ORIGINAL RESEARCH

Racial and Sex Disparities in Anticoagulation After Electrical Cardioversion for Atrial Fibrillation and Flutter

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BACKGROUND: Anticoagulation is indicated for 4 weeks after cardioversion in patients with atrial fibrillation/flutter. We sought to examine whether there is evidence of sex or racial disparity in anticoagulant prescription following cardioversion, and whether postcardioversion anticoagulation affects outcomes.

METHODS AND RESULTS: We identified a representative sample of Medicare patients who underwent elective electric cardioversion in an outpatient setting from 2015 to 2017. We identified patients who had an anticoagulant prescription for 3 months after the cardioversion date. Multivariable logistic regression was used to assess factors associated with a prescription of an anticoagulant after cardioversion. Cox regression analysis was used to test association of anticoagulation with a composite end point of 90-day mortality, ischemic stroke, or arterial embolism. The final study cohort included 7860 patients. Overall, 5510 patients (70.1%) received any anticoagulation following cardioversion, while 2350 (29.9%) did not. Patients who did not receive anticoagulation were younger, with a lower burden of most comorbidities. Patients were less likely to receive antico-agulation if they had dementia or atrial flutter, while patients with valvular heart disease, obesity, heart failure, peripheral vascular or coronary disease, or hypertension were more likely to receive anticoagulation. Female sex (adjusted odds ratio, 0.84; 95% CI, 0.75–0.92; *P*<0.001), Black and Hispanic race (adjusted odds ratio, 0.50; 95% CI, 0.38–0.65; and odds ratio, 0.56; 95% CI, 0.41–0.75, respectively; *P*<0.001) were independently associated with lower probability of anticoagulant prescription. Postcardioversion anticoagulation was associated with lower risk of the composite end point (adjusted hazard ratio, 0.38; 95% CI, 0.27–0.52; *P*<0.001).

CONCLUSIONS: Racial and sex disparities exist in anticoagulant prescription after outpatient elective cardioversion for atrial fibrillation.

Key Words: anticoagulation **■** atrial fibrillation **■** cardioversion **■** disparities

trial fibrillation (AF) is the most prevalent arrhythmia in the United States.¹ Electrical cardioversion is a procedure that is performed with the aim of restoring sinus rhythm.² The risk of ischemic stroke, thromboembolism, and mortality is heightened for the first few weeks following cardioversion. Thus, anticoagulation for at least 4 weeks after cardioversion, especially in individuals with CHA₂DS₂-VASc score ≥ 1 (congestive heart failure, hypertension, age \geq 75 years,

diabetes mellitus, previous stroke/transient ischemic attack, vascular disease, age 65–74 years, sex category), carries a class I in the current American Heart Association/American College of Cardiology and the European Society of Cardiology guidelines on management of AF.^{3,4}

Sex and racial disparities in the management of AF have been previously demonstrated. Women are less likely to undergo catheter ablation or cardioversion or

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CLINICAL PERSPECTIVE

What Is New?

- In patients who undergo elective outpatient direct-current cardioversion for atrial fibrillation/ flutter where postcardioversion anticoagulation is indicated for 4 weeks, Black, Hispanic, and female patients are less likely to receive anticoagulation.
- Lack of an anticoagulant prescription following direct-current cardioversion in patients with atrial fibrillation is associated with higher risk of mortality and ischemic stroke.

What Are the Clinical Implications?

 More efforts are needed to eliminate racial and sex disparity in receiving indicated anticoagulation for 4 weeks after elective direct-current cardioversion in patients with atrial fibrillation.

receive anticoagulation for stroke prophylaxis when indicated compared with men.^{5–7} Black patients are less likely to receive appropriate treatment compared with White patients.⁸ However, it is unclear if sex or racial disparities in the prescription of oral anticoagulation after cardioversion for AF exist across practices in the United States.

The aims of this study were (1) to examine whether there is evidence of sex or racial disparity in oral anticoagulant prescription after cardioversion and (2) to examine whether anticoagulation following cardioversion is associated with a protective effect against mortality and thromboembolism in a contemporary national cohort from the United States.

METHODS

Data used for the study are covered under a data use agreement with the Centers for Medicare and Medicaid Services and are not available for distribution by the authors but may be obtained from the Centers for Medicare and Medicaid Services with an approved data use agreement.

