Spinal Cord (2001) 39, 263–268

www.nature.com/sc

Original Article

Forced vital capacity in two large outpatient populations with chronic spinal cord injury

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Objective: To determine the expected vital capacity in persons with chronic spinal cord injury (SCI) in relation to injury level, completeness of injury, smoking and duration of injury, as an aid to diagnosis and management of respiratory complications.
Setting: A New York City veterans' hospital and a Los Angeles public rehabilitation hospital.
Methods: Case series from the two hospitals were pooled. Participants (adult outpatients with SCI of duration >1 year, not ventilator-dependent) were evaluated by conventional forced expiratory spirometry. Cross-sectional analysis was performed, using multiple regression, on the entire population and defined subgroups. The principal outcome measure was forced vital capacity (FVC).
Results: In the subjects with complete-motor lesions, FVC ranged from near 100% of normal predicted values in the group with low paraplegia, to less than 50% in those with high tetraplegia. Incomplete lesions mitigated FVC loss in tetraplegia. In subjects with paraplegia, longer duration of injury was associated with greater loss, and smoking-related loss was evident at older but not at younger ages, presumably due to greater pack years in older subjects.
Conclusions: Vital capacity/SCI level relationships determined here may have diagnostic and prognostic value. Smoking-related FVC loss is important in persons with SCI as in others, although at higher levels it may be obscured by SCI-related loss.
Sponsorship: Supported in part by National Institute of Disability and Rehabilitation Research, Office of Special Education and Rehabilitative Services, US Department of Education (Grants H133N00026, H133B30029, and H133B70011); Eastern Paralyzed Veterans Association; National Institute of Environmental Health Sciences (Grant 1P01ES90581-0); and US Environmental Protection Agency (Grant R826708-01-0).
Spinal Cord (2001) **39,** 263–268

Keywords: paraplegia; tetraplegia; vital capacity; smoking

Introduction

Among people with chronic spinal cord injury (SCI), respiratory disease is now the most common cause of death, and one of the most common medical complications.[1–4] Effective respiratory health management, which should reduce the risk of premature death and excess disability, requires clear understanding of the relationship between lung function impairment and the level and completeness of SCI. Lesions above L5 disable respiratory muscles, resulting in restriction of total lung capacity and vital capacity, increasing markedly at high thoracic and cervical lesion levels. Restriction may lead to atelectasis and chronic infection, which in turn may lead to chronic airway obstruction, with reduced expiratory flow rates and added disability due to breathlessness. Bronchial hyperreactivity also may result from higher-level SCI,[5–7] further increasing the risk of obstructive dysfunction. Nevertheless, most people with SCI retain reasonably normal expiratory flow rates relative to their attainable lung volumes.[8,9] Thus, restrictive dysfunction is the predominant respiratory manifestation of SCI.

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Smoking is a major cause of chronic lung dysfunction (primarily obstructive) in the general population[10] and probably also in the SCI population. Almenoff *et al*.,[8] studying 165 male outpatients with SCI at a New York City (NY) military veterans hospital, found statistically significant correlations of SCI level with forced vital capacity (FVC), forced expired volume in one second (FEV_1), and peak expiratory flow (PEF). They found statistically significant excess decrements in FEV_1, consistent with chronic airway obstruction, in paraplegic and low-tetraplegic current smokers. Linn *et al*.[9] similarly studied 187 male and 35 female adult outpatients at a public rehabilitation hospital in metropolitan Los Angeles (LA). Dysfunction related to SCI level and completeness was roughly similar in NY and LA. Smoking-related decrements appeared larger in LA, despite a younger population with presumably lower lifetime smoking doses. High tetraplegics did not show smoking-related deficits in NY or LA. This is explainable by selection bias: high tetraplegics with relatively more severe neurologic impairment, and thus more respiratory limitations, should be more strongly dissuaded from smoking.

Precise estimation of the relationship between lung function decrement and SCI level/completeness requires analysis of a large population, ie, pooling of data from multiple institutions. Unfortunately, instrumental and human factors can influence lung function measurements, so data pooling is seldom possible without *a priori* standardization.[11–13] However, pooling of the NY and LA studies appeared feasible, in that they were closely concurrent, and used similar test equipment which met performance standards of the American Thoracic Society (ATS).[14] Also, ATS-standard spirometric tests of healthy never-smokers in the United States NHANES-III survey[15] provide improved benchmarks for assessment of SCI- and smoking-related deficits. This study presents results from analyses of combined NY and LA outpatient populations, in relation to NHANES-III predictions.

