Gender and Its Impact on Postacute Secondary Medical Complications Following Spinal Cord Injury

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This study used a case-control design to examine gender-based differences in the occurrence of postacute secondary complications following spinal cord injury (SCI). Three participant cohorts (1 year postinjury, 5 years and more postinjury, and 10 years and more postinjury) were utilized. Men with SCI were matched, case for case, to women with SCI based on age at follow-up, marital status, educational background, category of neurologic impairment at rehabilitation discharge, American Spinal Injury Association (ASIA) impairment scale, etiology of injury, bladder management at rehabilitation discharge, and ventilator use at rehabilitation discharge. Results showed that gender was largely unrelated to subsequent development of medical complications. Study limitations and future directions are also discussed. Key words: *gender, secondary complications, spinal cord injury*

SPINAL CORD INJURY (SCI) is an important public health problem in the United States. Approximately 10,000 SCIs occur annually, and currently there are estimated to be between 183,000 and 230,000 individuals living with SCI in the United States.[1,2] Historically, women have comprised 18%–20% of the patients enrolled in the national database of the Model Spinal Cord Injury Care Systems (MSCICS).[2]

Individuals with SCI are living longer,[3] but a cure for SCI remains elusive. Because of this, clinicians have historically focused their efforts on improving the quality of life and preventing secondary medical complications in this population. Despite these efforts, secondary medical complications continue to be a significant source of morbidity and mortality.

The potential role of gender in the occurrence of secondary medical complications has not been elucidated to date. There has been a paucity of studies focusing on the potential impact of gender on complication occurrence in SCI patients. Despite this, it can be postulated that important differences might be evident because of anatomical differences, gender specific alterations in physiology, and psychosocial factors. For

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example, women have shorter urethras that might predispose to bacterial colonization. It is also our experience that women with SCI are more commonly managed with indwelling catheters secondary to the increased manual dexterity required to perform intermittent catheterization and the inability to use condom catheters. Physiologically, menopause and lower baseline bone densities might place women with SCI at greater risk for symptomatic osteoporosis and long bone fractures. These are just a few examples of how gender might theoretically affect complication occurrence in SCI patients.

Recent government legislation and policy changes within the National Institutes of Health (NIH) and the Food and Drug Administration (FDA)[4,5] have mandated a greater allocation of resources to medical issues that specifically impact women. These policies mandate the inclusion of women in government-supported clinical trials and the performance of gender analysis on study results. This increasing interest in women's health has also focused attention on medical issues facing women with disabilities including those in the SCI population.

No study, to our knowledge, has focused solely on whether gender is related to the incidence of secondary complications following SCI. In this study, we examined the relationship between gender and the occurrence of secondary medical complications while we attempted to control for social and medical characteristics along with severity of SCI.

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Method

Participants

Individuals seen for annual follow-up between January 1990 and December 1995 at one of the 18 Model Spinal Cord Injury Systems of Care funded by the Department of Education were considered for study. The 18 Model Systems are geographically dispersed throughout the United States and reflect both urban and rural catchment areas. Study participants in the SCI Model Systems have follow-up evaluations performed at 1, 2, and 5 years postinjury, and subsequently at 5-year intervals. During these evaluations, medical complications, which occurred in the preceding year, are documented. Data from follow-up evaluations are maintained at the National Spinal Cord Injury Statistical Center (NSCISC) located at the Spain Rehabilitation Center at the University of Alabama at Birmingham.

From the aforementioned patient population, two study cohorts were identified. The first cohort consisted of all 1 year ($n = 2{,}618$) follow-up evaluations, and the second cohort consisted of all 5 year or more ($n = 6{,}090$) follow-up evaluations. Using a case-control design, men were matched to women, case for case, on a variety of demographic and medical characteristics. The matching procedure was performed separately for each cohort. That is, the matching procedure attempted to match 470 women to 2,148 men in Cohort 1 and 1,001 women to 5,089 men in Cohort 2. Using these criteria, a total of 177 pairs were matched in Cohort 1 and 413 pairs in Cohort 2. To further examine the influence of injury duration on secondary medical complications, additional analysis was performed only on participants being seen for 10 years and more follow-up within Cohort 2. Seventy-eight pairs fit this description, and this patient group was labeled Cohort 3. Availability of data in the national database for specific variables influenced the selection of criteria used to match male/female patient pairs. A description of the criteria that was used to match patients follows:

1. *Age at injury*. Individuals were matched within 10 years.

