Published in final edited form as:
Am Heart J. 2013 June ; 165(6): 949–955.e3. doi:10.1016/j.ahj.2013.03.020.

Atrial Fibrillation Among Medicare Beneficiaries Hospitalized With Sepsis: Incidence and Risk Factors

Allan J. Walkey, MD, MSc[*], **Melissa A. Greiner, MS**[†], **Susan R. Heckbert, MD, PhD**[‡], **Paul N. Jensen, BA**[‡], **Jonathan P. Piccini, MD, MHS**[†,§], **Moritz F. Sinner, MD**[‖,¶], **Lesley H. Curtis, PhD**[†,§], and **Emelia J. Benjamin, MD, ScM**[**]

[*]Pulmonary Center and the Section of Pulmonary and Critical Care Medicine, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts

[†]Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina

[‡]Department of Epidemiology, University of Washington School of Public Health, Seattle, Washington

[§]Department of Medicine, Duke University School of Medicine, Durham, North Carolina

[‖]Cardiovascular Research Center, Massachusetts General Hospital, Charlestown, Massachusetts

[¶]Department of Medicine I, University Hospital Grosshadern, Ludwig Maximilians University, Munich, Germany

[**]Sections of Cardiovascular Medicine and Preventive Medicine, Department of Medicine, Boston University School of Medicine, and Department of Epidemiology, Boston University School of Public Health, Boston, Massachusetts

Abstract

Background—Newly-diagnosed atrial fibrillation (AF) during severe sepsis is associated with increased risks of in-hospital stroke and mortality. However, prevalence, incidence, and risk factors associated with AF during the sepsis syndromes are unclear.

Methods—We identified patients with preexisting, newly-diagnosed, or no AF in a nationally representative 5% sample of Medicare beneficiaries hospitalized with sepsis between 2004 and 2007. We identified multivariable-adjusted demographic and clinical characteristics associated with development of newly-diagnosed AF during a sepsis hospitalization.

Results—A total of 60,209 beneficiaries had a sepsis hospitalization. Mean age was 80.2 years, 44.4% were men, and 83.1% were white. AF occurred during 25.5% (95% CI, 25.2–25.9) of sepsis hospitalizations, including 18.3% (18.0%–18.7%) with preexisting AF and 7.2% (7.0%–7.4%) with newly-diagnosed AF. Patients with sepsis requiring intensive care had a greater risk of

Address for correspondence: Allan J. Walkey, MD, MSc, 72 East Concord Street, R-304, Boston, MA 02118-2526; telephone: 617-638-4844; alwalkey@bu.edu.

Financial Disclosures: Dr Piccini reported receiving research support from Bayer HealthCare, Boston Scientific, and Johnson & Johnson; and receiving personal income for participation on an advisory board for Sanofi-Aventis. Dr Curtis reported receiving research support from Johnson & Johnson. Drs Piccini and Curtis have made available online detailed listings of financial disclosures (http://www.dcri.duke.edu/about-us/conflict-of-interest/). No other disclosures were reported.

newly-diagnosed AF (10.7%; 95% CI, 10.3–11.1%) compared with patients who did not require intensive care (4.4%; 4.2–4.5%; $P < .001$). In multivariable analysis, factors associated with newly-diagnosed AF during sepsis included older age, white race, acute organ dysfunction, intensive care unit admission, mechanical ventilation, right heart catheterization, diagnosis of endocarditis, and coronary artery bypass graft surgery. Cardiovascular comorbid conditions generally were not associated with increased risk for newly-diagnosed AF during sepsis.

Conclusions—AF is common among critically ill patients with sepsis. Acute factors, rather than preexisting cardiovascular comorbid conditions, are associated with increased risk for newly-diagnosed AF during sepsis, suggesting that mechanisms of newly-diagnosed AF during sepsis may differ from the general population of patients with AF.

Keywords

Atrial Fibrillation; Hospitalization; Incidence; Prevalence; Sepsis

The sepsis syndromes are a leading cause of death[1] and arise from the systemic inflammatory response to infection.[2] Severe sepsis is associated with increased risk for newly-diagnosed atrial fibrillation (AF).[3] Patients who experience newly-diagnosed AF during severe sepsis have increased risks for in-hospital stroke and mortality.[3–5] Notably, more than 50% of patients with newly-diagnosed AF during severe sepsis do not survive to hospital discharge.[3] Thus far, incidence and risk factors for newly-diagnosed AF during the spectrum of sepsis syndromes have not been well characterized.

Clarifying the epidemiology of newly-diagnosed AF that occurs during sepsis may provide insights into its poorly understood mechanisms. Epidemiological insights may help to identify strategies for AF prevention, monitoring or risk modification during sepsis. To better define the burden of AF complicating the sepsis syndromes, we investigated the prevalence, incidence, and clinical and demographic features associated with AF during sepsis in a nationally representative 5% sample of Medicare beneficiaries.

