospitalization costs are consistently higher in Afib patients with LBBB over all the years. There is a gradual increase in mean hospitalization cost in both the groups

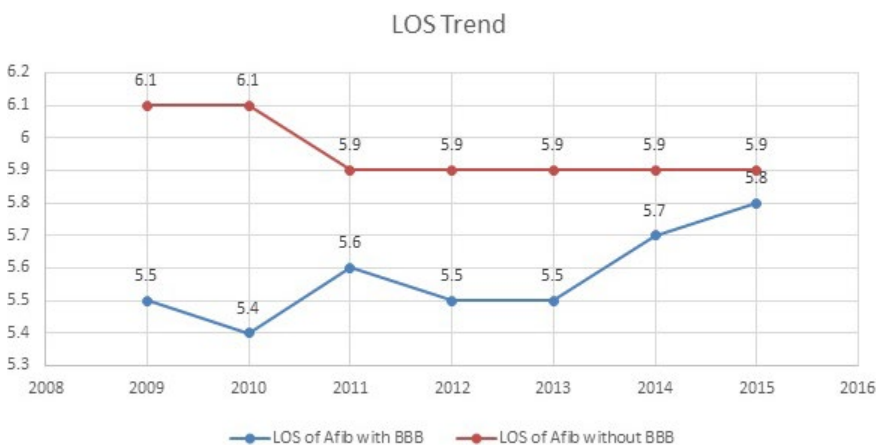


FIGURE 2 Compares the mean length of hospital stay in Afib patients with and without BBB. LOS was higher in the group Afib without BBB in the years 2009 and 2010

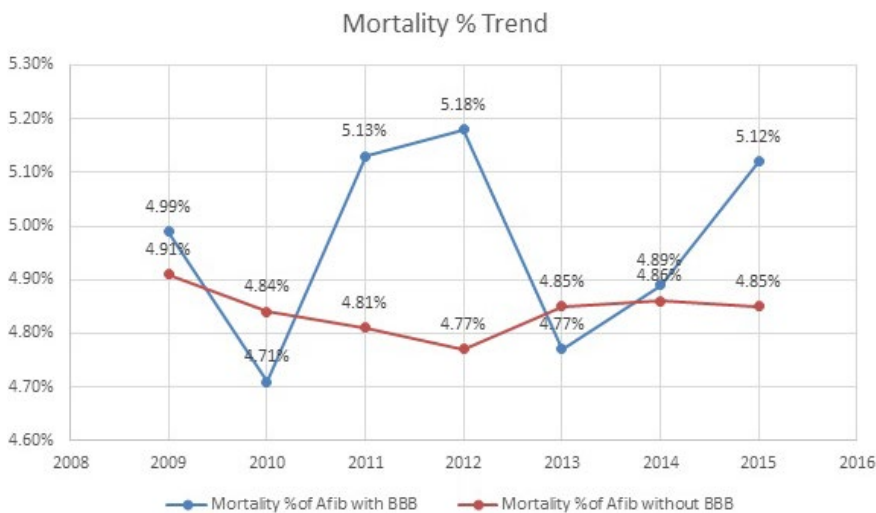


FIGURE 3 Compares the trends of inpatient mortality among Afib patients with and without BBB. The mortality stayed consistent in the non-BBB group, but varied significantly in the BBB group with highest mortality in year 2012

5 | LIMITATIONS

Our study has several limitations. First, it is a retrospective study using NIS database, leading to usual limitations such as recording bias and selection bias. Second, this study only proves an association between Afib and BBB, and does not provide any

information regarding causation. Also, the ventricular rate during Afib was not available, limiting our understanding of the rate effect of Afib on the remodeling of the bundle branches. Another limitation section of our study is massive data, and small changes in means or median can be significant merely because of the large sample size.

6 | CONCLUSIONS

Our study over a large NIS database from years 2009 to 2015 showed a significant association between the presence of Afib and BBB. The presence of BBB was associated with higher hospitalization costs in Afib but did not increase length of stay or inpatient mortality. Future studies are required to further assess the relationship between Afib and BBB, determining causation, and identifying short- and long-term effects of the presence of BBB on clinical outcomes in Afib patients.

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CONFLICTS OF INTEREST

Authors bear no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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