The Impact of Non-invasive Ventilation on Health Cost and Outcomes

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PURPOSE

- Chronic obstructive pulmonary disease (COPD) is a common disorder affecting approximately 7% of the U.S. population.[1] As COPD progresses, many patients develop chronic respiratory failure (CRF), which increases the risks of death and hospitalization, reduces quality of life, and increases health care costs.
- Treatment strategies such as non-invasive ventilation at home (NIVH) have been employed in an effort to mitigate these adverse outcomes. Despite conflicting data supporting improved outcomes for NIVH in COPD-CRF, its use is rapidly increasing. However, while NIVH use is rapidly increasing, fewer than 5% of patients with COPD-CRF are currently prescribed NIVH.[2]
- This study sought to understand the association of NIVH use with risk of mortality, hospitalizations, and ER visits.

METHODS

Data source

- Retrospective cohort study using the Medicare Limited Data Set (LDS) between 2012 and 2017. The LDS contains information on Medicare Part A and B for a randomly selected 5% sample of the Medicare fee-for-service population.[3]

Study cohort

- Patients were included who had a diagnosis of both CRF and COPD between 2012 and 2017, and were divided into a treatment group identified by receipt of NIVH within two months of initial CRF diagnosis (index date), and a control group defined by absence of NIVH treatment. All patients were enrolled in traditional fee-for service plans for at least 18 months.
- Patients were excluded if they had ever been diagnosed with obstructive sleep apnea or dementia.

Study outcomes

- The primary outcome of this study was overall survival (time to death). Secondary outcomes were time to first hospitalization, and time to first emergency room (ER) visit.
- All patients were followed until event occurrence or censoring.

Statistical analysis

- The association between NIVH and outcomes were estimated using time-to-event analyses (Cox regressions).
- The estimated hazard ratios (HRs) were allowed to be time-varying to account for violation of the Cox proportional hazard assumption.
- All outcomes were measured as time from index CRF diagnosis to first occurrence of a primary or secondary endpoint.
- Additionally, the absolute risk reduction (ARR), relative risk reduction (RRR), and the number needed to treat (NNT) were measured using a one-year time frame.
- Due to the observational nature of this study, two methods were employed to control for confounding and selection bias. Using both methods is a conservative approach as either can provide consistent estimates of treatment effects:
  1. Inverse probability weighting (IPTW): The control group was reweighted to more closely resemble the treatment group using stabilized inverse probability of treatment weights.
  2. Inclusion of controls in the Cox regressions.
- The set of demographic and clinical factors controlled for and used for matching included race/ethnicity, gender, age, region of the country, the components of the Charlson Comorbidity Index, total health care spending for 6 months prior to index date, county-level smoking prevalence, and comorbid hypercapnia.
- Bootstrap methods were used to calculate standard errors as both the propensity score estimation procedure and the regression models were computed with error.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Descriptive statistics

- The treatment group consisted of 410 COPD-CRF patients treated with NIVH, and the control group consisted of 36,247 COPD-CRF patients not treated with NIVH.
- Statistically significant differences in baseline demographic characteristics and clinical factors existed between the treatment and control group **(Table 1)**. Most notably, the treatment group was younger than the control group and had lower six-month pre-index date total healthcare spending.
- The IPTW weighting procedure achieved good balance between the treatment and control group **(Table 1)**. After reweighting, only gender was significant at the p<0.05 level.

Primary endpoint analysis results

- Patients receiving NIVH had a 38.3% reduction in risk of death compared to those not receiving NIVH (HR: 0.617, 95%CI: 0.462-0.772) at index date. This decreased risk of death for those receiving NIVH diminishes by 0.1% per day (HR: 1.001, 95%CI: 1.001-1.001) **(Table 2 & Figure 1A)**. After 69 weeks, the survival benefit of NIVH disappears **(calculated from Table 2).**
- One year from index date, 34.6% of patients receiving NIVH died versus 46.7% of patients not treated with NIVH. This translates to an ARR of 12.2%, yielding a RRR of 26.0%. The NNT to prevent death within the first year was 8.2 **(Table 3)**.

Secondary endpoints analysis results

- Hospitalizations
  - Patients receiving NIVH had 30.1% reduction in risk of hospitalization (HR 0.699, 95%CI, 0.582-0.844) at index date. The decreased risk of being hospitalized is constant over time **(Table 2 & Figure 1B)**
  - After one year, 66.3% of patients prescribed NIVH had been hospitalized versus 74.5% for those not using NIVH. This translates to an ARR of 11.3%, yielding a RRR of 15.1%. The NNT to prevent a first hospitalization within the first year was 8.9 **(Table 3)**.
- ER visits
  - Patients receiving NIVH had 45.5% reduction in risk of ER visit (HR 0.545, 95% CI, 0.450-0.639) **(Table 2)**. The decreased risk of having an ER visit for those receiving NIVH diminishes 0.1% per day (HR: 1.001, 95%CI: 1.001-1.001) **(Table 2 & Figure 1C)**; there is no decreased risk of having an ER visit for NIVH patients past 87 weeks **(calculated from Table 2).**
  - After one year, 73.4% of patients prescribed NIVH had been to the ER versus 89.1% for those not using NIVH. This translates to an ARR of 15.7%, yielding a RRR of 17.7%. The NNT to prevent a firster visit within the first year was 6.4 **(Table 3)**.