Methods

We obtained a nationally representative 5% sample of Medicare standard analytic files and corresponding denominator files from the Centers for Medicare & Medicaid Services (CMS) for 2004 through 2007. We chose September 30, 2007, as the termination date of the study, because inpatient diagnosis of AF after this date was no longer considered a “major complication or comorbidity” by CMS, a change that might bias estimates of incidence after the change.

Inpatient files contain institutional claims for facility costs covered under Medicare Part A, and outpatient files contain claims from institutional outpatient providers. Carrier files contain noninstitutional provider claims for services covered under Medicare Part B. Denominator files contain beneficiary demographic data and information about program eligibility and enrollment. We eliminated invalid records and restricted the analysis to beneficiaries living in the United States and enrolled in fee-for-service Medicare.

Patients

No gold standard exists for identification of sepsis in administrative data;[6] therefore, we used previously published validated methods. For the primary analysis, we selected a coding strategy with a high degree of specificity[3, 7] to identify patients for whom a diagnosis of septicemia or sepsis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 038.xx, 995.91, or 995.92) was reported on an inpatient

claim.[8] For the secondary analysis, we selected a strategy with greater sensitivity[7] to identify patients with severe sepsis on the basis of (*a*) a diagnosis of infection, including pneumonia, bacteremia or fungemia, gastrointestinal infection, urinary tract infection, skin or soft tissue infection, or endocarditis and (*b*) a diagnosis of renal, circulatory, respiratory, neurologic, hematologic, metabolic, or hepatic organ failure (Appendix Table 1) on an inpatient claim.[9]

For both analyses, we selected the first sepsis hospitalization for patients who had multiple hospitalizations, excluding hospitalizations with length of stay <1 day. We required that patients be at least 67 years of age and have continuous enrollment in fee-for-service Medicare for at least 2 years before the discharge date.

Outcomes

We identified beneficiaries with an AF or atrial flutter diagnosis on the sepsis hospitalization claim (*ICD-9-CM* code 427.31 or 427.32). We used claims files from 1991 through 2007 to identify a previous diagnosis of AF on an inpatient claim or 2 outpatient or physician claims within 365 days. As reported previously,[10, 11] we required 2 outpatient claims to improve the specificity of the AF classification by reducing the impact of rule-out diagnoses. Using these criteria, we defined beneficiaries as having newly-diagnosed disease if they had an inpatient AF claim concomitant with the index sepsis hospitalization but did not have a prior inpatient or 2 prior outpatient AF claims. Beneficiaries with AF claims both before and during the index sepsis hospitalization were defined as having preexisting AF.

Patient Characteristics

Medicare beneficiaries report race and ethnicity at the time of enrollment; we used the categories “black” and “white” and combined all others as “other”.[12] We derived rural classifications from Rural-Urban Commuting Area scores based on zip code of residence.[13, 14] We identified comorbid conditions using well-validated coding algorithms[15, 16] and searched all claims in the 365-day period preceding the sepsis hospitalization admission date for chronic obstructive pulmonary disease, diabetes mellitus, heart failure, hypertension, myocardial infarction, renal disease, and valvular heart disease (Appendix Table 1). Because conditions such as heart failure, myocardial infarction, and valvular heart disease may result from sepsis,[17] we included only claims made before the sepsis hospitalization to maintain the temporal relations between potential comorbid conditions and sepsis. We also created variables to indicate the presence of established[18, 19] AF risk factors for hypertension, valvular heart disease, and heart failure.

Acute Factors Associated With Sepsis Hospitalization

We searched *ICD-9-CM* diagnosis and procedure codes on the sepsis hospitalization claim to identify acute factors associated with the hospitalization (Appendix Table 1). Acute factors included number and types of acute organ failures (renal, circulatory, respiratory, neurologic, hematologic, metabolic, and hepatic), critical care interventions (mechanical ventilation, new-onset dialysis, and right heart catheterization), types of infection (pneumonia, bacteremia or fungemia, gastrointestinal infection, urinary tract infection, skin or soft tissue infection, and endocarditis), and common cardiac surgeries (coronary artery bypass graft, aortic valve replacement, and mitral valve replacement). We searched for inpatient revenue center codes 200 through 209 to identify intensive care admissions, and we calculated length of stay (ie, discharge date minus admission date). We identified patients who died in the hospital using the patient status code from the inpatient sepsis claim and the death date from the denominator file.

Statistical Analysis

We used descriptive statistics to evaluate patient characteristics and factors associated with sepsis hospitalizations in the primary and secondary cohorts. We present categorical variables as percentages and continuous variables as means with standard deviations or medians with interquartile ranges.

In each sepsis cohort, we calculated the age- and sex-adjusted proportions of patients with newly-diagnosed and preexisting AF in each year.[20] The pooled population for each constituted the standard population for age and sex adjustments. We used Cochran-Mantel-Haenszel nonzero correlation tests to test for temporal trends in sepsis-associated AF diagnosis from 2004 to 2007. We estimated the range of patients affected yearly with AF during sepsis using the specific primary analysis cohort as a lower bound and the sensitive secondary analysis cohort as the upper bound, and we divided these values by 0.05 to extrapolate from the 5% sample to the Medicare population. We calculated age- and sex-adjusted estimates of the proportion of patients with preexisting and newly-diagnosed AF in predefined subgroups with hypertension, valvular disease, heart failure and combination of these comorbidities.

