Loneliness and ED Visits in Chronic Obstructive Pulmonary Disease

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Abstract

The primary objective of this study was to investigate the association of loneliness and the incidence of ED visits in a large and well-characterized cohort of patients with severe chronic obstructive pulmonary disease (COPD); the association of loneliness with performance measures and health perception was the secondary objective. Baseline data were used from the National Emphysema Treatment Trial (NETT), which investigated the effectiveness of lung volume reduction surgery in patients with moderate-to-severe COPD. Patients received Quality of Wellbeing questionnaires, which asked about loneliness and social isolation. For comparing baseline variables between lonely and non-lonely subjects, we used $\chi^2$ tests for categorical variables and Wilcoxon tests for continuous variables. The association of loneliness with ED visits and health perception was assessed with a logistic model that adjusted for multiple critical confounders. The study took place from December 2002, to December 2004, with a follow-up period of 5 years to assess loneliness and 24 months to assess use of the emergency department. There were 1218 patients analyzed, mean age 65 (standard deviation [SD] 12), 47% were women, FEV 1% 41 (SD 12); 7.9% of participants reported feeling lonely. These individuals had worse health ratings, 6-minute walk tests (6MWTs), and breathlessness. Loneliness was independently associated with ED visits after adjusting for age, lung function, dyspnea, 6MWT, treatment, and gender, odds ratio (OR) 1.57 (95% confidence interval [CI], 1.005-2.466), $P = .04$. This study suggests that loneliness in patients with COPD is significantly and independently associated to ED visits and reduced health perception. Addressing loneliness of patients with COPD in the outpatient setting may contribute to improved health perception and less health care utilization.

Chronic obstructive pulmonary disease (COPD) is a common chronic condition, estimated to affect 11.7% of the population across the globe. This figure is expected to increase over the next 30 years with a subsequent rise in the number of deaths due to the condition. At present, it is the fourth most common cause of death in the United States. Anxiety, depression, and loneliness are commonly recognized psychologic comorbidities of COPD. Quality of life in patients with COPD is affected by these factors and comorbidities leading to an inability to engage in activities, decreased exercise capacity, and anxiety/depression.

Loneliness, in particular, is a significant obstacle for individuals living with COPD, as well as an overall public health concern. Loneliness can be defined as the feeling that one’s social relations are inadequate, leading to subjective dissatisfaction. This subsequently may contribute to a sense of distress and has been linked to adverse outcomes in mortality and mental health. Overall, loneliness seems to be increasing in the United States and prevails among older adults. Those with limited mobility—which can be seen in the COPD population because of progressive lethargy and dyspnea—are at increased risk for loneliness. Loneliness is associated with social-skill deficits and worse outcomes in mental health issues such as depression and anxiety, leading to worsening dyspnea. In addition, patient lack of understanding about their own diagnoses of COPD can lead to social isolation and increased mortality.

Similarly, the concept of social isolation, both objective and subjective, is associated with an increased risk of mortality and higher
health care utilization.\textsuperscript{13,14} It has been shown that persons who primarily use outpatient health care compared with inpatient health care feel less lonely and have a lower risk of depression.\textsuperscript{15} Patients who experience chronic loneliness have higher numbers of physician visits, particularly the emergency department,\textsuperscript{7} suggesting that there may be a cycle of illness and use of the health care system.\textsuperscript{14} There is a knowledge gap on the association of loneliness and health care utilization in COPD. We aimed to investigate that knowledge gap in a large and well-characterized cohort of patients with severe COPD.

\textbf{METHODS}

This study uses baseline data from the previously published National Emphysema Treatment Trial (NETT).\textsuperscript{16} NETT design and methodology has been previously detailed. The NETT was conducted in accordance with the amended Declaration of Helsinki. Local institutional review boards approved the NETT protocol, and written informed consent was obtained from all patients. The study took place from December 2002, to December 2004.

In brief, NETT consented participants from 17 centers who were included in their trial if nonsmokers (abstinent \(\geq 6\) months) with moderate-to-severe COPD. The primary outcome of the study was to investigate the effectiveness of lung volume reduction surgery (LVRS).

Pertinent to this study, loneliness was measured by a psychometrically validated question from the Quality of Wellbeing questionnaire: Do you feel lonely or socially isolated (yes/no).\textsuperscript{16} Patients were defined as not lonely if they responded “No days” to the question “Feelings of being lonely or isolated” at baseline. Patients were classified as lonely if they responded “Yesterday,” “2 days ago” or “3 days ago.” The patients were given the questionnaire at study enrollment. The follow-up period was 5 years to assess loneliness, and 24 months to assess use of the emergency department.

