Excess Risk of Bladder Cancer in Spinal Cord Injury: Evidence for an Association Between Indwelling Catheter Use and Bladder Cancer

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ABSTRACT. Groah SL, Weitzenkamp DA, Lammertse DP, Whiteneck GG, Lezotte DC, Hamman RF. Excess risk of bladder cancer in spinal cord injury: evidence for an association between indwelling catheter use and bladder cancer. Arch Phys Med Rehabil 2002;83:346-51.

Objectives: To evaluate whether the risk of bladder cancer is greater in individuals with spinal cord injury (SCI) than in the general population and whether indwelling catheter (IDC) use is a significant independent risk factor for bladder cancer.

Design: Historical cohort study in which subjects with SCI were stratified according to bladder management method and followed for the development of bladder cancer.

Setting: A large rehabilitation hospital in the Spinal Cord Injury Model Systems.

Participants: A total of 3670 patients with SCI who were evaluated for bladder cancer on at least 1 occasion by cystoscopy over a period of 1 to 47 years.

Interventions: Not applicable.

Main Outcome Measures: Bladder cancer occurring after SCI determined by diagnosis at our facility, by subject report, or by report of next of kin.

Results: Twenty-one cases of bladder cancer were found in the 3670 study participants. The risk of bladder cancer for subjects with SCI using IDC is 77 per 100,000 person-years, corresponding to an age- and gender-adjusted standardized morbidity ratio (SMR) of 25.4 (95% confidence interval [CI], 14.0–41.9) when compared with the general population. After controlling for age at injury, gender, level and completeness of SCI, history of bladder calculi, and smoking, those using solely IDC had a significantly greater risk of bladder cancer (relative risk [RR] = 4.9; 95% CI, 1.3–13.8) than those using nonindwelling methods. Mortality caused by bladder cancer in individuals with SCI was significantly greater than that of the US population (SMR = 70.6; 95% CI, 36.9–123.3).

Conclusions: Bladder cancer risk and mortality are heightened in SCI compared with the general population. IDC is a significant independent risk factor for the increased risk of and mortality caused by bladder cancer in the SCI population.

Key Words: Bladder cancer; Incidence; Mortality; Rehabiliation; Spinal cord injuries.

BLADDER CANCER is the fifth most common neoplasm and 12th leading cause of cancer mortality[1,2] in the United States, with an age-adjusted yearly incidence of 17 per 100,000 persons. Known risk factors for bladder cancer include male gender, smoking,[3-11] occupational exposure to aromatic amines in industrialized countries,[6,12] and schistosomiasis infection in endemic areas. The most common histologic type of bladder cancer is transitional cell carcinoma, occurring in approximately 90% of all cases, whereas squamous cell carcinoma, adenocarcinoma, and other mixed varieties comprise the remaining 10%.[4]

Bladder cancer research in spinal cord injury (SCI) is limited by the challenges inherent in following a large cohort of individuals with SCI long enough to allow for bladder cancer to develop. Often, cancer research is conducted retrospectively by using a case-control design to maximize financial and temporal efficiency because most types of cancer have long preclinical disease phases, thus limiting the use of a prospective design. The literature includes several studies reporting on the prevalence of bladder cancer in SCI,[13-20] which was calculated by dividing known bladder cancer cases by the number of SCI patients followed over a variable amount of time. There have been no studies in which a large cohort was followed prospectively, permitting the accurate calculation of disease risk in SCI. With the paucity of prospective data, we were prompted to examine the association between indwelling catheter (IDC) use and bladder cancer in SCI.

The purpose of this study was to examine and quantify the risk of bladder cancer in SCI compared with the US general population and to determine if IDC use is a risk factor for bladder cancer in SCI. We explored 4 hypotheses: (1) the incidence of bladder cancer is higher in the SCI population than in the general population; (2) compared with other bladder management methods, IDC use is associated with bladder cancer in the SC population; (3) there is an increasing risk of bladder cancer with increasing duration of IDC use; and (4) bladder cancer mortality is greater in individuals with SCI who use IDC as their primary means of bladder management than in those who do not.

METHODS

Study Design

A historical cohort study was designed by using the SCI population at Craig Hospital, a large SCI treatment center based in the Denver, CO, metropolitan area. Of all Colorado residents who incur an SCI that requires inpatient rehabilitation, approximately 75% are referred to Craig Hospital.

