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ORIGINAL RESEARCH

Incidence and Prognostic Implications of Readmissions Caused by Thrombotic Events After a Heart Failure Hospitalization

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BACKGROUND: Readmission occurs in 1 out of 3 patients with heart failure (HF). We aimed to study the incidence and prognostic implications of rehospitalizations because of arterial thromboembolism events (ATEs) and venous thromboembolism events (VTEs) after discharge in patients with HF.

METHODS AND RESULTS: We identified Medicare beneficiaries who were admitted with a primary diagnosis of HF from 2014 to 2019, with a hospital stay ranging between 3 and10 days, followed by discharge to home. We calculated incidence of ATEs (myocardial infarction, ischemic stroke, or systemic embolism) and VTEs (deep venous thrombosis and pulmonary embolism) up to 90 days after discharge. Out of 2 953 299 patients admitted with HF during the study period, a total of 585 353 patients met the inclusion criteria, and 36.6% were readmitted within 90 days of discharge. The incidence of readmission due ATEs, VTEs, HF, and all other reasons was 3.4%, 0.5%, 13.2%, and 19.5%, respectively. Incidence of thromboembolic events was highest within 14 days after discharge. Factors associated with ATEs included prior coronary, peripheral, or cerebrovascular disease and for VTEs included malignancy and prior liver or lung disease. ATE/VTE readmission had a 30-day mortality of 19.9%. After a median follow-up period of 25.6 months, ATE and VTE readmissions were associated with higher risk of mortality (hazard ratio, 2.76 [95% CI, 2.71–2.81] and 2.17 [95% CI, 2.08–2.27], respectively; $P<0.001$ for both) compared with no readmission on time-dependent Cox regression.

CONCLUSIONS: After a HF hospitalization, 3.9% of patients were readmitted with a thromboembolic event that was associated with 2- to 3-fold greater risk of mortality in follow-up.

Key Words: arterial thromboembolism ■ extended thromboprophylaxis ■ heart failure ■ venous thromboembolism

Heart failure (HF) is the leading cause of hospitalization in older adults, and ≈1 out of 3 of the patients are readmitted within 90 days after discharge.[1,2] Readmissions rates continue to increase despite the implementation of hospital readmission reduction programs.[3] The most vulnerable phase after HF hospitalization includes the first 6 months after discharge.[4] Readmissions after an HF hospitalization, regardless of the cause, are associated with increased mortality.[5] There are no universally accepted interventions to prevent rehospitalizations after an HF admission, but chronic disease management programs that involve a multidisciplinary team, disease-specific education, telemonitoring, and dynamic optimization of medical therapy have been proposed with modest benefit.[6]

The proinflammatory environment of acute illness, need for intravascular procedures, and unavoidable reduced mobility is thought to disrupt every aspect of Virchow's triad, resulting in thrombosis.[7] Hospitalization for medical illness is an important risk factor for venous

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CLINICAL PERSPECTIVE

What Is New?

- Patients discharged after a hospitalization for heart failure are at a high risk of both arterial and venous thromboembolic events in the immediate posthospitalization period.
- These events, in turn, impart a significant risk in short- and long-term mortality for patients with heart failure.

What Are the Clinical Implications?

- Our findings provide a basis for future studies on mitigation strategies, specifically extended duration antithrombotic agents, to reduce the risk of myocardial infarction, ischemic stroke, and venous thromboembolism in the immediate postdischarge period.
- Furthermore, this analysis also highlights the patients at highest risk for these events and the most vulnerable period after discharge to help guide prophylactic strategies.

Nonstandard Abbreviations and Acronyms

ATE	arterial thromboembolism events
VTE	venous thromboembolism events

thromboembolism events (VTEs).[8] This risk is particularly high in patients with a history of HF, which has been consistently demonstrated to be an independent risk factor for VTEs.[9] Furthermore, this risk for VTEs remains elevated beyond discharge from the HF hospitalization.[10,11]

The pathophysiology of VTEs and arterial thromboembolism events (ATEs) is overlapping, with many shared risk factors.[12–14] Post hoc analyses of prior randomized controlled trials of extended-duration pharmacological prophylaxis suggest a net clinical benefit when including ATEs (ischemic stroke, myocardial infarction) along with VTEs.[15–17] Although these analyses are intriguing, the incidence of an ATE after hospital discharge in a real-world population and its effect on patient outcomes remains unknown.

The objective of our study was to study the incidence, risk factors, and prognostic implications of rehospitalizations caused by ATEs and VTEs in patients with HF using a large administrative database.

