Research article

Associations with chest illness and mortality in chronic spinal cord injury

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Objective: Identify factors associated with chest illness and describe the relationship between chest illness and mortality in chronic spinal cord injury (SCI).
Design: Cross-sectional survey assessing chest illness and a prospective assessment of mortality.
Methods: Between 1994 and 2005, 430 persons with chronic SCI (mean ± SD), 52.0 ± 14.9 years old, and ≥4 years post SCI (20.5 ± 12.5 years) underwent spirometry, completed a health questionnaire, and reported any chest illness resulting in time off work, indoors, or in bed in the preceding 3 years. Deaths through 2007 were identified.
Outcome measures: Logistic regression assessing relationships with chest illness at baseline and Cox regression assessing the relationship between chest illness and mortality.
Results: Chest illness was reported by 139 persons (32.3%). Personal characteristics associated with chest illness were current smoking (odds ratio =2.15; 95% confidence interval =1.25–3.70 per each pack per day increase), chronic obstructive pulmonary disease (COPD) (3.52; 1.79–6.92), and heart disease (2.18; 1.14–4.16). Adjusting for age, subjects reporting previous chest illness had a non-significantly increased hazard ratio (HR) for mortality (1.30; 0.88–1.91). In a multivariable model, independent predictors of mortality were greater age, SCI level and completeness of injury, diabetes, a lower %-predicted forced expiratory volume in 1 second, heart disease, and smoking history. Adjusting for these covariates, the effect of a previous chest illness on mortality was attenuated (HR = 1.15; 0.77–1.73).
Conclusion: In chronic SCI, chest illness in the preceding 3 years was not an independent risk factor for mortality and was not associated with level and completeness of SCI, but was associated with current smoking, physician-diagnosed COPD, and heart disease history.

Keywords: Spinal cord injuries, Respiratory tract infections, Mortality

Introduction

Chest illnesses are an important cause of morbidity in persons with chronic spinal cord injury (SCI).[1,2] Injury to the cervical or thoracic regions of the spine results in various degrees of respiratory muscle weakness and paralysis depending on the level and severity of SCI. This leads to reduced pulmonary function and ineffective cough that impairs the clearance of mucus from the airways. As a result, in comparison to the able-bodied, persons with SCI are potentially more susceptible to the effects of respiratory illnesses such as bronchitis and pneumonia, and may have more severe illness and debilitation when afflicted with these disorders. In the years immediately following acute SCI, data from the US Spinal Cord Injury Model Systems registry indicate that diseases of the respiratory system, and in particular pneumonia, are the most common cause of death.[3] Persons with higher and more complete injuries are most at risk from dying of respiratory causes.

SCI increases the risk of premature death.[4–6] Although many studies have examined short-term

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mortality following acute SCI, few have focused on factors influencing long-term mortality. We previously examined mortality between 1994 and 2000 in 361 men with chronic SCI at the Veterans Affairs Boston Health Care System (VA Boston) (mean duration of SCI 17.5 years) and found a 47% increase compared to what would have been expected in the general population.[7] Adjusting for severity and completeness of SCI, a reduced percent-predicted forced expiratory volume in 1 second (FEV_1) was associated with greater mortality risk.[7] It has been shown that exacerbations in patients with chronic obstructive pulmonary disease (COPD) are positively related to mortality risk,[8] and it is plausible that a similar association exists in persons with SCI.

In this report, we extend our observations regarding mortality through 2007 in 430 participants enrolled in the VA Boston chronic SCI cohort. We hypothesized that a history of chest illness would be associated with level and completeness of injury and that a history of chest illness would be associated with an increased mortality risk.

Methods

Study population and chest illness definition

Between 1994 and 2005, 582 persons at least 1 year post SCI and age 22 years or older were enrolled in a longitudinal study assessing factors associated with respiratory health. Included were persons who did not require ventilator support and who did not have a tracheostomy. Details about this longitudinal cohort have been published elsewhere.[9] Briefly, VA Boston is one of 23 Department of Veterans Affairs SCI centers that provide health services to persons with acute and chronic SCI. The cohort included persons previously treated at VA Boston and those recruited by advertisement from the greater Boston area. The analysis excluded persons with other neurological conditions (history of polio, multiple sclerosis, or stroke, $n = 27$), with lung resection ($n = 5$), with no known date of injury ($n = 1$), without a detectable SCI level ($n = 16$), or who were unable to complete spirometry ($n = 10$). Study procedures followed the protocol approved by the VA Boston Institutional Review Board and were in accord with the ethical standards of the review board.

