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Impact of chronic obstructive pulmonary disease on readmission after hospitalization for acute heart failure: A nationally representative US cohort study

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ABSTRACT

Background: Patients hospitalized for heart failure (HF) are at high risk of readmission. Chronic obstructive pulmonary disease (COPD) is one of the most prevalent comorbidities in this population. However, few data and only small studies describe the impact of COPD on the risk of readmission.
Methods and results: Hospitalizations for HF were identified in the 2012 National Readmissions Database. We compared clinical characteristics and the risk of all-cause, cardiovascular (CV) and respiratory-related readmission for patients with and without COPD. We included 225,160 patients hospitalized for HF among whom 54,953 had comorbid COPD. Patients with COPD were younger (median age 76 years COPD versus 77 years without COPD; $p < 0.001$), had a higher burden of comorbidity and were more frequently male (53% versus 49%, $p < 0.001$). Thirty-day all-cause readmission risk was two-fold greater in patients with COPD compared to those without COPD (adjusted HR 2.02, 95%CI 1.97–2.08). Most readmissions were attributed to a CV cause, though fewer patients with COPD had a CV admission (49% versus 51% without COPD). COPD was independently associated with significantly more frequent unplanned respiratory-related readmission (adjusted HR 2.90, 95%CI 2.68–3.15) as well as CV readmission risk (adjusted HR 1.92, 95%CI 1.85–1.99).
Conclusions: In patients hospitalized for HF, most readmissions are due to a CV cause. However, patients with comorbid COPD are at a significantly elevated risk of respiratory in addition to CV-related readmission. These data stress the importance of a multidisciplinary management approach, including optimization of non-CV conditions, in order to reduce readmissions post index HF hospitalization.

1. Introduction

Despite advances in the treatment of chronic heart failure (HF), patients who are hospitalized for HF remain at high risk of readmission [1]. Readmission may have a profoundly negative impact on a patients' quality of life and represents a considerable economic burden for healthcare systems. Additionally, 30-day readmission rates are currently used by the Centers for Medicare and Medicaid Services to judge the quality of hospital care and penalties are accrued by hospitals with high readmission rates [2]. Importantly, however, not all readmissions are due to decompensated HF and in the pursuit of more effective and holistic HF care models, there has been growing emphasis on the management of non-cardiac comorbidities in this population [3,4]. Between 40% [5] and 80% [6] of patients with HF have two or more comorbidities, which may complicate management of their disease via misattribution of symptoms, accelerating disease progression, or due to adverse effects of polypharmacy, which may prevent optimal HF therapy.

Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity among patients with HF, with a reported prevalence of 10% to 40%, depending on the population under study and diagnostic criteria used [1,7–10]. Few studies have specifically examined the prognosis of patients with acute HF and concomitant COPD, and among these an increase in adverse outcomes, including hospitalization and death have been reported [7,10–12]. Whether this increase in risk is directly attributed to COPD or may be explained by a clustering of multiple chronic diseases in patients with hospitalized HF, is unclear. Furthermore, cause-specific hospitalization has been less well described in this population and is poorly captured in HF studies with a focus on cardiovascular outcomes. Such information is important for decisions regarding post-discharge care, resource allocation and the design of strategies to prevent readmission.

To address these areas of uncertainty, we compared the comorbidity profiles, frequency, and causes of readmission among patients with

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hospitalized HF, with and without COPD, in a large, contemporary and nationally representative US cohort. We hypothesized that hospitalized HF patients with COPD would have greater levels of comorbidity, but that COPD would be independently associated with an increased risk of readmission and specifically readmission due to a respiratory cause.

2. Methods

2.1. Data source

The study cohort was derived from the United States National Readmissions Database (NRD), which comes from a group of publicly available, all-payer databases developed by the Agency for Healthcare Research and Quality for the Healthcare Cost and Utilization project. The NRD contains discharge data from 27 US States, accounting for 57.8% of the US resident population and 56.6% percent of all US hospitalizations. All discharge records of patients treated in community hospitals, excluding rehabilitation and long-term acute care facilities are included. Patient linkage numbers are used to track a patient across hospitals within a state thus protecting the identity of individual patients, physicians, and hospitals. Outcomes in the NRD include national readmission rates, reasons for returning to the admitting hospital and discharge costs. In the present study we utilized data from the calendar year 2012. Ethical approval was not required for this study as NRD is a publicly available de-identified administrative database.