Methods

Data acquisition and classification

At both hospitals, forced expiratory spirometry was performed in routine follow-up examinations of outpatients with SCI of >1 year duration.[8,9] The analysis included 455 subjects – 216 in LA and 239 in NY – examined in 1993–1997 who had satisfactory data for FVC and predictor variables, and who showed no evidence of asthma or chronic bronchitis. In both institutions, similar spirometers and volumetric calibration syringes (SensorMedics, Yorba Linda, CA, USA) were used.

For each subject, the level of injury was defined as the lowest normal motor segment, determined by neurological examination following American Spinal Injury Association guidelines.[16] The lesion was classified as motor-incomplete if volitional motor function was preserved at sacral levels, and motor-complete if not. Subjects were stratified by level as high tetraplegics (C2–C5), low tetraplegics (C6–C8), high paraplegics (T1–T6), and low paraplegics (T7–L5). They were classified as never smokers, former smokers (quit >6 months before testing), or current smokers on the basis of interview information. Lifetime smoking dose ('pack years') data were incomplete, so dose effects were addressed by comparing smokers below and above the population mean age of 45 years, assuming that cumulative doses would be greater in the older group.

Table 1 presents characteristics of the population by SCI level category. The NY population was predominantly white non-Hispanic, while the LA population was predominantly Hispanic, of Mexican or Central American descent. Of 40 female subjects, 36 were from LA. Mean age and duration of injury were greater in NY (50 and 18 years respectively) than in LA (40 and 14 years respectively). For the 79% of current and former smokers with smoking history available, mean lifetime dose was 15 pack-years, maximum was 90 pack-years.

Table 1 Population characteristics by injury level

	C2–C5	*C6–C8*	*T1–T6*	*T7–L5*	*All*
Number	115	93	78	169	455
% Female[a]	8	2	17	9	9
% Black[a]	23	23	17	18	20
% Hispanic[a]	30	37	40	36	35
Age, mean ± SD	44 ± 14	44 ± 13	46 ± 15	47 ± 15	45 ± 14
Years since injury, mean ± SD	15 ± 10	15 ± 10	18 ± 14	17 ± 12	16 ± 11
% Motor-incomplete	22	31	13	34	27
% Current smokers	20	30	21	34	27
% Ever smoked	50	67	62	66	61
FVC, mean ± SD[b]	53 ± 16	69 ± 17	79 ± 15	88 ± 15	74 ± 21

[a]Subjects were white non-Hispanic males unless indicated otherwise. [b]Percentage of normal-predicted value from reference 15

Data analysis

We expressed each subject's FVC as a percentage of the value predicted from NHANES-III regression equations[15] to account for most of the variance due to height, age, sex and ethnic group. NHANES-III predictions based on the general US population of healthy nonsmokers are referred to here as 'normal-predicted' values. Predictions for our population based on the present analyses are referred to as 'SCI-predicted' values, and expressed as percentages of normal-predicted values. Regression analyses employed commercial statistical software (SPSS Inc., Chicago; Microsoft Inc., Redmond, WA, USA). Variables used to predict FVC included SCI level (from C1 = 1 to S5 = 30), duration of SCI (in years), and categorical variables (0 = false, 1 = true) for motor-incomplete lesion, ever smoking, and current smoking. Effects were considered statistically significant at $P < 0.05$. Preliminary analyses indicated that NY-LA differences in FVC were non-significant. By contrast, peak flows were significantly higher and FEV_1 values significantly lower in NY compared to LA, suggesting important differences in instruments and/or subject coaching techniques between cities, which precluded pooling their data for flow-related variables. Accordingly, analyses were limited to FVC, and were performed on the entire population or on subgroups defined by injury or smoking characteristics. To model the nonlinear effect of injury level across the entire range in motor-complete subjects, we tested logarithmic, polynomial, power, and nonparametrically smoothed functions. A logarithmic function gave the most satisfactory result in terms of biological plausibility, mathematical simplicity, and fit to the data.