Health ratings were determined using the 36-Item Short Form Survey Instrument (SF-36) question 1.\textsuperscript{16} The question reads: “In general, would you say your health is: 1-Excellent, 2-Very Good, 3-Good, 4-Fair, 5-Poor.”\textsuperscript{17}

The Modified Medical Research Council Dyspnea Scale (mMRC) is a tool widely used and recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines to stratify the severity of dyspnea in individuals with COPD. Using the mMRC scale, patients can quantify their shortness of breath on a scale ranging from 0 (dyspnea only with strenuous exercise) to 4 (too dyspneic to leave the house).

\textbf{Statistical Methods}

Baseline variables between non-lonely and lonely subjects were performed by using Wilcoxon tests for continuous variables and \(\chi^2\) tests for categorical variables. The association between loneliness and having any ED visits was assessed using a logistic model that adjusted for NETT study arm, age, \(\text{FEV}_1\), mMRC. The latter 3 variables comprise the Age, Dyspnea, Airflow Obstruction (ADO) Index.\textsuperscript{18} This is a tool that has been used to predict 2-year mortality in patients with COPD. We defined these variables \textit{a priori} to be included in the models, as they are considered as critical outcomes in COPD. We included the treatment arm as the whole cohort of the NETT study and also included gender to be investigated as a biological variable. All analyses were done using SAS version 9.4 (SAS Institute Inc., Cary, NC).

\textbf{RESULTS}

The follow-up period was 5 years to assess loneliness and 24 months to determine use of the emergency department. Patient characteristics are included in Table 1. In summary, 96 of 1217 subjects (7.9\%) were classified as lonely. Lonely patients were more likely to be women; 11\% of women were lonely compared with 6\% of men. In addition, lonely people had decreased 6-minute walk test (6MWT) distances, lower overall health ratings, and increased breathlessness (Table 1). Loneliness was significantly associated with increased use of the health care system, as represented by lonely patients being significantly more likely to visit the emergency department in the 5 years of follow-up of the study (Table 2) after adjusting for age, lung function, gender, dyspnea, 6MWT, and treatment arm. Lonely patients had ORs of 1.57 (95\% confidence interval [CI] of 1.005 to 2.466, \(P = .04\)) for having an
ED visit compared with patients who were not lonely. Loneliness was assessed yearly and was found to increase continuously over time, beginning with 8% at baseline and increasing to 14% by year 5. Marital status was included as an exploratory variable in the model for having any ED visits. When this model was performed, loneliness showed a trend toward significance, suggesting marital status and loneliness are strongly related ($P = 0.08$). Similarly, 5% of married patients were lonely compared with 13% of other patients. Finally, we explored the association of loneliness in relation to patient perception of general health. Loneliness was found to be significantly related to lower overall perception of general health ($P < 0.0001$) after adjusting for age, lung function, treatment arm, marital status, and breathlessness score, with lonely patients having health ratings 9.9 points lower than other patients (Table 3).

**DISCUSSION**

This study examined the relationship between loneliness and ED visits as a measure of health care utilization and the perception of general health in moderate-to-severe COPD. Our results suggest that loneliness is independently associated with more ED visits and worse perception of health. We confirm and extend the findings of other studies demonstrating worse outcomes for lonely people and those with other chronic conditions. However, this report includes a very well-characterized population of patients with COPD. Theeke et al demonstrated that patients with lung disease had higher levels of loneliness and that this loneliness also correlated with total number of chronic conditions. We showed that lonely patients had increased dyspnea, and this has been shown to lead to decreased time spent outside the home because of breathlessness, which may, in turn, create a cycle of worsening loneliness. Assisting this population in engagement in activities may be important in affecting overall well being. For example, Theeke et al showed that quality of life may be enhanced in survivors of stroke following interventions targeting loneliness, suggesting that assessment of loneliness be incorporated into routine clinical practice. We enthusiastically agree with other reports that recommend possible initiation of cognitive behavioral interventions or health coaching to target loneliness. In addition, loneliness has been shown as an independent risk factor for physical inactivity, and increased physical activity has been associated with healthy aging. In a study by Kara et al,
it was demonstrated that, as patients with COPD experience disease progression, their quality of life is affected, as increased breathlessness results in social isolation. Finally, it has been found that social isolation is linked to mortality. Our findings on the association loneliness with health status perception extend previous report regarding social isolation and a higher disease burden.