2. *Marital status at discharge from the SCI Care System*. Marital status was characterized as single, married, divorced, separated, widowed, other (unclassified), and unknown.

3. *Educational background*. This variable specifies the highest formal educational level completed at the time of injury. Designations included 8th grade or less, 9th through 11th grade, high-school diploma or general equivalency diploma (GED), associate degree (junior college degree), bachelor's degree, master's degree, doctorate (PhD, MD, JD, etc.), other (unclassified), and unknown.

4. *Category of neurologic impairment at rehabilitation discharge*. This variable documents the degree of neurologic injury present at discharge. Patients were classified as paraplegic (incomplete), paraplegic (complete), paraplegic (minimal deficit), tetraplegic (incomplete), tetraplegic (complete), tetraplegic (minimal deficit), normal neurologic, or unknown.

5. *American Spinal Injury Association (ASIA) impairment scale*.[6] This variable attempts to describe the degree of impairment. Categories are:

A (complete injury)—No sensory or motor function is preserved in the sacral segments S4-S5.

B (incomplete)—Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.

C (incomplete)—Motor function is preserved below the neurological level, and more than half of the key muscles below the neurological level have a muscle grade less than 3.

D (incomplete)—Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade greater than or equal to 3.

E (normal)—Sensory and motor function is normal.

U (unknown)—Self-explanatory.

6. *Etiology of injury*. Causes were grouped into four categories: vehicular, violence, sports, and other, which included falls.

7. *Method of bladder management at rehabilitation discharge*. Categories used to describe patients included:

None—The patient has a neurogenic bladder but does not follow any established program of bladder management.

Catheter free—The patient voids satisfactorily using any method of reflex stimulation or any form of extrinsic pressure.

Indwelling catheter—Bladder is emptied by any type of catheter, which is maintained through the urethra or a stoma.

Intermittent catheterization—The patient empties the bladder by frequent insertion of a urethral catheter in an on-going program of chronic management.

Normal micturition—The patient voids satisfactorily without using reflex stimulation or extrinsic bladder pressure voiding techniques. The bladder, however, may or may not have completely normal function.

8. *Ventilator use at rehabilitation discharge*. This variable documents the use of mechanical ventilation to sustain respiration at discharge.

9. *Duration since injury*. Patients were grouped according to their follow-up year (Year 1, Years 5–9, Years 10–14, and Years 15 and more).

Outcome measures

Gender differences within each cohort were examined for the following medical outcomes: number of rehospitalizations in the past year, number and severity of pressure ulcers, the presence or absence of autonomic dysreflexia, atelectasis/pneumonia, pulmonary embolism, deep vein thrombosis, calculi in the kidney or ureter, abnormal renal function, and long bone fractures in the lower extremities. Only complications that occurred in the year preceding reevaluation were documented when patients were seen for study follow-up. Abnormal renal function was defined by an abnormal glomerular filtration rate or abnormal testing with nuclear renal scan, intravenous pyelography, renal ultrasound, or serum creatinine. Chi-square analysis was used to determine between gender differences within each cohort. A .05 alpha level was used for significance.

Results

Demographic characteristics for the three matched cohorts are summarized in Table 1. The majority of participants were Caucasian and single. Although participants were unmatched for race, there were no statistically significant differences between genders in the three cohort groups. In general, most individuals had a high-school education. In all three cohorts, the leading cause of SCI was vehicular accidents followed by violence.

Analysis within Cohort 1 (Year 1 follow-up) indicated that medical complications were largely unrelated to gender. However, the proportion of individuals reporting two or more hospitalizations in the past year was significantly higher among men (14%) as compared to women (6%), $\chi^2(2) = 6.33$, $P < .05$. All other between-gender comparisons were nonsignificant.

Similarly, Cohort 2 (Year 5 and more follow-up) showed medical complications to be largely unrelated to gender. There was, however, a higher incidence of atelectasis/pneumonia in men (4%) compared to women (1.5%), $\chi^2(1) = 4.55$, $P < .05$ and significantly more men had abnormal renal function (3.5% compared to 0.5%), $\chi^2(2) = 9.54$, $P < .01$. In contrast to Cohort 1, the number of rehospitalizations was not significantly different within this cohort. It should be noted that the information on abnormal renal function had a substantial amount of missing data. Similarly, individuals with abnormal renal function might have been more likely to be seen for long-term follow-up. Focusing only on individuals being seen for 10 years or more follow-up (Cohort 3) revealed no significant gender differences.