Ethics Approval

The Institutional Review Board at the University of Iowa approved the study with waiver of informed consent.

Study Cohort and Data Source

Medicare patients from the 5% enhanced sample, who were enrolled in Fee-for-Service and Medicare Part D, and underwent elective electric cardioversion in an outpatient setting, for AF or atrial flutter were identified from March 2015 through October 2017, using Current Procedural Terminology codes 92960 and 92961. The Medicare Carrier (Parts B and C) standard analytic files, which includes outpatient encounters, physician billed services, including institutional and outpatient procedures, for a 5% representative rolling cohort of Medicare beneficiaries, was used to extract patients who underwent cardioversion using the above Current Procedural Terminology codes. The Inpatient Medicare Provider Analysis and Review (MedPar) file, which includes all inpatient admissions for Medicare beneficiaries, was used to extract all inpatient admissions. The inpatient admissions and outpatient encounters for 1 year before the cardioversion date were used as a look-back period to assess patients' comorbidities burden using billed International Classification of Diseases, Ninth Revision and Tenth Revision (ICD-9 and ICD-10) codes. We also calculated a frailty score that was validated in patients with heart failure, pneumonia, myocardial infarction and AF in prior studies.⁹⁻¹¹ The Medicare Beneficiary Summary file was used to extract patients' demographics, including age, sex, and race; enrollment dates; death dates; residence zip codes; and types of insurance plans for each patient. The race/ethnicity variable "Bene_Race_CD" is reported in inpatient and outpatient encounter claims by the hospital/provider. Finally, prescription medications were extracted from the Pharmacy Drug Event (Part D) file 5% sample, which includes pharmacy claims for Medicare beneficiaries who are enrolled in Part D. Variables included in the Part D file include prescribing physician, filling pharmacy, number of pills and number of days prescribed, and amount paid by plan and patient. We identified patients who filed a claim for an anticoagulant (warfarin, apixaban, rivaroxaban, or dabigatran) 3 months before and for 3 months after the cardioversion date. We also extracted procedures done up to 1 month before the cardioversion and determined patients who underwent transesophageal echocardiogram using Current Procedural Terminology codes (93312, 93314). We excluded patients who were enrolled in Medicare Advantage and patients who were not enrolled in Medicare Part D for at least 3 months before and 3 months after the date of the cardioversion. We also excluded patients who underwent cardioversion in the setting of an inpatient admission, emergency department visit, for ventricular arrhythmias or paroxysmal supraventricular tachycardia. We also extracted the physician specialty, and practice zip code from the cardioversion claim line.

Study Outcomes

Our primary interest was in factors associated with receipt of anticoagulation after cardioversion per guideline recommendations, specifically race and sex disparities. We were also interested in the disparities in patient outcomes and the association of postcardioversion anticoagulation with patient outcomes. We defined a composite outcome representing readmissions with a primary diagnosis of ischemic stroke, transient ischemic attack, or systemic embolism (including acute lower extremity embolic ischemia and splenic and renal infarction), and death within 90 days from the cardioversion date. Study follow-up was 90 days for the entire cohort, and end of follow-up was December 2017.

Statistical Analysis

Continuous variables are presented as mean and SD and compared using Student's t test if normally distributed, or presented as median and interguartile range and compared using the Mann-Whitney test if nonnormally distributed. Categorical variables are presented as counts and percentages and were compared using the chi-square test. Multivariable logistic regression was used to assess factors associated with prescription of a postcardioversion anticoagulant. Variables considered for this model included age, sex, race, comorbidities including frailty score, cardioversion indication (AF versus atrial flutter), provider specialty, and practice zip code. A practice was considered to be located in a rural area if it was located in a zip code designated rural by the Federal Office of Rural Health Policy. Variable selection was done in a stepwise approach, with a cutoff P value of 0.2 to enter the model and 0.1 to remain in the model. A second multivariable logistic regression model was constructed to assess factors associated with the composite end point. The exposure of interest in that model was receipt of postcardioversion anticoagulation after adjusting for measured confounders. To assess possible collinearity between different variables, variance inflation factor was calculated for each variable in the model. Both models with candidate variables included were planned a priori. Cox regression model was performed to examine the association of postcardioversion anticoagulation with the composite end point, and Kaplan-Meier curves for events were generated and compared with log-rank. In a second model, we analyzed the average treatment effect of postcardioversion anticoagulation on the composite outcome using an augmented inverse probability weighting model with a doubly robust estimator and bootstrapped corrected confidence intervals.¹² In a sensitivity analysis, we assessed the extent to which unmeasured confounders could explain an observed association between postcardioversion anticoagulation and the study primary outcome by calculating the E value for our results.13 The E value indicates the minimum strength of association that an unmeasured confounder would need to have with both the exposure and outcome to fully explain away a specific treatment-outcome association.¹³ All analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC) and R 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

