Disability and Health Journal 13 (2020) 100866

Contents lists available at ScienceDirect

Disability and Health Journal

journal homepage: www.disabilityandhealthjnl.com

Original Article

Patterns of inpatient care for prostate cancer in men with spina bifida

Ashley W. Johnston [a], Steven Wolf [b], Muhammad H. Alkazemi [c], Gina-Maria Pomann [b], Hadley Wood [d], John S. Wiener [a], Jonathan C. Routh, MD, MPH [a, *]

[a] Division of Urology, Duke University Medical Center, Durham, NC, USA
[b] Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC, USA
[c] School of Medicine, Duke University Medical Center, Durham, NC, USA
[d] Department of Urology, Cleveland Clinic, Cleveland, OH, USA

ARTICLE INFO

Article history:
Received 10 May 2019
Received in revised form
28 August 2019
Accepted 24 October 2019

Keywords:
Spina bifida
Prostate
Prostate cancer
Prostatectomy
Health care utilization

ABSTRACT

Background: Advances in medical care have increased the long-term survival of patients with spina bifida. Despite this growing population, limited knowledge is available on age-related illnesses in adults with spina bifida, particularly prostate cancer for which there is no published data.
Objective: Our aim was to describe inpatient care for prostate cancer in men with spina bifida in the United States.
Methods: We performed a descriptive, retrospective study utilizing the 1998 to 2014 National Inpatient Sample from the Healthcare Cost and Utilization Project. Weights were applied to the sample to make national level inferences. We identified all adult encounters (≥18 years old) with prostate cancer and spina bifida.
Results: We identified 253 encounters (mean age 64.9 years). Most were Caucasian (67.5%) and had public insurance (61.6%). 44% of encounters included a major urologic procedure. 38.4% of encounters included prostatectomies, 28.3% included lymph node dissections, and 7.8% included cystectomies. Robotic surgery was performed in 9.4%. Mean length of stay was 5.6 days (95% CI: 3.7, 7.5). The average total cost was $14,074 (95% CI: $8990.3, $19,158.6).
Conclusions: In this first-ever exploration of inpatient care for prostate cancer in men with spina bifida, we found that length of stay and total costs were higher in men with spina bifida. Almost half of encounters included a prostatectomy, cystectomy, and/or lymph node dissection. More detailed investigations are necessary to assess comparative treatment outcomes and complications, including prevalence and mortality rates of prostate cancer among adult men with SB.

Introduction

Spina bifida (SB) represents failure of fusion of the caudal neural tube and multiple variants including myelomenigocele and menigocele. It is the most common non-chromosomal, permanently disabling birth defect with a worldwide incidence of 4.5 per 1000 live births,[1] leads to a wide spectrum of cognitive and physical disabilities affecting neurologic, orthopedic, gastrointestinal, and genitourinary organ systems. SB frequently causes neurogenic bladder manifesting as voiding dysfunction, incontinence, reduced bladder compliance, and upper urinary tract deterioration.[2] The treatment of neurogenic bladder often requires clean intermittent catheterization and/or surgical intervention, including bladder augmentation, bladder neck reconstruction, urinary diversion, and/or insertion of artificial urinary sphincters.[3]

Fortunately, advancements in medical care have led to remarkedly increased long-term survival among individuals with SB.[4] At least 75% of patients with SB will survive into adulthood.[5] This has resulted in a rapidly expanding population of adults with SB, many of whom have undergone multiple abdominal surgeries.[6] Although focus is increasingly placed on optimizing transitional care from childhood to adulthood, very little data is available regarding the presentation and management of age-related illnesses in this expanding adult SB population. This includes prostate cancer (PCa), the second-leading cause of cancer-related death in

* Corresponding author. Duke University Medical Center, DUMC Box 3831, Durham, NC, 27710, USA.
E-mail addresses: Ashley.wietsma@duke.edu (A.W. Johnston), Steven.Wolf@duke.edu (S. Wolf), Muhammad.Alkazemi@duke.edu (M.H. Alkazemi), Gina-Maria.Pomann@duke.edu (G.-M. Pomann), WoodH@ccf.org (H. Wood), John.Wiener@duke.edu (J.S. Wiener), jonathan.routh@duke.edu (J.C. Routh).