Results

Analyses stratified by level of injury

In preliminary regression analyses, level, duration, motor-incomplete lesion, and ever smoking were found to be significant predictors in one or more injury level categories. An analysis including only those predictors was applied separately to each level category. For high tetraplegics (C2–C5), only the motor-incomplete effect was significant, predicting an improvement of FVC by 16 percentage points (95% confidence interval 9, 23; $P < 0.01$), relative to a motor-complete lesion. For low tetraplegics (C6–C8), effects of motor-incompleteness and injury level were significant ($P < 0.01$). A motor-incomplete lesion predicted FVC improvement by 10 percentage points (95% CI 3, 17); and a one-vertebra rise in lesion level predicted an additional nine percentage points FVC impairment (95% CI 3, 15).

For high (T1–T6) and low (T7–L5) paraplegics, estimated effects of level were similar – slightly more than one percentage point FVC decrement per one-vertebra rise in level, significant ($P < 0.05$) only in the T7–L5 group. Effects of injury duration were also significant in paraplegics – 0.33 percentage points loss per year after injury in T1–T6 (95% CI 0.09, 0.57), and 0.25 in T7–L5 (95% CI 0.05, 0.45). An alternative analysis with chronological age as a predictor instead of injury duration showed a similar pattern: the age effect was significant in paraplegics but not in tetraplegics. In still another analysis of paraplegics only, including both age and injury duration as predictors, the duration effect (−0.22 percentage points per year since injury, $P = 0.02$) predominated over the age effect (−0.08 percentage points per year, $P > 0.3$). The effect of motor-incomplete lesions was non-significant in paraplegics.

Smoking effects were significant only in low paraplegics. Those who had ever smoked showed FVC decrement averaging six percentage points ($P < 0.05$), relative to those who had never smoked. A separate analysis excluding former smokers showed an FVC decrement related to current smoking of seven percentage points ($P < 0.05$). In an analysis of all paraplegics stratified by age, the estimated effect of ever smoking was a decrement of one percentage point (not significant) in those under 45 years, *versus* seven percentage points ($P < 0.05$) in those 45 years and older.

Analyses including all levels of injury

Table 2 and Figure 1 present results from a regression analysis of all subjects with motor-incomplete lesions,

Table 2 Predicted and observed FVC by level, for persons with motor-complete lesions[a]

Level	*SCI-predicted*	*Observed mean* (range) *Never-smokers*	*All*
3 C3	–	–	52 (25–73)
4 C4	45	44 (17–62)	46 (15–72)
5 C5	52	48 (22–76)	50 (22–80)
6 C6	57	64 (43–84)	63 (40–84)
7 C7	62	77 (65–85)	67 (33–93)
8 C8	66	–	88 (65–107)
9 T1	70	–	82 (57–105)
10 T2	73	–	72 (61–81)
11 T3	76	76 (58–95)	76 (58–95)
12 T4	79	80 (55–104)	83 (55–104)
13 T5	81	84 (65–107)	73 (46–107)
14 T6	84	82 (60–98)	84 (60–100)
15 T7	86	74 (61–85)	79 (50–120)
16 T8	88	86 (78–96)	82 (62–96)
17 T9	90	–	85 (71–114)
18 T10	92	87 (73–116)	92 (61–124)
19 T11	93	92 (78–107)	87 (67–107)
20 T12	95	99 (82–116)	90 (53–116)
21 L1	97	–	95 (79–118)
22 L2	98	–	88 (68–103)
23 L3	99	–	–
24 L4	101	–	84 (76–98)

[a]Expressed in percentage of normal-predicted FVC from reference 15. Blanks indicate insufficient data (fewer than three measurements)