Table 1. Demographic characteristics of matched cohorts

	Cohort 1 (*n* = 354)		Cohort 2 (*n* = 826)		Cohort 3 (*n* = 156)	
Characteristics	**Men (*n* = 177)**	**Women (*n* = 177)**	**Men (*n* = 413)**	**Women (*n* = 413)**	**Men (*n* = 78)**	**Women (*n* = 78)**
Age at follow-up (*SD*)[a]	38.0 (17.1)	34.5 (14.7)	36.5 (11.1)	33.2 (9.2)	38.5 (8.8)	35.0 (5.7)
Education						
11th grade or less	134 (37.9%)		104 (12.6%)		12 (7.7%)	
High school or GED	180 (50.8%)		528 (63.9%)		88 (56.4%)	
More than high school	38 (10.7%)		184 (22.3%)		52 (33.3%)	
Unknown	2 (0.6%)		10 (1.2%)		4 (2.6%)	
Race						
Caucasian	107 (60.5%)	119 (67.2%)	301 (72.9%)	297 (71.9%)	59 (75.6%)	52 (66.7%)
African American	58 (32.8%)	37 (20.9%)	95 (23.0%)	84 (20.3%)	15 (19.2%)	20 (25.6%)
Other	12 (6.8%)	21 (11.9%)	17 (4.1%)	32 (7.7%)	4 (5.1%)	6 (7.7%)
Marital Status						
Single	262 (74.0%)		620 (75.1%)		112 (71.8%)	
Married	92 (26.0%)		202 (24.5%)		42 (26.9%)	
Unknown	0 (0.0%)		4 (0.5%)		2 (1.3%)	
Ventilator use at discharge						
Yes	0 (0.0%)		2 (0.2%)		0 (0.0%)	
No	354 (100.0%)		824 (99.8%)		156 (100.0%)	
Level of Impairment						
Paraplegia, incomplete	112 (31.6%)		106 (12.8%)		10 (6.4%)	
Paraplegia, complete	16 (4.5%)		390 (47.2%)		80 (51.3%)	
Tetraplegia, incomplete	180 (50.8%)		158 (19.1%)		14 (9.0%)	
Tetraplegia, complete	46 (13.0%)		170 (20.6%)		52 (33.3%)	
Unknown	0 (0.0%)		2 (0.2%)		0 (0.0%)	
ASIA Impairment Index						
A	62 (17.5%)		560 (67.8%)		132 (84.6%)	
B	50 (14.1%)		88 (10.7%)		10 (6.4%)	
C	70 (19.8%)		38 (4.6%)		2 (1.3%)	
D	172 (48.6%)		138 (16.7%)		12 (7.7%)	
E	0 (0.0%)		0 (0.0%)		0 (0.0%)	
Etiology of SCI						
Vehicular	186 (52.5%)		530 (64.2%)		98 (62.8%)	
Violence	56 (15.8%)		152 (18.4%)		36 (23.1%)	
Sports	10 (2.8%)		42 (5.1%)		12 (7.7%)	
Other	102 (28.8%)		102 (12.3%)		10 (6.4%)	
Time since injury						
5–9 years	NA		670 (81.1%)		NA	
10–14 years	NA		124 (15.0%)		124 (79.5%)	
≥ 15 years	NA		32 (3.9%)		32 (20.5%)	

[a]Individuals were matched within 10 years resulting in slight differences in average age between genders.

The occurrence of long bone fractures was relatively rare, and there was substantial missing data in all three cohorts. As a result, it is not possible to draw meaningful conclusions regarding this specific outcome. The results for study Cohorts 1, 2, and 3 are summarized in Table 2.

Discussion

Given the significant numbers of closely matched individuals, our study was remarkable for the relative paucity of significant differences between matched men and women in the occurrence rate of most SCI secondary complications. Statistically significant findings included a higher rehospitalization rate for men during postdischarge Year 1 that did not persist in the Year 5 and more and Year 10 and more cohorts. There was also a higher incidence in men of pneumonia/atelectasis in the Year 5 and more cohort, which was not evident in the other cohorts. The reason for this is unclear. Given the number of statistical comparisons made between genders, this isolated finding could be attributed to chance.