A total of 19 108 patients underwent a cardioversion for AF or atrial flutter during the study period. We excluded 5928 patients because they were not enrolled in Part D for at least 3 months before and after the cardioversion date, 219 patients because they were enrolled in Medicare Advantage, and 5101 patients who underwent a cardioversion in the setting of an inpatient admission or emergency department visit. The final study cohort included 7860 patients. Table 1 shows baseline characteristics for the study population. Overall, 5510 patients (70.1%) received anticoagulation following cardioversion, while 2350 (29.9%) did not. Patients who did not receive anticoagulation were younger (mean age, 72.9±10 versus 74.8±7.9 years; P<0.001), more likely to be women, of minority race, and with a lower burden of most comorbidities including heart failure, coronary artery disease, lung and kidney disease, anemia, prior bleeding, and prior ischemic stroke. Patients who did not receive anticoagulation had lower frailty scores (median, 2.4 [interguartile range, 0-7.4] versus 3.0 [interguartile range, 0-8.5]; P<0.01) and lower CHA₂DS₂-VASc scores (mean, 3.7±1.7 versus 4.2±1.7; P<0.01). Overall, AF was the indication for cardioversion in the majority of patients (89.2%), and 39.0% had a precardioversion transesophageal echocardiogram.

Postcardioversion Anticoagulation

In patients who received postcardioversion anticoagulation, apixaban was used in 39.3%, followed by warfarin (26.7%), rivaroxaban (26.7%), and dabigatran (7.3%). Figure 1 shows the logistic regression model for independent factors associated with postcardioversion anticoagulation. Patients were less likely to receive anticoagulation if they were women, Black, or Hispanic or had dementia or atrial flutter, while patients with valvular heart disease, obesity, hypertension, peripheral vascular or coronary artery disease, or systolic or diastolic heart failure, or who underwent precardioversion transesophageal echocardiogram were more likely to receive postcardioversion anticoagulation. Cardioversions performed in rural practices were associated with a lower probability of postcardioversion anticoagulation. Female sex (adjusted odds ratio [OR], 0.84; 95% Cl, 0.75–0.92; P<0.001), Black race and Hispanic ethnicity (adjusted OR, 0.50; 95% Cl, 0.38-0.65; and OR, 0.56; 95% Cl, 0.41-0.75, respectively; P<0.001 for both) were independently associated with lower probability of anticoagulation prescription.

