Association between urinary diversion and quality of life after radical cystectomy

Michael Metcalfe, MD,[1] Eric Estey, MD,[2] Niels-Erik Jacobsen, MD,[2] Don Voaklander, PhD,[3] Adrian S. Fairey, MD[2]

[1]Department of Urological Sciences, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada
[2]Division of Urology, Department of Surgery, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[3]Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada

METCALFE M, ESTEY E, JACOBSEN N-E, VOAKLANDER D, FAIREY AS. Association between urinary diversion and quality of life after radical cystectomy. *Can J Urol* 2013;20(1):6626-6631.

Introduction: *We examined the association between type of urinary diversion and quality of life (QoL) in patients who underwent radical cystectomy for primary bladder cancer using a validated, disease-specific instrument.*

Materials and methods: *A cohort of 314 consecutive patients treated with radical cystectomy and urinary diversion for primary bladder cancer between January 2000 and December 2006 was analyzed. Participants were mailed the validated Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index (FACT-VCI) questionnaire. Univariable and multivariable linear regression analyses were used to examine the association between type of urinary diversion (ileal conduit versus orthotopic neobladder) and QoL.*

Results: *Eighty-four out of 168 (50% response rate) evaluable patients completed the FACT-VCI questionnaire. The median follow up duration was 5.6 years (range, 2.1 to 9.3 years). ANOVA showed statistically significant differences favoring orthotopic neobladder urinary diversion with more favorable QoL scores on the FACT-VCI (mean difference 5.6 points, p = .03) and radical cystectomy-specific domain (mean difference 2.9 points, p = .05). However, multivariable linear regression analyses showed no statistically significant association between the type of urinary diversion and QoL (FACT-VCI: β = 4.1 points, p = .177; radical cystectomy-specific: β = 1.5 points, p = .390).*

Conclusions: *Type of urinary diversion was not associated with QoL after radical cystectomy. Randomized controlled trials comparing types of urinary diversion using validated, disease-specific QoL instruments are needed.*

Key Words: bladder cancer, radical cystectomy, urinary diversion, quality of life, Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index

Introduction

Radical cystectomy with pelvic lymph node dissection and urinary diversion is a standard treatment for muscle-invasive bladder cancer and high risk, non-muscle-invasive disease resistant to intravesical therapy.[1] Although the primary aim of treatment is cancer control, quality of life (QoL) is an important consideration in preoperative planning. Historically, incontinent ileal conduit urinary diversion (ICUD) was the main form of urinary tract reconstruction. However, this method was shown to be associated with decreased QoL and continent orthotopic neobladder urinary diversion (ONUD) emerged as an alternative based on the assumption of superior QoL.[2-6] Continent forms of urinary tract reconstruction also have disadvantages including increased technical difficulty and operative times, the need to leave hospital with an indwelling catheter, patient education, and malabsorption disorders.[7] Moreover, the current evidence suggesting a QoL benefit for ONUD are limited by retrospective study designs and a failure to incorporate validated QOL instrument.[2,7-10] A validated disease-specific QoL instrument has recently been developed for use in radical cystectomy patients.[11] The objective of the current study was to determine

Accepted for publication October 2012

Address correspondence to Dr. Adrian S. Fairey, USC Institute of Urology, 1441 Eastlake Avenue, Suite 7416, Los Angeles, CA 90089-9178

the association between type of urinary diversion (ICUD and ONUD) and QoL after radical cystectomy for primary bladder cancer using a validated, disease-specific instrument. We hypothesized that patients who received ONUD would have superior QoL compared to patients who received ICUD.

Materials and methods

University of Alberta radical cystectomy database

The University of Alberta radical cystectomy database is an ongoing, multi-institutional computerized database containing detailed and comprehensive demographic, clinical, pathologic, and outcome data on all adult patients with a diagnosis of primary bladder cancer treated with radical cystectomy in Edmonton, Canada from April 1994 forward.[12,13] The institutions involved provide tertiary care in a multidisciplinary fashion and are teaching centers of the University of Alberta. The University of Alberta Health Research Ethics Board approved the database and the current study.

