Do Countries or Hospitals With Longer Hospital Stays for Acute Heart Failure Have Lower Readmission Rates?

Findings From ASCEND-HF

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Background—Hospital readmission is an important clinical outcome of patients with heart failure. Its relation to length of stay for the initial hospitalization is not clear.

Methods and Results—We used hierarchical modeling of data from a clinical trial to examine variations in length of stay across countries and across hospitals in the United States and its association with readmission within 30 days of randomization. Main outcomes included associations between country-level length of stay and readmission rates, after adjustment for patient-level case mix; and associations between length of stay and readmission rates across sites in the United States. Across 27 countries with 389 sites and 6848 patients, mean length of stay ranged from 4.9 to 14.6 days (6.1 days in the United States). Rates of all-cause readmission ranged from 2.5% to 25.0% (17.8% in the United States). There was an inverse correlation between country-level mean length of stay and readmission (r=–0.52; P<0.01). After multivariable adjustment, each additional inpatient day across countries was associated with significantly lower risk of all-cause readmission (odds ratio, 0.86; 95% confidence interval, 0.75–0.98; P=0.02) and heart failure readmission (odds ratio, 0.79; 95% confidence interval, 0.69–0.99; P=0.03). Similar trends were observed across US study sites concerning readmission for any cause (odds ratio, 0.92; 95% confidence interval, 0.85–1.00; P=0.06) and readmission for heart failure (odds ratio, 0.90; 95% confidence interval, 0.80–1.01; P=0.07). Across countries and across US sites, longer median length of stay was independently associated with lower risk of readmission.

Conclusions—Countries with longer length of stay for heart failure hospitalizations had significantly lower rates of readmission within 30 days of randomization. These findings may have implications for developing strategies to prevent readmission, defining quality measures, and designing clinical trials in acute heart failure.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00475852.

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Key Words: heart failure ■ hospitalization ■ length of stay ■ outcome research ■ patient readmission

As the leading cause of hospital readmission, heart failure is a significant burden on healthcare systems.[1] In the United States alone, >$39 billion was spent on the care of patients with heart failure in 2010, with the majority spent on inpatient care.[2] The US Centers for Medicare and Medicaid Services publicly reports rates of readmission within 30 days of discharge from a heart failure hospitalization, and 30-day readmission rates are likely to be bundled to reimbursement for the index hospitalization. Given the focus on 30-day readmission by payers and policy makers, there is an urgent need to understand the role of length of stay and to develop treatments and management strategies that reduce a patient's risk of early readmission and mortality.

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Few strategies have proven efficacious in significantly reducing 30-day readmission rates.[3–6] Similarly, few clinical factors have been shown to reliably identify patients at high

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risk for early readmission. Some processes of care, such as early follow-up, are associated with modestly lower hospital-level rates of early readmission.[7] In myocardial infarction, country-level length of stay has been shown to be inversely related to early readmission.[8] However, the impact of length of stay on readmission rates for patients with heart failure, who often have multiple comorbid conditions and are readmitted for causes other than heart failure, is less clear.

We examined length of stay and readmission rates in the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF). We examined country-level variations in length of stay for patients with heart failure, the relationship between country-level length of stay and early readmission, and the relationship between site-level length of stay and early readmission in the United States.

Methods

Data Source

ASCEND-HF was a multinational, double-blind, placebo-controlled study designed to evaluate the effectiveness and safety of nesiritide in addition to standard care among patients with acute decompensated heart failure. Participants were randomly assigned to a study group within 48 hours of hospitalization. Detailed inclusion and exclusion criteria have been described previously.[9] The 2 primary end points were a composite end point of heart failure readmission or all-cause mortality up to 30 days after randomization and the change in dyspnea at 6 and 24 hours after study drug initiation.

Patient Characteristics and Outcome Data

Data on patient characteristics were collected at during the baseline hospitalization through the trial case report form. The case report form also collected information on all readmissions within 30 days of randomization. If a patient was readmitted, study staff documented the admission and discharge dates and the primary reason for the readmission. Hospitalization was defined as a stay of >24 hours from admission to discharge. For patients who were transferred to a second hospital, we combined the hospitalization days from both hospitals to determine their total inpatient length of stay.