Table 1. Baseline Demographics and Characteristics of the 2 Study Groups

Variable	Overall (N=7860)	Post-DCCV anticoagulation (N=5510)	No Post-DCCV anticoagulation (N=2350)	P Value
Age, y	74.2±8.6	74.8±7.9	72.9±10	<0.001
Male sex	4488 (57.1)	3242 (58.8)	1246 (53.0)	<0.001
White race	7123 (90.6)	5077 (92.1)	2046 (87.1)	<0.001
Black race	275 (3.5)	140 (2.5)	135 (5.7)	
Asian race	94 (1.2)	58 (1.1)	36 (1.5)	
Hispanic ethnicity	115 (2.6)	115 (2.1)	87 (3.7)	
Diabetes mellitus	2639 (33.6)	1859 (33.7)	780 (33.2)	0.6
Hypertension	6702 (85.3)	4869 (88.4)	1833 (78.0)	<0.001
History of heart failure	2593 (33.0)	2057 (37.2)	536 (22.8)	<0.001
Prior coronary artery disease	3497 (44.5)	2647 (48.0)	850 (36.2)	<0.001
Prior bleeding	1384 (17.6)	1013 (18.4)	371 (15.8)	0.006
Prior gastrointestinal bleed	602 (7.7)	431 (7.8)	171 (7.3)	0.4
Prior cerebral bleed	50 (0.6)	32 (0.6)	18 (0.8)	0.3
Prior ischemic stroke	1125 (14.3)	833 (15.1)	292 (12.4)	0.002
Prior smoking	1049 (13.4)	753 (13.7)	296 (12.6)	0.2
Peripheral artery disease	1832 (23.3)	1335 (24.2)	497 (21.2)	0.003
Liver disease	403 (5.1)	287 (5.2)	116 (4.9)	0.6
Chronic kidney disease	1078 (13.7)	815 (14.8)	263 (11.2)	<0.001
End-stage renal disease	108 (1.4)	71 (1.3)	37 (1.6)	0.3
Prior permanent pacemaker	826 (10.5)	647 (11.7)	179 (7.6)	<0.001
Prior intracardiac defibrillator	425 (5.4)	341 (6.2)	84 (3.6)	<0.001
Valvular heart disease	3300 (42.0)	2569 (46.6)	731 (31.1)	<0.001
Sleep apnea	1681 (21.4)	1295 (23.5)	386 (16.4)	<0.001
Dementia	319 (4.1)	196 (3.6)	123 (5.2)	0.001
Obesity	2046 (26.0)	1529 (27.8)	517 (22.0)	<0.001
Hypothyroid	1982 (25.2)	1417 (25.7)	565 (24.0)	0.1
Anemia	1981 (25.2)	1442 (26.2)	539 (22.9)	0.003
Metastatic tumor	154 (2.0)	104 (1.9)	50 (2.1)	0.5
Rheumatoid arthritis/ connective tissue disease	603 (7.7)	419 (7.6)	184 (7.8)	0.7
Lung disease	2260 (28.8)	1633 (29.6)	627 (26.7)	0.008
Depression	1027 (13.1)	704 (12.8)	323 (13.7)	0.2
Alcohol abuse	181 (2.4)	134 (2.4)	47 (2.0)	0.2
Frailty score	2.9 (0-8.2)	3.0 (0-8.5)	2.4 (0-7.4)	<0.001
Atrial flutter	849 (10.8)	563 (10.2)	286 (12.2)	0.01
Precardioversion TEE	3066 (39.0)	2458 (44.6)	608 (25.9)	<0.001
Precardioversion anticoagulation for at least 3-4 weeks	5299 (67.4)	4876 (88.5)	423 (18.0)	<0.001
Warfarin	1647 (21.0)	1484 (26.9)	163 (6.9)	
Apixaban	2005 (25.5)	1867 (33.9)	138 (5.9)	
Rivaroxaban	1454 (18.5)	1344 (24.4)	110 (4.7)	
Dabigatran	410 (5.2)	387 (7.0)	23 (1.0)	
CHA ₂ DS ₂ -VASc score	4.1±1.7	4.2±1.7	3.7±1.7	
1	403 (5.2)	200 (3.6)	203 (8.7)	<0.001
2	1046 (13.3)	631 (11.5)	415 (17.7)	
3	1599 (20.3)	1112 (20.2)	487 (20.7)	
4	1881 (23.9)	1349 (24.5)	532 (22.6)	

(Continued)

Table 1. (Continued)

Variable	Overall (N=7860)	Post-DCCV anticoagulation (N=5510)	No Post-DCCV anticoagulation (N=2350)	P Value
5	1438 (18.3)	1072 (19.5)	366 (15.6)	
6	836 (10.6)	634 (11.5)	202 (8.6)	
≥7	657 (8.4)	512 (9.3)	145 (6.2)	
Rural practice zip code	802 (10.4)	508 (9.2)	294 (12.5)	<0.001
Post-DCCV anticoagulation				
Warfarin		1470 (26.7)	NA	NA
Apixaban		2165 (39.3)	NA	
Rivaroxaban		1472 (26.7)	NA	
Dabigatran		403 (7.3)	NA	

Results are presented as n (%) and mean±standard deviation.

DCCV indicates direct-current cardioversion; NA, not applicable; and TEE, transesophageal echocardiography.