Using a respiratory questionnaire based on a survey from the American Thoracic Society (ATS) and the Division of Lung Diseases (ATS DLD-78),[10] participants were asked the following questions upon enrollment into the cohort: "'During the past year have you had any chest illness that has kept you off work, indoors at home, or in bed?" and "During the past 3 years have you had any chest illness that has kept you off work, indoors at home, or in bed?" Participants who responded "yes" to either question were identified as having a history of chest illness. This approach for querying chest illness in this cohort was previously validated.[11] To ensure that the 3-year period occurred entirely during the chronic SCI phase (starting one year post-injury), we excluded 93 persons who were less than four years post-injury at baseline. The remaining 430 persons included in the analyses were at least 4 years post-injury at the baseline study visit.

Health history

The respiratory health questionnaire (ATS DLD-78) with supplemental questions was used to obtain a standardized medical history that included diabetes, physician-diagnosed COPD (emphysema or chronic bronchitis), asthma, hypertension, and heart disease treated in the 10 years before study entry. Any wheeze was defined as wheeze reported with a cold, occasionally apart from colds, or on most days or nights. Chronic cough was defined as cough on most days for 3 consecutive months of the year, and chronic phlegm was defined similarly.

Spirometry

Pulmonary function testing was conducted according to ATS guidelines,[12] modified for SCI as previously described.[13,14] Briefly, participants were coached to provide three acceptable and reproducible efforts using a 10-1 water-seal spirometer (DSII) in 88% of the sessions or an 8-1 water seal portable spirometer in 2%. Beginning in March 2004 and for 10% of the sessions, a dry-rolling seal CPL spirometer system was used. Equipment was manufactured by Collins Pulmonary Diagnostics (currently nSpire Health, Inc., Longmont, CO, USA). The highest FEV_1 and forced vital capacity (FVC) values were used to calculate percent predicted FEV_1 and FVC using Hankinson's equations.[15]

Neurological exam, stature, and weight

At entry, motor level and completeness of injury were assessed based on the American Spinal Injury Association Impairment Scale (AIS) by record review and exam.[16,17] Motor incomplete SCI included AIS C (most key muscles below the neurological level grade $<3/5$) or AIS D (most muscles below the neurological level grade $\geq 3/5$). For analysis, persons were further grouped into cervical complete and AIS C (cervical motor complete (AIS A or B) and cervical AIS C), non-cervical complete and AIS C (thoracic or lower motor complete (AIS A or B) and thoracic or lower AIS C), and all others (AIS D). AIS C were grouped

with AIS A and B because of the small numbers of cervical AIS C ($N = 14$) and non-cervical AIS C ($N = 19$) participants. We later performed a sensitivity analysis on the effect of combining AIS C with AIS A and B. Stature was obtained by measuring body length from top of the head to the heel with the subject in a supine position. In individuals who declined length measurement or who had severe joint contractures that precluded accurate assessment, stature was self-reported.[11] Weight was directly measured at the research visit for most patients (91%), and was otherwise obtained via self report (8%) or medical record (1%).

Mortality

Deaths and dates of death through 31 December 2007 were identified through routine contacts with cohort participants for subsequent studies and through an online search of the Social Security Master Death Index. Additionally, the VA electronic medical record was reviewed for all veterans (71.9% of the cohort).