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. Requests for analytic statistical analysis system (SAS) codes may be sent to the corresponding author.

Study Cohort

We identified patients who were admitted with a primary diagnosis of HF between January 2014 and September 2019 from the Medicare Provider Analysis and Review 100% Files, using *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes (428.*, 402.01, 402.11, 402.91, 404.01, 404.11, 404.91, 404.03, 404.13, 404.93) and *Tenth Revision* (*ICD-10*) codes (I50.*, I11.0, I13.0, I13.2). If a patient was admitted more than once during the study period, only the first admission was included. We excluded patients who spent <3 days or >10 days in the hospital, patients who died in the hospital, and patients who were discharged to any destination other than home or home with health services. This was done to limit our study population to a more homogenous HF cohort. Because medication data were unavailable, we also excluded patients who had prior history of atrial fibrillation, a VTE (deep vein thrombosis or pulmonary embolism), or valve replacement surgery to exclude patients likely to be on anticoagulation. Patients who had <1 year of coverage by Medicare Fee-for-Service before the HF admission date were also excluded. We used a look-back period of 1 year to ascertain patients' comorbidities, using an algorithm developed by Elixhauser et al,[18] and using all *ICD* codes submitted in admissions claims to hospitals, skilled nursing facilities, and long-term acute care facilities in the year preceding the HF admission. We also used *ICD* diagnoses filed in the index HF admission claim if the present on admission flag was marked as yes. Patient demographics, including sex, race, and dates of enrollment, were derived from Medicare Beneficiary Summary Files.

Study Outcomes

The primary outcome of interest was the incidence of ATEs and VTEs up to 90 days after discharge from the HF admission. ATEs included acute myocardial infarction, ischemic stroke, and systemic embolism (splenic infarct, renal infarct, acute limb ischemia), and VTEs included deep venous thrombosis and pulmonary embolism. All patients included in the study were followed for 90 days after the HF admission. Secondary outcomes included the length of hospital stay in the subsequent admission because of the ATE or VTE, 30-day, 90-day, and long-term mortality after the ATE or VTE. The institutional review board of the Cleveland Clinic approved the study with waiver of informed consent.

Statistical Analysis

Categorical variables are reported as frequency and percentages and are compared using a χ^2 test. Continuous variables are reported as mean and standard deviation if normally distributed, or median and interquartile range if not normally distributed, and compared using the Student *t* test or Mann-Whitney test, respectively. For both ATEs and VTEs, we report incidence event rates as percent per day and cumulative incidence as percent over the 90 days after HF discharge. To study independent predictors associated with occurrence of an ATE and VTE, mixed-effects logistic regression models with the admitting hospital as a random intercept were used, with the ATE or VTE as the dependent variable, and patients age, sex, race, comorbidities, and length of HF admission stay as fixed-effects variables. To assess the effect of ATEs and VTEs on long-term mortality, a multivariable Cox regression model was performed using an ATE or VTE as a time-dependent covariate. To account for time dependency of the ATE or VTE, we depicted survival curves for the study cohort using Simon-Makuch plots and compared the 2 curves using the Mantel-Byar test.[19–21] Interaction and subgroup analyses were conducted in patients with diastolic versus systolic HF, for the study's primary and secondary outcomes.

Sensitivity Analyses

To compare the risk of an ATE and VTE in patients after a hospital admission with a primary diagnosis of HF with a control group, we performed 2 comparisons. First, we identified patients admitted with a primary diagnosis of alcohol intoxication, in the same period, and applied the same inclusion and exclusion criteria. We then performed propensity-score matching on age, sex, race, all comorbidities, and length of hospital stay between the 2 cohorts and compared the risk of an ATE and VTE within 90 days from the date of discharge using conditional logistic regression with strata of match identification, and asymptotic odds ratios (ORs) were estimated. Second, we identified patients admitted with a primary diagnosis of pyelonephritis and repeated the same analysis to compare the risk of a 90-day ATE and VTE between both cohorts.

The analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC), R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria), and GraphPad Prism version 8 (GraphPad Software, San Diego, CA).