Ninety-Day Outcomes

The composite outcome was higher in patients who did not receive postcardioversion anticoagulation (3.2% versus 1.2%; P<0.001). This was driven mainly by a higher incidence of 90-day mortality (2.9% versus 0.8%; P<0.001; Table 2). Figure 2 shows the full logistic regression model for the study primary outcome. Anticoagulation following cardioversion was independently associated with a lower risk of the primary outcome (adjusted OR, 0.28; 95% CI, 0.20-0.40; P<0.001). There was no evidence of collinearity in the model (Table S1). On augmented inverse probability weighting, average treatment effect of postcardioversion anticoagulation was -2.7% (95% Cl. -1.7% to -3.6%; P<0.01). On Cox regression analysis, postcardioversion anticoagulation was associated with lower risk of the composite end point compared with no anticoagulation (adjusted hazard ratio, 0.38; 95% CI, 0.27-0.52; P<0.001) (Figure 3). On sensitivity analysis, The E value for the adjusted OR of postcardioversion in the full model was 6.6, suggesting that an unobserved confounder associated with the study outcome and with the exposure (postcardioversion anticoagulation) with OR 6.6 and 6.6, respectively, after all covariate adjustment, can explain the observed relationship reported in our study and bring the risk estimate to the null.

DISCUSSION

In this study, we demonstrate several important findings. First, almost 30% of patients who underwent elective cardioversion in an outpatient setting for AF or atrial flutter did not receive any anticoagulation after cardioversion. Second, patients who identified as women, Black, or Hispanic or those who underwent cardioversion in a rural practice were less likely to receive appropriate anticoagulation after cardioversion. Third, postcardioversion anticoagulation was independently associated with a lower risk of 90-day mortality and ischemic stroke, with an average treatment effect of -2.7% (95% CI, -1.7% to -3.6%).

Anticoagulation for at least 4 weeks after cardioversion, regardless of thromboembolic risk, carries a class I recommendation in both the American Heart Association/American College of Cardiology and the European Society of Cardiology guidelines for management of AF.^{3,4} Earlier studies have shown that the risk of ischemic stroke and fatal embolism after cardioversion without anticoagulation can be as high as 5%.^{14,15} Contemporary studies reported a 2% rate of thromboembolic complications without anticoagulation compared with 0.3% with anticoagulation.² Thromboembolic events after cardioversion can happen because of embolization of a preformed atrial thrombus upon restoration of sinus rhythm, or because of de novo thrombus formation after cardioversion from depressed atrial mechanical function, a phenomenon known as atrial stunning.¹⁶ In atrial stunning, recovery of mechanical function of the atrium is delayed compared with the electrical recovery of "P" waves on surface ECG.¹⁷ In our study, the rate of the primary study end point, a composite of ischemic stroke, systemic embolism, and mortality on and off anticoagulation was 1.2% and 3.2%, respectively, comparable with previously reported rates.^{2,18,19} It is unclear why in our study the difference in the composite end point was driven mainly by difference in mortality and not in ischemic stroke. However, it is important to note that in our study, patients who did not receive anticoagulation after cardioversion were younger, had a lower burden of most comorbidities, had lower CHA₂DS₂-VASc score, and had lower frailty scores compared with patients who received anticoagulation.



Figure 1. Logistic regression model for factors associated with receipt of anticoagulation following elective electrical cardioversion.

DCCV indicates direct-current cardioversion; OR, odds ratio; and TEE, transesophageal echocardiography.

In our study, a history of dementia was significantly associated with a lower likelihood of anticoagulation after cardioversion. However, after adjusting for patient characteristics including frailty, patients who were women, Black, or Hispanic remained less likely to receive anticoagulation. Prior studies have demonstrated sex disparities in AF management. Women were less likely to be prescribed an antiarrhythmic medication or to undergo cardioversion or catheter ablation, compared with men.⁵⁻⁷ Women also were also less likely to receive chronic anticoagulation for permanent AF when indicated.²⁰ This is despite our recognition that women have a higher AF-related risk of fatal or disabling stroke than men.^{21,22} Several proposed mechanisms to explain the higher risk in women include hormonal factors, menopause, higher platelet activity, and higher thrombotic biomarkers.²³ Similarly, racial disparities in AF management have been shown in the past. Black patients are less likely to receive