It is our belief that even though clinicians might appreciate valid gender differences in complication occurrence as part of their daily practice, these differences are primarily attributable to the frequency of various patient characteristics (psychosocial and physiologic) varying between the sexes. The relative paucity of significant differences when men and women are matched for potential confounding variables argues against an increased risk of the studied complications based solely on gender.

McKinley and colleagues[7] recently examined the occurrence of long-term medical complications utilizing the SCI national database, but their study did not specifically focus on the potential impact of gender. In addition, multivariate analysis or other statistical methods were not used to control for confounding variables when identifying risk factors. Statistically significant findings included an increased incidence of pressure ulcers and abnormal renal testing in men. Women had a higher incidence of long bone fractures at follow-up Year 20. In an earlier study, Meyers et al.[8] examined rehospitalization rates in individuals with SCI and found no significant relationship to gender.

A Swedish study[9] utilized multivariate analysis to examine the relationship between various patient characteristics (i.e., gender, neurologic deficits, age at injury, duration of injury) and a variety of postacute medical problems. Men were at increased risk for sexual dysfunction and spasticity problems. Women were at increased risk for spinal deformity and long bone fractures. In our study, missing data prevented us from reaching any conclusions regarding the relationship between gender and long bone fractures.

Another recent study[10] examined complications in the acute rehabilitation setting. Men were noted to have a higher incidence of pressure ulcers, autonomic dysreflexia, deep vein thrombosis, pulmonary embolism, and abnormal renal testing. However, the differences were statistically significant only for abnormal renal testing.

Earlier studies utilizing the national SCI database to focus on secondary medical complications found men to be at significantly increased risk for autonomic dysreflexia, deep vein thrombosis, pulmonary embolism, and pressure ulcers.[11–13] Only in the study on pressure ulcer incidence was multivariate

Table 2. Study results

	Cohort 1 (n = 354)			Cohort 2 (n = 826)			Cohort 3[a] (n = 156)
Medical complications	**Men (%) n = 177**	**Women (%) n = 177**	***P***	**Men (%) n = 413**	**Women (%) n = 413**	***P***	***P***
Rehospitalizations							
None	107/171 (62.6)	124/175 (70.9)	**.042**	313/400 (78.3)	318/402 (79.1)	.378	.743
One	41/171 (24.0)	41/175 (23.4)		47/400 (11.8)	54/402 (13.4)		
Two or more	23/171 (13.5)	10/175 (5.7)		40/400 (10.0)	30/402 (7.5)		
Pressure ulcers (grade)							
No ulcers	121/137 (88.3)	130/143 (90.9)		146/190 (76.8)	157/208 (75.5)		
Grade 1	4/137 (2.9)	3/143 (2.1)	.349	11/190 (5.8)	20/208 (9.6)	.152	.761
Grade 2	10/137 (7.3)	5/143 (3.5)		21/190 (11.1)	13/208 (6.3)		
Grade 3 or more	2/137 (1.5)	5/143 (3.5)		12/190 (6.3)	18/208 (8.7)		
Pressure ulcers (#)							
None	121/137 (88.3)	130/143 (90.9)	.575	146/190 (76.8)	157/208 (75.5)	.389	.779
One	12/137 (8.8)	8/143 (5.6)		34/190 (17.9)	33/208 (15.9)		
Two or more	4/137 (2.9)	5/143 (3.5)		10/190 (5.3)	18/208 (8.7)		
Autonomic dysreflexia							
Yes	15/174 (8.6)	18/176 (10.2)	.607	49/404 (12.1)	42/403 (10.4)	.588	.708
No	159/174 (91.4)	158/176 (89.8)		355/404 (87.9)	361/403 (89.6)		
Atelectasis/pneumonia							
Yes	7/175 (4.0)	9/175 (5.1)	.609	16/403 (4.0)	6/398 (1.5)	**.033**	.360
No	168/175 (96.0)	166/175 (94.9)		387/403 (96.0)	392/398 (98.5)		
Mechanic ventilation[b]							
Yes (short-term)	0/173 (0.0)	2/174 (1.1)	.157	2/356 (0.6)	0/381 (0.0)	.341	NA
Yes (dependent)	0/173 (0.0)	0/174 (0.0)		1/356 (0.3)	1/381 (0.3)		
No	173/173 (100)	172/174 (98.9)		353/356 (99.2)	380/381 (99.7)		
Pulmonary embolism[b]							
Yes	0/175 (0.0)	0/175 (0.0)	NA	0/405 (0.0)	0/402 (0.0)	NA	NA
No	175/175 (100)	175/175 (100)		405/405 (100)	402/402 (100)		
Deep vein thrombosis[b]							
Yes	7/175 (4.0)	2/175 (1.1)	.091	3/404 (0.7)	8/402 (2.0)	.127	NA
No	168/175 (96.0)	173/175 (98.9)		401/404 (99.3)	394/402 (98.0)		
Renal calculi							
Yes	2/163 (1.2)	3/156 (1.9)	.250	12/388 (3.1)	9/373 (2.4)	.567	.362
No	161/163 (98.8)	153/156 (98.1)		376/388 (96.9)	364/373 (97.6)		
Renal function							
Normal	28/172 (16.3)	26/175 (14.9)	.830	68/397 (17.1)	63/395 (15.9)	**.009**	.303
Abnormal	3/172 (1.7)	2/175 (1.1)		14/397 (3.5)	2/395 (0.5)		
Not performed	141/172 (82.0)	147/175 (84.0)		315/397 (79.3)	330/395 (83.5)		
Long bone fractures							
Yes	1/58 (1.7)	0/68 (0.0)	.277	3/274 (1.1)	0/211 (0.0)	.127	.377
No	57/58 (98.3)	68/68 (100.0)		271/274 (98.9)	211/211 (100)		