2.2. Study population

We used the International Classification of Diseases 9th revision, Clinical Modification (ICD-9CM), Clinical Classification Software (CCS) code 108 to identify all hospitalizations with a primary reason of HF (ICD-9CM codes 398.91; 428.xx, Supplemental Table 1), akin to previous studies using the NRD [13,14]. We excluded rheumatic HF due to its predominant valvular sequelae and thus differential management to other causes of congestive HF. For analyses of 30-day readmission, patients with an index admission in December were excluded, and for analyses of 90-day readmission patients with an index admission in October, November and December were excluded (as 30-day and 90-day follow-up would not be available, respectively). For optimal accuracy, we excluded patients with missing data on demographics, length of stay (LOS) or index hospitalization survival status. Patients who were not resident in the state where the index hospitalization had taken place were also excluded as their subsequent hospitalizations could not be linked. Lastly, as COPD is generally diagnosed in older age, patients younger than 40 years were excluded [15] and for all patients, only non-elective (i.e. emergency) hospitalizations were studied (Fig. 1).

2.3. Definitions and outcomes

Readmissions and time from index hospitalization discharge to first readmission were identified according to the methods outlined by the Healthcare and Utilization Project [16]. If a patient had multiple readmissions within 30 days, only the first one was included in the analysis. Causes of readmission were identified using ICD-9CM codes in the primary diagnosis field (Supplemental Table 2). NRD specific "cm_" variables were used to identify co-morbidities. This was performed using available diagnoses and the diagnosis-related group coded on the discharge date. Co-morbidities were considered as those conditions not directly related to HF. These methods have been utilized in other studies [13,17].

Comorbidities included were: atrial fibrillation (AF), coronary artery disease (CAD), diabetes, obesity [defined as a Body Mass Index (BMI) > 30)], hypertension, liver disease, renal failure, cancer, anemia, peripheral vascular disease, weight loss, coagulopathy and depression. COPD status was not pre-defined in NRD. Thus, for each hospitalization, and patient, we identified whether an ICD-9 CM code for COPD was included in the patient's record and created a diagnostic label for prevalent COPD (Supplementary Table 1). These ICD-9CM codes have been previously used to identify COPD in administrative databases with high accuracy [18–20].

NRD variables were used to identify patients' demographic characteristics including age; gender, median household income category for patient's zip code, payer, discharge status, index hospitalization (baseline) in-hospital mortality and LOS. We did not have access to out-of-hospital mortality data. We therefore assumed that patients who were admitted only once and did not die in hospital were still alive at the end of 30-days, or 90-days, for the respective analyses. Other studies have used a similar approach [21,22]. To verify our findings, a sensitivity analysis was performed excluding all patients with no readmissions after the index hospitalization.

The primary outcome of this study was readmission due to any cause at 30-days. Secondary outcomes were readmission due to any cause at 90-days and respiratory-related or cardiovascular (CV) readmission at 30- and 90-days respectively. Outcomes were compared between hospitalized HF patients with and without COPD.

For the primary outcome of 30-day readmission risk, based on a sample of 217,979 observations (excluding patients who died during their index hospitalization) and a probability of readmission of 0.20 in the overall population, we had >95% power to detect a HR of 1.2, assuming a type I error rate (alpha) of 0.001.

2.4. Statistical analysis

Data are presented as frequency (%) for categorical variables and mean ± standard deviation (SD), or median and interquartile range (IQR) for non-normally distributed, continuous variables. Differences in baseline characteristics between patients with and without COPD were assessed using the Chi-square test for categorical variables and Kruskall-Wallis tests for continuous variables.