Table 2. Study End Points

	Post-DCCV anticoagulation (N=5510)	No Post-DCCV anticoagulation (N=2350)	P Value
30-day mortality	11 (0.2)	34 (1.5)	<0.001
90-day mortality	45 (0.8)	69 (2.9)	<0.001
90-day ischemic stroke or TIA	24 (0.4)	11 (0.4)	0.9
Composite end point	68 (1.2)	76 (3.2)	<0.001

Results are presented as n (%). DCCV, indicates direct current cardioversion; and TIA, transient ischemic attack.





anticoagulation for AF when indicated compared with White patients after adjusting for clinical differences.⁸ Our study extends these findings to show that racial disparities also exist in postcardioversion anticoagulation. It is important to note that Black race was shown to be a risk factor for stroke in AF, and a prior study demonstrated that a modified CHA₂DS₂-VASc-R score, after adding Black race, improved model fit to predict stroke risk.²⁴ Another important finding in our study is the disparities faced by Hispanic patients in postcardioversion anticoagulation compared with White patients. Hispanic people are one of the largest and fastest-growing minority populations in the United States. Prior studies have demonstrated that Hispanic patients are less likely to receive left atrial appendage occlusion or catheter ablation for AF.^{25,26} Hispanic patients are also less likely to receive direct oral anticoagulants and when prescribed warfarin have significantly lower time in therapeutic range.^{27,28} We expand on these findings by showing that Hispanic patients are less likely to receive indicated anticoagulation after undergoing elective electrical cardioversion for AF.

Another important finding in our study was that patients who underwent cardioversion in rural hospitals were less likely to receive postcardioversion anticoagulation. Almost 25% of the US general population reside in rural areas. Lower quality of healthcare outcomes in rural hospitals has been demonstrated in the past. In one study, adjusted mortality attributable to cardiovascular diseases was significantly higher in rural counties compared with urban counties, and the difference nearly doubled from 1999 to 2017.²⁹ Another study demonstrated higher in-hospital mortality in patients admitted with AF in rural hospitals compared with urban settings.³⁰ Finally, in our study, atrial flutter was independently associated with lower probability of anticoagulation following cardioversion. Risk of embolism after cardioversion for atrial flutter is similar to AF,³¹ and the American College of Cardiology/ American Heart Association and European Society of Cardiology guidelines recommend anticoagulation for at least 4 weeks after cardioversion for atrial flutter, in a fashion similar to AF.^{3,4}

Our study has several limitations. First, it included patients from the Medicare population, and thus results may not be generalized to the general population. Second, the risk of residual confounding in an observational study cannot be completely ruled out, although the calculated E value for our risk estimate is significantly high (6.6), which means that any unmeasured confounder should have a significantly high association (6.6 on risk ratio scale) with both the exposure and the outcome of the study after adjustment for measured confounders to bring our results to the null, which is unlikely. Third, we lacked information on echocardiogram and important variables such as ejection fraction, left atrial appendage ligation or occlusion, or concomitant antiplatelet therapy. Fourth, some patients might have been prescribed anticoagulation but did not fill the prescription, so part of the disparity observed could be attributable to these groups (women, Black or Hispanic patients) were less likely to fill their prescription for unclear reasons.



Figure 3. Kaplan-Meier curves for time to composite end point in the 2 study groups, compared by log-rank test.

In conclusion, oral anticoagulation is underused after elective electric cardioversion for AF/atrial flutter, with women and Black and Hispanic patients less likely to receive anticoagulation. Lack of anticoagulation after cardioversion is associated with higher mortality and ischemic stroke within 90 days.

ARTICLE INFORMATION

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Disclosures

None

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1.Variance inflation factor (VIF) for variables in the final logistic regression model for the study composite endpoint.

Variable	Variance inflation factor
Age	1.06888
Post cardioversion anticoagulation	1.04146
Alcohol abuse	1.01988
Anemia	1.19159
Diastolic Heart failure	1.1646
Systolic heart failure	1.1945
Chronic lung disease	1.0906
Diabetes mellitus	1.09141
Hypertension	1.11564
Metastatic tumor	1.01096
Weight loss	1.07916
Frailty score	1.40912