[a] For Cohort 3 where none of the findings reached statistical significance, only the *P* values are given for comparison. [b] For these complications, not applicable (NA) is used to denote when a *P* value could not be calculated because the complication in question failed to occur in any of the study participants.

analysis utilized to control for the impact of other variables.[12] In contrast, Waring and Karunas[14] used logistic regression modeling and found no correlation between gender and the occurrence of deep vein thrombosis and thromboembolism.

Our study is unique because of the methodology we used of examining complication occurrence in closely matched men and women. To our knowledge, we are the first investigators to primarily focus on gender-based differences in SCI-related complications using this approach. This distinction, along with differences in the outcomes studied, could be responsible for the discrepancies between our study and earlier studies.

In this investigation, we utilized the national database of the Model SCI Systems. This database is maintained at the NSCISC at the University of Alabama in Birmingham. Since its inception in 1973, over 25,000 individuals have been entered into the database.[1] This large cohort of patients made it possible for us to use the case-control methodology of matching pairs of women and men for various characteristics. This approach facilitates the comparison of similar individuals and therefore helps control for potentially confounding factors that could impact measured outcomes. As a result, the case-control design substantially increases the internal validity of the study in determining the specific effects of gender on secondary medical complications.

Despite the aforementioned strengths, the matching methodology has some limitations. It necessitates having a large cohort of study participants before the matching to ensure adequate numbers of matched pairs for statistical analysis. The number of criteria used to match individuals has a direct impact on the yield of matched pairs for study. The more criteria utilized, the fewer available pairs for analysis. This serves as a practical ceiling for the number of criteria that can be used to match patients. Therefore, the selection of matching criteria is very important. The potential impact of a variable on outcome cannot be controlled for unless study participants are matched for it.

Our selection of matching criteria was affected by the available information in the database, practical limitations on the number of criteria that could be included, and clinical judgment regarding what variables other than gender might affect complication occurrence. Despite these limitations, the high internal validity of the study design strongly supports the conclusion that gender is largely unrelated to the secondary medical complications that were studied. It is still possible that gender might impact secondary medical complications that are not recorded outcomes in the national database.

This study was designed to specifically detect differences in complication occurrence among men and women with SCI. It was not designed to define rates of occurrence and magnitude of differences in secondary complications and, therefore, should not be generalized to the overall SCI population. The study also used cross-sectional groups of patients for comparison. Longitudinal follow-up of specific cohorts was impractical because of increasing losses to follow-up as the duration from injury increased.[15]

The results of this study suggest that pursuing gender differences in complication occurrence may not be productive. Instead, resources and further investigation should focus on identifying variables that predict the development of secondary medical complications in male and female SCI patients.

Conclusion

Secondary medical complications continue to be a source of major mortality and morbidity in both male and female SCI patients. When other variables are controlled for, the independent effect of gender on secondary medical complications that are included in the national SCI database appears to be minimal. Our ability to comment specifically on gender and its relationship to fracture risk was hampered by missing data. In the future, it is vital that investigators continue their efforts to identify risk factors that place SCI patients at increased risk for secondary complications. Interventional strategies could then be devised to target these risk factors if modifiable.

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