https://doi.org/10.1016/j.dhjo.2019.100866
1936-6574/

American men.[7] Despite the high prevalence of PCa in the population at large, to our knowledge, there is no existing data on the diagnosis or treatment of PCa in men with SB. Previous studies on the management of PCa among men with spinal cord injuries (SCI) demonstrate a pattern of under-screening and more advanced cancers at presentation; indeed, 63% of men with SCI presented with T3/4 disease at the time of diagnosis versus 29% of men without SCI.[8] Additionally, patients with SCI undergoing surgical treatment for PCa had higher rates of postoperative complications than neurologically intact men.[9] If patterns seen in men with SCI are instructive, poor preventative care, insufficient screening, and inadequate treatment would be expected among men with SB.

Thus, there is a significant lack of knowledge on PCa diagnosis and treatment patterns in men with SB. Our objective was to perform an initial, descriptive analysis of in men with SB undergoing inpatient care in the United States for PCa. We analyzed a nationally representative administrative database to compare inpatient encounters for PCa in both adults with and without SB. We deliberately intended this to be an exploratory, hypothesis-generating analysis.

Methods

Data source

Following approval from our Institutional Review Board (No. 00088711), we performed a retrospective study utilizing the 1998 to 2014 National Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project (HCUP). The NIS approximates a 20% stratified sample of all discharges from U.S. hospitals, excluding rehabilitation and long-term acute care hospitals. National level estimates were calculated by applying weights to the sample.[10]

Cohorts

We identified all encounters of adults (age $\geq$ 18 years) with an *International Classification of Diseases, Clinical Modification, Ninth Edition* (ICD-9) diagnosis code for PCa (185) and SB (SB occulta: 756.17; SB with hydrocephalus: 741.0, 741.00, 741.01, 741.02, 741.03; SB without hydrocephalus: 741.9, 741.90, 741.91, 741.92, 741.93) from NIS during the years 1998–2014. The PCa encounters were divided into two cohorts: cohort SB - all encounters with both PCa and SB; cohort non-SB - all encounters with PCa and without SB.

Variables of interest

Cost of encounter, encounter length of stay (LOS), in-hospital death, and PCa surgical interventions were the variables of interest. Cost was estimated using cost-to-charge ratio files (CCR) from HCUP[11] by multiplying total charge of encounter by either the hospital-specific all-payer inpatient cost/charge ratio when available, or the group average all-payer inpatient cost/charge ratio otherwise. Oncologic prostate surgical interventions of interest were identified using ICD-9 codes (Prostatectomy: 60.3, 60.4, 60.5, 60.6, 60.61, 60.62, 60.69; Lymph node dissection: 40.29, 40.3, 40.50, 40.59; Cystectomy: 57.6, 57.7, 57.71, 57.79; Robotic surgery: 17.4, 17.41, 17.42, 17.43, 17.49). Surgical procedures were not mutually exclusive and any given encounter may have included more than one. With ICD-9 codes, there is not a specific code for robotic forms of surgeries; instead, we reported the presence of a robotic approach as an adjunct to any other surgery. Additionally, we reported the demographic features of SB and non-SB cohorts.

Statistical analysis

In order to take into account the complex sampling structure of the NIS and to make national level estimates, weighted descriptive statistics were used to describe both cohorts. As per the HCUP data use agreement, events occurring fewer than 15 times cannot be reported. Proc Surveyfreq was used for discrete variables and Proc Surveymeans was used for continuous variables. All analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