Statistical analyses

Cross-sectional associations with chest illness in the past 3 years were assessed using logistic regression (PROC LOGISTIC, SAS 9.1, Cary, NC, USA). Predictors of mortality through 2007 were assessed with Cox regression models (PROC PHREG). For both logistic and Cox regression models, variables with significant univariable associations at the 0.1 level were assessed in multivariable models. Percent predicted FEV_1 was the pulmonary function variable that showed the best association with chest illness and was thus used in survival modeling. Proportional hazards of the Cox model were assessed for individual covariates using a term for the variable multiplied by the natural log of time. Overall proportional hazard for the model was assessed using the proportionality test statement in PROC PHREG. The P value for linear trend of percent predicted FEV_1 in quartiles was obtained by assigning each quartile its median value and then entering the median values as a continuous variable in the multivariable survival model.

Results

Participant characteristics

The majority of participants were male (93.0%) and white (92.8%) with age of 52.0 ± 14.9 (mean ± standard deviation) years and 20.5 ± 12.5 years since SCI at study entry. In 382 participants (88.8%) SCI was due to trauma and 115 (26.7%) participants had cervical complete and AIS C, 189 (44.0%) had non-cervical complete and AIS C, and 126 (29.3%) were AIS D.

Prior chest illness

Chest illness in the 3 years prior to study entry was reported by 139 participants (32.3%) and was significantly associated with current smoking (Tables 1 and 2). After controlling for smoking, prior chest illness was significantly associated with female sex, doctor-diagnosed COPD, asthma, obstructive lung disease, heart disease requiring treatment in the past 10 years, chronic phlegm, and any wheeze (Table 2). There were suggestive effects of percent predicted FEV_1 and percent predicted FVC, but did not reach statistical significance. Current smoking (odds ratio (OR) = 2.15 per pack per day; 95% confidence interval (CI) = 1.25–3.70) and COPD (OR = 3.52; 95% CI = 1.79–6.92) were independently significant in a multivariable model (Table 3). After controlling for smoking status and COPD, heart disease requiring treatment in the past 10 years was the only other variable significantly associated with prior chest illness (Table 3). Any wheeze was strongly associated with prior chest illness when included in a multivariable model excluding smoking history (OR = 3.59; 95% CI = 2.25–5.73; Table 3). Adding pulmonary function variables to the multivariable chest illness models did not improve model fit.

Survival

There were 111 deaths (25.8%) (Table 1). Length of time in the study for each individual was calculated from date of initial clinic visit to date of death or 31 December 2007, whichever occurred first. Participants were followed for mean 8.08 ± 3.77 years, ranging from 0.04 to 13.82 years. Year of entry into the cohort was not significantly related to mortality. In an age-adjusted multivariable Cox regression model, cervical complete and AIS C (compared to all AIS D), non-cervical complete and AIS C (compared to all AIS D), current smoking packs per day (compared to never smokers), recent cessation of smoking (≤3 years) (compared to never smokers), diabetes, heart disease requiring treatment in the past 10 years, and lower percent predicted FEV_1 were each significantly associated with an increased hazard of death (Table 4). Adjusting for only age, subjects reporting chest illness in the past 3 years at study entry had a higher hazard for death than those who did not report chest illness (hazard ratio (HR) = 1.30; 95% CI = 0.88–1.91; data not shown), but this relationship was not statistically significant and was further attenuated in the multivariable model (HR = 1.15; 95% CI = 0.77–1.73; Table 4). We present a multivariable model with percent predicted FEV_1 in quartiles as it better satisfies the proportional hazards assumption and is easier to interpret clinically compared to a

Table 1 Descriptive statistics of 430 persons with chronic SCI with and without reported chest illness in the 3 years before study entry*