Statistical Analysis

Consistent with the main trial analyses of treatment efficacy, we limited our analysis to the modified intention-to-treat population. Similar to publicly reported readmission rates for Medicare beneficiaries, we included patients who died after discharge but excluded those who died before discharge or were still hospitalized at 30 days. For statistical stability, we also excluded countries that enrolled <20 patients. We used means, SDs, medians, and proportions, as appropriate, to describe the variables of interest. We calculated the correlation between length of stay and readmission using Pearson correlation coefficient analysis. To account for the hierarchical nature of the data, in which patients were clustered within sites and sites were clustered within countries, we used a 3-level logistic regression model (ie, country, site, patient) to evaluate the relationships between country-level mean lengths of stay for the index admission and country-level readmission rates within 30 days after randomization. We used a 2-level logistic regression model to evaluate the relationships between site-level mean lengths of stay for the index admission and readmission rates among sites in the United States. We included 2 random intercepts accounting for the clustering effects of sites and countries in the all-country analysis and 1 random intercept accounting for the clustering effect of different sites in the US analysis. Consistent with other post hoc analyses investigating postdischarge outcomes in ASCEND-HF,[10] we included the following patient-level variables in each model: age, history of cerebrovascular disease, history of chronic obstructive pulmonary disease, history of depression, heart failure readmission 1 year before the index admission, severity of baseline dyspnea, elevated jugular venous pressure, systolic blood pressure, sodium, blood urea nitrogen, and creatinine. To account for differential periods of time when patients with shorter and longer lengths of stay were at risk for readmission, we included a covariate representing days from the index discharge to death, dropout, or 30 after randomization in the logistic models. We performed the analysis across all countries and across US sites only, given US policy interests and public reporting of hospital-level 30-day readmission rates for patients with heart failure. We evaluated rates of readmission for any cause and for heart failure.

We used SAS version 9.2 (SAS Institute Inc, Cary, NC) for all analyses. The Institutional Review Board of the Duke University Health System approved this study.

Results

ASCEND-HF enrolled 7141 participants at 398 sites in 30 countries in North America, Latin America, Europe, and Asia between May 2007 and August 2010. The modified intention-to-treat analysis of the 7007 patients who received the study drug revealed no significant findings concerning the primary end points. There were 9.4% of patients in the nesiritide group and 10.1% of patients in the placebo group who experienced hospital readmission because of heart failure or who died from any cause within 30 days (P=0.31). There were no significant differences in 30-day or 180-day mortality between the groups.

After excluding countries that enrolled fewer than 20 patients (n=25) and patients who died before discharge from the index hospitalization (n=151) or were still hospitalized at 30 days (n=141), we derived a final study population of 6824 patients from 389 sites in 27 countries. Of these, 779 (11.4%) were readmitted for any cause within 30 days, and 366 (5.4%) were readmitted for heart failure. Eighty-one patients (1.2%) died after discharge from the index hospitalization and had no readmission within 30 days. Of the 2684 patients in the United States, 477 (17.8%) patients were readmitted for any cause within 30 days and 236 (8.8%) patients were readmitted for heart failure.

Table 1 shows the baseline characteristics of the study population. Patients readmitted within 30 days were more likely to have been hospitalized for heart failure in the year before admission and to have comorbid conditions. Patients readmitted within 30 days were more likely to have lower blood pressure and hemoglobin level, and higher B-type natriuretic peptide, blood urea nitrogen, and creatinine levels.

