Research Article

Comparison of Quality of Life of Patients Following Cystectomy for Malignant Versus Benign Urinary Bladder Pathology

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Abstract

Introduction: We assess post-operative quality of life (QoL) for cystectomy and ileal conduit urinary diversion (C_x) patients in Northern Ireland, comparing those with malignant and benign indications for surgery.

Methods: We reviewed notes C_x patients, between 1992 and 2010. A QoL-questionnaire (EORTC QLQ-C30) was distributed to surviving patients, additionally post-procedure general-practitioner (GP) attendances for suspected and proven urinary tract infections (UTI) and related hospital admissions were logged.

Results: Eighty C_x cases were identified in the study period. 31 deceased patients were excluded from study. All patients underwent C_x for benign (C_B) (n=26) or malignant (C_M) (n=23) bladder/pelvic conditions. Mean age in these groups was 45.7 and 65.8 years respectively. Mean number of GP visits with suspected UTI was 77.8 for C_B and 31.1 for C_M (p<0.001). Mean number of hospital admissions for procedure related complications was 19 for C_B and 6for C_M (p <0.001). EORTC QLQ-C30 questionnaire; the average functional and symptom scale were both worse post-operatively for C_M, however the global health related QoL was better in these patients.

Conclusion: We hypothesise that patient expectation of outcomes differ between C_x for benign and malignant conditions contributing to significantly different QoL outcomes. Outcomes in the well-studied malignant group cannot be directly applied to those with benign indications for surgery. Those undergoing C_x for benign conditions have significantly more unplanned healthcare attendances post-operatively. Further detailed study of QoL in benign cystectomy is needed.

INTRODUCTION

Being one of the most common urological cancers, bladder cancer affects more than 380,000 new patients a year worldwide with more than150, 000 deaths [1,2].

Radical cystectomy (RC) remains the gold standard surgical treatment for MIBC [3]. However, RC is a major operation carrying significant morbidity and mortality. In 2010-2011 in Northern Ireland 83 patients underwent cystectomy for muscle invasive bladder cancer [4].

On the other hand, benign painful bladder conditions are highly prevalent in western countries, with a substantially higher female-to-male ratio of 9:1 [5]. These conditions represent a heterogeneous spectrum of disorders, which are still poorly defined.

QUALITY OF LIFE (QOL)

Urinary diversion for lower urinary tract malignancy and dysfunction is a major intervention with significant recognised complications; hence QoL becomes an important factor to consider. Health-related quality of life (HRQoL) refers to the physical, psychological, and social domains of health that are influenced by a person's experiences, beliefs, expectations, and perceptions. It is measured with questions, or items, whose answers can be converted to numerical scores [6,7].

HRQoL instruments can be either generic or disease-specific. There are several disease specific HRQoL instrument for bladder cancer but there is no HRQoL dedicated for cystectomy in patients with benign bladder conditions. In order to assess these outcomes we used an updated version of the European Organization for Research and Treatment of Cancer QoL questionnaire (EORTC-QLQC30, version 3). This version of the EORTC-QLQC30 contains 30 items that are grouped into five functional scales (physical, role, emotional, cognitive, and social), 8 symptoms scales (fatigue, nausea and vomiting, pain, dyspnoea, appetite loss, constipation, diarrhoea and financial difficulties), and 2 global HRQoL scale (health and QoL questions). The broadness of this instrument

makes it generally applicable to all cancer states and adaptable for QoL in benign conditions, but may lack the specificity to address issues that may be unique to a particular disease [8].

METHODS

A retrospective review of consecutive cystectomy and ileal conduit urinary diversion cases performed at our institution between January 1992 and 2010 was performed. Those included RC performed for patients with MIBC, *Bacillus Calmette–Guér* in refractory cancer and carcinoma-*in-situ* (CIS). In addition, cases that underwent cystectomy and conduit for benign lower urinary tract conditions were also reviewed during the same period. Data was obtained from the hospital electronic records and patients' case notes.

FOLLOW UP

RC patients were followed according to the hospital protocol including CT scan of chest, abdomen and pelvis, at 3,6,12,18,24 months and annually thereafter for 10 years. For the benign cystectomy group, follow up was individualised accordingly, with patients who demonstrate resolution of their preoperative symptoms being discharged from urology follow up.

OUTCOME MEASURES AND STATISTICAL ANALYSIS

Primary outcome measure was assessed using EORTC QLQ-C30 version-3. Following consent, surviving patients completed current and retrospective pre-operative scoring. Secondary outcomes were measured indirectly by recording all post procedure general practitioner (GP) attendances for suspected and microbiologically proven urinary tract infections (UTI) and related hospital admissions.