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Development of the Database

A comprehensive database was developed in 1979 to follow individuals treated for SCI at our facility. Information on subjects who had a SCI before the database was developed and who survived to 1979 was entered into the database at their next evaluation, whereas information on persons who died before 1979 was not recorded. Data collected after construction of the database were abstracted for this study.

Identification of the Study Population

Participants included individuals listed in the database who incurred an SCI between 1950 and 1997 and who were known to have survived at least 1 year. Participants were eligible for the study if initial screening cystoscopy, performed at any time post-SCI, documented the presence or absence of bladder cancer. Seventy-five percent of the entire cohort completed initial screening within 3 years of injury.

There were 9112 patients with SCI treated at our institution between 1950 and 1997, of whom 4078 were excluded because they had less than 1 year of follow-up. Another 1364 were excluded because of insufficient data about their method of bladder management. The remaining 3670 patients whose initial cystoscopic screen did not reveal bladder cancer were entered into the study from the time of their SCI to the last known follow-up or death.

Description of Cohorts

Participants were stratified according to their bladder management techniques since the SCI. The majority of patients had used either an indwelling urethral catheter, indwelling suprapubic catheter, intermittent catheterization, external condom catheter, or spontaneous voiding as their primary method of bladder management. It was assumed that all participants were catheter free before their SCI.

Participants were divided into 2 primary bladder management groups: IDC use and nonindwelling catheter use (NIDC). A third group, comprised of patients who used both indwelling and nonindwelling methods (Multi), was developed for those who had changed bladder management methods. The IDC group included those who used either urethral or suprapubic catheters. The NIDC group included those persons spontaneously voiding, using external condom collectors, or intermittent catheterization. Intermittent catheterization was included in the NIDC group because we felt that brief exposure of the urethra and bladder to the catheter during intermittent catheterization was clinically insignificant compared with continuous exposure to an IDC.

A method of bladder management was included only if it was used for more than 1 year. We defined multiple bladder management techniques as the use of both indwelling and nonindwelling methods, each for 1 year or more. The purpose of this time designation was to exclude brief periods of change in bladder management methods that we assumed were not clinically significant. Further, by including a separate cohort with a mixed experience of indwelling and nonindwelling methods use, we were better able to address dose-response relationships between catheter use and bladder cancer.

Method of Follow-up

Participants had variable lengths of routine follow-up after SCI. Demographic variables and method of bladder management were recorded on initial inpatient admission and discharge for outpatient visits. Participants had variable lengths of routine follow-up after SCI, which were summed, thereby permitting a calculation of the person-time contribution for each type of bladder management technique. For individuals who received their initial SCI rehabilitation at another hospital and who had different initial and current methods of bladder management, we reviewed their medical records to determine the person-time contribution for each type of management. If a medical record was incomplete, that individual was assumed to have contributed 50% of the amount of time with undetermined bladder management to each of the 2 groups. Individuals contributed person-time to the analysis from time of SCI to the most recent cystoscopy documenting bladder cancer status. The mean follow-up interval for the population was 2 years, with 94% of a random sample having received screening cystoscopy during follow-up. Biopsies were performed on a case-by-case basis when there was clinical suspicion of cancer on cystoscopy. Participants were assumed to remain cancer free if initial and subsequent cystoscopies did not reveal evidence of bladder cancer. Data were collected on patients through December 31, 1998.

Ascertaining and Validating Bladder Cancer Status

Incident cases of bladder cancer occurring between 1979 and 1998 and defined according to the International Classification of Diseases[21] codes 188.0 to 188.9 and V10.5 served as the basis of the study. Bladder cancer status was initially ascertained through malignant findings from a bladder biopsy and subsequent pathology reports when available (n = 17, 80%), from self-reports (n = 2, 10%), or from reports by next of kin (n = 2, 10%). All cases diagnosed at our institution were confirmed by biopsy, and reports of biopsy results were obtained for patients diagnosed at other institutions. Available pathology slides and reports were reviewed by a single pathologist who was blinded to bladder management method, bladder cancer status, and previous histologic diagnoses.

Identification of the "General Population"

Information on individuals with SCI was compared with data from the US population. Age- and gender-specific incidence and mortality data were obtained from the National Cancer Institute, Surveillance Epidemiology and End Results[2] (SEER), referred to here as "general population" data. The SEER program currently collects and publishes cancer incidence and survival data from 11 population-based cancer registries and 3 supplemental registries covering approximately 14% of the US population.[2] The intra-SEER variability of bladder cancer incidence between the registries ranges from 2 to 20 per 100,000 population. Because the SCI population was comprised of a large proportion of individuals from states other than Colorado, the total SEER population data was believed to be the most comparable of available databases, as opposed to a single SEER registry.