Table 2 shows country-level estimates of mean length of stay and rates of readmission within 30 days of randomization. Mean age ranged from 57.7 to 75.9 years. Systolic blood pressure ranged from 117.8 to 133.5 mm Hg. Heart rate ranged from 75.2 to 91.1 beats per minute. Country-level mean length of stay ranged from 4.9 to 14.6 days. Mean length of stay among US sites was 6.1 days. Mean country-level all-cause readmission rates ranged from 2.5% to 25.0%. The readmission rate among US sites was 17.8%. Figure 1 shows the inverse correlation between country-level mean length of stay and readmission rates (r=–0.52; P<0.01). To explore the possible nonlinear relationship between length of stay and readmission, we added a quadratic term of mean length of stay in all models, and it was not significant across countries (P=0.25) or across US sites (P=0.45). As shown in Figure 2, after multivariable adjustment, each 1-day increase in the mean length of stay across countries was independently associated with a

Table 1. Baseline Characteristics of the Study Population

Variables	Not Readmitted Within 30 Days (n=6045)*	Readmitted Within 30 Days (n=779)*	*P* Value
Age, median (IQR), y	66.0 (56.0–76.0)	68.0 (56.0–77.0)	0.14
Female sex, %	34.0	34.4	0.83
Race, n (%)			<0.01
Asian	1590 (26.3)	112 (14.4)	
Black	883 (14.6)	172 (22.1)	
White	3297 (54.5)	473 (60.7)	
Other	274 (4.5)	22 (2.8)	
Comorbid conditions, n (%)			
Atrial fibrillation or flutter	2193 (36.3)	345 (44.3)	<0.01
Chronic respiratory disease	920 (15.2)	193 (24.8)	<0.01
Coronary artery disease	3249 (53.8)	479 (61.2)	<0.01
Depression	434 (7.2)	105 (13.5)	<0.01
Diabetes mellitus	2509 (41.5)	390 (50.1)	<0.01
Heart failure 1 y before admission	2204 (36.5)	422 (54.2)	<0.01
Hypertension	4334 (71.7)	605 (77.7)	<0.01
Myocardial infarction	2073 (34.3)	301 (38.7)	0.02
Clinical values, median (IQR)			
Blood pressure, mm Hg			
Systolic	124.0 (110.0–140.0)	121.0 (110.0–137.0)	<0.01
Diastolic	75.0 (67.0–84.0)	72.0 (64.0–82.0)	<0.01
Blood urea nitrogen, mg/dL	25.0 (17.7–37.4)	28.1 (19.0–40.1)	<0.01
Creatinine, μmol/L	106.1 (88.4–135.0)	114.9 (96.4–150.3)	<0.01
Ejection fraction, %	30.0 (20.0–36.0)	28.0 (20.0–39.0)	0.78
Heart rate, beats per minute	82.0 (72.0–95.0)	81.0 (70.0–93.0)	0.11
BNP	958.0 (526.0–1801.0)	1140.0 (634.0–2065.2)	<0.01
N-terminal pro-BNP	4277.6 (2002.1–8704.9)	5467.8 (2759.1–10841.5)	<0.01
Hemoglobin, g/dL	12.7 (11.4–14.1)	12.4 (11.0–13.6)	<0.01
Sodium, mmol/L	139.0 (136.0–141.0)	138.7 (136.0–141.0)	0.11

BNP indicates B-type natriuretic peptide; and IQR, interquartile range.
*Ascertained during 30 days from randomization.

lower risk of all-cause readmission (odds ratio [OR], 0.86; 95% confidence interval [CI], 0.75–0.98; *P*=0.02) and heart failure readmission (OR, 0.79; 95% CI, 0.69–0.99; *P*=0.03). Similar trends were observed when we examined mean length of stay across US study sites concerning readmission for any cause (OR, 0.92; 95% CI, 0.85–1.00; *P*=0.06) and readmission for heart failure (OR, 0.90; 95% CI, 0.80–1.01; *P*=0.07). In sensitivity analyses, we substituted the mean length of stay with median length of stay. In countries with longer median length of stay, patients experienced a lower risk of all-cause readmission (OR, 0.86; 95% CI, 0.76–0.97; *P*=0.02) and heart failure readmission (OR, 0.83; 95% CI, 0.69–0.99; *P*=0.04). Similarly, among US sites, median length of stay was associated with a lower risk of all-cause readmission (OR, 0.91; 95% CI, 0.83–1.00; *P*=0.04) and heart failure readmission (OR, 0.86; 95% CI, 0.75–0.98; *P*=0.02).