The EORTC QLQ-C30 manual was followed in assessing the outcome; an average raw score was obtained for the different Functional items, symptom items and global items (Table 1).

In order to standardise the raw score, linear scale was then obtained for all the items according to the following formula:

–   A high score for a functional scale represents a high / healthy level of functioning.

–   A high score for the global health status / QoL represents a high QoL.

–   A high score for a symptom scale / item represents a high level of symptomatology.

StatsDirect™ system was utilised for statistical analysis. Differences in patient characteristics were assessed with the Mann-Whitney **U** or chi-square test, as appropriate. The Friedman test was used to compare the primary and the secondary study outcomes between the two groups. Statistical significance was set at 0.05.

RESULTS

Eighty case notes were reviewed. Data for 49 patients was included with 31 deceased patients excluded from the study. No peri-operative deaths were recorded. One cohort (C_B) included those who had urinary diversion for benign bladder conditions (n=26). The other (C_M) included those who had urinary diversion for malignant bladder conditions (n=23). 12 C_B patients and 13C_M patients responded to postal questionnaires. One patient was

excluded from C_M due to a significant amount of untraceable data (Figure 1).

Median age in C_B was 42years (range 25-80) and for C_M was 67years (range 52-80). Patients' demographics and surgical indications are summarized in Table 2. The mean follow up for these groups was 6.9 and 6.7 years respectively.

EORTC QLQ-C30 questionnaire response rate was 49.1% (C_B-46.1%, C_M-52.1%). The average functional scale was worse post-operatively for C_M, with only 3 patients reporting improvements, but not at a statistically significant level. (C_B: 7 worse, 5 improved; C_M: 8 worse, 3 improved, 1 no change, p=0.541) (Figure 2). Similarly, the post-operative average symptom scale was worse for C_M (C_B: 6 improved, 6 worse; C_M: 3 improved, 9 worse, *p*=0.103) (Figure 3). On the other hand the global QoL was significantly better for C_M (C_B: 3 better, 6 worse, 3 no change; C_M: 8 better, 1 worse and 3 no change, *p*=0.022) (Figure 4).

Mean number of GP visits with suspected UTI in C_B was 77.8 (range 7-234), and in C_M was 24.2 (range 4-93), *p*<0.001. Mean number of confirmed UTI in C_B was 31.1 (range 1-110), in was 9.4 (range 0-68), *p*=0.003 (Figure 5). Mean number of hospital admissions for procedure related complications in C_B was 19 (0-39), in C_M was 6 (0-14), *p*<0.0001. The total number of procedure related complications was 9 in C_B and 8 in C_M. However, there was no difference in the number of patients requiring further surgical intervention in the two groups (Table 3).

DISCUSSION

The "gold standard" operation for MIBC, cystectomy and ileal conduit remains to be the very last resort, and in the eyes of many urologists, a drastic option for benign bladder conditions [9]. It carries an undoubtedly significant morbidity and mortality.

There are several studies looking at the effect of this operation on health related QoL in MIBC patient [10,11]. Minimal data exists on HRQoL in patients with benign indications for cystectomy, to our knowledge there have been no studies comparing the HRQoL in cystectomy patients for malignancy against those undergoing the operation for benign bladder conditions.

Those with benign bladder conditions requiring bladder removal did experience better functional and symptom outcomes in QoL assessment than the malignant group. However, our results suggest a significant difference in global HRQoL between the two cohorts, with the MIBC patients reporting better outcomes. The authors hypothesise that multiple factors contribute to these unexpected differences.

Cancer diagnosis is considered an experience of loss and is a continuous threat to the patient's life. Accordingly, MIBC patients usually need to change priorities and disengage from many commitments in order to cope with the multiple medical, social, psychological and financial implications of their conditions [12]. These observations concur with Singer et al., who demonstrated in their study that cystectomy patients, as opposed to those with superficial bladder cancer, reported more fatigue, appetite loss and decreased role functioning [13]. A 2013 study looking at the different QoL measurements in hematuria patients found that patients with MIBC tend to have a lower level of anxiety than those with alternative diagnosis' [14]. Patient expectations following a diagnosis of cancer are significantly altered. This may explain why despite poorer functional and symptom scores the MIBC group performed better in global outcomes.

Table 1: Scoring the QLQ-C30 version 3.0.

