Association of atrial fibrillation and various cancer subtypes

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Abstract

Background: Studies have shown that the incidence of atrial fibrillation (AF) in cancer is most likely due to the presence of inflammatory markers. The purpose of our study is to determine the association of AF with different cancer subtypes and its impact on in-hospital outcomes.

Methods: Data were obtained from the National Inpatient Sample database between 2005 and 2015. Patients with various cancers and AF were studied. ICD-9-CM codes were utilized to verify variables. Patients were divided into three age groups: Group 1 (age < 65 years), Group 2 (age 65-80 years), and Group 3 (age > 80 years). Statistical analysis was performed using Pearson chi-square and binary logistic regression analysis to determine the association of individual cancers with AF.

Results: The prevalence of AF was 14.6% among total study patients (n = 46 030 380). After adjusting for confounding variables through multivariate regression analysis, AF showed significant association in Group 1 with lung cancer (odds ratio, OR = 1.92), multiple myeloma (OR = 1.59), non-Hodgkin lymphoma (OR = 1.55), respiratory cancer (OR = 1.55), prostate cancer (OR = 1.20), leukemia (OR = 1.12), and Hodgkin’s lymphoma (OR = 1.03). In Group 2, the association of AF with multiple myeloma (1.21), lung cancer (OR = 1.15), Hodgkin lymphoma (OR = 1.15), non-Hodgkin lymphoma (OR = 1.12), respiratory cancer (OR = 1.08), prostate cancer (OR = 1.06), leukemia (OR = 1.14), and colon cancer (OR = 1.01) were significant. In Group 3, AF showed significant association with non-Hodgkin lymphoma (OR = 1.06), prostate (OR = 1.03), leukemia (OR = 1.03), Hodgkin’s lymphoma (OR = 1.02), multiple myeloma (OR = 1.01), colon cancer (OR = 1.01), and breast cancer (OR = 1.01). The highest mortality was found in lung cancer in age <80 and prostate cancer in age >80.

Conclusion: In patients age <80 years, AF has significant association with lung cancer and multiple myeloma, whereas in patients age >80 years, it has significant association with non-Hodgkin lymphoma and prostate cancer. In patients age <80 years, increased mortality was seen in AF with lung cancer and in patients age >80 years, increased mortality was seen in those with AF and prostate cancer.
1 | INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in the United States. Its prevalence and incidence increase every year.\(^1\)\(^2\) AF has been associated with an increased risk of stroke, myocardial infarction, dementia, heart failure, CKD, venous thromboembolism, and mortality.\(^3\)\(^4\)

Risk factors associated with an increased risk of atrial fibrillation include older age, obesity, diabetes, cardiomyopathy, myocarditis, pneumonia, COPD, pulmonary embolism (PE), hypertension, and cancer.\(^3\)\(^4\) The bidirectional relation of AF and cancer is not well known and needs further research studies. Individual factors that influence the development of atrial fibrillation are genetics, aging, hypoxia, electrolyte abnormalities, systemic inflammation, and neurohormonal changes. Cancer treatment, including chemotherapy and radiation therapy, may lead to structural damage that increases the risk of atrial fibrillation. Chemotherapy is also strongly associated with inducing systemic inflammation.

Our study hypothesized that certain cancers (increase systemic inflammation, electrolyte abnormalities, and neurohormonal changes which) increase the development of AF compared with other cancers. The purpose of our study is to determine the association of AF with different cancers and its subsequent impact on in-hospital outcomes.

2 | METHODS

2.1 | Data source

The present study was conducted using the National Inpatient Sample (NIS) database, the largest inpatient database in the United States. The NIS is a part of the Healthcare Cost and Utilization Project developed by the Agency for Healthcare Research and Quality. The data were collected from 48 states. NIS represents more than 97% of the US population, and the data have an average of 7-8 million discharges each year. NIS data are obtained from more than 7 million hospital stays each year, and it estimates more than 35 million hospitalizations nationally. Each admission contains information on patient characteristics, including demographics, comorbidities, complications, as well as the primary and secondary discharge diagnoses. This has been explained in detail in previous studies.\(^5\)\(^6\) The International Classification of Disease, 9th revision, Clinical Modification (ICD 9-CM) codes were used to identify diagnosis in the NIS database.\(^7\)

Data included in this study were obtained between January 2005 and October 2015, as data before October 2015 included the use of ICD-9-CM codes. NIS data include the charge-to-cost ratio. Charges showed the amount the hospital bills for services while cost represents how much the service costs including utilities cost, supplies, and wages. The study cohort was derived from a deidentified and publicly available database; hence, the study was considered exempt from the formal approval of the institutional review board.