Among patients with no prior AF claims, we used multivariable modified Poisson regression models to estimate relative risks[21, 22] for factors associated with newly-diagnosed disease during a sepsis hospitalization. We adjusted for age, sex, race, comorbid conditions, rural/urban location, geographic region, acute factors associated with the sepsis hospitalization, and year of the sepsis hospitalization. In sensitivity analysis, we excluded patients who underwent cardiac surgery[23] and those who were diagnosed with endocarditis[24]—conditions that confer high risk for acute AF—during the sepsis hospitalization.

We used SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina) for all analyses. We chose a 2-tailed threshold of .05 for statistical significance. The Institutional Review Board of the Duke University Health System approved the study.

This work was supported by grants R01HL092577, RC1HL101056, and R01HL102214 from the National Heart, Lung, and Blood Institute; and by grant R01AG028321 from the National Institute on Aging. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Results

We identified 60,209 beneficiaries with sepsis in the primary analysis during the 3.75-year study period. Table 1 shows baseline characteristics and acute factors in the primary analysis cohort. Patients had a median of 1 acute organ failure (interquartile range, 0–2) and a length of stay of 7 days (4–14); 24.7% died during the hospitalization. In the secondary analysis cohort, baseline characteristics were similar (Appendix Table 2).

Overall, 25.5% of patients (95% CI, 25.2%–25.9%) had an AF diagnosis during the sepsis hospitalization; 18.3% (18.0%–18.7%) had preexisting disease, and 7.2% (7.0%–7.4%) had newly-diagnosed disease. Although the age- and sex-adjusted proportion of patients with preexisting disease increased slightly from 2004 to 2007, the proportion with newly-diagnosed AF did not change (Table 2). Patients admitted to intensive care had greater prevalence and incidence of AF than patients without intensive care (Table 3). Newly-diagnosed and preexisting AF risks in the secondary analysis cohort were similar to those in the primary cohort (Appendix Table 3). We estimate that AF affects 80,000 to 170,000 Medicare beneficiaries with sepsis annually, and that 20,000 to 50,000 experience newly-diagnosed AF during a sepsis hospitalization.

Among patients with standard risk factors for AF, age- and sex-adjusted proportions with preexisting AF were higher than the proportions with newly-diagnosed AF (Figure). Table 4 shows factors associated with newly-diagnosed AF in multivariable analysis. Associated demographic characteristics included older age and white race. Acute factors included acute organ dysfunction, endocarditis, coronary artery bypass graft surgery, admission to intensive care, mechanical ventilation, and right heart catheterization. Most cardiovascular conditions and risk factors, such as heart failure, myocardial infarction, hypertension, and valvular heart disease, were not significantly associated with increased risk for newly-diagnosed AF in the context of sepsis. History of chronic obstructive pulmonary disease, diabetes mellitus, or renal disease was associated with decreased risk of AF during sepsis. Sensitivity analyses that excluded endocarditis and patients after cardiac surgery were consistent with findings from the primary analysis (Appendix Table 4).

Discussion

We observed that AF occurs in more than 25% of Medicare beneficiaries hospitalized with sepsis, with 7.2% of sepsis patients experiencing newly-diagnosed AF. In addition, we demonstrated that newly-diagnosed AF during sepsis has a different risk factor profile than the general population of patients with AF. Factors associated with newly-diagnosed AF during sepsis included older age, white race, and greater severity of acute illness. However, most standard risk factors for AF, including heart failure, myocardial infarction, and valve disease, [18, 19] were not associated with newly-diagnosed AF in patients hospitalized with sepsis. Our findings suggest that newly-diagnosed AF during sepsis may have different mechanisms than AF in other settings.

Consistent with the association of newly-diagnosed AF with greater acute illness severity, age- and sex-adjusted incidence of AF in patients not admitted to intensive care (4.4%) was significantly lower than in patients who required intensive care (10.7%). The estimates of intensive care-associated incidence are within the range of AF incidence (6%–31%) reported in small, single-center studies of patients admitted to intensive care with severe sepsis.[4, 5] The wide range of AF incidence during severe sepsis in previous studies may be related to differences in sepsis severity, intensive care unit type, demographic characteristics, methods for ascertaining AF diagnoses, or random variation in small samples. Our results demonstrate that about 1 in 20 Medicare beneficiaries hospitalized with sepsis outside of intensive care experience newly-diagnosed AF, compared with 1 in 10 beneficiaries with sepsis requiring intensive care.