Characteristic	Prior chest illness *N* = 139 (32.3)	No prior chest illness *N* = 291 (67.7)
Deceased	42 (30.2)	69 (23.7)
Female	14 (10.1)	16 (5.5)
Nonwhite	8 (5.8)	23 (7.9)
Age (years)	52.8 (14.8)	51.6 (14.9)
Job status		
Employed/student	47 (33.8)	102 (35.1)
Unemployed/retired	92 (66.2)	189 (64.9)
Years post-injury	21.6 (12.1)	20.0 (12.7)
Level of injury		
Cervical complete and AIS C	42 (30.2)	73 (25.1)
Non-cervical complete and AIS C	52 (37.4)	137 (47.1)
AIS D	45 (32.4)	81 (27.8)
Body mass index continuous	27.3 (6.7)	26.6 (5.3)
Underweight (<18.5)	6 (4.3)	8 (2.8)
Normal (≥18.5 to <25.0)	53 (38.1)	113 (38.8)
Overweight (≥25.0 to <30.0)	38 (27.3)	98 (33.7)
Obese (≥30.0)	42 (30.2)	72 (24.7)
Smoking status		
Never smoker	37 (26.6)	109 (37.5)
Ex-smoker	60 (43.2)	124 (42.6)
Quit >3 years	53 (38.1)	112 (38.5)
Quit ≤3 years	7 (5.0)	12 (4.1)
Current smoker	42 (30.2)	58 (19.9)
Current packs per day	0.91 (0.60)	0.71 (0.46)
COPD	27 (19.4)	16 (5.5)
Asthma	25 (18.0)	22 (7.6)
Obstructive lung disease (asthma or COPD)	40 (28.8)	33 (11.3)
Hypertension	47 (33.8)	96 (33.0)
Diabetes	18 (13.9)	32 (11.0)
Heart disease treated in past 10 years	24 (17.3)	23 (7.9)
Chronic cough	34 (24.5)	45 (15.5)
Chronic phlegm	42 (30.2)	48 (16.5)
Any wheeze	105 (75.5)	122 (41.9)
FEV_1/FVC	0.772 (0.099)	0.784 (0.099)
$FEV_1/FVC \leq 0.7$	25 (18.0)	49 (16.8)
% Predicted FEV1	72.9 (20.0)	76.6 (20.2)
% Predicted FVC	73.5 (20.2)	76.0 (18.8)

*For categorical variables the number (percent) and mean (standard deviation) for continuous variables are displayed.

continuous measure of percent predicted FEV_1. The multivariable model satisfies the Cox regression proportional hazards assumption overall and for each individual variable.

We performed a sensitivity analysis to assess the influence of our SCI level and severity categorization on the results and whether the association between history of chest illness and mortality was modified by level and severity of SCI (data not shown). Removing $n = 33$ AIS C from the multivariable model did not change the HR for the relationship between chest illness and mortality (HR = 1.14; 95% CI = 0.73–1.76). Additionally, there was no association between chest illness and mortality among only motor completes (HR = 1.31; 95% CI = 0.78–2.20), or when further restricting to cervical motor completes (HR = 1.02; 95% CI = 0.40–2.55), adjusting for the same covariates as the multivariable survival model in Table 4.

Discussion

In 430 persons at least 4 years post SCI, self-reported history of chest illness in the past 3 years was most strongly associated with current smoking, doctor diagnosed COPD, and prior heart disease. However, a history of chest illness assessed at study entry was not an independent predictor of mortality assessed over a mean of 8.1 years. This suggests that while a chest illness history may be related to morbidity, it does not have a substantial independent effect on the long-term mortality of persons with chronic SCI who have survived at least 4 years.

A prior study found that acute respiratory illness in SCI patients increased the risk of 60-day mortality.[18] The fact that our findings differ further supports the concept that the risks for short- and long-term mortality in SCI patients are not the same. Previous studies that have used outpatient visits for acute respiratory

Table 2 Logistic regression models of self-reported chest illness in the past 3 years ($N = 430$)