	Scale	Number of items	Item range	Version 3 Item numbers
Functional scales				
Physical functioning (revised)*	PF2	5	3	1 to 5
Role functioning (revised)**	RF2	2	3	6,7
Emotional functioning	EF	4	3	21 to 24
Cognitive functioning	CF	2	3	20,25
Social functioning	SF	2	3	26,27
Symptom scales/items				
Fatigue	FA	3	3	10,12,18
Nausea & vomiting	NV	2	3	14,15
Pain	PA	2	3	9,19
Dyspnoea	DY	1	3	8
Insomnia	SL	1	3	11
Appetite loss	AP	1	3	13
Constipation	CO	1	3	16
Diarrhoea	DI	1	3	17
Functional difficulties	FI	1	3	28

*__Item range__ is the difference between the possible maximum and the minimum response to individual items; most items take values from 1 to 4, giving range = 3.
** (revised) scales are those that have been changed since version 1.0

Table 2: Patient demographics.

	Benign	Malignant	*p* value
Mean age (yrs)	45.7	65.8	*p*<0.0001
Range	25-80	52-80	
Male	1	7	*p*<0.0001
Female	11	5	*p*<0.0001
Benign pelvic conditions			
CPPS	6		
Urge Incontinence	1		
Bladder injury	1		
Radiation cystitis	1		
Recurrent UTIs	2		
Neurogenic bladder	1		
Cancer conditions			
TCC G3pT1 (primary treatment)		3	
TCC G3pT2		3	
TCC G3pT3		2	
urethral TCC		1	
multifocal TCC		1	
SCC		1	
G3 pT1 with BCG failure		1	
Mean (Range) Follow Up (yrs)	6.9 (2-17)	6.7 (1-17)	
Mean (Range) no. of GP visits	77.8 (7-234)	24.2 (4-93)	*p*<0.0001
Mean (Range) no. of UTIs	31.1 (1-110)	9.4 (0-68)	*p*=0.003
QLQ-C30 questionnaire response	46.1%	52.1%	

Conversely patients undergoing cystectomy and diversion for benign indications will have failed to respond to bladder conserving measures, and will often suffer from chronic intractable symptoms. Given this, the improvements in symptom scores are not surprising. Of concern from respondents is the significant deterioration in global health following cystectomy. Again this may reflect patient expectations of outcomes and inadequate pre-operative counselling. With the advancement of surgery and the adoption of laparoscopic cystectomy, reports about improving the patients' QoL are being reported, albeit on small cohorts [15]. Another important cohort of benign cystectomy procedures, which includes those with intractable radiation induced fistulae with incontinence in our series is lacking. The assumption is that those patients would have a significant improvement of their QoL, as published by Al Hussein et al. [16]. Another factor that includes refinement of the technique of the operation is to use

Table 3: Complications rates.