Study design

This investigation was a retrospective cohort study of consecutive database patients treated between January 2000 and December 2006. All patients identified to be alive on November 1, 2008 were mailed a study package. The package contained a cover letter stating the purpose of the study, a Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index (FACT-VCI) questionnaire, and a postage paid business reply letter. Participants were asked to complete and return the completed questionnaire to the investigators by mail. A modified Total Design Method was utilized to optimize response rates. This strategy included the initial mailing of the study package and a follow up phone call 6 weeks later to those subjects who had not yet responded. The primary analysis examined the association between type of urinary diversion and QoL.

Treatment

All patients underwent a surgical procedure that included radical cystectomy, pelvic lymph node dissection, and urinary tract diversion as previously described.[12,13] The extent of pelvic lymphadenectomy varied based on surgeon preference. The type of urinary diversion was either ICUD or ONUD (Studer Pouch).[14]

Outcomes

The primary outcome was QoL. It was assessed by the Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index (FACT-VCI) scale.[11] The FACT-VCI is a HRQoL assessment tool that includes physical, social/family, emotional, and functional well-being subscales that are relevant to all cancer patients. It also includes a subscale labeled "additional concerns" that is comprised of items relevant to patients treated with radical cystectomy and urinary diversion. These include four bowel and appetite related items, five urinary related items, two sexual impact items, two self-image items, and four items that assess the impact of urinary diversion on day-to-day life. The FACT-VCI has been found to be reliable, valid, responsive, brief, and easy to administer.[11]

Statistical analysis

Data was analyzed using SPSS version 15.0 software. Univariable and multivariable linear regression analyses were used to examine the association between type of urinary diversion and QoL. Variables included in the multivariable models were age, gender, comorbidity status, duration of follow up, and pathologic T stage. To avoid the exclusion of patients who completed the QoL questionnaire but had missing QoL data, missing values were imputed using the multiple imputation method.[15] Regression methods were used for continuous variables. Missing-at-random assumptions were made. All statistical tests were be two-sided ($p < 0.05$).

Results

Data collection

Between January 2000 and December 2006, 314 patients underwent radical cystectomy for primary bladder cancer in Edmonton, Canada. One hundred sixty-eight out of 314 patients (53%) were alive on November 1, 2008. Eighty-four out of 168 patients (50%) completed the questionnaire and returned it for analysis. The median follow up duration of these patients was 5.6 years (range, 2.1 to 9.3 years).

Baseline characteristics

Table 1 presents the baseline characteristics of patients who responded and patients who did not respond to the study invitation. There were no statistically significant differences between responders and non-responders except for the type of urinary diversion (ICUD 55% versus ONUD 35%, $p = 0.02$).

Table 2 presents the baseline characteristics and clinical outcomes of patients who responded to the study invitation stratified by type of urinary diversion. Fifty-three out of 84 patients (63%) received an ICUD and 31 out of 84 patients (37%) received an ONUD. There were no statistically significant differences between the groups except for age ($p < 0.01$) and gender ($p = 0.03$).

TABLE 1. **Baseline characteristics of patients who responded and those who did not respond to the study invitation**

Variable	All patients (n = 168)	Responders (n = 84)	Non-responders (n = 84)	p value
Mean age (years)	64	66	63	0.06
Gender				
Male (%)	137	72 (86)	65 (77)	0.16
Female (%)	31	12 (14)	19 (23)	
Comorbidity status*				
None/mild (%)	61	32 (38)	29 (35)	0.87
Moderate (%)	75	37 (44)	38 (45)	
Severe (%)	32	17 (20)	15 (18)	
Type of urinary diversion				
Ileal conduit (%)	118	65 (77)	53 (63)	0.02
Orthotopic neobladder (%)	48	17 (23)	31 (37)	
Adjuvant chemotherapy (%)	23	10 (12)	13 (15)	0.50
Length of stay (days)	15	15	15	0.99
Estimated blood loss (mL)	1099	1032	1168	0.18
Pathologic T stage				
≤ T2 (%)	118	63 (75)	55 (65)	0.18
≥ T3 (%)	50	21 (25)	29 (35)	