RESULTS

Figure 1 shows the flowchart diagram to summarize the study cohort creation. Out of 2 953 299 patients

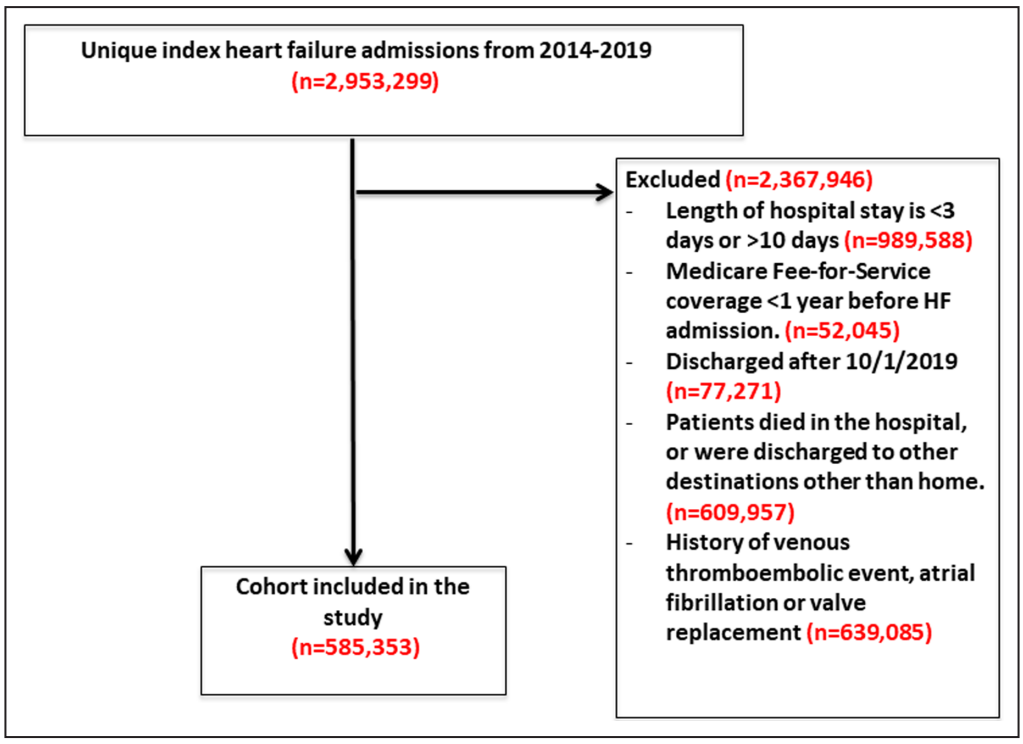

Figure 1. Flowchart of the study cohort.
Flowchart diagram for creation of the study cohort with inclusion and exclusion criteria. HF indicates heart failure.

Table 1. Baseline Characteristics of the Study Cohort

Characteristic	Value
Average age, y	73.4±12.2
Women	52.6%
Race and ethnicity	
White	63.4%
Black	23.1%
Asian	2.2%
Hispanic	9.2%
Comorbidities	
Coronary artery disease	61.1%
Valve disease	28.0%
Peripheral artery disease	17.3%
Stroke	5.0%
Paralysis	3.2%
Hypothyroidism	19.9%
Lymphoma	1.4%
Metastatic cancer	1.7%
Tumor without metastasis	3.0%
Connective tissue disease	4.8%
Diabetes	56.4%
Hypertension	93.1%
Tobacco use	19.0%
Obesity	30.8%
Anemia	41.9%
Chronic kidney disease	43.7%
Chronic lung disease	44.8%
Liver disease	4.8%
Median length of stay, d	4 (IQR, 3–6)

IQR indicates interquartile range.

admitted with HF during the study period, a total of 585 353 hospitalizations of unique patients met the inclusion criteria. The average age of the study cohort was 73.4 years (±12.2 years), of which 52.6% were women, and prevalence of diastolic HF was 19.5%. The study cohort had significant burden of most comorbidities including a history of hypertension (93.1%), coronary artery disease (61.1%), diabetes (56.4%), chronic kidney disease (43.7%), and chronic lung disease (44.8%) (Table 1). The median length of HF hospital stay was 4 days (interquartile range, 3–6 days).

At the 90-day mark, a total of 214 348 (36.6%) patients were readmitted to the hospital. The proportion of patients readmitted because of thrombotic events, HF, and other reasons was 10.7%, 36.1%, and 53.3%, respectively.