Variable	OR[†]	aOR[‡]	95% CI[‡]	P value[‡]
Female	1.93	2.21	1.04–4.71	0.040
Nonwhite	0.71	0.80	0.34–1.84	0.591
Age	1.01	1.01	0.99–1.02	0.281
Job status				
Employed/student	0.95	1.04	0.67–1.60	0.869
Unemployed/retired	Ref			
Years post injury	1.01	1.01	1.00–1.03	0.127
Level of injury				
Cervical complete and AIS C	1.04	1.17	0.68–2.01	0.896
Non-cervical complete and AIS C	0.68	0.76	0.46–1.24	0.265
AIS D	Ref			
BMI				
Underweight (<18.5)	1.60	1.68	0.55–5.13	0.368
Normal (≥18.5 to <25.0)	Ref			
Overweight (≥25.0 to <30.0)	0.83	0.85	0.51–1.40	0.143
Obese (≥30.0)	1.24	1.24	0.74–2.06	0.737
Smoking status				
Never smoker	Ref			
Ex-smoker	1.38	–	0.87–2.17	0.167
Current smoker packs per day	2.35*	–	1.39–3.97	0.002
COPD	4.14*	3.81	1.95–7.41	<0.001
Asthma	2.68*	2.78	1.50–5.18	0.001
Obstructive lung disease	3.16*	3.03	1.79–5.11	<0.001
Hypertension	1.04	1.09	0.70–1.68	0.710
Diabetes	1.20	1.20	0.64–2.23	0.577
Heart disease in past 10 years	2.43*	2.45	1.31–4.57	0.005
Chronic cough	1.77*	1.45	0.86–2.46	0.166
Chronic phlegm	2.19*	1.87	1.13–3.07	0.014
Any wheeze	4.28*	3.95	2.49–6.25	<0.001
FEV_1/FVC	0.29	0.67	0.08–5.92	0.719
$FEV_1/FVC \leq 0.7$	1.08	0.92	0.53–1.60	0.773
% Predicted FEV1	0.99	0.99	0.98–1.00	0.088
% Predicted FEV1 in quartiles				0.212
Quartile 1 – (28–61%)	1.34	1.32	0.74–2.34	
Quartile 2 – (61–78%)	1.30	1.29	0.72–2.29	
Quartile 3 – (78–90%)	0.77	0.75	0.41–1.37	
Quartile 4 – (90–132%)	Ref			
% Predicted FVC	0.99	0.99	0.98–1.00	0.105
% Predicted FVC in quartiles				0.162
Quartile 1 – (25–61%)	1.27	1.44	0.81–2.55	
Quartile 2 – (61–78%)	0.97	1.02	0.57–1.82	
Quartile 3 – (78–89%)	0.64	0.73	0.40–1.34	
Quartile 4 – (89–124%)	Ref			

[†]Crude odds ratio.
[‡]Odds ratio adjusted for smoking status (never smoker, ex-smoker, current smoker packs per day).
*$P < 0.05$ for the crude odds ratio.
Ref, reference group.

Table 3 Multivariable logistic regression models of self-reported chest illness in the past 3 years ($N = 430$)

Variable	Odds ratio	95% Confidence interval	P value
Model 1			
Smoking status			
Never smoker	Ref		
Ex-smoker	1.21	0.76–1.94	0.422
Current smoker packs per day	2.15	1.25–3.70	0.006
COPD	3.52	1.79–6.92	<0.001
Heart disease in past 10 years	2.18	1.14–4.16	0.018
Model 2			
Any wheeze	3.59	2.25–5.73	<0.001
COPD	2.40	1.20–4.79	0.013
Heart disease in past 10 years	1.87	0.97–3.61	0.062

Ref, reference group.

Table 4 Multivariable Cox regression model assessing mortality ($N = 430$)

Variable	Hazard ratio	95% confidence interval	P value
Age	1.07	1.06–1.09	<0.001
Level of injury			
Cervical complete and AIS C	2.15	1.18–3.93	0.013
Non-cervical complete and AIS C	1.88	1.14–3.09	0.013
AIS D	Ref		
Never smoker	Ref		
Quit >3 years	1.11	0.72–1.71	0.634
Quit ≤3 years	3.37	1.44–7.90	0.005
Current smoker packs per day	1.80	1.20–2.71	0.004
Diabetes	1.75	1.06–2.91	0.030
Heart disease in past 10 years	2.18	1.29–3.67	0.004
% Predicted FEV1			
Quartile 1 – (25–61%)	3.57	1.91–6.67	<0.001
Quartile 2 – (61–78%)	2.37	1.25–4.48	0.008
Quartile 3 – (78–89%)	2.21	1.15–4.28	0.018
Quartile 4 – (89–124%)	Ref		
P value for trend			<0.001
Chest illness in past 3 years	1.15	0.77–1.73	0.491

Ref, reference group.