Postadmission characteristics representing greater severity of acute illness and race were associated with newly-diagnosed AF. Associations between acute factors such as new organ failures, intensive care, mechanical ventilation, and right heart catheterization support the hypothesis that abnormalities that characterize sepsis may act as triggers of AF. A substantially higher risk for atrial fibrillation associated with white race has been previously well -described in studies of community-dwelling adults[19, 25] and in post-operative patients.[26] Recent genetic studies have determined that in admixed African Americans, AF risk is higher in those with more European ancestry.[27] The possibility that genetic variation interacts with potential AF triggers of sepsis warrants further study.

In contrast, many cardiovascular comorbid conditions previously identified as AF risk factors—such as hypertension, heart failure, and diabetes mellitus[18, 19]—were not associated with increased risk of newly-diagnosed AF in patients with sepsis. The lack of associations between cardiovascular comorbid conditions and increased risk for newly-diagnosed AF in sepsis was suggested in previous studies,[4, 5] though prior studies did not have statistical power to detect risk factors with moderate effect sizes for newly-diagnosed AF. In contrast

to our findings, the previous population-based study of newly-diagnosed AF during severe sepsis in California found an association between heart failure and newly-diagnosed AF.[3] However, temporality between heart failure and severe sepsis (ie, comorbidity vs. complication when both diagnoses are coded as "present on admission") in the California State Inpatient Database was less clear than the timing of comorbid conditions identified through past claims in our present study. Factors associated with an acute illness such as sepsis may overwhelm the AF risks associated with traditional cardiovascular comorbid conditions. Acute, and potentially modifiable, risk factors are likely important to the development of AF during sepsis and warrant further evaluation.

Paradoxically, many comorbid conditions previously described as AF risk factors (eg, diabetes mellitus,[19, 28] chronic obstructive pulmonary disease,[29] and renal disease[30]) were associated with decreased risk for newly-diagnosed AF during sepsis. Patients with diabetes mellitus are at lower risk for inflammatory complications of sepsis, such as acute respiratory distress syndrome.[31] Other potential explanations include the possibility that patients with standard cardiovascular AF risk factors may have previously acquired preexisiting AF and thus were not at risk for newly-diagnosed AF (ie, were depleted), that patients with newly-diagnosed AF during sepsis may have had less contact with the health care system and fewer opportunities for comorbidity claims prior to the sepsis hospitalization, or that diabetes mellitus, chronic obstructive pulmonary disease, or renal disease may confer protection against the development of AF through unclear mechanisms. Further study using prospective ascertainment of comorbid conditions is warranted to explore these possible explanations.

Our study has several limitations. First, strategies for identifying AF and sepsis in claims data are highly specific, but insensitive;[7, 16] we likely underestimated the burden of AF during sepsis. Second, because available slots for coding are limited, diagnoses that may not affect hospital reimbursement may be crowded out in favor of better-reimbursed diagnoses. For this reason, we adjusted for cardiovascular conditions diagnosed before the sepsis hospitalization, and we chose acute factors that increase reimbursement (such as procedures). However, we may not have accounted for some clinically important risk factors, such as obesity, that have previously been shown to be poorly ascertained with administrative data.[32] Third, timing of events during the index hospitalization could not be ascertained in claims data. Therefore, we did not include potential comorbidity claims during the hospitalization that may have occurred after sepsis onset, which may have resulted in underestimation of comorbidity prevalence.

Furthermore, we could not confirm that AF occurred during sepsis, only during a hospitalization with sepsis. In addition, we not exclude the possibility that patients with newly-diagnosed AF may have had undetected AF present prior to the sepsis hospitalization.[33] Validated algorithms that might discriminate between paroxysmal, persistent, and permanent atrial fibrillation using Medicare claims data are not currently available. Prospective studies are needed to confirm the findings. Finally, the results do not necessarily reflect characteristics of AF during sepsis in patients not enrolled in fee-for-service Medicare, such as younger patients and those enrolled in private insurance plans.

Conclusion

Our findings indicate that each year about 20,000 to 50,000 Medicare beneficiaries experience newly-diagnosed AF during a sepsis hospitalization. In addition, we demonstrate that acute factors, rather than standard AF risk factors, are associated with increased risk for newly-diagnosed AF during sepsis. Currently, little evidence guides prevention, management, and prognostication of sepsis-associated AF,[34] a condition associated with

increased short-term health care resource use, in-hospital stroke risk, and high in-hospital mortality.[3–5] Investigations that further enhance understanding of the mechanisms underlying newly-diagnosed AF during sepsis may provide important insights into novel strategies for its prevention and treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Damon M. Seils, MA, Duke University, provided editorial assistance and prepared the manuscript. Mr Seils did not receive compensation for his assistance apart from his employment at the institution where the study was conducted.