2.2 | Diagnosis codes for AF and cancer

Clinical Classifications Software (CCS) codes from 11 to 43 which are for nonspecific and specific malignant cancers were used for extraction of specific cancers which were included in our study. The NIS data provide up to 30 CCS diagnoses for each inpatient visit.

We extracted cancer and AF hospitalizations using appropriate ICD-9-CM diagnosis codes in primary or secondary diagnosis (Table S1). Furthermore, we documented the following comorbidities: hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, deficiency anemia, hypothyroidism, coronary artery disease, smoking, obesity, and chronic kidney disease (CKD) in our study cohort. The present study included prostate cancer, lung cancer, colon cancer, other respiratory/intrathoracic cancer, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma (NHL), leukemia, and multiple myeloma (MM).

2.3 | Subgroups

The data were separated into three groups based on age as follows: Group 1: 18-64, Group 2: 65-80, and Group 3: >80 years. Figure 1 illustrates the patient distribution into three groups.

2.4 | Figures

In figures, the individual cancers were merged to create four groups: gastrointestinal, respiratory, hematologic, and prostate cancers. The
prevalence and mortality incidence of each group with AF is shown in the graphs.

2.5 | Statistical analysis

All the data extraction and analysis were done using SAS statistical software, version 9.4. All continuous variables were compared using Student’s t test, and categorical variables were analyzed using the Pearson chi-square test. Categorical data were presented as weighted frequency in percentages. Continuous data were presented as mean ± standard deviation. A P-value of <.05 was considered statistically significant. Three models of multivariate regression analysis were made. After adjusting for age, hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, hypothyroidism, thyrotoxicosis, coronary artery disease, obesity, and collagen vascular disease, the association of AF with different cancers was analyzed. Logistic regression data were reported as odds ratios with a 95% confidence interval.

The primary outcome of our study was to determine which cancer had the highest association of AF. Secondary outcomes included in-hospital mortality, length of stay, and hospitalization costs.

3 | RESULT

Between the years 2005 and 2015, a total number of 46 897 124 adult hospitalizations were identified with a cancer diagnosis. After excluding 866 744 patients of <18 years, 40 030 380 were included in the study. The incidence of AF in these cancer patients was 14.6%.

3.2 | Comparison of cancer and AF coincidence/odds ratio in subgroups

In Group 1, the prevalence of AF was highest in lung cancer (20.8% vs 10.9%) followed by prostate cancer (8.1% vs 6.5%), Hodgkin’s lymphoma (1.9% vs 1.6%), NHL (7.5% vs 6.6%), leukemia (5.6% vs 6.6%), and multiple myeloma (3.2% vs 1.9%) (Table 1). In Group 2, the prevalence of AF was highest in lung cancer (18.8% vs 15.9%) followed by prostate cancer (17.5% vs 16.4%), NHL (6.2% vs 5.6%), leukemia (4.8% vs 4.3%), multiple myeloma (1.8% vs 1.5%) and Hodgkin’s lymphoma (0.5% vs 0.4%) (Table 2). AF prevalence was lower in Group 2 compared with Group 1. In Group 3, the prevalence of AF was found to be elevated only in prostate cancer (21.3% vs 20.8%), NHL (5.3% vs 5.0%), and leukemia (4.8% vs 4.7%) (Table 3).

The study results showed AF prevalence with prostate, respiratory, hematologic, and GI cancers (Figure 2). The study showed that with increasing age, the difference between the prevalence of AF with cancer groups compared with those without AF is not statistically significant (Figure 2). In patients aged >80, the prevalence of AF with prostate, respiratory, hematologic, and GI cancers is not statistically significant to those without AF.