As shown in Table 2, the combined incidence of ATEs and/or VTEs was 3.9%, and HF was 13.2% of the entire cohort. The incidence of myocardial infarction was 2.6%, acute ischemic stroke was 0.8%, and acute deep vein thrombosis or pulmonary embolism was 0.6%. The incidence of an ATE was modestly higher in

Table 2. Reasons for 90-Day Readmission After a HF Hospitalization

Diagnosis at readmission	N	% of all admissions	% of all readmissions
Overall, N=585 353			
Arterial thromboembolic events	19 767	3.4%	9.2%
Acute myocardial infarction	14 712	2.5%	6.9%
Acute ischemic stroke	4693	0.8%	2.2%
Systemic arterial embolism	362	0.1%	0.2%
Venous thrombotic events	3064	0.5%	1.4%
HF	77 343	13.2%	36.1%
Other reasons	114 174	19.5%	53.3%
Systolic HF, N=471 176			
Arterial thromboembolic events	16 816	3.6%	9.8%
Acute myocardial infarction	12 632	2.7%	7.3%
Acute ischemic stroke	3889	0.8%	2.3%
Systemic arterial embolism	302	0.06%	0.2%
Venous thrombotic events	2397	0.5%	1.4%
HF	64 314	13.7%	37.4%
Other reasons	88 590	18.8%	51.5%
Diastolic HF, N=114 177			
Arterial thromboembolic events	2951	2.6%	7.0%
Acute myocardial infarction	2089	1.8%	5.0%
Acute ischemic stroke	804	0.7%	1.9%
Systemic arterial embolism	60	0.05%	0.1%
Venous thrombotic events	667	0.6%	1.6%
HF	13 029	11.4%	30.9%
Other reasons	25 584	22.4%	60.6%

Causes for readmission within 90 days of index hospital admission for heart failure. Percentages as a proportion of both all index HF hospitalizations and all readmissions are shown. HF indicates heart failure.

systolic HF compared with diastolic HF. The cumulative incidence and the daily incidence rates of ATEs and VTEs after discharge are depicted in Figures 2A and 2B. The median length of subsequent hospital stays for ATEs or VTEs was 4 days (interquartile range, 3–6 days). During this readmission, in-hospital mortality was 6.2%. Furthermore, 30-day mortality was 19.9%.

Tables 3 and 4 summarize the results of the final multivariable logistic regression model, listing variables associated with an ATE and VTE after HF discharge, respectively. Systolic HF, prior history of coronary artery disease, ischemic stroke, and peripheral artery

