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ORIGINAL ARTICLE

Bladder cancer in spinal cord injury patients

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Study design: Retrospective review.
Objective: Spinal cord injury is a known risk factor for bladder cancer. The risk of bladder cancer has been reported at 16–28 times higher than the general population. Earlier studies have identified indwelling catheters as risk factors. We examined the characteristics of bladder cancers in a spinal cord injury (SCI) population.
Setting: Long Beach VA Hospital Spinal Cord Injury Unit, Long Beach, California
Methods: We reviewed SCI patients seen and diagnosed with bladder tumors between January 1983 and January 2007. Data collected included time since diagnosis, method of diagnosis, form of bladder management, pathologic type, treatment of the tumor, and outcome.
Results: A total of 32 patients with bladder cancer were identified out of 1319 seen. Tumors found were 46.9% squamous cell carcinoma (SCC), 31.3% transitional cell carcinoma (TCC), 9.4% adenocarcinoma, and 12.5% mixed TCC and SCC. The primary form of bladder management was 44% urethral catheter for a mean of 33.3 years, 48% external catheter for a mean of 37.4 years, and 8% intermittent catheterization for a mean of 24.5 years. Nineteen patients had a known method of cancer detection with 42% found on screening cystoscopy.
Conclusions: The pathologic makeup of the tumors is similar to that reported earlier. Over 50% of patients diagnosed with bladder cancer in our population did not have an indwelling catheter. This suggests that the neurogenic bladder, not the indwelling catheter, may be the risk factor for bladder cancer. Urologists should consider diligent, long-term screening of all patients with SCI for bladder cancer and not just those with indwelling catheters.
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Keywords: spinal cord injuries; urinary bladder neoplasms; catheterization

Introduction

Bladder tumors in the spinal cord injury (SCI) patient are a well-recognized phenomenon. Although controlled prospective studies are lacking, several retrospective studies have suggested that the relative risk of a bladder neoplasm is 16–28 times that of a normal population.[1–4] SCI patients are also known to have a different spectrum of disease than the general population with a significantly higher proportion of squamous cell carcinoma (SCC) compared with transitional cell carcinoma (TCC), and a lower age and a higher stage at diagnosis.[5] We examined the risk factors and characteristic of bladder tumors in an SCI population.

Materials and methods

All SCI patients at the Long Beach Veterans Administration diagnosed with bladder tumors between January 1983 and January 2007 were reviewed.

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A total of 32 patients with tumors were identified out of approximately 1319 patients seen and followed by urology, and data was collected on each patient including the time since their diagnosis, management of their bladder, the number and method of identification of the bladder tumors, the method of treatment of the tumors, and the end result of their disease.

Results

A retrospective review of patients seen at the Spinal Cord Injury Unit of the Long Beach Veterans Administration Hospital found 32 patients with bladder tumors out of 1319 patients seen and followed by urology. Of these tumors, 15 (46.9%) were SCC, 10 (31.3%) were TCC, 3 (9.4%) were adenocarcinoma, and 4 (12.5%) had mixed TCC and SCC. The tumors were identified for a mean of 34 (range 16–62) years after the initial SCI (Table 1).

Overall, 25 patients with tumors had information available regarding their bladder management. Of these, 4 patients (16%) managed their bladders with clean intermittent

Table 1 Patient demographics by tumor type

	All tumors	*SCC*	*TCC*	*Adeno*	*TCC + SCC*
Total (%)	32 (100)	15 (46.9)	10 (32.3)	3 (9.4)	4 (12.5)
Time in years from injury to diagnosis (range)	34 years (0–58)	44 (14–55)	50 (0–58)	41 (34–53)	45 (33–55)
Underwent cystectomy (%)	27 (84)	14 (93.3)	7 (70)	3 (100)	3 (100)
Died (%)	23 (71.9)	11(73.3)	7 (70)	2 (66.7)	2 (66.7)
Years after diagnosis (range)	3.8 (0–20)	5.1 (0–20)	1.7 (0–5)	5 (2–8)	3 (0–6)
Tobacco use (%)	21 (70)	7 (50)	9 (90)	3 (100)	1 (50)
Pack years (range)	58 (10–180)	44.7 (18–100)	65.6 (10–180)	77 (25–150)	10

Abbreviations: SCC, squamous cell carcinoma; TCC, transitional cell carcinoma.