The uniqueness of this report is that we found that loneliness is independently associated with increased ED visits and health perception after adjusting for the most meaningful confounders in COPD in a very large and well-characterized population with a meaningful follow-up period. Our results also agree with previous reports. A study by Geller et al showed that loneliness predicted use of the emergency department as demonstrated by those with above-average loneliness scores made use of the hospital’s emergency department 60% more per year than those who scored less than the mean. Molloy et al has also illustrated that in adults older than age 65, increased loneliness was associated with hospitalization. Our study further confirms that lonely patients make more use of the emergency department but in a much larger and well-characterized cohort of patients with severe COPD. It is possible that a higher degree of neediness and lack of support for health-related decision making is associated with uncertainty, stress, and higher likelihood of visiting emergency departments. Of note, loneliness was almost as significant when adjusted to marital status, suggesting that even married patients may experience feelings of isolation.

**STRENGTHS AND LIMITATIONS**

This is the largest report that shows an association between loneliness and health care utilization adjusted for most meaningful factors in COPD. We acknowledge that loneliness was not measured by a specific loneliness tool. However, the question used has been tested and is part of a highly validated tool (Quality of Wellbeing questionnaire) in the COPD population. Although question number 1 of the SF-36, determining patients’ perceptions of general health, has been widely used, it has not been specifically validated in COPD. Despite this, the brevity of these assessments allows for use in routine, busy clinical practice in both the inpatient and outpatient settings.

**TABLE 2. Loneliness as a Determinant of Any ED Visits, Adjusted for Age, Sex, Post-FEV1% predicted, and MRC**

| Variable                        | Odds Ratio (95% CI) | P value |
|---------------------------------|---------------------|---------|
| Feeling lonely or isolated      | 1.57 (1.01,2.47)    | .04     |
| Medical treatment               | 0.82 (0.64,1.05)    | .11     |
| Sex, male                       | 1.04 (0.79,1.36)    | .80     |
| Age                             | 0.97 (0.95,0.99)    | .01     |
| Post-BD FEV1% pred              | 1.01 (0.99,1.03)    | .23     |
| 6-minute walk distance in feet  | 1.00 (1.00,1.00)    | .99     |
| mMRC dyspnea scale              | 1.01 (0.88,1.16)    | .90     |

CI = confidence interval; DF = degrees of freedom; Post-BD FEV1% pred = postbronchodilator forced expiratory volume in 1 second; mMRC scale = Medical Research Council dyspnea scale.

**TABLE 3. Loneliness as a Determinant of Perception of General Health**

| Variable                        | Parameter Estimate (standard error) | P value |
|---------------------------------|-------------------------------------|---------|
| Feeling lonely or isolated      | -9.92 (2.14)                        | <.0001  |
| Medical treatment               | -0.03 (1.14)                        | .98     |
| Sex, male                       | -0.99 (1.23)                        | .42     |
| Age                             | 0.71 (0.10)                         | <.0001  |
| Post BD FEV1% pred              | 0.12 (0.09)                         | .17     |
| mMRC dyspnea scale              | -4.05 (0.63)                        | <.0001  |

mMRC scale = modified Medical Research Council dyspnea scale; Post-BD FEV1% pred = postbronchodilator forced expiratory volume in 1 second.

**CONCLUSION**

Loneliness is an important public health issue, particularly in those with chronic illness such as COPD. This study shows that increased loneliness is significantly associated with a high incidence of visits to emergency departments and poorer perception of health in patients with moderate-to-severe COPD. In addition, our study demonstrates that loneliness is related to worse perception of general health from the patient perspective, and it is possible that even married patients experience feelings of social isolation. It is plausible that addressing loneliness in the outpatient setting may ultimately contribute to decreased ED visits and improved quality of life for this population by improving perceptions of health.
The methods of assessment of loneliness in this study are brief, which can allow for them to be employed effectively by clinicians. Our report suggests the need of frequent assessment of loneliness in routine practice.

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Abbreviations and Acronyms. COPD = chronic obstructive pulmonary disease; FEV1 = forced expiratory volume in 1 second; LVRS = lung volume reduction surgery; mMRC = modified medical research council; NETT = National Emphysema Treatment Trial; SF-36 = 36-item Short Form Survey Instrument; 6MWT = 6-minute walk test

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REFERENCES

1. GOLD website. Global Initiative for Chronic Obstructive Lung Disease. Available at: https://goldcopd.org/wp-content/uploads/2018/02/WMS-GOLD-2018-Feb-Final-to-print-v2.pdf. Accessed June 7, 2018.

2. Smith MC, Wrobel JP. Epidemiology and clinical impact of major comorbidities in patients with COPD. Int J Chron Obstruct Pulmon Dis. 2014;9:871-888.

3. Kara M, Mirici A. Loneliness, depression, and social support of Turkish patients with chronic obstructive pulmonary disease and their spouses. J Nurs Scholarsh. 2004;36(4):331-336.