Abbreviations

AF	atrial fibrillation
CMS	Centers for Medicare & Medicaid Services
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification

References

1. Minino AM, Xu J, Kochanek KD, Tejada-Vera B. Death in the United States, 2007. NCHS Data Brief. 2009; (26):1–8. [PubMed: 20018136]
2. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest. 1992; 101:1644–1655. [PubMed: 1303622]
3. Walkey AJ, Wiener RS, Ghobrial JM, et al. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. JAMA. 2011; 306:2248–2254. [PubMed: 22081378]
4. Salman S, Bajwa A, Gajic O, et al. Paroxysmal atrial fibrillation in critically ill patients with sepsis. J Intensive Care Med. 2008; 23:178–183. [PubMed: 18443011]
5. Christian SA, Schorr C, Ferchau L, et al. Clinical characteristics and outcomes of septic patients with new-onset atrial fibrillation. J Crit Care. 2008; 23:532–536. [PubMed: 19056018]
6. Wilhems SB, Huss FR, Granath G, et al. Assessment of severe sepsis in Sweden using different ways of abstracting International Classification of Disease codes: difficulties with methods and interpretation of results. Crit Care Med. 2010; 38:1442–1449. [PubMed: 20400903]
7. Iwashyna TJ, Odden A, Rohde J, et al. Identifying Patients With Severe Sepsis Using Administrative Claims: Patient-Level Validation of the Angus Implementation of the International Consensus Conference Definition of Severe Sepsis. Med Care. 2012 in press.
8. Martin GS, Mannino DM, Eaton S, et al. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003; 348:1546–1554. [PubMed: 12700374]
9. Angus DC, Linde-Zwirble WT, Lidicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001; 29:1303–1310. [PubMed: 11445675]
10. Klabunde CN, Potosky AL, Legler JM, et al. Development of a comorbidity index using physician claims data. J Clin Epidemiol. 2000; 53:1258–1267. [PubMed: 11146273]
11. Welch HG, Sharp SM, Gottlieb DJ, et al. Geographic variation in diagnosis frequency and risk of death among Medicare beneficiaries. JAMA. 2011; 305:1113–1118. [PubMed: 21406648]

12. Arday SL, Arday DR, Monroe S, et al. HCFA's racial and ethnic data: current accuracy and recent improvements. Health Care Financ Rev. 2000; 21:107–116. [PubMed: 11481739]
13. [Accessed February 1, 2012] Rural Urban Commuting Area Codes. [WWAMI Rural Health Research Center web site]. Available at: http://depts.washington.edu/uwruca/ruca-uses.php/
14. [Accessed February 1, 2012] Rural-Urban Commuting Area Codes. [Economic Research Services, US Department of Agriculture web site]. Available at: http://www.ers.usda.gov/Data/RuralUrbanCommutingAreaCodes/
15. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005; 43:1130–1139. [PubMed: 16224307]
16. Birman-Deych E, Waterman AD, Yan Y, et al. Accuracy of ICD-9-CM codes for identifying cardiovascular and stroke risk factors. Med Care. 2005; 43:480–485. [PubMed: 15838413]
17. Merx MW, Weber C. Sepsis and the heart. Circulation. 2007; 116:793–802. [PubMed: 17698745]
18. Schnabel RB, Sullivan LM, Levy D, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. Lancet. 2009; 373:739–745. [PubMed: 19249635]
19. Chamberlain AM, Agarwal SK, Folsom AR, et al. A clinical risk score for atrial fibrillation in a biracial prospective cohort (from the Atherosclerosis Risk in Communities [ARIC] study). Am J Cardiol. 2011; 107:85–91. [PubMed: 21146692]
20. Brenner H, Arndt V, Gefeller O, et al. An alternative approach to age adjustment of cancer survival rates. Eur J Cancer. 2004; 40:2317–2322. [PubMed: 15454258]
21. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004; 159:702–706. [PubMed: 15033648]
22. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol. 2005; 162:199–200. [PubMed: 15987728]
23. Hogue CW Jr, Creswell LL, Gutterman DD, et al. Epidemiology, mechanisms, and risks: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. Chest. 2005; 128:9S–16S. [PubMed: 16167659]
24. Gaca JG, Sheng S, Daneshmand MA, et al. Outcomes for endocarditis surgery in North America: a simplified risk scoring system. J Thorac Cardiovasc Surg. 2011; 141:98–106. e1-2. [PubMed: 21168017]
25. Jensen PN, Thacker EL, Dublin S, et al. Racial differences in the incidence of and risk factors for atrial fibrillation in older adults: The Cardiovascular Health Study. J Am Geriatr Soc. 2013; 61:276–280. [PubMed: 23320758]
26. Bhave PD, Goldman LE, Vittinghoff E, et al. Incidence, predictors, and outcomes associated with postoperative atrial fibrillation after major noncardiac surgery. Am Heart J. 2012; 164:918–924. [PubMed: 23194493]
27. Marcus GM, Alonso A, Peralta CA, et al. European ancestry as a risk factor for atrial fibrillation in African Americans. Circulation. 2010; 122:2009–2015. [PubMed: 21098467]
28. Benjamin EJ, Levy D, Vaziri SM, et al. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA. 1994; 271:840–844. [PubMed: 8114238]
29. Buch P, Friberg J, Scharling H, et al. Reduced lung function and risk of atrial fibrillation in the Copenhagen City Heart Study. Eur Respir J. 2003; 21:1012–1016. [PubMed: 12797497]
30. Winkelmayer WC, Patrick AR, Liu J, et al. The increasing prevalence of atrial fibrillation among hemodialysis patients. J Am Soc Nephrol. 2011; 22:349–357. [PubMed: 21233416]
31. Moss M, Guidot DM, Steinberg KP, et al. Diabetic patients have a decreased incidence of acute respiratory distress syndrome. Crit Care Med. 2000; 28:2187–2192. [PubMed: 10921539]
32. Goff SL, Pekow PS, Markenson G, et al. Validity of using ICD-9-CM codes to identify selected categories of obstetric complications, procedures and co-morbidities. Paediatr Perinat Epidemiol. 2012; 26:421–429. [PubMed: 22882786]
33. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med. 2012; 366:120–129. [PubMed: 22236222]