Limitations

- Due to the observational nature of this study, we used IPTW and regression controls simultaneously to control for potential confounding or selection bias. These techniques provide consistent estimates of treatment effects if either one or both of the models (the regression model or the propensity score model) are properly specified.
- The LDS data do not include information that enabled us to identify the different types of CRF.
- Information on the frequency and duration of NIVH treatment is not included in the LDS data. Hence, this study cannot answer questions regarding the level of compliance with NIVH needed to achieve improved clinical outcomes.

Conclusions

- Use of NIVH among COPD-CRF patients was associated with a statistically significant and clinically meaningful reduction in the risk of death, hospitalization, and ER visit compared to similar patients not treated with NIVH.

Clinical Implications

- Physicians caring for COPD-CRF patients should consider prescribing NIVH treatment to reduce patient mortality, hospitalizations, and ER visits.

Table 1. Balance diagnostics

	Treatment group (unweighted)	Control group (unweighted)	Difference in means p-value	Treatment group (weighted)	Control group (weighted)	Difference in means p-value
Patient count	410	36,247		773	36,096	
Age at index date (Mean, SD)	70.3 (10.8)	75.0 (10.9)	<0.001	74.8 (10.3)	75.0 (10.9)	0.75
Male	43.4%	44.2%	0.76	37.5%	44.0%	0.04
Race						
White	86.6%	87.9%	0.43	89.9%	88.0%	0.29
Black	7.6%	8.0%	0.73	6.0%	7.9%	0.14
Other	5.9%	4.1%	0.08	4.2%	4.1%	0.92
Medical spending 6 months pre-index date (Mean, SD)	$18,350 ($24,418)	$33,027 ($50,901)	<0.001	$26,916 ($35,883)	$32,742 ($50,579)	0.08
Comorbidities						
Cerebrovascular disease	14.1%	21.9%	<0.001	19.4%	21.8%	0.42
Congestive heart failure	32.0%	43.8%	<0.001	44.2%	43.7%	0.89
Chronic pulmonary disease†	89.8%	82.2%	<0.001	83.5%	82.3%	0.73
Diabetes	21.2%	20.9%	0.86	23.0%	20.9%	0.56
Any malignancy, except neoplasm of the skin	11.0%	15.3%	0.02	16.2%	15.2%	0.74
Moderate/severe liver disease	0.5%	1.2%	0.18	0.8%	1.2%	0.47
Myocardial infarction	8.0%	15.7%	<0.001	13.9%	15.6%	0.53
Peptic ulcer disease	1.0%	3.2%	0.01	4.3%	3.2%	0.65
Peripheral vascular disease	19.3%	30.9%	<0.001	30.7%	30.6%	0.95
Renal disease	12.7%	28.2%	<0.001	24.6%	28.0%	0.36

Note: Chronic pulmonary disease was measured within 6 months prior to index date. 42 patients in the treatment sample received COPD diagnosis at index date, i.e., the same date as the CRF diagnosis. Abbreviations: SD = Standard deviation

Table 2. Primary and secondary results, hazard ratios

	HR (95% CI)
Overall survival	0.617*** (0.462, 0.772)
Change in HR over time for overall survival	1.001*** (1.001, 1.001)
Time to first hospitalization	0.699*** (0.582, 0.844)
Change in HR over time for time to first hospitalization	1.000 (0.999, 1.000)
Time to first ER visit	0.545*** (0.450, 0.639)
Change in HR over time for time to first ER visit	1.001*** (1.000, 1.001)

*** p<0.01, ** p<0.05, *p<0.1

Abbreviations: CI = Confidence interval, ER = Emergency room, HR = Hazard Ratio, NIVH = Non-invasive ventilation at home

Table 3. One –year absolute risk reduction, relative risk reduction, and number needed to treat, by outcome

Outcome	% with event (treatment group)	% with event (control group)	Absolute risk reduction (95% CI)	Relative risk reduction (95% CI)	Number needed to treat (95% CI)
One-year mortality	34.6%*** (28.0%, 42.8%)	46.7%*** (46.2%, 47.2%)	12.2%*** (4.1%, 18.5%)	26.0%*** (8.5%, 39.7%)	8.2 (5.4, 24.4)
Hospitalizations	63.3%*** (58.0%, 68.3%)	74.5%*** (74.1%, 75.0%)	11.3%*** (5.9%, 16.7%)	15.1%*** (8.0%, 22.3%)	8.9 (6.0, 17.0)
ER visits	73.4%*** (68.7%, 77.6%)	89.1%*** (88.8%, 89.5%)	15.7%*** (11.4%, 20.4%)	17.7%*** (12.8%, 23.0%)	6.4 (4.9, 8.8)

*** p<0.01, ** p<0.05, *p<0.1

Abbreviations: ER = Emergency room

Figure 1. Stratified Kaplan-Meier failure curves for A) overall survival (death rate), B) time to first hospitalization, C) time to first ER visit

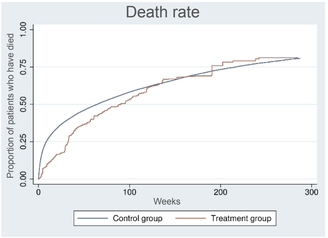

Figure 1A

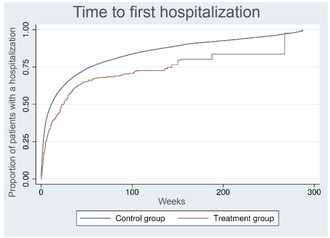

Figure 1B

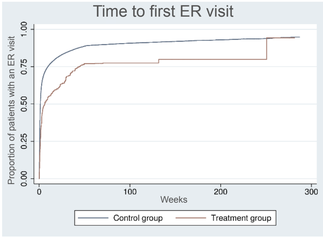

Figure 1C

DISCLOSURES

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