Cox proportional hazards regression models were conducted to test the association between COPD and 30-day or 90-day all-cause, CV and respiratory-related readmission. Multivariable analyses adjusted for baseline characteristics with a p-value of 0.1 in univariate analyses (age, gender, comorbidities and index LOS). Time to first 30-day, or 90-day readmission was analyzed for the entire hospitalized HF cohort and separately, stratified by COPD status. Potential interactions between COPD status and baseline variables were explored. Patients with a single (index) admission only were censored at 30-days or 90-days, respectively, in primary analyses. Kaplan-Meier curves were used to compare 30-day and 90-day readmission rates between HF patients with and without COPD. Patients who died during their index hospital admission were excluded. No variables used in the main analyses had missing data. Statistical analyses were performed using R software 3.4.4. All p-values were two-sided; $p < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline characteristics

Among 225,160 patients hospitalized for HF, 54,953 (24.4%) had a concomitant diagnosis of COPD. Baseline characteristics of the study population are presented in Table 1. When compared to patients without COPD, HF patients with COPD were, on average, younger, more frequently male and had a higher overall burden of comorbidity (Table 1).

Data regarding income was available for 222,002 (98.6%) patients. Approximately half of the total study population were in middle income brackets, 26th–75th percentiles, with equal proportions of patients with and without COPD. However, a greater number of patients with COPD occupied the lowest income bracket, 0 to 25th percentile (34% with COPD vs. 31% without COPD). Insurer details were available for 224,399 (99%) patients. Patients with COPD were more likely to be insured by Medicare (81% vs. 76%) as compared to those without COPD and less likely to have private insurance (7% vs. 11%) or self-pay status (4% vs. 6%) (Supplemental Table 3).

3.2. Index hospitalization

In total, 7181 (3.19%) patients died during their index HF hospitalization. Fewer patients with comorbid COPD died, as compared to those without COPD (2.8% vs. 3.3%). However, patients with COPD had a similar length of index hospital admission (median inter-quartile range [IQR] 4 [3–7] days with COPD and 4 [2–6] days without COPD) and accompanying greater cost of hospitalization (median charge $26,269 with COPD vs. $25,000 for patients without COPD). Discharge destination also differed by COPD status. Patients with COPD were more likely to be discharged to home health care (26% COPD vs. 24% no COPD) or transferred to a skilled nursing facility (20% COPD vs. 18% no COPD) rather than discharged home, with or without additional support (Supplemental Table 3).

3.3. Readmission rates, reasons and risk factors

Overall, 65,237 (29%) patients in this cohort were readmitted to hospital, including 24,646 (45%) patients with COPD and 40,591 (24%) patients without COPD. Median [IQR] time to first readmission was shorter in those with COPD (47 [18–106] days) as compared to those without (51 [19–115] days, $p < 0.001$). Comorbid COPD was also associated with a higher frequency of 30-day (17% COPD vs. 8% no COPD, $p < 0.001$) and 90-day (34% COPD vs. 17% no COPD, $p < 0.001$) readmission (Fig. 3 e-component, Supplemental Fig. 1).

Compared with patients without COPD, those with COPD were twice as likely to be readmitted within 30 days of discharge following their index hospitalization even after adjusting for differences in baseline characteristics and LOS [adjusted HR 2.02, 95%CI 1.97 to 2.08]; at 90 days the risk of readmission was greater still (adjusted HR: 2.12, 95%CI 2.07 to 2.16).