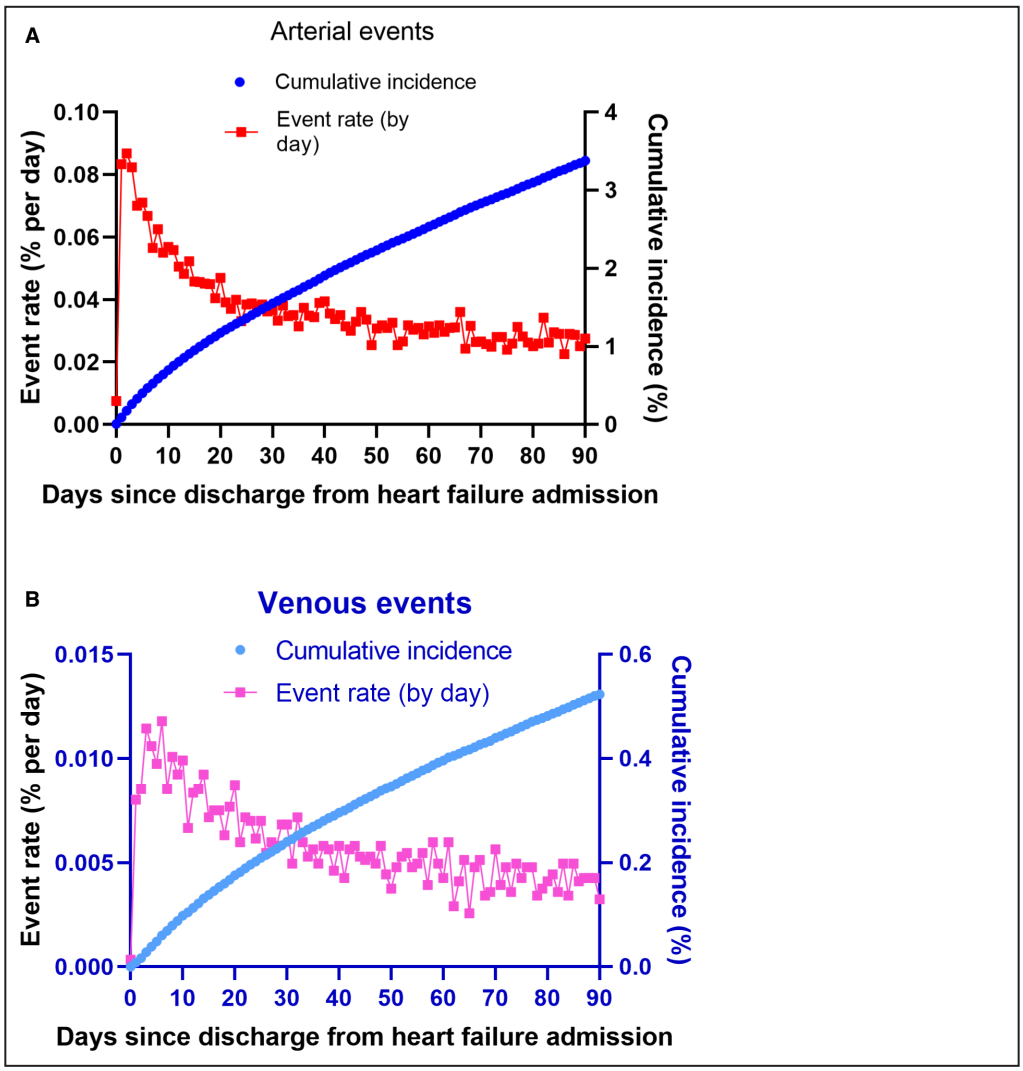

Figure 2. Timing of study end points after hospital discharge.
Daily event and cumulative incidence of (**A**) arterial thromboembolism events (ischemic stroke, myocardial infarction, or systemic embolism) and (**B**) venous thromboembolism events (deep venous thrombosis and pulmonary embolism), after hospital discharge from index heart failure admission.

disease was most strongly associated with a postdischarge ATE, whereas a history of malignancy, prior chronic lung disease, liver disease, and Black race was associated with a higher risk of a VTE.

Cox regression analysis with ATEs, VTEs, HF, and all other reasons for readmission as time-dependent covariates revealed hazard ratios (HRs) of 2.76 (95% CI, 2.71–2.81), 2.17 (95% CI, 2.08–2.27), 2.26 (95% CI, 2.24–2.28), and 1.89 (95% CI, 1.87–1.91), $P<0.001$ for all, respectively, for mortality (Table 5) over a median follow-up period of 25.6 months (interquartile range, 12.5–44.8 months). In subgroup analysis, an ATE was associated with higher long-term mortality in both systolic HF (HR, 2.84 [95% CI, 2.79–2.90]; $P<0.001$) and diastolic HF (HR, 2.43 [95% CI, 2.33–2.53]; $P<0.001$, $P_{interaction}<0.01$). A VTE also was associated with higher long-term mortality in both systolic HF (HR, 2.29 [95% CI, 2.18–2.41]; $P<0.001$) and diastolic HF (HR, 1.85 [95% CI, 1.69–2.02], $P<0.001$, $P_{interaction}=0.02$). Time-dependent Simon-Makuch curves for survival with a postdischarge ATE are shown in Figure 3. Figure 4 depicts the long-term Simon-Makuch survival curves for patients with a postdischarge VTE as a time-dependent covariate.

Sensitivity Analyses

When compared with admission with alcohol intoxication, the risk of an ATE (OR, 2.56 [95% CI, 2.14–3.07]; $P<0.001$) and of a VTE (OR, 1.72 [95% CI, 1.28–2.29]; $P<0.001$) was significantly higher in the HF cohort. When compared with patients admitted with pyelonephritis, the risk of an ATE (OR, 2.38 [95% CI,

Table 3. Final Multivariable Logistic Regression Model for Arterial Thromboembolic Events

Variable	Odds ratio	95% CI	*P* value
Prior coronary artery disease	1.90	1.83–1.98	<0.001
Paralysis	1.37	1.27–1.48	<0.001
Prior ischemic stroke	1.40	1.32–1.48	<0.001
Drug abuse	1.23	1.1–1.39	<0.001
Peripheral vascular disease	1.29	1.24–1.34	<0.001
Diabetes	1.16	1.12–1.2	<0.001
Chronic kidney disease	1.12	1.08–1.16	<0.001
Hypertension	1.13	1.05–1.22	0.001
Valve disease	1.15	1.11–1.19	<0.001
Anemia	1.09	1.05–1.12	<0.001
Age	1.007	1.005–1.009	<0.001
Female sex	1.04	1.01–1.07	0.03
Liver disease	0.88	0.81–0.96	0.004
Pulmonary hypertension	0.78	0.73–0.83	<0.001
White race	Reference		
Black race	1.00	0.96–1.04	0.06
Other race*	1.08	0.9–1.28	0.8
Asian race	1.22	1.11–1.34	0.003
Hispanic ethnicity	1.14	1.09–1.2	0.02
Native American race	1.06	0.87–1.29	0.9
Smoking	1.05	1.00–1.09	0.04
Systolic heart failure	1.25	1.21–1.32	<0.001

Final multivariate logistic regression model listing ORs (reference is White race) of various risk factors associated with postdischarge acute myocardial infarction, ischemic stroke, and/or systemic embolism within 90 days after discharge from a heart failure hospitalization. OR indicates odds ratio.