End Points

End points included diagnosis of bladder cancer or death from any cause. Bladder cancer was confirmed as described previously and included a primary diagnosis of cancer occurring in the bladder or the perivesicle area (urethra or suprapubic tract). For subjects who died from any cause, their most recent follow-up documenting bladder cancer status was used as the final data collection point. This was done because the subject could have potentially developed and subsequently died from bladder cancer after the most recent follow-up and without our knowledge.

Statistical Analysis

Univariate investigations of the cohorts with respect to age and duration of SCI, level and completeness of SCI, and gender

were performed with the NIDC group as the reference. Chi-square and independent *t* tests were used to detect any differences between the groups that might have contributed to an altered risk of bladder cancer.

Person-time follow-up for each participant was computed from the time of SCI to the date of diagnosis of bladder cancer, death from any cause, or last known follow-up in which bladder cancer status was assessed by cystoscopy. Fifty percent of participants were injured before the database was developed in 1979. For these individuals, we included their person-time contribution from time of SCI to entry into the database, according to the initial recorded method of bladder management. We assumed that the presenting type of bladder management had been used since SCI. In a random sample of participants, we determined the classification error inherent in this assumption to be 6%, which was equally distributed between the 2 primary bladder management groups. Comparisons of the baseline demographic and risk factor data for the participants injured before or after the database was developed revealed that the 2 groups were similar except that there were fewer occurrences of bladder calculi in the group injured before 1979. Analyses revealed this error to have a negligible impact on the calculations of bladder cancer risk. By including total person-time experience since SCI in our calculations, we attempted to avoid overestimation of bladder cancer risk.

The incidence of bladder cancer was calculated for each bladder management group by dividing the number of participants with bladder cancer by the total person time of the cohort. Age adjustment was performed by using the direct method, with the total SCI population as the standard.

A standardized morbidity ratio (SMR) was calculated to evaluate bladder cancer risk in the SCI population exposed to IDC compared with that of the general population. By using age- and gender-specific incidence rates of bladder cancer obtained from the SEER registry, we compared the observed number of bladder cancer cases among those with SCI with the number of bladder cancer cases expected if individuals with SCI had the same morbidity experience as the general population. Confidence intervals (CIs) for the SMR were obtained by using the method of Breslow and Day.[22]

Cox proportional hazards regression analyses[23] were used to examine the relation between bladder cancer development and method of bladder management. Analyses were performed for eligible subjects beginning at the time of SCI. Covariates included age at SCI, duration of SCI, cervical level of SCI, American Spinal Injury Association (ASIA) classification[24] describing completeness of SCI (A = complete, B = sensory incomplete, C and D = motor incomplete, E = complete motor and sensory recovery), gender, and a history of bladder calculi (modeled as a time-dependent dichotomous covariate). With the exception of gender, only significant terms were retained in the final model. The number of covariates included in the final model was limited by few bladder cancer cases. Model fit was determined based on the -2 log-likelihood ratio test, which has a chi-square distribution with degrees of freedom equal to the number of estimated parameters.[25] Log-log plots were parallel, indicating that there were no departures from the proportional hazards assumptions for any covariate included in the multivariate regression model. Regression results are expressed as rate ratios and approximate 95% CIs.

Then, by using life-table techniques, each person's probability of not developing bladder cancer during the entire period from entry into the study through their last follow-up of known bladder cancer status was computed as the cumulative product of his probabilities of not developing bladder cancer at each year. The probability of not developing bladder cancer in any year was calculated as 1 minus the probability of developing bladder cancer at a particular age during that year.

The attributable risk (AR) was used to provide information about the absolute effect of IDC use on bladder cancer. The AR was calculated by subtracting the incidence of bladder cancer in the NIDC group from the incidence of bladder cancer in the IDC group. Under the null hypothesis, if there is no relationship between IDC use and bladder cancer the AR would be zero. The AR percentage is the proportion of disease attributable to IDC use. It is calculated as the AR divided by the rate of disease among those exposed to IDC multiplied by 100.

All persons alive with bladder cancer (or next of kin if the subject was deceased) were contacted for confirmation of vital status. Of those deceased, death certificates were obtained in all but 2 cases. Mortality rates from bladder cancer were calculated by dividing the number of subjects who died because of bladder cancer by the total person-time experience with SCI for each of the bladder management groups. These were compared with the general population obtained from SEER data by using a SMR as described previously and adjusting for age and gender.