Table 2 Method of bladder management

	All tumors	*SCC*	*TCC*	*Adeno*	*TCC + SCC*
Total	25	9	9	3	1
Foley (%)	14 (56)	2 (22.2)	7 (77.7)	3 (100)	2 (66.7)
Years (range)	26.7 (1–53)	31 (30–32)	21 (1–53)	30 (20–50)	37.5 (20–55)
CIC (%)	4 (16)	1 (11.1)	1 (11.1)	0 (0)	1 (33.3)
Years (range)	17.3 (3–33)	16	17	NA	33
SPT (%)	2 (8)	1 (11.1)	1 (11.1)	0 (0)	0 (0)
Years (range)	2.5 (2–3)	3	2	NA	NA
EDD (%)	14 (56)	5 (55.6)	5 (55.6)	2 (66.7)	1 (33.3)
Years (range)	32 (1–55)	42.8 (18–50)	41 (32–50)	10.5 (1–20)	33

Abbreviations: SCC, squamous cell carcinoma; TCC, transitional cell carcinoma.

catheterization for a mean of 17.3 years (range 3–33 years), 14 patients (56%) had an indwelling urethral catheter to free gravity drainage for a mean of 26.7 years (range 1–53 years), 2 patients (8%) had a suprapubic catheter for a mean of 2.5 years (range 2–3 years), and 14 patients (56%) managed their bladder with an external catheter for a mean of 32 years (range 1–55 years). Several patients used multiple forms of bladder management over the course of their disease (Table 2).

All 32 patients had information available about the stage of their tumor. A total of 6 (20.6%) had Stage 1, 3 (10.3%) had Stage II, 11 (37.9%) had Stage III, 9 (20.6%) had Stage IV, and 3 (10.3%) had CIS (Table 3).

A total of 9 of the 32 patients (28.1%) were alive as of January 2007 with 23 (71.9%) having died. Of those patients who are deceased, a cause of death could be identified for 21 of them with 9 (42.8%) having died of their bladder tumor at a mean of 2.4 years after initial diagnosis (range 0–9) (Table 1).

A total of 21 out of 30 patients (70%) who had information available used tobacco for a mean of 58 pack years (range 10–180 pack years) (Table 1).

Squamous cell carcinoma

Of the 15 patients with SCC, 14 (93.3%) eventually underwent a cystectomy and 11 of the 15 died at a mean of 5.1 years after diagnosis with 6 dying because of their disease (range 0–20 years). A total of 13 patients had staging information available with 1 patient (7.6%) with Stage II disease, 6 patients (46.1%) with Stage III disease, 3 patients (23.1%) with Stage IV disease, and 3 patients (23.1%) with CIS. Of the nine patients for whom bladder management information was available, one (11.1%) used clean intermittent catheterization for 16 years, two (22.2%) used an indwelling urethral catheter for a mean of 31 years (range 30–32 years), one (11.1%) used a suprapubic tube for 3 years, and five (55.6%) used external catheters for a mean of 42.8 years (range 18–50 years). A total of 7 out of 14 patients (50%) used tobacco for a mean of 44.7 pack years (range 18–100 pack years).

Transitional cell carcinoma

Of the 10 patients with TCC, 7 (70%) eventually underwent cystectomy and 7 out of 10 died at a mean of 1.7 years after diagnosis (range 0–5 years) with 2 dying of their disease. All 10 patients had staging information available with 5 patients (50%) having Stage I disease, 4 patients (40%) with Stage III disease, and 1 patient (10%) with Stage IV disease. A total of 9 patients had information regarding bladder management available and among them 1 (11.1%) used clean intermittent catheterization for 17 years, 7 (77.8%) had an indwelling urethral catheter for a mean of 21 years (range 1–53 years), 1 (11.1%) had a suprapubic catheter for 2 years, and 5 (55.6%) had an external catheter for a mean of 41 years (range 32–50 years). Several patients used multiple forms of bladder management over the course of their SCI. Nine patients (90%) used tobacco for a mean of 65.6 pack years (range 10–180 pack years).