34. Kanji S, Stewart R, Fergusson DA, et al. Treatment of new-onset atrial fibrillation in noncardiac intensive care unit patients: a systematic review of randomized controlled trials. Crit Care Med. 2008; 36:1620–1624. [PubMed: 18434899]

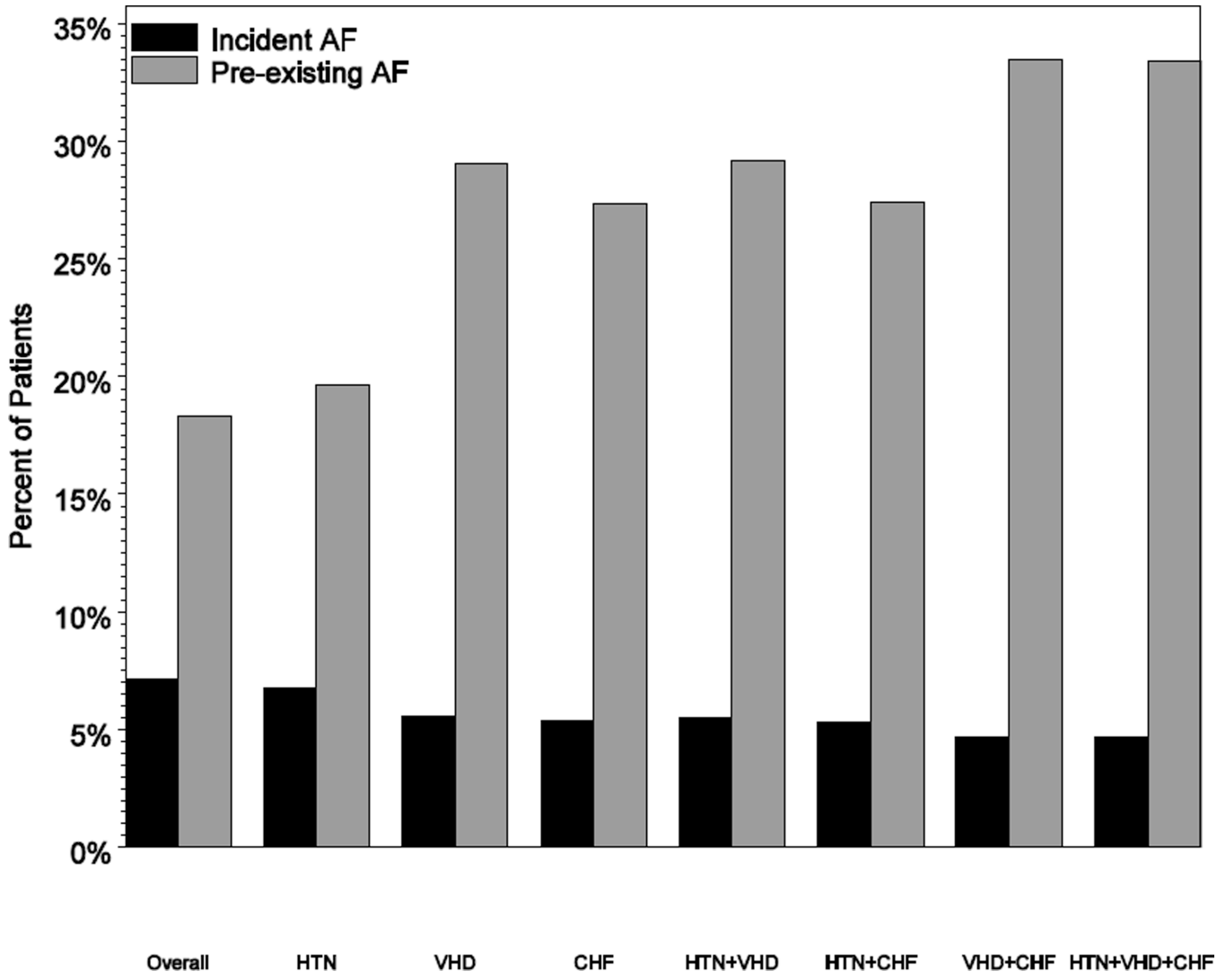

Figure 1.