P values of $\leq .05$ were considered indicative of statistical significance. Statistical Package for the Social Sciences[a] was used for data management.

RESULTS

A total of 3670 participants, contributing 39,729 person-years of follow-up, were available for the main analysis. This included 1628 in the NIDC group contributing 15,226 person-years, 314 in the Multi group contributing 4411 person-years, and 1728 in the IDC group contributing 20,092 person-years. At study completion, 24 subjects with SCI had developed bladder cancer.

Three bladder cancer cases were eliminated from the main analysis. In 1 case, the patient had a history of bladder cancer before SCI; in another, the bladder cancer was detected on initial screening cystoscopy; and in the third case, the reviewing pathologist determined that the carcinoma did not originate in the bladder. Of the cases eliminated, 1 occurred in the NIDC group, whereas 2 occurred in the IDC group. Of the remaining 21 cases used in the main analyses, 15 were in the IDC group, and 3 each were in the Multi and NIDC groups. Mean age at diagnosis of bladder cancer was 48 years (range, 29–72y; standard error [SE], 2.9y), and mean duration of SCI at time of diagnosis was 20 years (range, 12–40y; SE, 1.7y).

Demographic data were examined according to the bladder management method in table 1. Mean age at SCI and gender distribution were consistent across the 3 groups. The IDC group was more likely to have a cervical level of SCI ($\chi^2_2 = 381.15$, $P < .0001$) and an ASIA class A complete SCI ($\chi^2_2 = 112.05$, $P < .0001$) than the NIDC group.

Analyses of potential risk factors for bladder cancer revealed a significantly greater proportion of participants who used IDC (46% of IDC group, 39% of Multi group) developed bladder calculi compared with the 10% in the NIDC group ($\chi^2_2 = 537.64$, $P < .0001$). Thirty-one percent of the IDC group had a history of pyelonephritis, compared with 33% of the NIDC group ($\chi^2_1 = 1.4$, $P = .24$). There were no documented cases of bladder schistosomiasis in any of the cohorts.

Age-adjusted analyses revealed that increasing exposure to IDC use was associated with bladder cancer in SCI. The IDC group had an age-adjusted rate of 77 per 100,000 person-years, compared with rates of 56.1 and 18.6 per 100,000 person-years in the Multi and NIDC groups, respectively.

As shown in table 2, after age and gender adjustment, participants with SCI were 15.2 (95% CI, 9.2–23.3) times more

Table 1: Comparison of Subject Demographic Data at Entry Into Study by Bladder Management Method*

Factor	NIDC	Multi	IDC
No. of subjects	1628	314	1728
Age at SCI (y)			
1–9	0%	0%	0%
10–19	4%	0%	3%
20–29	23%	11%	20%
30–39	28%	31%	30%
40–49	24%	29%	26%
50–59	13%	17%	12%
60–69	7%	8%	7%
70–79	0%	3%	2%
80–89	0%	1%	0%
Mean age at SCI (y)	30	29	29
Gender			
Male	80%	85%	80%
Female	20%	15%	20%
Level of SCI			
Cervical*	35%	40%	68%
Thoracic*	54%	56%	30%
Lumbosacral*	11%	4%	2%
ASIA classification			
A*	47%	60%	65%
B*	14%	18%	20%
C	13%	9%	11%
D*	25%	13%	4%
E	1%	0%	0%
Median duration of bladder management time (y)			
NIDC	9.8	7.3	NA
IDC	NA	6.9	11.8

Abbreviation: NA, not applicable.
* $P < .05$.

likely to develop bladder cancer than the general population. Of those using IDC only as their method of bladder management, the observed 15 cases of bladder cancer were compared with an expected 0.6 cases, yielding a ratio of 25.4 (95% CI, 14.0–41.9).

Cox regression models were constructed independently to examine bladder management method, age at SCI, gender, ASIA classification, level of SCI, and history of bladder calculi (table 3). Only bladder management method and age at SCI significantly predicted bladder cancer. ASIA classification, level of SCI, and a history of bladder calculi did not contribute significantly to the model, nor were there any significant interactions between these and other covariates. After adjustment for potential risk factors, the risk of bladder cancer was 4.9 (95% CI, 1.3–13.8) times greater in those using IDC compared with those using NIDC. Male gender did not significantly contribute to the model (relative risk [RR] = 1.9; 95% CI, 0.6–6.8) but was included because it is a well-documented risk factor for disease.