*Multiracial or unknown/unreported.

Table 4. Final Multivariable Logistic Regression Model for Venous Thromboembolic Events

Variable	Odds ratio	95% CI	*P* value
Metastasis	2.48	1.98–3.11	<0.0001
Tumor without metastasis	1.76	1.44–2.16	<0.0001
Drug use	1.52	1.26–1.83	<0.0001
Weight loss	1.36	1.16–1.58	<0.0001
Lymphoma	1.35	1–1.84	0.0525
Pulmonary circulatory disease	1.26	1.1–1.45	0.0009
Coagulopathy	1.21	1.04–1.4	0.0136
Chronic lung disease	1.2	1.1–1.31	<0.0001
Prior coronary artery disease	0.9	0.83–0.99	0.0251
Anemia	0.88	0.8–0.97	0.0118
Valve disease	0.88	0.8–0.97	0.0134
Diabetes	0.85	0.78–0.93	0.0004
Hypertension	0.79	0.68–0.91	0.0015
Chronic kidney disease	0.79	0.72–0.87	<0.0001
Female sex	1.11	1.01–1.23	0.0438
White race	Reference		
Black race	1.31	1.19–1.45	<0.0001
Other race*	0.92	0.57–1.49	0.9476
Asian race	0.61	0.41–0.9	0.0269
Hispanic ethnicity	0.77	0.65–0.92	0.098
Native American race	0.88	0.52–1.49	0.8738
Length of hospital stay	1.03	1.01–1.06	0.0082

Final multivariate logistic regression model listing odds ratios (reference is White race) of various risk factors associated with postdischarge deep vein thrombosis and/or pulmonary embolism within 90 days after discharge from a heart failure hospitalization. OR indicates odds ratio.

*Multiracial or unknown/unreported.

1.97–2.98]; *P*<0.001) and a VTE (OR, 1.44 [95% CI, 1.08–1.93]; *P*=0.01) was also significantly higher in the HF cohort.

DISCUSSION

In this study, which included over 500 000 patients hospitalized with HF, we report several key findings. First, thrombotic events account for 1 in 10 readmissions, with ATEs accounting for the majority of thromboembolic events. Second, the incidence of thromboembolic events is highest within 2 weeks of discharge. Third, conventional risk factors, such as a history of prior coronary, peripheral, or cerebrovascular arterial disease, were associated with a higher risk of postdischarge ATEs, whereas malignancy, prior lung or liver disease, and Black race were associated with a higher risk of postdischarge VTEs. Finally, thromboembolic events are associated with more than a 2-fold increase in the risk of mortality over a median follow-up period of 27.4 months.

There are several common molecular cascades that have been reported in the pathophysiology of HF and thrombosis. For example, inflammatory cytokines, such as TNF-α (tumor necrosis factor-α), IL-1 (interleukin-1), and IL-6 (interleukin 6), have been long known to be upregulated in HF and may have a prognostic role in this patient population.[22–24] Interestingly, these pathways are also associated with both arterial and venous thrombosis.[25–28] Furthermore, downstream upregulation of tissue factor and neutrophil extracellular traps are now thought to contribute to both HF and propagation of intravascular thrombosis.[29] In light of this overlapping pathophysiology, the clinical correlation of these conditions as demonstrated in our study is not surprising.

Although real-world postdischarge data on the incidence of arterial thromboembolic events in patients with HF are lacking, our findings are concordant with previously published reports from HF clinical trials. In an analysis of the HF network trials that included 744 subjects admitted because of acute HF with prominent congestion and renal dysfunction, 26% of patients were readmitted during the first 30 days.