Age- and Sex-Adjusted Proportion of Subjects with Preexisting or Newly-diagnosed Sepsis-Associated Atrial Fibrillation across Standard Risk Factors

Abbreviations: HTN, hypertension; VHD, valvular heart disease; CHF, congestive heart failure.

Table 1

Baseline Characteristics and Acute Factors in the Primary Analysis Cohort of Medicare Beneficiaries Hospitalized With Sepsis

Characteristic	Patients (N = 60,209)
Age	
Mean (SD), y	80.2 (7.5)
Median (interquartile range), y	80.0 (74.0–86.0)
Age group	
67–74 y	15,635 (26.0)
75–84 y	26,940 (44.7)
≥ 85 y	17,634 (29.3)
Male, No. (%)	26,752 (44.4)
Race, No. (%)	
Black	7215 (12.0)
White	50,030 (83.1)
Other	2964 (4.9)
Comorbid conditions, No. (%)	
Chronic obstructive pulmonary disease	25,747 (42.8)
Diabetes mellitus	25,786 (42.8)
Heart failure	27,078 (45.0)
Hypertension	49,683 (82.5)
Myocardial infarction	8879 (14.7)
Renal disease	14,363 (23.9)
Valvular heart disease	16,588 (27.6)
Rural/urban, No. (%)	
Small or isolated small rural	7338 (12.2)
Large rural	7338 (12.2)
Urban	45,533 (75.6)
US geographic region, No. (%)	
Midwest	14,785 (24.6)
Northeast	11,922 (19.8)
South	25,222 (41.9)
West	8280 (13.8)
No. of acute organ failures during sepsis hospitalization	
Mean (SD)	1 (1)
Median (interquartile range)	1 (0–2)
Any acute organ failure, No. (%)	34,660 (57.6)
Circulatory failure	11,555 (19.2)
Hematologic failure	4444 (7.4)
Hepatic failure	1062 (1.8)
Metabolic failure	4214 (7.0)
Neurologic failure	2101 (3.5)

Characteristic	Patients (N = 60,209)
Renal failure	18,907 (31.4)
Respiratory failure	15,404 (25.6)
Critical care intervention, No. (%)	
Mechanical ventilation	10,105 (16.8)
New-onset dialysis	684 (1.1)
Right heart catheterization	647 (1.1)
Infection, No. (%)	
Bacteremia or fungemia	59,195 (98.3)
Endocarditis	739 (1.2)
Gastrointestinal	4755 (7.9)
Pneumonia	16,420 (27.3)
Skin or soft tissue	3295 (5.5)
Urinary tract	25,335 (42.1)
Cardiac surgery, No. (%)	439 (0.7)
Aortic valve replacement	140 (0.2)
Coronary artery bypass graft	364 (0.6)
Mitral valve replacement	57 (0.1)
Any intensive care unit stay, No. (%)	26,412 (43.9)
Length of stay	
Mean (SD), d	11.2 (12.9)
Median (interquartile range), d	7.0 (4.0–14.0)

Table 2

Age- and Sex-Adjusted Risk of Atrial Fibrillation among Medicare Beneficiaries Hospitalized With Sepsis between 2004 and 2007*

	Overall (N = 60,209)	2004 (n = 16,092)	2005 (n = 16,418)	2006 (n = 15,941)	2007 (n = 11,758)†	*P* Value for Trend
Any AF coded during inpatient stay, No. (%)	15,365 (25.5)	4009 (24.9)	4221 (25.7)	4063 (25.5)	3066 (26.1)	.05
95% CI for the proportion	25.2–25.9	24.2–25.6	25.0–26.4	24.8–26.2	25.3–26.9	
Preexisting AF	11,045 (18.3)	2838 (17.6)	2994 (18.2)	2965 (18.6)	2245 (19.1)	.001
95% CI for the proportion	18.0–18.7	17.0–18.2	17.6–18.8	18.0–19.2	18.4–19.8	
Newly-diagnosed AF	4320 (7.2)	1171 (7.3)	1227 (7.5)	1098 (6.9)	821 (7.0)	.12
95% CI for the proportion	7.0–7.4	6.9–7.7	7.1–7.9	6.5–7.3	6.5–7.4	

Abbreviation: AF, atrial fibrillation.

*Percentages are standardized to the age and sex distributions of the pooled cohorts of patients with a sepsis hospitalization.

†January through September 2007.

Table 3

Age- and Sex-Adjusted Risk of Atrial Fibrillation Among Medicare Beneficiaries Hospitalized With Sepsis Between 2004 and 2007 According to Intensive Care Unit Admission Status*

	No Intensive Care (n = 33,797)	Intensive Care (n = 26,412)	*P* Value
Any AF coded during inpatient stay, No. (%)	7131 (20.8)	8234 (31.6)	<.001
95% CI for the proportion	20.4–21.2	31.0–32.2	
Pre-existing AF	5616 (16.4)	5429 (20.9)	<.001
95% CI for the proportion	16.0–16.8	20.4–21.4	
Newly-diagnosed AF	1515 (4.4)	2805 (10.7)	<.001
95% CI for the proportion	4.2–4.6	10.3–11.1	

Abbreviation: AF, atrial fibrillation.