infections as a measure of chest illness may not be directly comparable to our self-reported measure and may represent more serious illnesses.[18,19] Additionally, our results differ from findings in patients with COPD where associations between exacerbations and mortality have been reported.[8]

Level and completeness of SCI was not related to chest illness in the 3 years prior to study entry, a finding similar to the study by Stolzmann *et al.*[11] where chest illness risk in persons in the same cohort was studied prospectively. However, the cross-sectional predictors of chest illness history in the presented multivariable model differ slightly from those in the prospective analysis.[11] Namely, after controlling for smoking and COPD, any wheeze and a lower percent predicted FEV_1 were associated with prospective chest illness, but they were not independently associated with chest illness in our cross-sectional analysis. Current smoking and any wheeze were each strongly associated with prior chest illness when modeled separately, and in a single predictor model there was a suggestive effect of a reduced percent predicted FEV_1 on chest illness ($P = 0.088$). Compared to this study, the previous prospective study included follow-up for chest illness over a longer time period (an average of 5.1 years as compared to a 3-year recall) and accounted for recurrent chest illness within an individual, and so more chest illnesses were reported ($n = 247$). Therefore, it is likely that greater statistical power in the prospective study permitted inclusion of additional predictor variables compared to the current cross-sectional study. Regardless, both this retrospective study and previous prospective study demonstrate the importance of factors other than level and severity of SCI in determining chest illness risk.[11]

In our previous report based on 36 deaths in 348 participants through 2000,[7] SCI level and completeness was not a significant predictor of mortality. However, in the current analysis, in a larger cohort with more deaths, level and severity of SCI was a risk factor for mortality even when controlling for the other main predictors of mortality. Our results confirm the findings of prior studies of long-term mortality in chronic SCI, including increased risks of mortality due to level and severity of injury.[4,5,20–22] In addition, our findings are similar to studies in the general population showing that heart disease,[23,24] diabetes,[24,25] reduced pulmonary function,[26–28] and cigarette smoking[29] are determinants of mortality. This study demonstrates and confirms the contribution of reduced pulmonary function, smoking, heart disease, and diabetes to greater mortality in chronic SCI independent of level and severity of injury. The risk of mortality in current and recent smokers, persons with diabetes, or persons with heart disease was similar to the risk of mortality due to cervical and non-cervical complete or AIS C status (as compared to AIS D).

A history of chest illness resulting in time off work, indoors at home, or in bed was not an independent predictor of mortality, but chest illness was associated with smoking history, heart disease, and reduced pulmonary function, and these factors were related to an increased risk of mortality. Therefore, the occurrence of chest illness may identify persons in poor health who are at a greater risk of mortality due to other clinical factors but is not predictive of mortality itself.

Study limitations

A limitation of this study is that the main variable of interest, chest illness that kept one off work, at home indoors, or in bed in the past 3 years, was queried by self-report. However, the events reported reflect significant illnesses likely to prompt recall, and we also previously validated this question with medical records.[11] In addition, the results of this study are applicable to patients with chronic SCI who survived at least 4 years and who do not require tracheostomy or mechanical ventilation, and are not generalizable to the entire SCI population. Strengths of this study include a large cohort of persons with chronic SCI, the use of a standardized health questionnaire to assess multiple personal risk factors for chest illness, and the prospective assessment of mortality.

Conclusion

Factors not directly related to SCI are the most important correlates of chest illness reported over 3 years. SCI level and completeness of injury, reduced pulmonary function, heart disease history, smoking, and diabetes are predictors of mortality, while history of chest illness is not significantly associated with long-term mortality in chronic SCI.

Disclaimer statements

Contributors VAD has made substantial contributions to the design, analysis, statistical support, and writing of this manuscript. KLS has made substantial contributions to the design, analysis, and writing of this manuscript. DRG has made substantial contributions to the statistical support and writing of this manuscript. RB has made substantial contributions to the design and writing of this manuscript. CGT has made substantial contributions to the design and writing of this manuscript. LRM has made substantial contributions to the design and writing of this manuscript. EG has made substantial contributions to the design, analysis, and writing of this manuscript.

Conflicts of interest None.

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