Table 5. Cox Regression Analysis for Long-Term Mortality in Patients Readmitted After a Heart Failure Hospitalization

Variable	Hazard ratio	95% CI	*P* value
Arterial thromboembolism	2.76	2.71–2.81	<0.001
Venous thromboembolism	2.17	2.08–2.27	<0.001
Heart failure readmission	2.26	2.24–2.28	<0.001
Other reason readmission	1.89	1.87–1.91	<0.001
Metastasis	2.63	2.57–2.69	<0.001
Tumor without metastasis	1.36	1.33–1.38	<0.001
Lymphoma	1.32	1.29–1.36	<0.001
Weight loss	1.35	1.33–1.36	<0.001
Chronic kidney disease	1.26	1.25–1.27	<0.001
Coagulopathy	1.21	1.19–1.22	<0.001
Liver disease	1.2	1.18–1.22	<0.001
Peripheral vascular disease	1.17	1.16–1.18	<0.001
Paralysis	1.17	1.14–1.19	<0.001
Chronic lung disease	1.15	1.14–1.15	<0.001
Pulmonary vascular disease	1.15	1.14–1.17	<0.001
Anemia	1.14	1.13–1.15	<0.001
Smoking	1.09	1.08–1.10	<0.001
Drug abuse	1.07	1.04–1.09	<0.001
Prior coronary artery disease	1.08	1.07–1.09	<0.001
Diabetes	1.06	1.05–1.07	<0.001
Valvular heart disease	1.05	1.04–1.06	<0.001
Age	1.03	1.03–1.03	<0.001
Hypertension	0.87	0.86–0.89	<0.001
Male sex	1.15	1.14–1.16	<0.001
White race	Reference		
Black race	0.87	0.87–0.88	<0.001
Asian race	0.83	0.81–0.85	<0.001
Hispanic ethnicity	0.91	0.90–0.92	<0.001
Native American race	1.11	1.06–1.16	<0.001

The above are results of Cox regression analysis for long-term mortality in patients readmitted within 90 days post-discharge after a heart failure hospitalization. Hazard ratios are listed for various risk factors as a time dependent covariate.

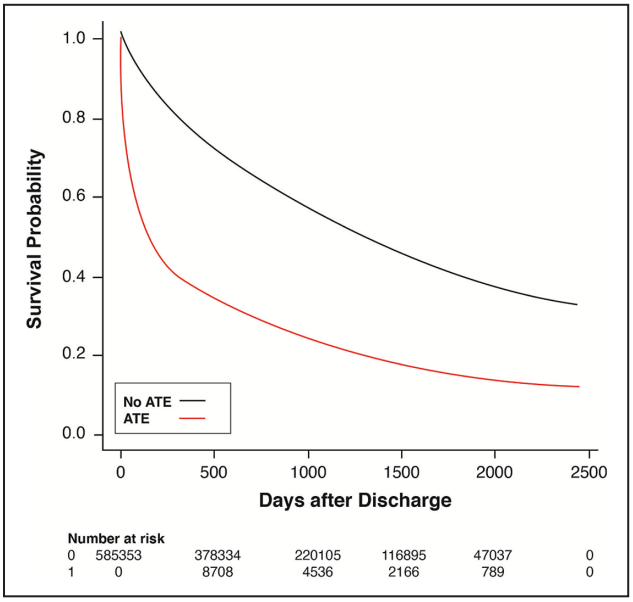

Figure 3. Long-term survival in patients who develop an arterial thromboembolism event (ATE) after discharge from index heart failure admission.
Simon-Makuch curves for long-term survival over time with ATEs as time-dependent covariates. Mantel-Byar test, $P<0.001$.

Non-HF cardiovascular indications accounted for 23% of readmissions. Approximately half of those patients had a possible ATE. The small sample size of that study limited any analysis to evaluate the impact of ATE on patient survival.[30] There are also some insights about postdischarge ATEs in the general medical population after hospital discharge. These are described in post hoc analyses of large clinical trials of extended thromboprophylaxis such as the APEX (Acute Medically Ill VTE [Venous Thromboembolism] Prevention with Extended Duration Betrixaban),[31] MARINER (Medically Ill Patient Assessment of Rivaroxaban Versus Placebo in Reducing Post-Discharge Venous Thrombo-Embolism Risk),[32] and MAGELLAN (Multicenter, Randomized, Parallel Group Efficacy and Safety Study for the Prevention of Venous Thromboembolism in Hospitalized Acutely Ill Medical Patients Comparing Rivaroxaban With Enoxaparin) trials.[33] In the MAGELLAN and MARINER trials, the 45-day postdischarge rate of myocardial infarction and nonhemorrhagic stroke was 0.2% and 0.5%, respectively, in the control group.[32,33] Similarly, the rate in the control group of the APEX study for nonhemorrhagic stroke was 0.6%, and acute myocardial infarction was 0.6% within 77 days after discharge.[31] In addition, underuse of coronary artery disease testing has been reported among patients admitted with new-onset HF.[34]

