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**Retrospective Study**

30-day readmission in patients with heart failure with preserved ejection fraction: Insights from the Nationwide Readmission Database.

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**Abstract**

**BACKGROUND**

There are rising numbers of patients who have heart failure with preserved ejection fraction (HFpEF). Poorly understood pathophysiology of heart failure with preserved and reduced ejection fraction and due to sparsity of studies, the management of HFpEF is challenging.

**AIM**

Aim of our study is to determine the hospital readmission rate within 30 days of acute or acute on chronic heart failure with preserved ejection fraction and its effect on mortality and burden on health care in the United States.

**METHODS**

We performed a retrospective study using the Agency for Health-care Research and Quality’s Health-care Cost and Utilization Project (HCUP), Nationwide Readmissions Database (NRD) for the year of 2017. We collected data on hospital readmissions of 60,514 adults hospitalized for acute or acute on chronic heart failure with preserved ejection fraction. The primary outcome was the rate of all-cause readmission within 30 days of discharge. Secondary outcomes were cause of readmission, mortality rate in
readmitted and index patients, length of stay, total hospitalization costs and charges. Independent risk factors for readmission were identified using Cox regression analysis.

RESULTS
The thirty day readmission rate was 21%. About 9.17% of readmissions were in setting of acute on chronic diastolic heart failure. Hypertensive chronic kidney disease with heart failure (1,245; 9.7%) was the most common readmission diagnosis. Readmitted patients had higher in-hospital mortality (7.9% vs 2.9%, \( P = 0.000 \)). Our study showed Medicaid insurance, higher Charlson co-morbidity score, patient admitted to teaching hospital and longer stay in the hospital were significant variables associated with higher readmission rates. Lower readmission rate was found in residents of small metropolitan or micropolitan area, older age, female gender, private insurance or no insurance were associated with lower risk of readmission.

CONCLUSION
We found that patients hospitalized for acute or acute on chronic HFrEF, the thirty day readmission rate was 21%. Readmission cases were had higher mortality rate and increased healthcare resource utilization. Most common cause of readmissions were cardio-renal syndrome.

INTRODUCTION
The prevalence of heart failure (HF) constantly increasing over time. About 6.2 million adults \( \geq 20 \) years of age diagnosed with heart failure during the years 2013 and 2016 in the USA, which was lower in 2009 to 2012 with an estimated 5.7 million HF diagnosis\(^1\). HFrEF is a clinical syndrome with patients having signs and symptoms of heart failure with normal or near normal left ventricle (LV) ejection fraction as a result of high LV filling pressure \(^2\)[3].

Among HF hospitalizations, approximately half are characterized by heart failure with preserved ejection fraction (HFrEF)\(^4\). The prevalence of HFrEF compared to heart
failure with reduced ejection fraction, seems to be going up due to increasing elderly population.

The total cost associated with HF patients treatment for 2012 was $30.7 billion. According to Medicare, from 2009 to 2012 the median risk-standardized 30-day readmission rate for HF was 23.0% \footnote{1,5}. Readmissions get higher attention from researchers and policy makers as they are recognized as being related to deficient medical care and a preventable cause of higher healthcare expenditure. The Affordable Care Act introduced a financial penalty for higher readmissions for hospitals that are capped at 3% of a hospital’s total Medicare payments for 2015 and beyond. Previously, Medicare’s diagnosis-related group payment system lacked a financial disincentive to reduce readmissions \footnote{6}. The Centers for Medicare and Medicaid Services’ (CMS) Hospital Readmission Reduction Program currently only assesses risk-adjusted 30-day readmission rates for heart failure, acute myocardial infarctions, pneumonia, chronic obstructive pulmonary disease, and elective total knee and hip arthroplasty \footnote{7}.

The objective of our study was to use the Healthcare Cost and Utilization Project (HCUP), Nationwide Readmission Database (NRD) 2017 database to assess HFpEF readmission rate, compare mortality rate between the index hospitalization and readmissions, assess etiologies, and determine predictors of HFpEF readmissions to recognize areas of improvement and implement the targeted interventions.