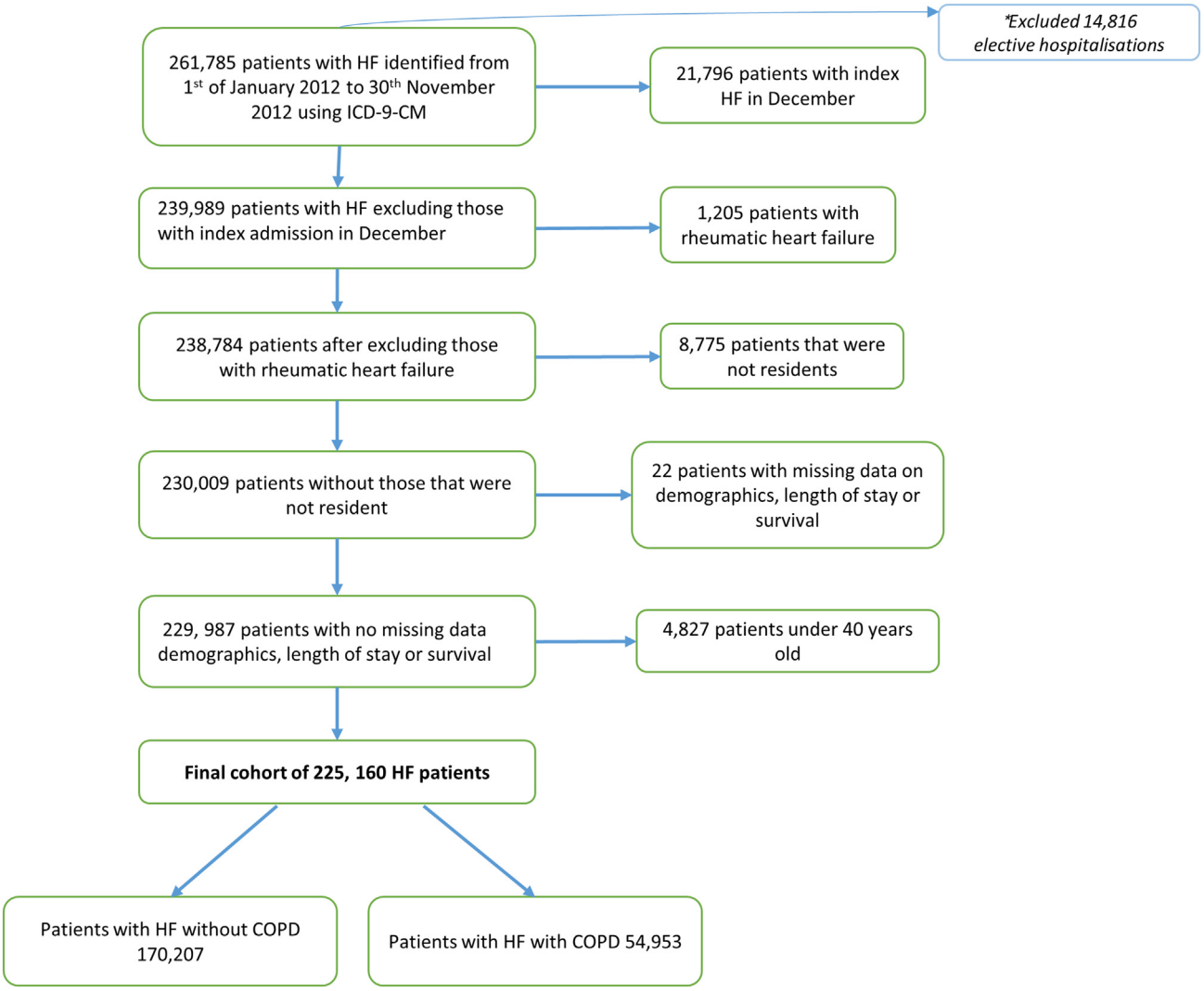

Fig. 1. Flowchart of the study population.

When 30-day readmission data were stratified by COPD status, female gender, baseline diabetes, renal failure, anemia and index admission LOS were associated with an increased risk of readmission, regardless of COPD status (Fig. 4 e-component, Supplemental Table 4). Conversely, AF, CAD, liver disease, cancer and peripheral vascular disease were only associated with an increased risk of readmission in patients without COPD. Readmission risk tended to be lower in patients above 70 years of age, but was statistically significant among the subset of patients with COPD, likely to reflect a competing risk of death or transfer to skilled facilities among elderly persons.

Similar associations were observed for 90-day readmissions, with the exception of renal failure which displayed a more marked effect in patients without COPD (p-value for interaction with COPD <0.001, Supplemental Fig. 2). An inverse association between age and readmission risk was also evident in patients older than 70 years, regardless of COPD status.