Discussion

In this analysis of data from the largest multinational trial to date among patients with acute decompensated heart failure, we found that mean length of stay and early readmission rates varied considerably across countries. After adjustment for patient characteristics, country-level variability in sample size, and days at risk for readmission, longer length of stay was associated with a lower risk of early readmission. Using median length of stay, we observed significant relationships across countries and across US sites.

The frequency of hospitalizations among patients with heart failure constitutes a major challenge for aging populations in healthcare systems with significant vulnerabilities in transitional care. Risk-adjusted readmission rates for US hospitals are reported publically to incentivize local practices for improving care. In addition, bundled payments for US hospitals are being evaluated and payment reductions for those with high readmission rates for heart failure have been implemented.[11,12] In response to these payment reforms, hospitals are joining national quality-improvement campaigns, such as Hospital to Home and Target: HF, to share best practices.[13,14] However, few treatments of patients with acute decompensated heart failure have been found to effective in randomized trials, and fewer have been evaluated using an end point of 30-day all-cause readmission. Early postdischarge follow-up

Table 2. Length of Stay and 30-Day All-Cause Readmission Rates Among Patients Discharged Alive With Length of Stay <30 Days

Countries	Patients, n	Length of Stay, Mean (SD), d	Readmission Rate,* %	Correlation	
				r	*P* Value
Argentina	209	6.6 (3.6)	11.0	–0.06	0.35
Australia	32	8.6 (4.7)	15.6	–0.02	0.93
Brazil	134	9.2 (5.2)	7.5	0.02	0.81
Bulgaria	65	7.0 (2.5)	6.2	0.11	0.40
Canada	445	9.3 (5.6)	14.2	–0.07	0.15
Chile	47	8.3 (4.3)	10.6	–0.07	0.63
China	293	11.9 (5.4)	4.4	0.07	0.20
Columbia	30	8.0 (3.8)	16.7	0.20	0.30
France	91	9.2 (4.1)	13.2	–0.14	0.20
Greece	45	7.8 (5.0)	6.7	–0.02	0.18
India	973	4.9 (2.4)	3.8	0.05	0.12
Israel	75	5.2 (3.1)	18.7	0.09	0.42
Italy	64	10.1 (5.2)	4.7	–0.12	0.35
Lithuania	88	12.2 (5.4)	3.4	–0.16	0.14
Malaysia	73	6.6 (3.4)	17.8	0.13	0.29
Mexico	214	5.4 (2.6)	3.3	0.02	0.82
Netherlands	130	9.1 (5.0)	3.1	–0.09	0.30
Norway	51	9.7 (6.8)	3.9	0.02	0.87
Poland	259	9.1 (5.1)	8.5	–0.01	0.90
Romania	47	10.5 (3.0)	4.3	0.22	0.15
Russia	278	14.6 (5.1)	2.5	0.08	0.21
Singapore	52	5.3 (2.6)	25.0	0.03	0.83
South Korea	145	8.9 (4.3)	5.5	–0.06	0.49
Taiwan	71	8.3 (5.8)	19.7	0.02	0.87
Thailand	46	6.4 (3.4)	10.9	–0.12	0.48
Ukraine	183	10.9 (4.3)	2.7	0.19	0.01
United States	2684	6.1 (4.0)	17.8	–0.01	0.55

*Ascertained during 30 days from randomization.

is associated with lower readmission rates,[7] but it is unclear whether extending inpatient stays has a similar influence. Consistent with observations in other disease states,[8,15] our findings provide evidence that shorter lengths of stay have an adverse impact on short-term outcomes. Our findings from this international data set are also consistent with trends noted among Medicare beneficiaries in the United States.[16] This highlights the importance of understanding country-level differences in length of stay within a multinational trial when determining the relevance of results for a specific population.