**MATERIALS AND METHODS**

We performed a retrospective analysis of the NRD database of 2017. Our study populations were derived from the HCUP NRD database. The NRD database is sponsored by the agency for healthcare research and quality. It is an administrative database which records de-identified admission data to acute care hospitals during that specific year. The NRD includes discharges for patients with and without repeat hospital visits in a year and those who have died in the hospital.
In 2017 approximately eighteen million discharges were recorded from 2454 participating hospitals. Variable “NRD_visitlink” was used to identify the patients and the time between the two admissions was obtained by subtracting the variable “NRD_DaysToEvent.” Subtracting length of stay of index admissions from time between two admissions provided the interval time to readmission. Index hospitalizations were studied between January to November to facilitate identification of 30-day readmission rates for all discharged patients for the 2017 calendar year. During this specified period, index hospitalizations were defined as non-elective admission with a primary International Classification of Diseases and Related Health Problems (ICD)-10 diagnosis code of acute diastolic heart failure/HFpEF, (I5031) or acute on chronic HFpEF (I5033). Index hospitalizations were excluded if: (1) the patients were younger than 18 years, (2) the patient died during the index hospitalization, (3) there was no information on the length of stay (LOS).

We extracted baseline patient characteristics such as age, discharge destination, sex, primary expected payer, and median household income from the NRD database. Charlson comorbidity index was used to see the effect of chronic comorbidities of patients on primary and secondary outcomes [8]. Hospital-level variables included bed size, rural/urban location, and teaching status. Discharge to a rehabilitation facility was also obtained.

The primary outcome was defined as any non-elective, non-traumatic readmission that occurred within the first 30 days of discharge from the index hospitalization. For index hospitalizations with more than one readmission within 30 days, only the first readmission was included.

Secondary outcomes were (1) in-hospital mortality rate for index admissions; (2) 30-day mortality rate for index admissions; (3) ten most common principal diagnosis for readmission; (4) in-hospital mortality rate during readmissions; (5) resource utilization
due to readmission: LOS, total hospitalizations cost and charges; (6) Independent risk factors for admissions.

For the in-patient mortality rate, we used the patient’s recorded vitals at discharge which are directly coded in the NRD database. The thirty-day mortality was calculated by following the patient’s vital status at discharge after any readmission within 30-day of index admission.

Total hospitalization charge is the amount that hospitals billed for the entire hospital stay but not equal to the actual cost of care. The HCUP provides hospital-specific cost to charge ratios based on all-payer inpatient cost. We used this information to calculate total cost of hospitalization by multiplying total hospitalization charges by the cost to charge ratio.

We obtained the ten most common reasons for readmission by tallying the principal diagnosis for each readmission. Independent risk factors for readmission were identified using Cox regression analysis. The statistical analyses were performed using STATA statistical software (StataCorp LLC, College Station, Texas 77845 USA). P values <0.005 was considered statistically significant.

RESULTS
The study included 60,514 adult patients with acute and acute on chronic HFpEF admitted between January to November in 2017, of which 61.1% of patients were female. The mean age was 74.8 years. About 59.4% patients had Charlson comorbidity index greater than three. The majority of patients came from large metropolitan areas [46%] and had Medicare insurance (82.4%). The number of patients discharged to rehabilitation facilities was minimal [0.098%]. Teaching hospitals had a comparatively higher admission rate of 58.9% compared to non-teaching hospitals. Table 1 summarizes details of patient and hospital level characteristic of index admission.
The 30-day rate of readmission was 21%. Only 1,175 (9.17%) of readmissions were associated with an admitting diagnosis of acute on chronic HFrEF. Figure 1 shows the Kaplan-Meier survival curve, which showed the total time at risk was 850,749 days, with the initial readmission occurring at day one and the last readmission at day twenty-eight. Hypertensive chronic kidney disease with heart failure (1,245; 9.7%) was the most common diagnosis of readmission. Figure 2 shows the ten most common etiologies of readmission. Readmissions showed with higher in-hospital mortality compared to index admission (7.9% vs 2.9%, \( P = 0.000 \)).

Readmission was associated with a total of 81,997 hospital days. Total inpatient health care related financial burden was $206 million in costs and $779 million in charges. Statistically significant predictors of higher rate of 30-day readmission were, higher Charlson comorbidity index (CCI) (1.08, 1.06-1.09, \( P = 0.000 \)), Medicaid insurance (1.15, 1.05-1.27, \( P = 0.004 \)), longer LOS in the hospital (1.01, 1.01-1.02, \( P = 0.000 \)) and teaching hospital admissions (1.09, 1.04-1.15, \( P = 0.001 \)). Lower readmission risk was associated with female gender (0.91, 0.86-0.95, \( P = 0.000 \)), elderly patients (0.99, 0.993-0.997, \( P = 0.000 \)), patients from micropolitan area (0.83, 0.77-0.90, \( P = 0.000 \)) or small metropolitan (0.91, 0.86-0.97, \( P = 0.003 \)), private insurance (0.85, 0.77-0.93, \( P = 0.000 \)) or self-paying patients (0.70, 0.53-0.93, \( P = 0.015 \)). Interestingly, discharges to rehabilitation did not show significant effect on re-admission rate (0.67, 0.28-1.6, \( P = 0.381 \)). Table 2 displays the independent predictors of 30-day readmission.