After applying the HCUP weighting schema, we identified 253 SB cohort encounters and 3,852,896 non-SB cohort encounters (Table 1). As expected, all encounters for both cohorts were male. The mean age of encounters in the SB cohort was 64.9 years old (95% CI: 62.2, 67.5) compared to 72 years old (95% CI: 71.8, 72.2) in the non-SB cohort. The mean age for the SB cohort decreased overtime from 69.3 years (95% CI: 65.5, 73.1) in 1998–2006 to 61.8 years (95% CI 58.3, 65.2) in 2011–2014. Conversley, in the non-SB cohort, the average age was relatively stable from 72.6 years (95% CI: 72.4, 72.8) in 1998–2006 to 71.4 years (95% CI: 71.2, 71.6) in 2011–2014. The majority of encounters in both cohorts were for white patients (67.5% SB cohort, 60.9% in the non-SB cohort) with public insurance (61.6% SB cohort, 68.2% non-SB cohort). The largest portion (28.3%) of encounters in the SB cohort were in the 4th income quartile (highest) compared to 17.6% in the non-SB cohort. To adhere to HCUP data use agreement to report only 15 + events, we grouped years as 1998–2006, 2007–2010 and 2011–2014. For the SB cohort, there was an even spread of encounters across each time interval. In contrast, over half (53.6%) of encounters for non-SB patients occurred in 1998–2006 with a decreasing number of encounters in later time intervals.

We found that 44.3% of SB cohort encounters included a urologic surgical procedure in the treatment of PCa versus 30.5% of non-SB cohort encounters (Table 2). Surgeries of interest included prostatectomies, cystectomies, and lymph node dissections. These procedures were not mutually exclusive, thus any given encounter could include one or more. The proportions of each surgery were observed to be larger in the SB cohort than those in the non-SB cohort. Prostatectomies were performed in 38.4% of SB encounters and 29.5% of non-SB encounters; this included transabdominal,

Table 1
Demographic data.

	SB Cohort (n = 253)	Non-SB Cohort (n = 3852896)
Age		
Mean (95% CI)	64.9 (62.2, 67.5)	72 (71.8, 72.2)
Median (IQR)	64 (57.7, 68.5)	71.8 (63, 80.6)
Race		
Missing	53 (21%)	722001 (18.7%)
White	171 (67.5%)	2347542 (60.9%)
Black/Other	29 (11.5%)	783353 (20.3%)
Primary payer		
Missing	0	5277 (0.2%)
Public	156 (61.6%)	2629491 (68.2%)
Private/Other	97 (38.4%)	1218226 (31.6%)
Median household income (quartile)		
Missing	58 (22.8%)	1247375 (32.4%)
1	18 (7.1%)	640855 (16.6%)
2	58 (23%)	644924 (16.7%)
3	48 (18.8%)	640194 (16.6%)
4	72 (28.3%)	679208 (17.6%)
Year of Admission		
1998–2006	91 (35.9%)	2065042 (53.6%)
2007–2010	81 (31.8%)	950306 (24.7%)
2011–2014	82 (32.3%)	837647 (21.7%)

Table 2
Surgical patterns of care for PCa encounters.

	SB Cohort (n = 253)	Non-SB Cohort (n = 3852896)
PCa Surgical Procedure	112 (44.3%)	1176179 (30.5%)
Prostatectomy	97 (38.4%)	1135648 (29.5%)
Lymph Node Dissection	72 (28.3%)	642320 (16.7%)
Cystectomy	20 (7.8%)	24645 (0.6%)
Robotic	24 (9.4%)	307270 (8%)

perineal, and minimally invasive approaches. 28.3% of SB encounters include lymph node dissections, including simple, regional, and radical, versus 16.7% of non-SB encounters. Cystectomies, which include both partial and radical, were seen in 7.8% of SB encounters versus a fraction (0.6%) of non-SB encounters. Robotic surgical approaches, a separate ICD-9 code, were performed in 9.4% of encounters for the SB cohort and 8% of non-SB encounters.