*comorbidity status was assessed using the Adult Comorbidity Evaluation-27 instrument

TABLE 2. **Baseline characteristics and clinical outcomes stratified by type of urinary diversion**

Variable	ICUD (n = 53)	ONUD (n = 31)	p value
Mean age (years)	68	62	< 0.01
Gender			
Male (%)	42 (79)	30 (97)	
Female (%)	11 (21)	1 (3)	0.03
Comorbidity status*			
None/mild (%)	21 (40)	11 (35)	
Moderate (%)	21 (40)	16 (52)	
Severe (%)	11 (20)	4 (13)	0.49
Adjuvant chemotherapy (%)	8 (15)	5 (16)	0.90
Length of stay (days)	15	14	0.96
Estimated blood loss (mL)	1027	1042	0.91
Pathologic T stage			
≤ T2 (%)	37 (70)	26 (84)	
≥ T3 (%)	16 (30)	5 (16)	0.15
Any complication with 90 days of surgery (%)	20 (38)	17 (54)	0.13

*comorbidity status was assessed using the Adult Comorbidity Evaluation-27 instrument
ICUD = ileal conduit urinary diversion; ONUD = orthotopic neobladder urinary diversion

TABLE 3. **Univariable analysis of urinary diversion and quality of life**

Variable	Overall (n = 84)	ICUD (n = 53)	ONUD (n = 31)	p value
FACT-VCI (44 questions, 168 points)	79	76	82	0.03
Radical cystectomy-specific (17 questions, 68 points)	28	27	29	0.05
FACT-General (27 questions, 108 points)	51	50	52	0.13
Social/family well being (6 questions, 24 points)	20	19	21	0.19
Physical well being (7 questions, 28 points)	4	4	4	0.47
Emotional well being (6 questions, 24 points)	6	7	6	0.34

ICUD = ileal conduit urinary diversion; ONUD = orthotopic neobladder urinary diversion; FACT-VCI = Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index

Association between type of urinary diversion and QoL

Table 3 presents the results of the univariable analysis examining the association between type of urinary diversion and QoL. ANOVA showed statistically significant differences between groups favoring ONUD with more favorable scores on the FACT-VCI (p = 0.03) and radical cystectomy-specific domain (p = 0.05). There were no statistical significant differences between groups for any other QoL domain.

Table 4 presents the results of the multivariable analysis examining the association between type of urinary diversion and QoL (FACT-VCI and radical cystectomy-specific domain). Multivariable analysis showed no independent association between the type of urinary diversion and QoL (FACT-VCI, p = 0.177; radical cystectomy-specific domain, p = 0.399). However, age was independently associated with the radical cystectomy-specific domain (p = 0.049).

Discussion

Quality of life is recognized as an important outcome measure in urologic oncology. In fact, many patients value quality of life as much as, if not more than, quantity of life.[16] Bladder cancer survivors who receive radical cystectomy and urinary diversion experience a number of side effects that may affect QoL including urinary and sexual dysfunction, physical and emotional dysfunction, and changes in body image.[16] Therefore, there is a clear need to accurately document QoL in this patient population.

TABLE 4. **Multivariable analysis of urinary diversion and quality of life**

	Variable		FACT-VCI	Radical cystectomy-specific		
	β value	95% CI	p value	β value	95% CI	p value
Age	-0.2	-0.5 to 0.1	0.211	-0.2	-0.4 to -0.1	0.049
Gender	2.9	-5.0 to 10.9	0.463	0.6	-4.0 to 5.2	0.790
Comorbidity	-0.5	-3.6 to 2.5	0.731	0.9	-0.9 to 2.7	0.318
Duration of follow up	0.3	-1.5 to 1.0	0.672	-0.1	-0.8 to 0.6	0.841
pTstage	-2.7	-8.6 to 3.2	0.371	1.0	-4.5 to 2.4	0.555
Type of urinary diversion	4.0	-1.9 to 10.0	0.177	1.5	-1.9 to 4.9	0.399