Adenocarcinoma

Of the three patients with adenocarcinoma all three (100%) underwent cystectomy and two eventually died at a mean of 5 years after diagnosis (range 2–8 years) with none dying of their disease. All three patients had information regarding

Table 3 Stage of bladder tumors at diagnosis

Tumor type (total patients with known staging)	*Stage*	*Number of patients (%)*
Overall (32)	1	6 (20.6)
	2	3 (10.3)
	3	11 (37.9)
	4	9 (20.6)
	CIS	3 (10.3)
Squamous cell carcinoma (13)	1	0 (0)
	2	1 (7.6)
	3	6 (46.1)
	4	3 (23.1)
	CIS	3 (23.1)
Transitional cell carcinoma (10)	1	5 (50)
	2	0 (0)
	3	4 (40)
	4	1 (10)
	CIS	0 (0)
Adenocarcinoma (3)	1	1 (33.3)
	2	1 (33.3)
	3	0 (0)
	4	1 (33.3)
	CIS	0 (0)
Mixed transitional and squamous cell carcinoma (3)	1	0 (0)
	2	1 (33.3)
	3	1 (33.3)
	4	1 (33.3)
	CIS	0 (0)

staging and one patient (33.3%) each had Stage I, II, and IV disease. All three patients (100%) had a history of Foley catheter use for a mean of 30 years (range 20–50 years) and two patients (66.7%) also had a history of external catheter use for a mean of 10.5 years (range 1–20 years). All three patients used tobacco for a mean of 77 pack years (range 25–150 pack years).

Mixed TCC and SCC

All three (100%) of the patients with mixed tumors underwent cystectomy and two of the three died at a mean of 3 years after diagnosis (range 0–6) with one dying of their disease. Three patients had staging information with one patient each (33.3%) having Stage II, III, and disease. One patient (33.3%) had a history of clean intermittent catheterization for 33 years, two patients (66.7%) had a history of Foley catheter use for a mean of 37.5 years (range 20–55 years), and one (33.3%) used an external catheter for 33 years. Two of the patients had information available regarding tobacco use and one of the two (50%) used tobacco for 10 pack years.

Method of detection of tumors

The method of detection of the tumor was known in 19 patients. Eight patients (42.1%) had screening cystoscopies with their annual examination, which detected a tumor. Seven patients (36.8%) reported hematuria. Five of these had a cystoscopy based solely on the hematuria, and two reported hematuria at their annual screening cystoscopy. One patient (5.2%) had a positive voided cytology, which led to a cystoscopy and discovery of his tumor. Three patients (15.7%) had findings on annual radiologic workup (ultrasound or CT scan), which led to cystoscopy and two patients (10.5%) had a scrotal abscess, which led to cystoscopy. The date of the last cystoscopy was available on 15 patients, and a mean of 1.6 years (range 0.7–5.5 years) had passed since their last cystoscopy.

Discussion

Bladder tumors in the SCI patient are a well-recognized phenomenon. Most earlier studies have shown that the relative risk of a bladder neoplasm in the spinal cord injured population is 16–28 times higher than that of the general population.[1–3] Recently, this increase has come into some question with a study showing no increase in cancer rates among a spinal cord injured population.[4] The patient population in this study did not undergo formal screening and had a much lower rate of tobacco use than in other studied populations, but it does suggest that further, well-controlled studies need to be performed to determine the true incidence of bladder neoplasms in spinal cord injured populations.

SCI patients are also known to have a different spectrum of disease than the general population with a significantly higher proportion of SCC compared with TCC, a lower age at diagnosis and a higher stage.[5]

We present one of the largest series of SCI patients with bladder tumors with 32 patients examined out of a total population of 1319 patients seen. In this study, several items of interest were noted. First, the distribution of tumors seen was similar to earlier studies with SCC representing approximately 1/3 of the tumors and TCC representing almost 1/2 (Table 1). Interestingly, adenocarcinoma represented 9.4%, which is significantly above the quoted rate of 2% in the general population.[6] This increase has also been seen in earlier studies with West *et al*.[5] reporting adenocarcinoma representing 10% of their bladder tumors. One of the known risk factors for adenocarcinoma of the bladder, much like in other bladder malignancies, is chronic irritation. The increase in adenocarcinoma could potentially be due to chronic irritation from catheterization, chronic urinary tract infections, bladder stones, or perhaps an intrinsic change in the neurogenic bladder.[6]

Also seen in this study are a high number of patients with bladder tumors who did not have an indwelling catheter (Table 2). Earlier studies have identified potential risk factors for bladder tumors in the SCI population. These have included indwelling catheter for >10 years, frequent UTIs, and frequent bladder stones.[2,5–7] In patients with SCC in our study, however, 55% used an external catheter for a mean of 40+ years with only 22.2% having had an indwelling catheter. Some of these patients may have had an indwelling catheter early in their injury, which was not documented, but with 40+ years of using an external catheter, the majority of their bladder management had been with an external catheter. Earlier studies have suggested that the nature of the neurogenic bladder itself may lead to an increased risk of tumors because of the interaction of the

bladder mucosa with a high volume of urine that is often seen in the neurogenic bladder.[5] The current findings seem to support this.