The mean cost of the SB cohort encounters was $14,074 (95% CI: $8990.3, $19,158.6) compared to $10,369 ($10,205.8, $10,532.4) in the non-SB cohort (Table 3). The median cost of the SB cohort was $8616 (IQR: $5479.8, $14,366) compared to $7809.3 (IQR: $4720.4, $12,389) in the non-SB cohort. The mean LOS for the SB cohort was 5.6 days (95% CI: 3.7, 7.5) compared to 4.6 days (4.53, 4.64) in the non-SB cohort. The median LOS for the SB cohort was 2.8 days (IQR: 1.5, 5.4) compared to 2.6 days (IQR: 1.3, 5) in the non-SB cohort. Over time, mean LOS of in the non-SB cohort was unchanged ranging from 4.2 days (95% CI: 4.1, 4.3) 2007–2010 to 4.9 (95% CI: 4.8, 4.9) in 1998–2006. Conversely, the mean LOS in the SB cohort decreased overtime from 7.2 days (95% CI: 4.5, 10) in 1998–2006 to 5.9 days (95% CI: 2.4, 9.4) in 2011–2014. In-hospital deaths occurred in 3.7% of non-SB encounters, which was similar to the rate in SB cohort patients.

Discussion

To our knowledge, this is the first report of treatment of PCa among adults with SB. In describing the treatment patterns of PCa in men with SB and in men without SB, estimated LOS and total cost were observed to be higher in men with SB cohort. Overall rates of surgical procedures for the treatment of PCa were higher for men with SB. Almost half of inpatient encounters for patients with SB included major urologic operative procedures such as prostatectomies, cystectomies, and lymph node dissections. Surgical management included both open and robotic approaches. Rates of all surgeries of interest were higher for men with SB compared to those without SB. The rate of in-hospital death was similar in encounters for men with SB vs. those without SB.

PCa is the most commonly diagnosed cancer in men. The average age at the time of diagnosis is 66 years.[7] Regarding PCa diagnosis, the utility of PSA has been a topic of debate. In 2012, the United States Preventative Task Force recommended against PSA screening to which the American Urological Association published recommendations in 2013 that PSA screening should be a shared decision-making process. These recent changes in the role of screening likely influenced our findings to an unknown degree. Given that there was a difference in patient age among the time periods sampled, however, we think that this was likely to play a large role.

Table 3
In-hospital outcomes.

	SB Cohort (n = 253)	Non-SB Cohort (n = 3852896)
Length of Stay		
Mean (SE)	5.6 (3.7, 7.5)	4.6 (4.53, 4.64)
Median (IQR)	2.8 (1.5, 5.4)	2.6 (1.3, 5)
Cost		
Mean (SE)	$14,074 ($8990.3, $19,158.6)	$10,369 ($10,205.8, $10,532.4)
Median (IQR)	$8616 ($5479.8, $14,366)	$7809.3 ($4720.4, $12,389)
In-hospital death		
Missing	[a]	3061 (0.08%)
Death	[a]	143412 (3.7%)

[a] In adherence with HCUP data use agreement, events < 15 cannot be reported.

Following diagnosis, risk stratification based on staging and pathology is performed. These guidelines by the National Comprehensive Cancer Network and American Urological Association aid in the development treatment plans. In general terms, treatment can consist of long-tern observation, hormonal management, radiation therapy, or surgery. Of these, only the latter is typically managed in the inpatient environment.

These data are similar to the existing literature on patients with PCa and neurogenic bladder not secondary to SB. Hospital stay after surgical management of PCa was significantly longer for men with SCI than men without SCI, which is comparable to our reported longer LOS for encounters of men with SB. Similar to our reported increased rates of cystectomy and prostatectomy in men with SB, Gammon et al.[9] found that the rate of cystoprostatectomy was higher than expected in men with SCI as compared to neurologically intact men. It is unclear if these higher rates of cystoprostatectomy in men with SCI are due to concomitant bladder dysfunction, bladder cancer, or more advanced prostate cancer. Similarly, in our study, the NIS database is limited in its ability to differentiate between PCa and urothelial carcinoma as the indication for cystoprostatectomy. It has been shown that patients with SCI tend to be diagnosed with more advanced stage and grade PCa.[8] Further investigations are needed to determine a the pattern of advanced disease in men with SB.