FACT-VCI = Functional Assessment of Cancer Therapy–Vanderbilt Cystectomy Index

In the current study, we examined the association between type of urinary diversion and QoL after radical cystectomy for primary bladder cancer using a validated, disease-specific instrument. Contrary to our hypothesis, we found that the type of urinary diversion was not independently associated with QoL. However, younger age was independently associated with increased radical cystectomy-specific QoL issues including bowel function, self-image, sexual impact of UD and managing their urinary diversion and how it impacts their day-to-day life.

The main finding of this study was that the type of urinary diversion was not independently associated with QoL after radical cystectomy. These data support and extend findings from three previous retrospective studies. Using the FACT-VCI instrument, Large et al[17] showed no difference in QoL in bladder cancer patients who received an ONUD or Indiana Pouch urinary diversion. Similarly, two additional studies found no QoL difference in bladder cancer patients who received an ONUD or ICUD using the Medical Outcomes Study 36-Item Short Form questionnaire[18] and European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30)[19] instruments. However, our data are in contrast to the results reported in another study. Using the EORTC QLQ-30, Hobisch et al[20] found superior QoL in bladder cancer patients who received an ONUD compared to patients who received an ICUD. Reasons for these discrepant findings are unknown but may be related to differences in patient characteristics, study design, and/or outcome assessment. Nonetheless, in aggregate, existing data using validated instruments have reported mixed results and do not support the assertion that one type of urinary diversion is superior to another with regard to QoL.

Another finding of the current study was that younger age was independently associated with increased radical cystectomy-specific QoL. Unfortunately, it is difficult to compare this finding with existing data since no study has examined age using a validated QoL instrument. Nonetheless, it is in contrast to prior data that found no association between age and QoL.[21,22] Clearly, our finding should be interpreted with caution and additional research examining the association between age and QoL using validated, disease-specific instruments is warranted.

Our study had strengths that merit comment. Strengths include a relatively large sample size and use of standardized, self-administered questionnaire.

Our study also had important limitations that need to be considered when interpreting the findings. First, it was a non-randomized, retrospective analysis with the potential to introduce bias from confounding factors. The choice of type of urinary diversion recommended to patients was a complex decision and may have been influenced by many factors that could also impact QoL such as comorbidity status, performance status, and extent of disease. Second, the response rate was only 50%, we did not obtain a baseline assessment of QoL, and our QoL assessment occurred at one non-standardized point in time after surgery. All of these factors introduce the possibility of bias from confounding factors. Importantly, however, we included relevant covariables (e.g., age, comorbidity status, duration of follow up) in our multivariable analysis of QoL. Third, there was a difference in the proportion of patients in the ICUD and ONUD groups who responded to the study invitation. Although we used a modified total design method to optimize our response rate, a higher proportion of patients who had ICUD provided QoL data compared to patients who had ONUD. Unfortunately, the lower response rate may be a result of not performing the questionnaire in the physician's office. Previous studies have used an office-based questionnaire with higher response rates and baseline data but lack of use of a standardized questionnaire.[10,23]

In summary, type of urinary diversion was not independently associated with QoL after radical cystectomy. However, younger age was independently associated with increased radical cystectomy-specific QoL. Randomized controlled trials comparing types of urinary diversion using validated, disease-specific QoL instruments are urgently needed. □