The recommendations for screening in this population have also been somewhat controversial and earlier recommendations have varied widely. Current VA guidelines for SCI patients state that a cystoscopy is to be performed every 10 years for patients with indwelling urethral catheter, suprapubic tubes, or who use tobacco. They also recommend that cystoscopy be performed for indications including new onset retention, recurrent UTIs, stones, or hematuria.[8] Others have advocated screening SCI patients with an indwelling catheter after 8–10 years of use with yearly cystoscopy, cytology, and possible biopsy.[9] Recent studies by Razdan *et al*. in 2003[10] and Kitahara *et al*. in 2006[11] show that the majority of urologists are performing annual cystoscopies for patients with long-term indwelling catheters, and 75–88% perform them if the patient has an indication such as hematuria or bladder stones. There has also been some interest in the use of urine tumor markers for screening. A paper by Davies *et al*. in 2005[12] confirmed that cystoscopy is presently the best screening tool for bladder cancer in SCI population. In a prospective study looking at screening with urine cytology and urine tumor markers in an SCI population, they found three patients with bladder cancer over a 5-year period on cystoscopy, none of whom had positive cytology, BTA stat, or survivin assay.

At our institution, we attempt to perform a yearly screening cystoscopy on all patients with indwelling catheters for any length of time, especially those who have had one in place for >10 years. We also perform a cystoscopy on any patient with hematuria, recurrent urinary tract infections, or any other urologic complaints indicating need for a cystoscopy (that is, frequency, change in bladder functioning, clogging of catheter, etc). We do not routinely take random bladder biopsies, but are aggressive in biopsying any abnormal appearing areas and frequently take cytologies.

This study suggests that screening needs to be continued diligently and indefinitely in spinal cord patients as bladder tumors were identified for a mean of 34 years after their initiating injury. The length of time since the injury may itself be a risk factor for the development of bladder tumors. As the bladder is exposed chronically to relatively static urine, irritation from an indwelling catheter, bladder stone, and/or UTIs, it is going to develop changes in the cells. As these cells undergo metaplasia to cope with these irritants, it is inevitable that eventually some of them will undergo dysplasia and begin the process of tumorogenesis. As with any similar process, the longer the irritant is present, the more likely that dysplasia and tumors will develop.

Furthermore, performing an annual cystoscopy in asymptomatic patients with risk factors such as an indwelling catheter, recurrent urinary tract infections or bladder stones remain important as 6 patients out of 19 diagnosed tumors (31.5%) would have been missed if cystoscopy was performed solely for symptoms. As such, it may be prudent to perform a cystoscopy in high-risk groups at a higher frequency than that recommended by the VA guidelines.

This diligence in screening remains especially important because of the aggressive and rapidly growing nature of bladder tumors in spinal cord patients. In our study, the tumors tended to be aggressive with 58.4% of the tumors presenting in Stage III or IV and 43% of the patients with available information died of their tumor at a mean of 2.4 years after diagnosis. Furthermore, patients had a mean of only 1.6 years since their last cystoscopy indicating that, despite surveillance and early detection, these tumors are also fast growing (Table 3). Both of these findings have been noted in earlier studies.[3,11,13–16] The reason for the rapid and aggressive nature of these tumors is unknown. In other populations with bladder cancer, approximately 25% will present with muscle invasive disease,[6] whereas in this study over 1/2 had advanced disease at presentation. In other populations, bladder cancer is thought to be due to a general field defect, often because of a systemic irritant such as tobacco leading to the growth and development of cancers. The mechanism may be different in SCI patients with chronic, focal irritation of the bladder because of stones, UTIs, catheters, or urinary stasis having a function in creating more aggressive tumors.

Conclusion

Our study suggests that an indwelling catheter is not the sole source of the increased risk of bladder neoplasm that appears to exist in the spinal cord injured population. Although it is a relatively small study, it suggests that a high index of suspicion needs to be maintained with spinal cord patients with or without indwelling catheters. Furthermore, tumors can happen, and are most common, several decades after the initial injury suggesting that a vigilant attitude toward annual screening cystoscopies needs to be maintained for the life of the patient.

Conflict of interest

The authors declare no conflict of interest.

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