The association of AF with cancer was assessed using multivariate regression analysis (Table 4). Each independent predictor, including AF, was analyzed using multivariate regression analysis, and results were reported as an odds ratio with a 95% confidence interval. After multivariate regression analysis, in Group 1, a significantly higher odds of having AF was seen with lung cancer (1.92), multiple myeloma (1.59), NHL (1.55), respiratory cancer (1.55), prostate cancer (1.20), leukemia (1.12), and Hodgkin’s lymphoma (1.03) (Table 4). Pancreatic (0.79), colon (0.93), breast (0.70), and thyroid (0.6) cancers showed decreased association with AF. In Group 2, AF was significantly associated with multiple myeloma (1.21), lung cancer (1.15), Hodgkin’s lymphoma (1.15), NHL (1.12), respiratory cancer (1.08), prostate cancer
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3.1 Comparison of secondary outcomes (mortality, length of stay, cost) in subgroups

The secondary clinical outcomes of the study are shown in Tables 1-3. In all age groups, the mortality, hospitalization costs, and length of stay was higher in cancer patients with AF compared with those without AF. In Group 1, mortality was highest in lung cancer (36.9% vs 24.7%), followed by leukemia (9.9% vs 8%), MM (4.3% vs 2.5%),

(Continues)
| Characteristics         | Cancers with AF | Cancers without AF | P-value |
|-------------------------|-----------------|--------------------|---------|
| **Gender**              |                 |                    |         |
| Male                    | 1 792 995 (58.3%) | 7 924 758 (50.8%)  | <.0001  |
| Female                  | 1 283 525 (41.7%) | 7 679 425 (49.2%)  |         |
| *Missing – 4003*        |                 |                    |         |
| **Race**                |                 |                    | <.0001  |
| Caucasians              | 2 353 070 (76.5%) | 10 654 565 (68.3%) |         |
| African-Americans       | 176 748 (5.7%)   | 1 445 919 (9.3%)   |         |
| Others                  | 546 735 (17.8%)  | 3 506 546 (22.5%)  |         |
| *Missing – 1123*        |                 |                    |         |
| **BMI**                 |                 |                    | <.0001  |
| **Cancers**             |                 |                    |         |
| Colon                   | 325 335 (10.65%) | 1 659 302 (10.63%) | .003    |
| Pancreas                | 49 049 (1.6%)    | 362 896 (2.3%)     | <.0001  |
| Lung                    | 578 309 (18.8%)  | 2 477 666 (15.9%)  | <.0001  |
| Other respiratory       | 6469 (0.24%)     | 31 572 (0.21%)     | .005    |
| Breast                  | 447 345 (14.5%)  | 2 483 820 (15.9%)  | <.0001  |
| Prostate                | 538 850 (17.5%)  | 2 564 687 (16.4%)  | <.0001  |
| Thyroid                 | 36 886 (1.2%)    | 199 940 (1.3%)     | <.0001  |
| Hodgkins                | 14 896 (0.5%)    | 59 563 (0.4%)      | <.0001  |
| Non-Hodgkins            | 190 080 (6.2%)   | 874 527 (5.6%)     | <.0001  |
| Leukemia                | 147 709 (4.8%)   | 671 398 (4.3%)     | <.0001  |
| Multiple myeloma        | 84 372 (2.7%)    | 373 153 (2.4%)     | <.0001  |
| **AHRQ comorbidities**  |                 |                    |         |
| Coronary arterial disease | 1 127 748 (36.6%) | 3 714 817 (23.8%) | <.0001  |
| Obstructive sleep apnea | 213 675 (6.9%)   | 553 450 (3.5%)     | <.0001  |
| Congestive heart failure | 223 895 (7.3%)   | 363 096 (2.3%)     | <.0001  |
| Valvular disease        | 274 048 (8.9%)   | 573 855 (3.7%)     | <.0001  |
| Chronic pulmonary disease | 989 132 (32.1%) | 3 745 872 (24%)    | <.0001  |
| Hypertension            | 2 051 799 (66.7%) | 9 586 878 (61.4%) | <.0001  |
| Diabetes mellitus       | 967 174 (31.4%)  | 4 251 791 (27.2%)  | <.0001  |
| Hypothyroidism          | 470 337 (15.3%)  | 2 017 313 (12.9%)  | <.0001  |
| Renal failure           | 569 866 (18.5%)  | 1 796 852 (11.5%)  | <.0001  |
| Obesity                 | 312 301 (10.1%)  | 1 167 477 (7.5%)   | <.0001  |
| Alcohol abuse           | 70 535 (2.3%)    | 323 822 (2.1%)     | <.0001  |
| Drug abuse              | 12 832 (0.4%)    | 84 183 (0.5%)      | <.0001  |
| RA/Collagen Vascular Disease | 93 517 (3%)   | 430 026 (2.8%)     | <.0001  |
| **Outcomes**            |                 |                    |         |
| In-hospital mortality   | 183 767 (5.9%)   | 637 237 (4.1%)     | <.0001  |
| *Missing – 8544*        | Adjusted odds ratio* | 1.31 (1.30-1.32) | <.0001  |
| Total hospitalization cost, $ (mean ± SD) | 15 994 ± 20 353 | 13 144 ± 16 108 | <.0001  |