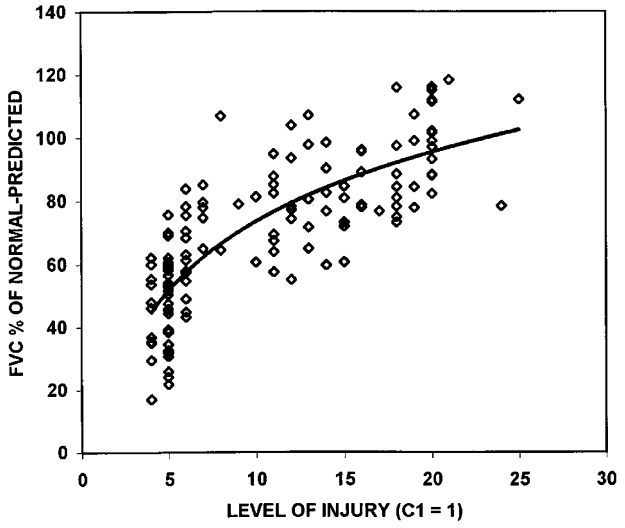

Figure 1 Individual measurements of FVC (% of normal-predicted) for never-smokers with motor-complete lesions, as a function of injury level (lowest normal neurological level), and best-fit regression line

with logarithmic transformation of injury level to allow for its nonlinear effect. Figure 1 shows FVC data points for motor-complete never-smokers as a function of injury level, and the best-fit regression line representing the equation:

$$V = 1.73 + 31.08 \text{ In } L \qquad (1)$$

in which V is SCI-predicted FVC (per cent of normal-predicted FVC) and L is level of injury. (Injury duration was not a significant predictor). Table 2 shows for each level the FVC predicted from equation 1 and the range of values actually measured. Many T7 and higher paraplegics, as well as most tetraplegics, fell below the lower normal limit, which is approximately 80% of normal-predicted.[15]

In subjects with motor-incomplete lesions, preliminary regression results did not differ significantly among the four injury level categories, so all 121 motor-incomplete subjects were analyzed together. Estimated effects were: level, 1.4 percentage points per vertebra ($P<0.005$); injury duration, -0.38 percentage points per year ($P<0.005$); ever smoking, -6.5 percentage points ($P=0.02$) – similar to effects in motor-complete paraplegics. Analysis of motor-incomplete never-smokers yielded the following regression equation:

$$V = 70.19 + 1.473 \text{ L} \quad 0.3065 \text{ D} \qquad (2)$$

in which V is SCI-predicted FVC (as a percentage of normal predicted), L is level of injury, and D is duration of injury in years. The duration effect approached significance in this analysis ($P=0.06$). Figure 2 shows a plot of motor-incomplete never-smokers' FVC as a function of level, with best-fit regression line, ignoring the duration effect. Table 3 shows FVC predicted from equation 2, along with observed means and ranges at each level with sufficient data.

Table 3 Predicted and observed FVC by level, for persons with motor-incomplete lesions[a]

Level	*SCI-predicted*[b]	*Observed mean* (range) *Never-smokers*	*All*
3 C3	70	–	58 (32–82)
4 C4	71	–	60 (49–98)
5 C5	73	71 (50–94)	69 (50–94)
6 C6	74	75 (39–97)	71 (39–97)
7 C7	76	87 (74–100)	84 (50–116)
8 C8	77	–	–
9 T1	79	–	–
10 T2	80	–	–
11 T3	82	–	–
12 T4	83	–	76 (64–89)
13 T5	85	–	–
14 T6	86	–	99 (87–121)
15 T7	88	–	–
16 T8	89	–	80 (69–99)
17 T9	91	–	–
18 T10	92	–	–
19 T11	94	–	99 (91–107)
20 T12	95	97 (93–100)	91 (66–111)
21 L1	97	101 (85–111)	96 (71–112)
22 L2	98	–	–
23 L3	99	81 (60–92)	75 (58–92)
24 L4	101	–	88 (46–114)

[a]Expressed in percentage of normal-predicted FVC from reference 15. Blanks indicate insufficient data (fewer than three measurements). [b]Assuming mean (15 years) duration of injury. Predicted value would be approximately five percentage points higher at minimum (1 year) duration