4. Jang SM, Kim KU, Na HJ, et al. Depression is a major determinant of both disease-specific and generic health-related quality of life in people with severe COPD. Chron Respir Dis. 2010;16:1-10.

5. Williams V, Bruton A, Ellis-hill C, Mphenzen K. What really matters to patients living with chronic obstructive pulmonary disease? An exploratory study. Chron Respir Dis. 2007;4(2):77-85.

6. Petrie T, Mallory J, Barnes E, Petrone A, Barr T, Theeeke L. A systematic review of loneliness and common chronic physical conditions in adults. Open Resp J. 2015;8(suppl 2):113-132.

7. Heinrich LM, Guillame E. The clinical significance of loneliness: a literature review. Clin Psychol Rev. 2006;26(6):695-718.

8. Cacioppo S, Grippi AJ, London S, Goossens L, Cacioppo JT. Loneliness: clinical import and interventions. Perspect Psychol Sci. 2015;10(2):238-249.

9. Luo Y, Hawley LC, Wake LJ, Cacioppo JT. Loneliness, health, and mortality in old age: a national longitudinal study. Soc Sci Med. 2012;74(6):907-914.

10. Ayazi R, Aktürk U, Erci B, Öztürk H, Aşlan H. Relationship between depression and loneliness in elderly and examination of influential factors. Arch Gerontol Geriatr. 2012;55(3):348-354.

11. Wang J, Mann F, Lloyd-Evans B, Ma R, Johnson S. Associations between loneliness and perceived social support and outcomes of mental health problems: a systematic review. BMC Psychiatry. 2018;18(1):56.

12. Wong SS, Abdullah N, Abdullah A, et al. Unmet needs of patients with chronic obstructive pulmonary disease (COPD): a qualitative study on patients and doctors. BMC Fam Pract. 2014;15(1):67.

13. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 2010;7(7):e1000316.

14. Gerst-Emerson K, Jayawardhana J. Loneliness as a public health issue: the impact of loneliness on health care utilization among older adults. Am J Public Health. 2013;103(5):1013-1019.

15. Jakobsson U, Kristensson J, Hallberg IR, Midlov P. Psychosocial perspectives on health care utilization among frail elderly people: an explorative study. Arch Gerontol Geriatr. 2011;52(3):290-294.

16. Fishman A, Martinez F, Naurheim K, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059-2073.

17. Bowlung A. Just one question: if one question works, why ask several? J Epidemiol Community Health. 2005;59(5):342-345.

18. Abu hussein N, Terriet G, Schoenenberger L, et al. The ADO index as a predictor of two-year mortality in general practice-based chronic obstructive pulmonary disease cohorts. Respir. 2014;88(3):208-214.

19. Theeke LA, Mallow J. Loneliness and quality of life in chronically ill rural older adults. Am J Nurs. 2013;113(3):28-37.

20. Theeke L, Horstman P, Mallow J, et al. Quality of life and loneliness in stroke survivors living in Appalachia. J Neurosci Nurs. 2014;46(6):e3-e15.

21. Benzo R, Vickers K, Novotny PJ, et al. Health coaching and chronic obstructive pulmonary disease rehospitalization: a randomized study. Am J Respir Crit Care Med. 2016;194(6):672-680.

22. Hawley LC, Thisted RA, Cacioppo JT. Loneliness predicts reduced physical activity: cross-sectional & longitudinal analyses. Health Psychol. 2009;28(3):354-363.

23. Peal NM, Mclure RJ, Bartlett HP. Behavioral determinants of healthy aging. Am J Prev Med. 2005;28(3):298-304.

24. Steptoe A, Shankar A, Demaakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. Proc Natl Acad Sci U S A. 2013;110(15):5797-5801.

25. Cantarero-Prieto D, Pascual-Sáez M, Blázquez-Fernández C. Social isolation and multiple chronic diseases after age 50: a European macro-regional analysis. PLoS One. 2018;13(10):e0205062.

26. Geller J, Janson P, Mqgovern E, Valdini A. Loneliness as a predictor of hospital emergency department use. J Fam Pract. 1999;48(10):801-804.

27. Molloy GJ, Miggee HM, O’Neill D, Conroy RM. Loneliness and emergency and planned hospitalizations in a community sample of older adults. J Am Geriatr Soc. 2010;58(8):1538-1541.

28. Taube E, Kristensson J, Sandberg M, Midlov P, Jakobsson U. Loneliness and health care consumption among older people. Scand J Caring Sci. 2015;29(3):435-443.

29. Kaplan RM, Atkins GJ, Timms R. Validity of a quality of well-being scale as an outcome measure in chronic obstructive pulmonary disease. J Chronic Dis. 1984;37(2):85-95.