The most frequent reason for readmission within 30-days was due to a CV cause (50.9% of all admissions). Respiratory disease was the second most frequent cause of readmission (13.3% of all admissions, 26% of non-CV admissions, Supplemental Fig. 3). Marginally fewer patients with COPD had a primary CV readmission within 30-days, as compared to patients without COPD (49% vs. 51%, p-value <0.001). However, a significantly higher proportion of HF patients with COPD were readmitted for respiratory-related reasons vs. HF patients without COPD (16% vs. 11%, $p < 0.001$) (Fig. 2).

The 30 and 90-day CV and HF-related readmission rates were higher in patients with COPD as compared to those without COPD, even after adjusting for differences in baseline characteristics. Importantly, however, COPD also exhibited a greater than two-fold increased risk of readmission due to a respiratory cause, as compared to those without COPD, and more than three-fold increased readmission risk when COPD was attributed as the specific cause. Albeit, the overall number of COPD-related admissions in both groups was low (Table 2).

4. Discussion

In this large, nationally representative cohort of patients with an index hospitalization for HF in the US, comorbid COPD was present in 1 in 4 patients. When compared to HF patients without COPD, those with COPD exhibited a two-fold increased risk of readmission due to any cause. This included more frequent HF as well as respiratory-related readmissions. Although, the most common reason for readmission was due to a CV cause, the risk of a respiratory-related readmission was two-fold greater, and COPD-specific readmission three-fold greater, in patients with COPD as compared to those without. These findings suggest a difference in the short-term trajectory following index HF hospitalization for patients with COPD with a particularly heightened risk of respiratory disease-exacerbation.

Table 1
Baseline characteristics by COPD status

	Overall (N = 225,160)	No COPD (N = 170,207)	COPD (N = 54,953)	p-Value
Gender				<0.001
Male	111,753 (50%)	82,751 (49%)	29,002 (53%)	
Female	113,407 (50%)	87,456 (51%)	25,951 (47%)	
Age (years)				
Median (IQR)	76.00 (65.00, 85.00)	77 (64.00, 86.00)	76 (66.00, 84.00)	<0.001
Atrial fibrillation	92,653 (41%)	68,968 (41%)	23,685 (43%)	<0.001
Coronary artery disease	122,372 (54%)	89,545 (53%)	32,827 (60%)	<0.001
Obesity[a]	39,514 (18%)	28,848 (17%)	10,666 (19%)	<0.001
Weight loss	10,410 (5%)	7750 (5%)	2660 (5%)	0.05
Peripheral vascular disorders	27,884 (12%)	19,259 (11%)	8625 (16%)	<0.001
Coagulopathy	13,374 (6%)	10,115 (6%)	3259 (6%)	0.92
Renal failure	90,764 (40%)	67,715 (40%)	23,049 (42%)	<0.001
Liver disease	6642 (3%)	4882 (3%)	1760 (3%)	<0.001
Diabetes	75,966 (34%)	56,632 (33%)	19,334 (35%)	<0.001
Cancer	6603 (3%)	4835 (3%)	1768 (3%)	<0.001
Anemia	69,719 (31%)	51,806 (30%)	17,913 (33%)	<0.001
Hypertension	173,646 (77%)	131,565 (77%)	42,081 (77%)	<0.001
Depression	20,634 (9%)	14,619 (9%)	6015 (11%)	<0.001
LOS (days)				
Median (IQR)	4.00 (2.00, 6.00)	4 (2.00, 6.00)	4 (3.00, 7.00)	<0.001
In-hospital mortality	7181 (3.19%)	5655 (3.3%)	1526 (2.8%)	<0.001

IQR: interquartile range; LOS: length of stay.
[a] Obesity was defined as Body Mass Index (BMI) > 30.

4.1. Prevalence of COPD and comorbidities in patients hospitalized for HF

The present analysis represents one of the largest studies to date of patients with hospitalized HF (n = 225,160). Our reported prevalence of COPD is similar to contemporary studies, using electronic health records and clinical studies of HF cohorts where COPD status was clinician-verified [9,23]).