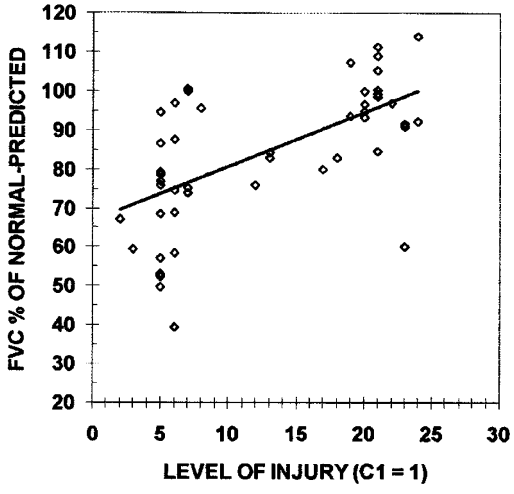

Figure 2 Individual measurements of FVC (% of normal-predicted) for never-smokers with motor-incomplete lesions, as a function of injury level (lowest normal neurological level), and best-fit regression line

Discussion

Increased duration (or earlier date) of injury was associated with lower FVC, independent of age, both here and in the earlier analysis of LA subjects.[9] This might reflect accelerated lung function losses due to respiratory complications in the chronic phase of SCI. If so, persons injured in their twenties would have appreciable risk of excess respiratory disability by late middle age, even if they do not smoke. If some older potential subjects have been lost to study due to respiratory complications causing early death or ventilator dependence, then the prospects for the overall SCI population would be even less favorable than our results indicate. A more optimistic alternative explanation is that improvements in management during the acute phase of SCI have preserved more respiratory muscle function in people injured more recently, and thereby mitigated their FVC losses in comparison with people injured earlier. As discussed previously,[9] clear understanding of duration effects and their causes will require longitudinal studies.

Despite limitations of our data on smoking, the association of smoking with FVC loss was clear, except in individuals with high-level injuries and low FVC related to injury *per se*. The loss was most evident in older subjects with presumably higher lifetime smoking doses. Most studies of smoking effects in able-bodied populations have focused on airway obstruction (ie, FEV_1) rather than FVC, but FVC losses have been observed cross-sectionally[17,18] and longitudinally.[19] Current information, though not definitive, is consistent with the possibility that losses are larger in SCI than in able-bodied populations. From findings by Dockery *et al*[18] we would project a four percentage-point mean FVC decrement in able-bodied people resembling our 45 years-and-older paraplegics who ever smoked in terms of their mean age, current smoking prevalence, and available pack-year data; whereas our subjects' observed decrement was seven percentage points. Although differences between current and former smokers were not clear in the present analyses, the earlier separate NY and LA studies,[8,9] as well as numerous studies of able-bodied populations,[10,18,19] attest to long-term lung function benefits from stopping smoking.

In able-bodied populations, larger vital capacity predicts longer life,[20,21] for reasons not completely understood. In the SCI population, lower injury levels are associated both with larger vital capacity[8,9] and with longer, healthier life.[1–4] It is likely (though not certain) that within any given level of injury, smaller FVC means greater risk of respiratory complications and early death. Accordingly, careful long-term respiratory management seems especially important for individuals with low FVC relative to their SCI-predicted values. This should not imply complacency about others with relatively good preservation of FVC after SCI: they may be abnormally susceptible to respiratory infections even if their lung function is well within the able-bodied normal range.

By the nature of our analyses, the FVC predictions are relatively uncertain for the relatively uncommon lowest cervical and highest thoracic injury levels. For the lowest levels of paraplegia, also uncommon, normal-predicted values appear valid. Wide variability of FVC even among healthy never-smokers (roughly from 80–120% of normal-predicted values specific to sex, ethnic group and height[15]) somewhat limits its prognostic value for individuals with or without SCI. Even so, improved understanding of relationships among SCI, lung function, and long-term respiratory health may emerge from further studies (preferably longitudinal) of SCI populations with detailed neurological characterization and thorough documentation of environmental risk factors (including smoking) and respiratory-illness history.

Acknowledgements

The authors thank Jerry Valencia and Clementine Brown (pulmonary technologists, Rancho Los Amigos National Rehabilitation Center), and Sheryl Terrell (medical research associate, Rancho Los Amigos National Rehabilitation Center) for their assistance. Supported in part by National Institute of Disability and Rehabilitation Research, Office of Special Education and Rehabilitative Services, US Department of Education (Grants H133N00026, H133B30029, and H133B70011); Eastern Paralyzed Veterans Association; National Institute of Environmental Health Sciences (Grant 1P01ES90581-0); and US Environmental Protection Agency (Grant R826708-01-0).

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