Patients with SB represent a high-risk surgical population. Loftus et al.[6] reported a complication rate of 92% when undergoing urologic surgeries even at centers of excellence. Medical comorbidities and extensive past surgical histories of multiple intra-abdominal procedures including urinary diversions and urologic reconstructive procedures likely contribute to this elevated risk, as well as impaired mobility, neurogenic bowel, and greater obesity rates. Despite these known increased operative risks of patients with SB, we found higher operative rates for the SB population compared to the non-SB population. Although our descriptive analysis did not evaluate postoperative complication rates, LOS and total cost were higher for men with SB which may reflect increased postoperative complications. However, the in-hospital death rate was similar to rates of non-SB patients. Additionally, patients were treated both with open and minimally invasive approaches. Future investigations would need to assess outcomes both from surgical and oncologic perspectives for the treatment of PCa in the SB population.

The findings of our study should be considered within the context of its design limitations. NIS represents a 20% stratified sample of US hospital admissions. While NIS is specifically designed by HCUP to produce a representative sample, it was impossible to guarantee that representativeness in any given year or combination of years. Consequently, results derived from NIS may not be generalizable to the broader community. In particular, non-participation by specific centers with high SB or PCa volumes (both surgical and non-surgical) may have reduced the accuracy of our estimates overall. We note, however, that NIS provides meticulous tracking and frequent updates of discharge and hospital weights to minimize risk of sampling bias.

Because NIS represents admission-based rather than patient-based data, it was impossible to track a given patient across time. We were unable to assess neither longer-term outcomes nor whether individual patients had multiple admissions. For the SB

cohort, there were 4 encounters that may have been repeated encounters for the same patient within a given year (all were from the same hospital with identical demographic features). While this potential duplication could have been a limitation, we performed a sensitivity analysis by excluding those patients; this analysis provided similar estimates of cost and LOS. Therefore, all 4 were included in the final analysis. Furthermore, since NIS represents inpatient care, PCa diagnosis and treatment (hormonal and radiation) occurring in outpatient settings were not captured.

Due to the relatively small sample size, covariance estimation for continuous variables (such as cost or LOS) was problematic. This led us to exclude year from the stratification procedures, which may have resulted in bias in the estimation of variance for continuous variables.

NIS may be affected by miscoding bias; i.e., our analysis depends in part on the accuracy of diagnosis and procedure coding in NIS. Though the accuracy level of NIS is high for an administrative database, it was possible at least some portion of our cohort may be incorrectly coded. We would note that the NIS database was rigorously monitored and audited for coding accuracy and, therefore, represented a reasonably reliable snapshot of the characteristics of an inpatient surgical cohort. It is important to note that these data cannot be construed to represent an analysis of causality. For example, it was impossible to differentiate between patients who were incidentally diagnosed with PCa after a cystectomy for urothelial carcinoma and those who underwent a cystectomy for PCa (rather than a prostatectomy) due to previous urinary reconstructions or outlet procedures. Additionally, granular data regarding PCa staging and pathology is not include in NIS, thus identified encounters may represent admission for oncologic management of advanced cancer. Of note, this may explain our 3.7% mortality rate for the non-SB population which is higher than previously reported post-prostatectomy mortality rates which are <1%.[12] Again, the aim of this manuscript was to *describe* patterns of care rather than to *explain* why those patterns occurred. Selection bias may be an issue in these data, as it is likely that patient selection played a significant role in whether to perform surgery for men with PCa, and, if so, what procedure to perform. Clinical experience and the extant SCI literature led us to initially suspect, for example, that we would see a larger proportion of non-surgical encounters and a larger proportion of cystectomy encounters than might be expected for men with PCa without SB. However, these data unfortunately cannot be used to prove nor to refute this suspicion. As noted throughout this manuscript, we would again stress that these analyses were explicitly designed to be exploratory and hypothesis-generating rather than definitive and hypothesis-proving.

Conclusion

This novel report of inpatient encounters of men with SB and PCa. Surgical treatment included both open and robotic approaches to prostatectomies, cystectomies, and lymph node dissections, which occurred in more than a third of the encounters. LOS, total costs, and rates of operative procedures were higher in encounters for men with SB compared to men without SB. As an initial foray into the burden of age-related illnesses in adults with SB, particularly PCa, this descriptive analysis presents a potentially important insight into the long-term issues that adults with SB contend with as they age. Further studies of these and other data sources are currently underway which hopefully will shed more light the prevalence of PCa and outcomes of treatment among adult men with SB.