Patients with HF and COPD had a greater overall burden of comorbidity and shorter time to first readmission, but lower in-hospital mortality, as compared to those without COPD ($p < 0.001$). Interestingly, two recent European studies reported higher in-hospital mortality among patients with HF and comorbid COPD versus HF alone [10,11]. In our cohort, patients with comorbid COPD were marginally younger than those without, which may have contributed to a lower in-hospital mortality. Other potential explanations for the unexpectedly lower rate of in-hospital mortality for patients with COPD may include specific therapeutic strategies, such as oral steroids, which may unintentionally treat other conditions besides COPD, or other unrecorded differences in management that may not be completely captured by routinely collected electronic health record data. Alternatively and more plausibly, this may be a chance finding, as can occur in the analyses of large datasets.

We found patients with comorbid COPD were not older than those without COPD. Previous research on age differences between these groups are inconsistent: some studies report patients with comorbid COPD to be older than those without [11], whilst some report the opposite [7]. Interestingly, all studies have distinct inclusion criteria for participants, ranging from a requirement to be over 18 years old [7], to over 40 years [10] or even 65 years old [24]. The variability of inclusion criteria across studies likely explains the heterogeneous results and adds difficulty in comparing them across the literature. Nonetheless, our result suggests patients' greater comorbidity burden cannot exclusively be attributed to older age and highlight a high risk subgroup.

4.2. Risk and causes of readmission in patients hospitalized for HF

In keeping with our hypothesis, patients with HF and COPD were more likely to be readmitted as compared to those without COPD. This finding is comparable to previous studies reporting higher readmission rates in patients with HF and COPD [11,25].

Importantly, however, whilst previous studies [10–12] showed an increased risk of CV or HF readmission in the long term (i.e. over one year or more), our study highlights a heightened risk within the immediate post-discharge period, within 30 and 90 days. Potential contributors to this early risk include a greater burden of comorbidity and sustained low-grade inflammation associated with COPD, which may increase in time. The plausibility of this assumption is enhanced in our study by the increasing trend in risk of CV readmission 90-days post first discharge (an increase of 5% compared to the 30-day results, respectively 7% for HF specific readmission, Table 2). In addition, possible under-recognition or suboptimal treatment of HF symptoms in this group of patients may also affect CV risk.

As the most frequent reason for hospitalization overall was still due to a CV cause, including HF, the need for optimal HF therapy and early identification of post-discharge HF decompensation in this population remains paramount.

This study has also highlighted an independent positive association between comorbid COPD and the risk of respiratory-related readmission, in particular due to COPD exacerbation. Whilst this may be expected, if true, it suggests a potential opportunity for COPD-targeted therapy to improve outcomes in this subgroup. An alternative consideration is that, due to overlapping symptoms and signs with HF, a proportion of CV or HF-related readmissions may be (mis)attributed (or coded) as being due to COPD in patients with this comorbidity. The fact, that the national hospital penalty program [26] has created financial incentives to encourage documentation of comorbid conditions, may have led to more sensitive detection of COPD (including potential false positive diagnoses). Ibrahim et al. [27] reported that greater than half of the reduction in the risk-adjusted readmission risk for three targeted conditions, including HF, may be attributed to an increase in "up coding" of severity of illness based on comorbid diseases. Differentiation of these hypotheses will need prospective evaluation and confirmation, but would be important to ensure appropriate care pathways were followed for patients with HF and COPD.

Finally, the present study, identified differences in the risk factors for readmission between patients with and without COPD. The fact that recognized risk factors for readmission in the non-COPD cohort (AF, CAD and renal failure) were not found to be predictive of readmission in patients with COPD, may suggest a greater prognostic impact of COPD in this timeframe (Fig. 4, Supplemental Table 4). Hence, our results support a need for early recognition and optimization of COPD management in patients who present to hospital with acute decompensated HF.