*Adjusted for race, gender, AHRQ comorbidities
Table 3: Patient-Level Characteristics of Cancers with atrial fibrillation versus Cancers without atrial fibrillation in 2005-2015 of Patients age > 80

| Characteristics                  | Cancers with AF | Cancers without AF | P-value |
|----------------------------------|-----------------|--------------------|---------|
| **N = 10 385 908**               | **N = 2 947 870 (28.4%)** | **N = 7 438 038 (71.6%)** |         |
| Gender                           |                 |                    |         |
| Male                             | 1 478 166 (50.1%) | 3 457 198 (46.5%)  | <.0001  |
| Female                           | 1 469 620 (49.9%) | 3 980 158 (53.5%)  |         |
| *Missing – 767                   |                 |                    |         |
| Race                             |                 |                    |         |
| Caucasians                       | 2 379 865 (80.7%) | 5 444 503 (73.2%)  | <.0001  |
| African-Americans                | 99 393 (3.4%)   | 495 031 (6.7%)     |         |
| Others                           | 468 505 (15.9%) | 1 497 883 (20.1%)  |         |
| *Missing – 729                   |                 |                    |         |
| Cancers                          |                 |                    |         |
| Colon                            | 455 176 (15.4%) | 1 146 301 (15.4%)  | .23     |
| Pancreas                         | 34 103 (1.2%)   | 120 725 (1.6%)     | <.0001  |
| Lung                             | 276 181 (9.48%) | 699 986 (9.43%)    | .03     |
| Other respiratory                | 4187 (.1%)      | 11 659 (0.2%)      | <.0001  |
| Breast                           | 590 118 (20%)   | 1 494 638 (20.1%)  | <.0001  |
| Prostate                         | 628 403 (21.3%) | 1 529 972 (20.6%)  | <.0001  |
| Thyroid                          | 24 876 (0.8%)   | 62 965 (0.8%)      | .67     |
| Hodgkins                         | 7187 (0.26%)    | 17 142 (0.24%)     | <.0001  |
| Non-Hodgkins                     | 155 224 (5.3%)  | 372 270 (5%)       | <.0001  |
| Leukemia                         | 142 707 (4.8%)  | 351 605 (4.7%)     | <.0001  |
| Multiple myeloma                 | 52 551 (1.8%)   | 133 623 (1.8%)     | .13     |
| AHRQ Comorbidities               |                 |                    |         |
| Coronary arterial disease        | 1 148 642 (38.9%) | 2 269 628 (30.5%)  | <.0001  |
| Obstructive sleep apnea          | 84 818 (2.9%)   | 116 202 (1.6%)     | <.0001  |
| Cardiomyopathy                   | 182 271 (6.2%)  | 196 675 (2.6%)     | <.0001  |
| Valvular disease                 | 372 294 (12.6%) | 503 057 (6.8%)     | <.0001  |
| Chronic pulmonary disease        | 760 224 (25.8%) | 1 560 519 (20.9%)  | <.0001  |
| Hypertension                     | 2 029 505 (68.8%) | 4 957 509 (66.6%)  | <.0001  |
| Diabetes mellitus                | 685 548 (23.3%) | 1 684 862 (22.6%)  | <.0001  |
| Hypothyroidism                   | 606 761 (20.6%) | 1 325 029 (17.8%)  | <.0001  |
| Renal failure                    | 689 878 (23.4%) | 1 303 194 (17.5%)  | <.0001  |
| Obesity                          | 102 487 (3.5%)  | 213 728 (2.9%)     | <.0001  |
| Alcohol abuse                    | 21 989 (0.74%)  | 50 743 (0.72%)     | <.0001  |
| Drug abuse                       | 4187 (0.1%)     | 11 639 (0.2%)      | <.0001  |
| RA/Collagen vascular disease     | 84 424 (2.9%)   | 201 790 (2.7%)     | <.0001  |
| Outcomes                         |                 |                    |         |
| In-hospital mortality            | 190 809 (6.5%)  | 363 563 (4.9%)     | <.0001  |
| *Missing – 6380                  | Adjusted odds ratio*<sup>a</sup> 1.23 (1.21-1.23) |                  |         |
| Length of stay, days (mean ± SD) | 5.9 ± 5.8       | 5.3 ± 5.6          | <.0001  |
| Total hospitalization cost, $ (mean ± SD) | 12 338 ± 14 079 | 10 678 ± 12 538   | <.0001  |