Mean length of stay during index admissions was 5.2 days and 6.4 days during readmission. Readmitted patients had higher LOS (Coefficient 1.15 95%CI 0.99-1.31, \( P = 0.000 \)). Total cost of hospitalization was higher for readmitted patients (USD 4831, 95%CI 4251- 5410, \( P = 0.000 \)). Table 3 describes primary and secondary outcome details.

**DISCUSSION**
Heart failure readmission is one of the major outcomes measured by CMS. Several studies have analyzed the burden of heart failure to identify the predictors related to readmission \(^{[4,9,10]}\), however most of these combined heart failure as a single entity, with only a few studies focusing on HFrEF specific readmission \(^{[10]}\). This study specifically evaluates heart failure with preserved ejection fraction readmission rates and outcomes using the latest NRD database available at the time of study.

The patient population involved was primarily elderly, with a mean age of 74.8 years and predominantly female (61.4%) in line with previous studies \(^{[11]}\)\(^{[12]}\)\(^{[13]}\). About 59.4% of patients had CCI greater than three. A prior study had shown a mean CCI of 2.9\(^{[12]}\). Another study revealed a higher percentage of patients with CCI > 3\(^{[14]}\).

The 30-day rate of readmission was 21%, which is comparable to other studies \(^{[11]}\)\(^{[14]}\)\(^{[15]}\). A study by Arora et al \(^{[11]}\) using the NRD database of 2013 and 2014 showed a readmission rate of 18.5% and this is likely due to the increasing prevalence of HFrEF among the elderly accounting for increased readmission rates.

About 1,175 (9.17%) of readmissions were admitted with acute on chronic HFrEF. The most common readmission diagnosis was heart failure associated with hypertensive chronic kidney disease (1,245; 9.7%). Combining all cardiac readmission reasons, our study found about 26.3% readmissions were due to cardiac etiologies. A prior study has reported higher numbers (approx. 41-50%) in this category \(^{[11]}\). A study done by Parag Goyal et al in 2018\(^{[14]}\) showed a higher percentage of non-cardiac causes of readmission. This significant reduction in cardiac cause as readmission reason is encouraging, as it could be due to improvement in treatment modalities for HFrEF. This is despite the fact that there is no established goal directed medical therapy for this condition or use of monitoring modalities such as Cardiomems, which have been proven to reduce readmission rate.

Significant predictors of increased 30-day readmission rate were Medicaid insurance, higher CCI, patient admitted to a teaching hospital and longer LOS in the hospital.
Higher CCI is an obvious indicator of high readmission rate as multiple comorbidities are associated with frequent hospitalizations. Previous studies demonstrated that patients with HFP EF are also diagnosed with multiple comorbidities \cite{16,17}. We have not further analyzed individual medical conditions associated with heart failure readmission, although it would be interesting to see how these conditions affect frequent readmission. Teaching hospital patient populations are generally complex and that could explain higher readmissions. Similarly, longer LOS is explained during readmissions as this happens with sicker patients, consistent with a study by Bergethon \textit{et al.}\cite{18}.

Residence in a small metropolitan (or micropolitan area), older age, female sex, private or no insurance were associated with lower odds of readmission. Raquel Lopez Vilella \textit{et al.}\cite{19} has shown that female gender is associated with higher number of readmissions when compared to males, independent of the left ventricular ejection fraction (females = 33.5\% vs. males = 26.8\%; $p = 0.009$). Our study has shown lower odds of readmissions in females. The study by Manemann \textit{et al.}\cite{20} revealed that the rural population with heart failure has increased risk of death but reduced risk of emergency department visits as well as hospitalizations. Our study has shown residence in small metropolitan or micropolitan is a predictor of decreased risk of readmission. This might be due to the decreased or delayed access to health care facilities. Further study in this direction will help find the gaps in healthcare access in these areas.