Table 2: Age- and Gender-Adjusted SMR of Bladder Cancer Compared With Bladder Cancer in the General Population

Bladder Management Method	Observed	Expected	Observed/Expected	95% CI
NIDC	3	0.6	5.0	1.1–14.6
Multi	3	0.2	15.8	3.6–46.1
IDC	15	0.6	25.4	14.0–41.9
All SCI	21	1.4	15.2	9.2–23.3

Table 3: RRs of Bladder Cancer, CIs, and *P* Values Obtained From Cox Regression Analysis

Risk Factor	RR	95% CI	*P* Value
Bladder management technique			
IDC use	4.9	1.3–13.8	.02
Multiple catheter use	4.0	0.8–20.2	.49
Age at SCI	1.1	1.1–1.2	.01
Male gender	1.9	0.6–6.8	.83
History of bladder calculi	1.1	0.5–2.9	.34
Cervical level of SCI	0.5	0.1–4.2	.76
ASIA Impairment Scale class A	NR	NS	.14

Abbreviations: NR, not reported due to high variability; NS, nonsignificant.

By using Kaplan-Meier techniques, the cumulative morbidity of persons surviving without bladder cancer was shown by comparing subjects who used IDC for more than 1 year with those who did not use IDC (fig 1). There was an increase in morbidity from bladder cancer occurring at approximately 15 to 25 years post-SCI, which was not seen to the same degree in persons using NIDC methods ($P = .03$).

When we examined the influence of duration of IDC use in 10-year increments, we found no cases of bladder cancer within the first 9 years of SCI. The risk of bladder cancer was 86.8 per 100,000 person-years in those who used IDC 10 to 19 years and increased to 398.1 per 100,000 person-years in those who used IDC for 20 years or more (RR = 4.6; 95% CI, 1.5–14.0).

Calculations of AR revealed that IDC was responsible for 34.1 cases of bladder cancer per 100,000 person-years of SCI. This yielded an AR percentage of 55.8% for IDC use, whereas male gender and bladder calculi were responsible for fewer cases of bladder cancer, at 32.9% and 10.7%, respectively. In those using IDC only, IDC was responsible for 58.4 cases per 100,000 person-years, or 64.8% of all bladder cancer occurring in the IDC population.

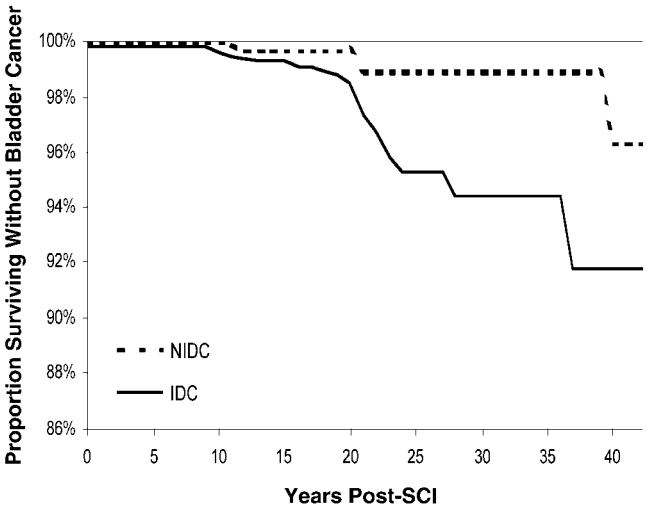

Fig 1. Cumulative morbidity of bladder cancer by bladder management method and years post-SCI.

At the completion of this study, 13 persons with bladder cancer had died, with the cause of death identified as bladder cancer in 12. Of the 12, 10 had solely used IDC, whereas 2 used multiple techniques (mean IDC use, 20y; range, 10–29y; SE, 2.3y). There were no bladder cancer mortality cases in the NIDC group. The age-adjusted bladder cancer mortality rate was 52 per 100,000 person-years for those using IDC versus 40.8 per 100,000 person-years for those using Multi bladder management methods. SMR adjusted for age and gender revealed that the SCI population had a bladder cancer mortality risk 70.6 (95% CI, 36.9–123.3) times that of the general population.

DISCUSSION

In this historical cohort study of 3670 people with SCI, use of IDC as a primary means of bladder management was found to be associated with a heightened risk and mortality of bladder cancer, after controlling for potential risk factors. Those using IDC alone experienced a 25-fold greater risk of bladder cancer than the general population; disease occurred in subjects with 12 or more years of IDC use and in patients as young as 29 years.