*Adjusted for race, gender, AHRQ comorbidities
prostate cancer (2.6% vs 2.1%), and Hodgkin's disease (1.8% vs 1.3%), (Table 5). In Group 2, the highest mortality was found in lung cancer (33.3% vs 30.2%), followed by prostate cancer (10.4% vs 8.8%), leukemia (8.4% vs 7.9%), NHL (7.4% vs 6.5%), MM (3.7% vs 3.3%), and Hodgkin's lymphoma (0.6% vs 0.5%) (Table 5). The mortality in Group 3 was highest in prostate cancer (18% vs 17.5%), followed by colon cancer (14.7% vs 13.9%), breast cancer (15.5% vs 13.9%), NHL (6.7% vs 6.3%), and thyroid cancer (0.7% vs 0.6%) (Table 5).

The figures further report the mortality incidence. Figure 3 shows AF mortality incidence in prostate, respiratory, hematologic, and GI cancers. In Figure 3, age <65 (Group 1), mortality was highest in the AF group with prostate, respiratory, and hematologic cancers. At age 65-80, the mortality incidence although elevated in the AF group with prostate, respiratory, and hematologic cancers. Group 3 (age >80) shows that patients with AF and prostate cancer have higher mortality.

4 | DISCUSSION

This case-control study evaluates the risk of atrial fibrillation in 11 different cancer subtypes. Our study’s core finding was that in patients younger than age 65, AF has the highest association with lung cancer followed by MM and NHL compared with other cancers. At age 65-80, AF’s association was most significant in MM, followed by lung and Hodgkin’s cancers. In the age group >80, the
The strongest association of AF was seen with NHL, followed by prostate cancer and leukemia. The mortality, length of stay, and hospitalization costs were higher in all three age groups with AF and cancer compared with those without AF. The highest incidence of mortality with AF in age <65 years was seen with lung cancer followed by leukemia, whereas in age 65-80 years, lung cancer followed by prostate cancer, and in age >80 years, the highest mortality incidence of AF was found in prostate cancer followed by colon cancer.

The study of the association between cancers and cardiovascular diseases is referred to as oncocardiology. Several clinical studies have demonstrated increased levels of pro-inflammatory markers in both AF and cancers. A case-control study found higher levels of CRP in patients with AF than without AF. Another population-based cohort study found elevated CRP associated with the presence of AF. These findings imply that inflammation can induce the structural and electrophysiological remodeling responsible for arrhythmias. Inflammation and autonomic dysfunction have been suggested to underlie this association. Several clinical studies have demonstrated increased levels of pro-inflammatory markers in both AF and cancers. A case-control study found higher levels of CRP in patients with AF than without AF. Another population-based cohort study found elevated CRP associated with the presence of AF. These findings imply that inflammation can induce the structural and electrophysiological remodeling responsible for arrhythmias. Inflammation and autonomic dysfunction have been suggested to underlie this association. Studies have shown higher CRP levels in cancer patients compared with controls. Autonomic dysfunction is another mechanism that may lead to the association of AF and cancer. An imbalance between the sympathetic and the parasympathetic system activities has been
associated with AF. This autonomic dysfunction is also found to some degree in cancer patients. The pain and emotional stress associated with cancer results in increased sympathetic activity predisposing to atrial fibrillation. Emotional distress also explains the increased risk of AF within 90 days after a cancer diagnosis. A new cancer diagnosis can be anxiety-provoking resulting in increased emotional distress in this period. Studies have shown an increased risk of AF secondary to subclinical hyperthyroidism which alters the structure and function of the heart. It has been hypothesized that tumors release thyroid hormones including thyroid-stimulating hormones (TSH) and triiodothyronine (T3). Therefore, an abnormal release of thyroid hormone-like peptides could be a possible mechanism for AF in cancer. Hypercoagulability associated with a neoplastic state leading to pulmonary microembolism is an additional mechanism leading to the development of AF.