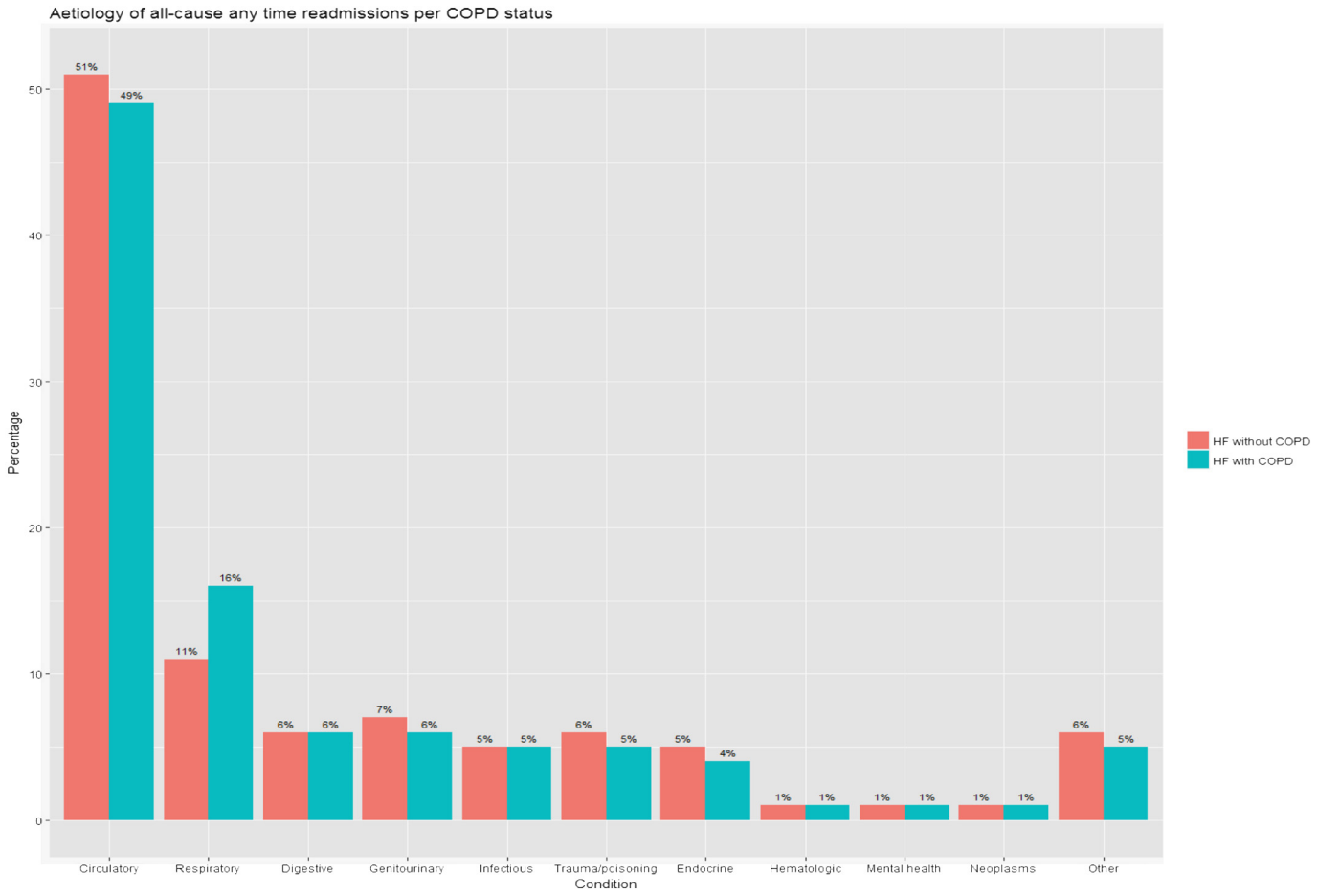

Fig. 2. Causes of readmission in patients with an index hospitalization for heart failure.

5. Limitations

This study has several limitations. Firstly, we did not have access to data regarding post-discharge death, which may have had a differential impact on the risk of readmission between patients with and without COPD. Interestingly, previous studies report conflicting findings regarding the competing risk of out-of-hospital mortality [28,29] and these data are not currently included in the assessment of US hospital performance. Nevertheless, to address this relevant limitation, we conducted a sensitivity analysis excluding patients with no data after the index admission (i.e. the sensitivity dataset comprised only those patients with one or more readmissions). There was no material change

Table 2
Association between COPD and readmission.