Although there have been several reports of the multiyear prevalence of bladder cancer in SCI,[13-20,26,27] to date there have been no accurate reports of the incidence of bladder cancer in SCI using duration of exposure to different types of bladder management methods. Melzak's[14] initial study of bladder cancer in SCI showed that 290 per 100,000 persons with SCI developed bladder cancer over many years. Depending on the method of diagnosis and characteristics of the population, the period prevalence (proportion of a population affected by disease during a specified period of time) of bladder cancer in SCI reported in more recent studies ranges from .27% to 10%.[13-18] Melzak[14] noted the mean age of bladder cancer onset was 51 years, and disease occurred as early as 13 years post-SCI. Similarly, we noted that mean age at bladder cancer diagnosis was 48 years, and mean time after SCI to bladder cancer was 20 years, whereas 6 cases presented between 12 and 13 years post-SCI. This is in contrast to the general population, in which bladder cancer typically does not occur in those younger than 60 years of age.[2]

Gender is a well-documented risk factor for bladder cancer in the general population, with men having nearly 4 times the risk of women.[3] Male gender was associated with a 2-fold risk of bladder cancer in our study, although this was not statistically significant. Stratified analyses revealed that gender was neither a confounder nor an effect modifier.

Bladder calculi in persons using IDC have been associated with urinary tract infection[28-31] and bladder cancer.[32] In our study population, there was a clear association between IDC use and bladder cancer, but a relation between bladder calculi and bladder cancer was not evident, as shown by the Cox regression results.

There are several drawbacks in this study that are inherent in historical cohort studies. The data include a large estimated proportion although a random sample showed a minimal error in our estimation, which was equally distributed between the 2 major groups of interest, thereby minimally affecting the results. We believe it is more accurate to add these known years of catheter use to the denominator used in the calculations of disease incidence, thereby avoiding an overestimation of disease risk.

We do not believe this study was biased by heightened clinical suspicion for bladder cancer in persons using IDC because the proportion of participants screened with cystoscopy was equivalent across bladder management groups, and screening resulted in the diagnosis of 2 cases (1 each in the IDC and Multi groups). Relatively few cases limited certain analyses, including evaluating the effect of potential interactions between covariates and the effect of duration of IDC use on bladder cancer risk.

Finally, because of limitations in the database, we cannot rule out the possibility that some unmeasured confounder such as urinary tract infection, family history of bladder cancer, history of occupational exposure to aromatic amines, or smoking accounted for some of the associations we found. Because smoking status was not available from the database, we further investigated a random sample of the total SCI population to obtain more information on the effect of smoking on bladder cancer status. This post hoc analysis showed that there was neither a significant difference in smoking status between the groups according to method of bladder management nor a significant difference when individuals with SCI were compared with general population data. Further, the RR of bladder cancer from IDC use remained relatively unchanged (RR = 4.4; 95% CI, 2.5–7.8) when we adjusted for smoking status.

This study has several critical strengths over those reported in the literature. This is the first prospective study of a large cohort with SCI that has been followed for many years, thereby allowing the calculation of bladder cancer risk in individuals exposed to different bladder management methods. The risk of bladder cancer has been miscalculated in previous studies[13-16,18,26,27,32] because exposure time information was not used in the calculations. This is the first study that has quantified the risk of bladder cancer from several risk factors while accounting for potential confounders and changing bladder management methods. Additionally, we were able to suggest a dose-response relation between IDC use and bladder cancer by including the Multi group as an intermediary risk group.

The results of this study are valid for individuals with SCI according to their bladder management method. Comparisons revealed our SCI population to be demographically similar to that of the Spinal Cord Injury Model Systems[33] database. However, our patient population uses IDC proportionally more than patient populations at other SCI centers. Therefore, the total SCI population risk is primarily applicable to other populations with similar distributions of bladder management. Similarly, these results are not necessarily generalizable to the catheterized, non-SCI populations because there may be other factors unique to the neurologic injury that occur with SCI that alters the risk of disease in this population.

CONCLUSIONS

The results of this historic prospective study offer strong support of our hypotheses that bladder cancer incidence and mortality are significantly higher in SCI than the general population, and that this heightened risk is primarily caused by IDC use. With a younger age at onset and heightened mortality rate, we submit that the type of bladder cancer and the course of the disease seen in SCI are unique from that typically seen in the general population. This may warrant more aggressive screening in certain high-risk subpopulations. Further, this information is especially critical when counseling SCI patients on long-term bladder management options because the majority will have several decades of potential exposure to IDC.

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Supplier

a. Version 12.0; SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.