References

1. Stein JP, Lieskowsky G, Cote R et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol* 2001;19(3):666-675.
2. Gerharz EW, Mansson A, Mansson W et al. Quality of life after cystectomy and urinary diversion: an evidence based analysis. *J Urol* 2005;174(5):1729-1736.
3. Henningsohn L, Wijkstrom H, Dickman P et al. Distressful symptoms after radical cystectomy with urinary diversion for urinary bladder cancer: a Swedish population-based study. *Eur Urol* 2001;40(2):151-162.
4. Madersbacher S, Studer UE. Contemporary cystectomy and urinary diversion. *World J Urol* 2002;20(3):151-157.
5. Hautmann RE, Stenzl A, Studer U et al. Urinary diversion. *Urology* 2007;69(S1):17-49.
6. Gore JL, Litwin MS. Quality of care in bladder cancer: trends in urinary diversion following radical cystectomy. *World J Urol* 2009;27(1):45-50.
7. Porter MP, Penson DF. Health related quality of life after radical cystectomy and urinary diversion for bladder cancer: a systematic review and critical analysis of the literature. *J Urol* 2005; 173(4):1318-1322.

8. Lee C. Quality of life following incontinent cutaneous and orthotopic urinary diversions. *Curr Treat Options Oncol* 2009;10(3): 275-286.
9. Wright JL. Quality-of-life assessment in patients with bladder cancer. *Nat Clin Pract Urol* 2007;4(3):147-154.
10. Somani BK, Gimlin D, Fayers P et al. Quality of life and body image for bladder cancer patients undergoing radical cystectomy and urinary diversion--a prospective cohort study with a systematic review of literature. *Urology* 2009;74(5):1138-43.
11. Cookson MS, Dutta SC, Chang SS et al. Health related quality of life in patients treated with radical cystectomy and urinary diversion for urothelial carcinoma of the bladder: development and validation of a new disease specific questionnaire. *J Urol* 2003;170(5):1926-1930.
12. Fairey AS, Chetner MP, Metcalfe J et al. Association among age, comorbidity and clinical outcomes after radical cystectomy: results from the Alberta Urology Radical Cystectomy Database. *J Urol* 2008;180(1):128-134.
13. Fairey AS, Jacobsen NE, Chetner MP et al. Associations between comorbidity, and overall survival and bladder cancer specific survival after radical cystectomy: results from the Alberta Urology Institute Radical Cystectomy database. *J Urol* 2009;182(1):85-92.
14. Studer UE, Stenzl A, Mansson W et al. Bladder replacement and urinary diversion. *Eur Urol* 2000;38(6):790-800.
15. Rubin DB. Multiple imputation after 18+ years. *J Am Stat Assoc* 1996;91:473-489.
16. Botteman M, Pashos C, Hauser R et al. Quality of life aspects of bladder cancer: a review of the literature. *Qual Life Res* 2003; 12(6):675-688.
17. Large MC, Katz MH, Shikanov S et al. Orthotopic neobladder versus Indiana pouch in women: a comparison of health related quality of life outcomes. *J Urol* 2010;183(1):201-206.
18. Hara I, Miyake H, Hara S et al. Health-related quality of life after radical cystectomy for bladder cancer: a comparison of ileal conduit and orthotopic bladder replacement. *BJU Int* 2002;89(1):10-3.
19. Protogerou V, Moschou M, Antoniou N et al. Modified S-pouch neobladder vs ileal conduit and a matched control population: a quality-of-life survey. *BJU Int* 2004;94(3):350-354.
20. Hobisch A, Tosun K, Kinzl J et al. Quality of life after cystectomy and orthotopic neobladder versus ileal conduit urinary diversion. *World J Urol* 2000;18(5):338-344.
21. Saika T, Arata R, Tsushima T et al. Health-related quality of life after radical cystectomy for bladder cancer in elderly patients with an ileal conduit, ureterocutaneostomy, or orthotopic urinary reservoir: a comparative questionnaire survey. *Acta Med Okayama* 2007;61(4):199-203.
22. Sogni F, Brausi M, Bruno F et al. Morbidity and quality of life in elderly patients receiving ileal conduit or orthotopic neobladder after radical cystectomy for invasive bladder cancer. *Urology* 2008; 71(5):919-923.
23. Hardt J, Fillpas D, Hohenfellner R, Egle UT. Quality of life in patients with bladder carcinoma after cystectomy: first results of a prospective study. *Qual Life Res* 2000;9(1):1-12.