In previously published studies, the elevated VTE risk within 90 days after hospital discharge has been reported as ≈2.5% in medical patients,[10,17] and between 1.5% and 2.5% in patients admitted with HF.[10,11,35] In a Medicare crossover analysis, the cumulative incidence of a VTE after hospitalization for new-onset HF was 1.5% at 30 days.[11] Similarly, in clinical trials that assessed extended-duration pharmacological prophylaxis, the incidence of a VTE was reported to be 0.8% to 5.7%.[31–33,36,37] Our study reported a VTE cumulative incidence of 0.6% at 90 days. The lower rate of VTE may be attributed to 2 main factors. First, we excluded patients with a prior history of a VTE. Second, outpatient diagnosis and management of VTEs were not captured. In a prior study from the ARIC (Atherosclerosis Risk in Communities) cohort, incident HF was associated with higher risk of long-term VTE, and the risk was similar between diastolic and systolic HF.[38]

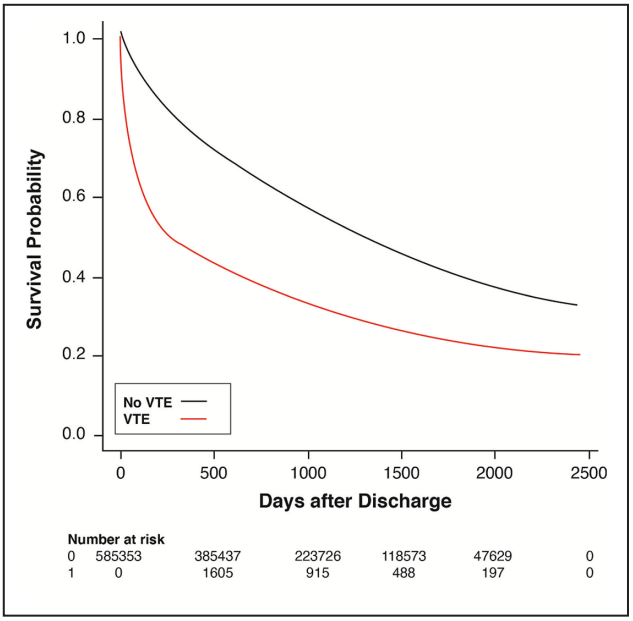

Figure 4. Long-term survival in patients who develop a venous thromboembolism event (VTE) after discharge from index heart failure admission.
Simon-Makuch curves for long-term survival over time with VTEs as time-dependent covariates. Mantel-Byar test, $P<0.001$.

An important finding of our study was the significant impact on survival and long-term mortality associated with a 90-day postdischarge thrombotic event. About 1 in 5 patients readmitted with a thromboembolic event died within 30 days of discharge from the index hospital admission. This was higher when compared with patients readmitted for other causes. These results are striking when considering that this analysis was limited to patients who did not have prolonged hospital stays (ie, >10 days) and were deemed well enough to be discharged home. Furthermore, the risk of longer-term mortality was entirely realized in the first few months after the event, as demonstrated in the survival curves. This highlights the value of postdischarge ATE or VTE as a poor prognostic marker in patients with HF.

This analysis also identifies a high-risk patient population that may most benefit from mitigations strategies such as extended thromboprophylaxis after hospital discharge. The benefit of postdischarge thromboprophylaxis with direct oral anticoagulants in reducing myocardial infarction and nonhemorrhagic stroke has been suggested in a high-VTE-risk patient population.[15–17] Similar studies need to be conducted in a high-ATE-risk cohort to understand the impact of antithrombotic agents in this patient population.

Our study has several limitations. First, because the study cohort was derived from an administrative database, there is potential for misclassification related to coding errors, especially with the transition from *ICD-9* to *ICD-10* codes. To limit the inclusion of misclassified patients, we only included patients with the appropriate *ICD* codes if included as the primary diagnosis or first secondary diagnosis. Second, outpatient events were not captured. Third, we lacked information of anticoagulation therapy and other inpatient or postdischarge medications that might have affected the outcomes. However, we excluded patients with diagnoses associated with anticoagulation therapy including prior history of atrial fibrillation, venous thromboembolism, and valve replacement.

In conclusion, thrombotic events are responsible for 1 out of 10 readmissions after an HF hospitalization. The highest risk of thrombotic events is within the first 14 days after discharge. Patients with venous or arterial thromboembolism suffered a 30-day mortality rate of 19.9%. The occurrence of a thrombotic events is associated with a 2- to 3-times higher risk of long-term mortality. Further research on mitigation strategies is warranted.

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Disclosures

None.

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