Private insurance and no insurance are two extreme ends of the spectrum, and our study showed a lower rate of readmissions with both. The lower rate of readmission could be explained by the fact that the patients with private insurance have good preventive and acute care along with good access to healthcare compared to patients with no insurance. Patients with no insurance may have delayed care and died before even hospital readmissions.
Interestingly, discharges to rehabilitation facilities had no effect on readmission. There are some contradicting results as per recent studies. Arora et al. [4] had shown increased risk of readmission in patients discharged to rehabilitation facilities. A study by Gupta et al. [21] has shown no effect on readmission rate based on discharge to hospital-based skilled nursing facility on chronic conditions like congestive heart failure, although this study showed lower readmission rate for acute conditions like acute myocardial infarction and pneumonia. This study’s results aligned to our study even though currently we do not see many hospital-based skilled nursing facilities compared to free standing skilled nursing facilities. This result could be due to a different patient population which requires discharge to a skilled nursing facility due to their complex medical history. Further research in this regard will certainly help to find the associated factors.

Our study showed increased in-hospital mortality in readmitted patients when compared to index admission (7.9% vs 2.9%, \( P = 0.000 \)). Multiple studies have shown readmission cases are associated with increased mortality [22][23][24]. This seems to be aligned to the predictors of readmissions, as these patients are generally sicker with multiple comorbidities. It would be helpful to analyze the basic characteristics of these patients, which could further highlight mortality related to cardiac vs non cardiac causes.

Mean LOS during index admissions was 5.2 days while it was 6.4 days for readmission. Several studies have shown that increased LOS has a negative effect on readmission rate, with longer index LOS correlating with a higher risk for readmission [24][25][26]. This finding is similar to our study result, which we hypothesize could be due to sicker patients and those with multiple comorbidities requiring a longer LOS, portending to higher readmission rates.
Total cost of hospitalization was higher for readmitted patients. 81,997 hospital days were associated with readmissions. Total economic burden associated with readmissions was $206 million in costs and $779 million in charges. A study by Finger et al [27] using NRD HCUP databases showed the total economic burden of readmissions for congestive HF patients was approximately $2,728 million in 2013. This study did not further differentiate between the cost associated with heart failure with reduced ejection fraction and HFrEF. However, given the increasing prevalence of HFrEF, it is likely that HFrEF will soon, if not already, account for the majority of the economic burden of heart failure and targeted interventions are required to reduce the economic burden while improving patient care by identifying key variables involved.

CONCLUSION
For patients hospitalized for acute or acute on chronic HFrEF, 30-day readmission rate is comparable to recent studies, although readmissions were associated with higher mortality and resource utilization compared to index admission. Multiple comorbidities were associated with increased risk of readmission. Most readmissions were due to hypertensive chronic kidney disease with heart failure.

ARTICLE HIGHLIGHTS
Research background
Heart failure with preserved ejection fraction is growing problem with high risk for readmissions. To highlight cause and effect of this condition will further help making guidelines to treat and prevent readmissions.

Research motivation
This study will help understanding important variables associated with readmissions risks and burden on the American health care resource utilization.

Research objectives
The main research objective is to identify common hospital and patient related variables of increased or decreased risk of readmission in patient with heart failure with preserved ejection fraction. Identifying these variables can help the clinicians as well as the researchers to further modify these variables to improve the morbidity as well as financial burden.

Research methods
This study has used National Readmissions Dataset of year 2017 to obtain the patient with heart failure with preserved ejection fractions using international calcification of Diseases (ICD) codes -10. This was a restrospective study. COX regression analysis was used to identify the significant variables on readmission rate.

Research results
This study clearly able to show different hospital related and patient related variables which have effect on increase risk of readmissions. Also, we found some interesting results showing the variables with decrease risk of readmissions. Some of these results align with recent study result but some other shows different results which needs further research to see new change in this condition dynamics.

Research conclusions
Our result shows the rate of readmissions are similar to recent studies which means we have to work harder to reduce this rate.
We were able to provide different variables which are easy to modify which can reduce risk of readmissions. Our study showed discharge to rehabilitation facility has no effect on rate of readmissions.

Research perspectives
Further study in this important topic will be helpful to determine the ongoing change in handling this condition and decreasing its effect both on the patients as well as for the health care sector.

ACKNOWLEDGEMENTS

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