Since 1984, when the current reimbursement model was introduced in the United States, there have been strong incentives to reduce lengths of stay to maximize hospital profitability. The consequent reduction in hospital lengths of stay has been accompanied by increases in postdischarge readmission rates,[17] which may have resulted in greater overall costs among patients with heart failure. In comparing the average spending for a heart failure hospitalization and the 30 days after discharge, postdischarge care and 30-day readmissions account for the difference between high-resource-use and low-resource-use hospitals, whereas index hospitalization costs are similar.[11] Therefore, identifying the appropriate length of stay for patients and efficient transitions of care to ambulatory settings are critical components of providing not only patient-centered care but also more cost-effective care. As a result, provider responsibilities during a hospitalization for heart failure can extend beyond ensuring clinical stability to include educating patients and families, reconciling inpatient and outpatient medication regimens, improving discharge planning, initiating multidisciplinary interventions, ensuring timely follow-up with outpatient providers, coordinating care with ambulatory services, and potentially using remote monitoring strategies.[7,18–23] Using an additional inpatient day as an intervention, allowing providers not only to ensure clinical stability but also to use locally available strategies for care coordination may warrant further investigation. Defining parameters for patient stability and optimal risk thresholds for discharge can help guide both clinical judgment and policy making toward more effective transitions of care.

With the trend toward globalization in clinical research and international differences in patterns of care,[24–26] it is important to identify country-level factors that may confound a treatment's effect on clinical end points. In this study, length of stay as a country-level factor was significantly correlated with early readmission. Other post hoc analyses have demonstrated that heterogeneity in trial results may be related in part to underlying country-level differences. In the Platelet Inhibition and Patient Outcomes (PLATO) trial, for example, aspirin

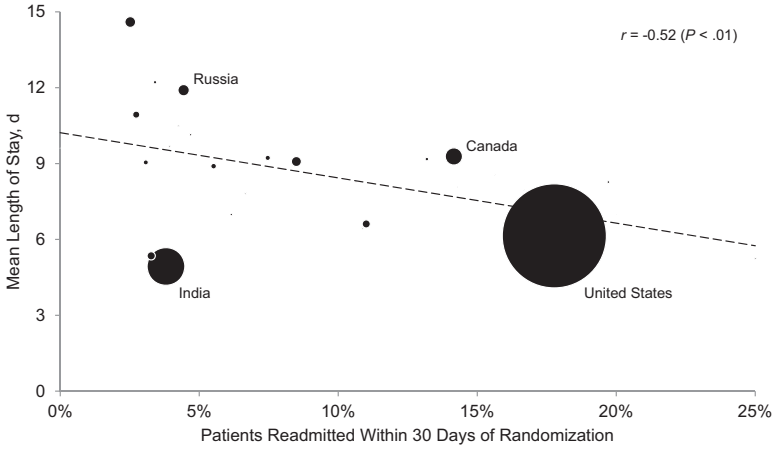

Figure 1. Country-level relationship of early all-cause readmission with mean length of stay for index heart failure hospitalizations. Each circle represents a country that enrolled a patient in the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF). The size of each circle is proportional to the country-level sample size.