Our study showed the association of AF in all cancer subtypes. As discussed above, this increased risk of AF is possibly due to an inflammatory state and autonomic dysfunction in cancer patients. A meta-analysis by Yuan et al suggested an increased risk of AF in cancer patients. Jacobson et al showed an increased incidence of AF in all cancer subtypes evaluated. A case-control study by Erichson et al concluded that colorectal cancer patients are at increased risk of AF compared with controls. The same study also showed an increased risk for all types of cancers. In our study, we evaluated the association of AF with multivariate regression analysis. In multivariate regression analysis, we adjusted for hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, hypothyroidism, thyrotoxicosis, coronary artery disease, obesity, and collagen vascular disease. We divided the patients into three groups based on age as age has a significant effect on AF prevalence. Previous studies have shown that age is an independent risk factor for AF development. Our study showed that the association of AF in those <65 years was highest in lung cancer followed by MM, NHL, and other respiratory cancer/intrathoracic cancers. At age 65-80 years, the association of AF was highest in MM followed by lung cancer and Hodgkin lymphoma. The odds ratio of lung cancer and MM in age 65-80 years is lower compared with those <65, which shows that age has an impact on the development of AF. Our finding supports the study findings of Jacobson et al which showed lung cancer as the strongest risk for AF. In age >80 years, the association of AF was highest in NHL and prostate cancer. Colon cancer and breast cancer showed a significant association with the development of AF in age >80 years, although it showed a decreased risk of AF in age <80 years. Wassermeth-Smoller et al similarly showed an increased association of AF with breast and colorectal cancer. In our study, lung cancer and MM had the strongest association with AF. Lung cancer increases the risk of AF due to its aggressive nature which may be responsible for the increased inflammatory effect. The anatomical location of lung cancer increases the risk of cardiotoxicity during radiation therapy as well as direct invasion. Similarly, paraneoplastic syndromes associated with lung cancer may be a possible mechanism for the increased risk of AF.

Two cancer subtypes, pancreatic and thyroid cancer, had decreased association of AF after adjusting for the above variables. The prevalence of AF in thyroid and pancreatic cancer in our population was lower than the majority of other cancers. Our finding that pancreatic cancer does not significantly increase the risk of AF is contradicting to the previous study by Jacobson et al. Jacobson et al also similarly noted nonsignificant association between endocrine cancer and risk of developing AF likely secondary to under power study. The development of AF in pancreatic cancer may be low because of the higher mortality of pancreatic cancer. Due to high mortality, these patients often die prior to developing AF. Chemotherapy can induce AF through cardiotoxicity. Our study lacked adjustment for treatment which may have resulted in confounding.

Our study also evaluated the effect of AF on mortality in cancer patients. We found higher mortality in cancer with AF group compared with those without AF group. In our study, the highest mortality of AF in those <65 years was seen with lung cancer followed by leukemia, in age >65-80 years, lung cancer followed by prostate cancer, and in age >80 years, prostate cancer followed by colon cancer.

The implications from these findings are that close surveillance and early management of atrial fibrillation may serve to reduce the burden of healthcare costs. Before application to clinical practice, further studies with better designs are necessary.

5 | LIMITATION

Our study has several limitations. The nature of the database limited can determine whether the patient developed AF before or after the development of their respective cancers. As our study sample is large and representative of US hospitals, after adjusting for other comorbidities, we were able to demonstrate that most of the cancers could be an independent risk factor of AF. We relied on diagnosis codes for cancer subtypes and AF, which could potentially lead to exposure and outcome misclassification, however, both ICD codes for AF and cancers are validated and used in several studies. We did not investigate the severity and stages of cancers which could affect the development of AF. In addition, we did not study the effect of chemotherapy on the development of AF. Our study did not investigate the pathophysiology and mechanism behind the association of AF and cancer types and the higher mortality associated with cancer; however, possible hypothesis will be that certain cancer cause more systemic inflammation in different age groups and that is why they increase the development of AF. Finally, the patient population was limited to inpatient, and cancer patients without hospitalization were not be included in this study.

6 | CONCLUSION

In the age group <80, our study found that lung cancer and multiple myeloma have a strong association with AF, whereas thyroid and
pancreatic cancers have no association with AF at any age. In age >80, NHL and prostate cancer have a significant association with AF. The highest mortality incidence in age <80 was found in lung cancer and age >80 was seen in prostate cancer.

CONFLICT OF INTEREST
None.

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

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