	COPD	No COPD	Unadjusted HR[a] (95% CI)	Adjusted HR[a] (95% CI)
	Number of events (%)[b]	Number of events (%)[b]		
All-cause readmission				
30-day	9238 (16.8%)	14,430 (8.4%)	2.06 (2, 2.11)	2.02 (1.97, 2.08)
90-day	15,535 (33.7%)	23,982 (17.5%)	2.07 (2.02, 2.11)	2.12 (2.07, 2.16)
CV readmission				
30-day	4586 (8.3%)	7458 (4.3%)	1.98 (1.90, 2.05)	1.92 (1.85, 1.99)
90-day	7747 (16.8%)	12,479 (9.1%)	2.03 (1.97, 2.08)	1.97 (1.91, 2.03)
HF readmission				
30-day	3025 (5.5%)	4664 (2.7%)	2.08 (2, 2.18)	2.05 (1.96, 2.15)
90-day	5135 (11%)	7786 (5.7%)	2.15 (2.08, 2.23)	2.12 (2.05, 2.20)
Respiratory readmission				
30-day	1170 (2.1%)	1258 (0.73%)	2.99 (2.76, 3.24)	2.90 (2.68, 3.15)
90-day	1940 (4.2%)	2000 (14.6%)	3.16 (2.97, 3.37)	3.08 (2.90, 3.29)
COPD readmission				
30-day	82 (0.14%)	55 (0.03%)	4.80 (3.14, 6.76)	4.76 (3.37, 6.72)
90-day	139 (0.3%)	92 9 (0.07%)	4.95 (3.8, 6.44)	4.82 (3.7, 6.03)

HR adjusted for age, gender, diabetes, hypertension, obesity, renal failure, liver disease, cancer, weight loss, peripheral vascular disease, coagulopathy, anemia, depression, length of stay
CI, confidence intervals; COPD, chronic obstructive pulmonary disease; CV, cardiovascular.

[a] COPD vs. no COPD.

[b] Calculated as number of events/total number of patients (30-day denominator COPD: 53,427; no COPD: 164,552; 90-day denominator COPD: 46,090; no COPD: 136,608). Note: the denominator used for 90 day readmission did not include patients with an index HF hospitalization in the months of October, November and December – see Methods.

to the associations observed from the main analysis, with the exception of a change in CV readmission risk (Supplemental Table 5). Whilst this analysis does not completely circumvent the lack of post-discharge death data, it suggests that the difference in risk of all-cause, HF, and respiratory-related readmission between the two groups cannot be entirely explained by a competing risk of death. Therefore our data support a detrimental effect of COPD.

Secondly, this is a retrospective analysis of administrative data, subject to recognized limitations of large data sources (e.g. potential coding errors resulting in diagnosis inaccuracy). We used ICD-9CM codes to identify COPD, a strategy that has been used in studies using large administrative databases, in the US and elsewhere. Studies where such codes were validated report an accuracy of 85%, deemed acceptable for epidemiological research [18,20]. Whilst the gold standard for diagnosing COPD is spirometry, this was not documented for this cohort. Moreover, spirometric-diagnosis of COPD has only been used in a minority of studies of HF patients and its interpretation may be problematic during acute HF decompensation, leading to misclassification [11].

Similarly, information regarding potential confounders including clinical stage of HF (e.g. New York Heart Association class), cardiac function, and treatment were unavailable.

Lastly, the NRD tracks readmissions within a single calendar year only, thus our numbers are only representative of this time period and may be underestimated.

6. Conclusion

In a large, nationally representative, US cohort, we have demonstrated that COPD increases the short-term risk of readmission in patients hospitalized for HF. Although most hospitalizations were due to a CV cause, COPD was additionally independently associated with significantly more frequent respiratory-related readmissions, including COPD exacerbation. Risk factors for readmission, also differed between patients with and without COPD. These data suggest that COPD status is a relevant consideration in the holistic management of patients with acute decompensated HF and for clinicians and policy makers designing strategies to reduce both respiratory and CV readmissions in this population. Future studies should evaluate whether concurrent evaluation and optimization of COPD management, for those with the comorbidity, would reduce readmission rates, among patients with acute decompensated HF.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.04.087.

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