*Percentages are standardized to the age and sex distributions of the pooled cohorts of patients with a sepsis hospitalization.

Table 4

Factors Associated With Newly-diagnosed Atrial Fibrillation During Hospitalization With Sepsis*

Variable	Unadjusted Risk Ratio (95% CI)	*P* Value	Adjusted Risk Ratio (95% CI)	*P* Value
Age				
67–74 years	1.00 [Reference]		1.00 [Reference]	
75–84 years	1.26 (1.18–1.36)	<.001	1.33 (1.24–1.43)	<.001
≥ 85 years	1.44 (1.33–1.55)	<.001	1.67 (1.55–1.81)	<.001
Male	1.06 (1.00–1.12)	.04	1.01 (0.96–1.07)	.66
Race				
Black	0.63 (0.57–0.70)	<.001	0.64 (0.58–0.71)	<.001
White	1.00 [Reference]		1.00 [Reference]	
Other	0.69 (0.59–0.79)	<.001	0.66 (0.57–0.77)	<.001
Comorbid conditions				
Chronic obstructive pulmonary disease	0.94 (0.89–1.00)	.04	0.91 (0.86–0.97)	.004
Diabetes mellitus	0.82 (0.78–0.87)	<.001	0.92 (0.87–0.98)	.007
Heart failure	0.94 (0.88–1.00)	.04	0.97 (0.91–1.03)	.33
Hypertension	0.88 (0.83–0.95)	<.001	0.97 (0.90–1.04)	.37
Myocardial infarction	0.94 (0.86–1.03)	.20	0.95 (0.87–1.04)	.30
Renal disease	0.77 (0.72–0.84)	<.001	0.82 (0.76–0.89)	<.001
Valvular heart disease	1.01 (0.94–1.08)	.83	0.99 (0.92–1.06)	.70
Rural/urban				
Small or isolated small rural	0.80 (0.73–0.88)	<.001	0.88 (0.80–0.97)	.009
Large rural	0.85 (0.78–0.94)	<.001	0.93 (0.85–1.02)	.10
Urban	1.00 [Reference]		1.00 [Reference]	
US geographic region				
Midwest	1.07 (1.00–1.15)	.05	1.07 (0.99–1.15)	.07
Northeast	1.12 (1.04–1.21)	.004	1.03 (0.95–1.11)	.50
South	1.00 [Reference]		1.00 [Reference]	
West	1.10 (1.01–1.20)	.03	1.02 (0.94–1.11)	.63
Any intensive care unit stay	2.47 (2.32–2.62)	<.001	2.02 (1.89–2.17)	<.001
Length of stay > 7 days	1.83 (1.73–1.94)	<.001	1.48 (1.39–1.57)	<.001
Any organ failure	1.77 (1.66–1.88)	<.001	1.25 (1.16–1.34)	<.001
Critical care interventions				
Mechanical ventilation	1.76 (1.65–1.87)	<.001	1.08 (1.00–1.16)	.04
New-onset dialysis	1.57 (1.28–1.93)	<.001	1.01 (0.82–1.25)	.91
Right heart catheterization	2.00 (1.66–2.41)	<.001	1.36 (1.12–1.64)	.002
Infections				
Endocarditis	1.54 (1.23–1.92)	<.001	1.36 (1.09–1.69)	.007
Gastrointestinal	1.18 (1.08–1.30)	<.001	0.92 (0.84,1.01)	.10
Pneumonia	1.24 (1.17–1.32)	<.001	1.06 (1.00,1.13)	.05
Skin or soft tissue	0.80 (0.70–0.93)	.003	0.86 (0.75,0.99)	.04
Urinary tract	0.71 (0.67–0.75)	<.001	0.84 (0.79,0.89)	<.001

Variable	Unadjusted Risk Ratio (95% CI)	*P* Value	Adjusted Risk Ratio (95% CI)	*P* Value
Cardiothoracic surgeries				
Aortic valve replacement	3.32 (2.51–4.38)	<.001	1.37 (1.00,1.88)	.05
Coronary artery bypass graft surgery	3.26 (2.75–3.87)	<.001	1.89 (1.53,2.32)	<.001
Mitral valve replacement	3.91 (2.57–5.95)	<.001	1.30 (0.84,1.99)	.24
Year				
2004	1.00 [Reference]		1.00 [Reference]	
2005	1.04 (0.96–1.12)	.34	1.01 (0.94,1.09)	.70
2006	0.96 (0.89–1.04)	.31	0.95 (0.88,1.02)	.15
2007	0.99 (0.91–1.08)	.78	0.96 (0.88,1.04)	.33

*The adjusted analysis using modified Poisson regression models included all listed variables. The sample size of 41,460 excluded 11,045 patients in the primary analysis cohort with preexisting AF and 7704 patients with a prior code for AF but no AF coded during the index sepsis hospitalization.