Author contributions

AW Johnston - Project development, Manuscript writing.

S Wolf - Project development, Data management, Data analysis, Manuscript editing.

MH Alkazemi - Project development, Manuscript writing.

GM Pomann - Project development, Data analysis, Manuscript editing.

H Wood - Project development, Manuscript editing.

JS Wiener - Project development, Manuscript editing.

JC Routh - Project development, Data management, Manuscript editing.

Disclosure of potential conflicts of interest

The authors have no potential or real conflicts of interest relevant to this research.

Research involving human participants and/or animals

Our Institutional Review Board reviewed this research and determined it to be exempt, non-human-subjects research (No. 00088711).

Informed consent

As exempt, non-human-subjects research, informed consent was not obtained. This research was a retrospective analysis of completely deidentified dataset.

Funding

None.

References

1. Snow-Lisy DC, Yerkes EB, Cheng EY. Update on urological management of spina bifida from prenatal diagnosis to adulthood. *J Urol*. 2015;194:288–296. Available at: http://www.ncbi.nlm.nih.gov/pubmed/25839383. Accessed October 10, 2017.
2. Lloyd JC, Wiener JS, Gargollo PC, et al. Contemporary epidemiological trends in complex congenital genitourinary anomalies. *J Urol*. 2013;190:1590–1595. Available at: https://www.sciencedirect.com/science/article/pii/S0022534713040846?via%3Dihub. Accessed May 3, 2018.
3. Wang H-HS, Lloyd JC, Wiener JS, et al. Nationwide trends and variations in urological surgical interventions and renal outcome in patients with spina bifida. *J Urol*. 2016;195:1189–1195. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26926542. Accessed October 10, 2017.
4. Shin M, Kucik JE, Siffel C, et al. Improved survival among children with spina bifida in the United States. *J Pediatr*. 2012;161(e3):1132–1137. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22727874. Accessed October 4, 2017.
5. Bowman RM, McLone DG, Grant JA, et al. Spina bifida outcome: a 25-year prospective. *Pediatr Neurosurg*. 2001;34:114–120. Available at: https://www.karger.com/Article/FullText/56005. Accessed August 8, 2019.
6. Loftus CJ, Moore DC, Cohn JA, et al. Postoperative complications of patients with spina bifida undergoing urologic laparotomy: a multi-institutional analysis. *Urology*. 2017;108:233–236. Available at: https://www.sciencedirect.com/science/article/pii/S0090429517306398?via%3Dihub. Accessed May 3, 2018.
7. Siegel RL, Miller KD, Jemal A. Cancer statistics. *CA. Canc. J. Clin.* 2018;68:7–30. https://doi.org/10.3322/caac.21442. Available at: . Accessed June 14, 2018.
8. Scott PA, Perkash I, Mode D, et al. Prostate cancer diagnosed in spinal cord-injured patients is more commonly advanced stage than in able-bodied patients. *Urology*. 2004;63:509–512. Available at: https://www.sciencedirect.com/science/article/pii/S009042950301118X. Accessed May 3, 2018.
9. Gammon SR, Berni KC, Virgo KS, et al. Surgical treatment for prostate cancer in patients with prior spinal cord injury. *Ann Surg Oncol*. 2005;12:674–678. Available at: http://www.springerlink.com/index/10.1245/ASO.2005.10.010. Accessed May 3, 2018.
10. Anon: HCUP-US NIS overview. Available at: https://www.hcup-us.ahrq.gov/nisoverview.jsp; 2017. Accessed October 4, 2017.
11. Anon. HCUP-US cost-to-charge ratio files. Available at: https://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp. Accessed June 14, 2018.
12. Björklund J, Folkvaljon Y, Cole A, et al. Postoperative mortality 90 days after robot-assisted laparoscopic prostatectomy and retropubic radical prostatectomy: a nationwide population-based study. *BJU Int*. 2016;118:302–306. Available at: http://www.ncbi.nlm.nih.gov/pubmed/26762928. Accessed August 8, 2019.