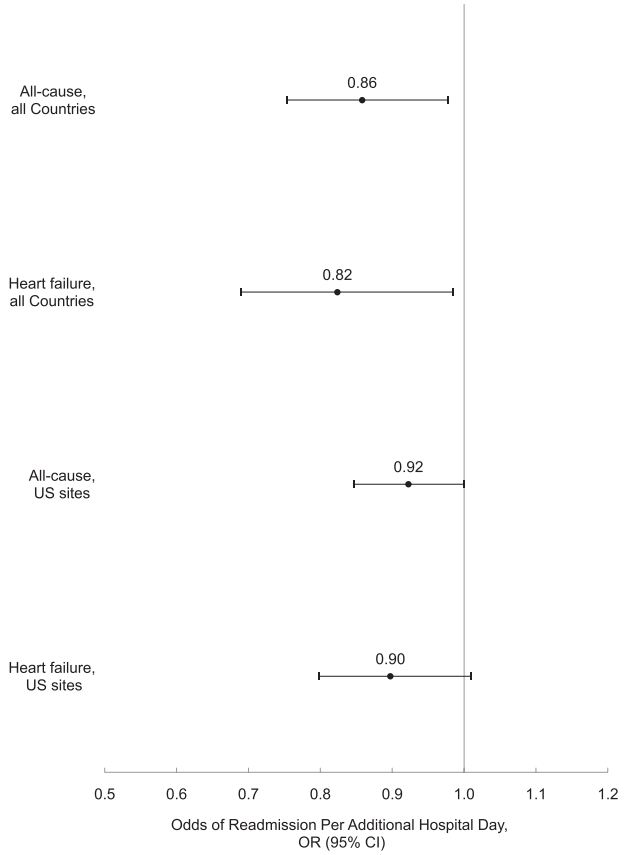

Figure 2. Multilevel modeling of relationships between mean length of stay and readmission across all countries and across US sites. Odds ratios (ORs) were adjusted for age; history of cerebrovascular disease; history of chronic obstructive pulmonary disease; history of depression; heart failure readmission 1 year before the index admission; severity of baseline dyspnea; elevated jugular venous pressure; systolic blood pressure <140 mm Hg; sodium <140 mmol/L; blood urea nitrogen; creatinine; and days from index discharge to death, dropout, or day 30 after randomization. CI indicates confidence interval.

maintenance dose may have explained regional differences in the efficacy of ticagrelor among patients with acute coronary syndrome.[27] Regional variations in the use of evidence-based therapies may have also influenced treatment effects in multinational heart failure trials.[28]

Our study has some limitations. First, despite adjustment for multiple patient-level covariates in the multilevel models, residual or unmeasured confounding may remain. Second, early readmission among US sites was lower in this study than found in Medicare data, likely because of differences in the age of the study population resulting from selection of patients into a clinical trial. Sites participating in a clinical trial may similarly be subject to selection bias. They may possess resources and infrastructure that distinguish them from hospitals that care for patients with heart failure but do not participate in clinical trials. Third, readmissions in this trial data set were ascertained over 30 days from randomization (median time from hospitalization to randomization in placebo arm, 15.7 hours), which may have led to lower readmission rates than the postdischarge rates reported for Medicare beneficiaries. Thus, the findings may not be generalizable to the Medicare heart failure population that is often the focus of readmission policies in the United States. Nevertheless, it is important that ASCEND-HF was not only the largest trial performed among patients with acute decompensated heart failure but was also a pragmatic trial with few exclusion criteria.[9]

Conclusions

Patients treated in countries with longer lengths of stay for heart failure hospitalizations had significantly lower rates of readmission within 30 days of randomization. Findings were similar among sites in the United States, where each 1-day increase in the mean length of stay at the site level was independently associated with a lower risk of all-cause and heart failure readmission. These findings may have implications for developing tactics to prevent readmission, defining quality measures, and designing clinical trials in acute heart failure.

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CLINICAL PERSPECTIVE

Heart failure (HF) is the leading cause of early readmissions in the United States and is a focus of payers and policy makers. Currently, there are few interventions and processes of care associated with reductions in 30-day readmission rates. In this analysis of data from the largest multinational trial to date among patients with acute decompensated heart failure, we found that patients treated in countries with longer lengths of stay for heart failure hospitalizations had significantly lower rates of early readmission. Among US sites, we found that each 1-day increase in the mean length of stay was independently associated with a lower risk of all-cause and heart failure readmission. Consistent with observations in other disease states, our findings provide evidence that shorter lengths of stay for HF patients are associated with less favorable outcomes in terms of this metric. Identifying the appropriate length of stay for patients and efficient transitions of care to ambulatory settings are critical components of providing not only patient-centered care but also more cost-effective care.

Do Countries or Hospitals With Longer Hospital Stays for Acute Heart Failure Have Lower Readmission Rates?: Findings From ASCEND-HF

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