Complication	Malignant	Intervention	Benign	Intervention
Incisional hernia	3	2	2	2
Anastomotic stricture	2	1	2	
Stomal problems	2	1	4	2
Prolonged ileus	1		0	
Bleeding	1		0	
Severe sepsis	0		1	
Total	9	4	8	4
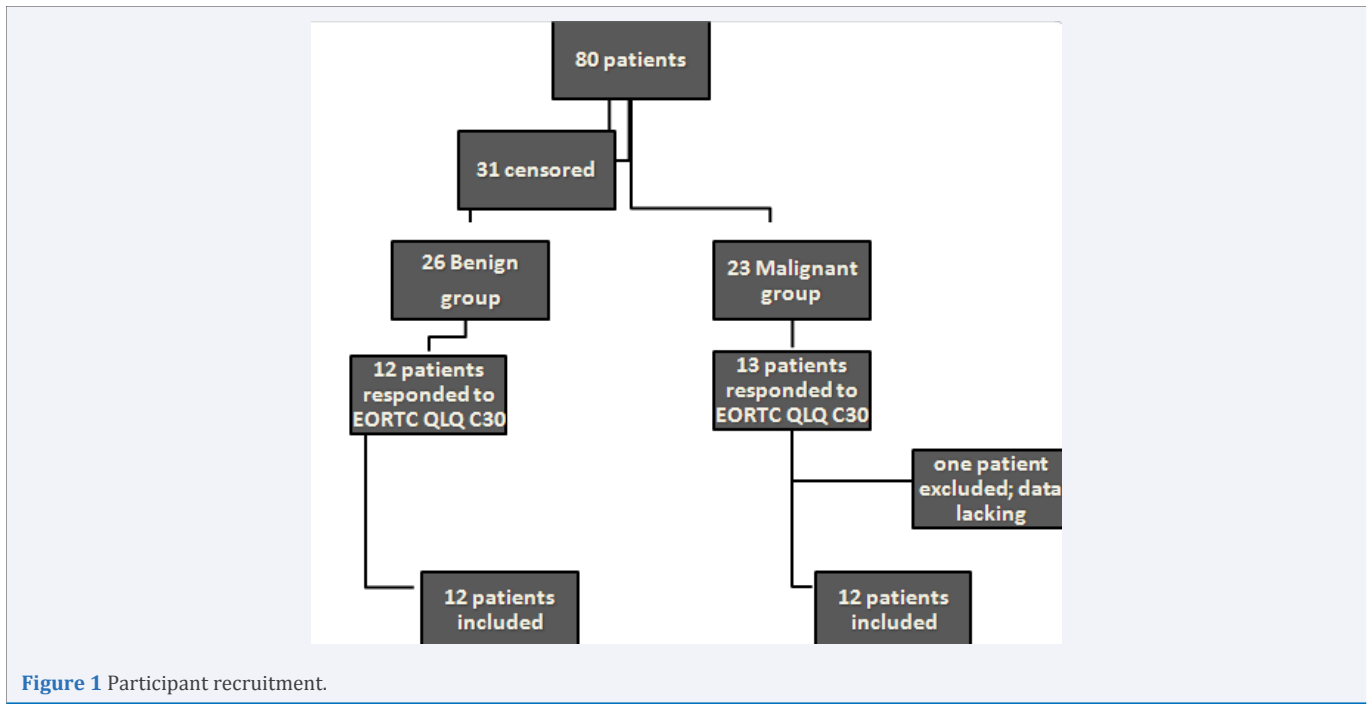
Figure 1 Participant recruitment.
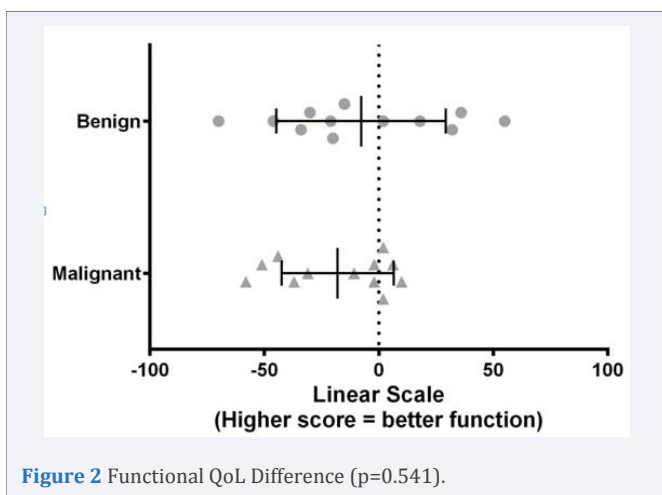
Figure 2 Functional QoL Difference (p=0.541).

a single stoma cutaneous ureterostomy, as opposed to using an ileal conduit urine diversion. This approach obviates the need for the extensive bowel anastomosis and should minimise the risk of peri-operative leak and the resultant complications. Longo N and colleagues have shown a significant peri-operative outcome with that undergoing single stoma ureterostomy diversion, but they failed to translate this into the actual patients' QoL [17].

Significant difference in both suspected and confirmed UTI was seen between the groups, one possible explanation would be pre-existing colonisation of the urinary tract in those with chronic bladder conditions, with inadequate treatment. Additionally due to associated medical issues this group may have more frequent interactions with healthcare professionals, with a resultant inevitable urinalysis. The incidence of positive urine culture in ileal conduit urine diversion patient could be as high as 75%, but
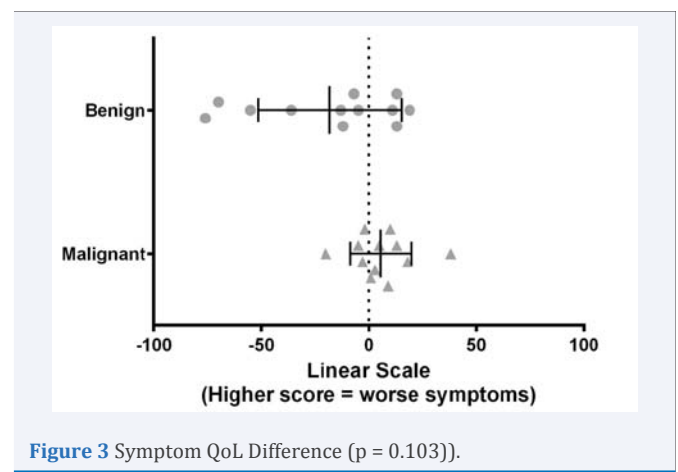
Figure 3 Symptom QoL Difference (p = 0.103)).

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Figure 4 Global QoL Difference (p=0.0223).

Figure 5 Mean General Practitioner Consultations for UTI.

it is often difficult to identify those with significant positive urine culture requiring treatment, especially in the absence of objective clinical signs of infection.

This study is limited by a number of factors. A significant difference between the ages of the two population groups was observed, with patients having malignant bladder conditions being older. This may act as a confounder for the functional and sympt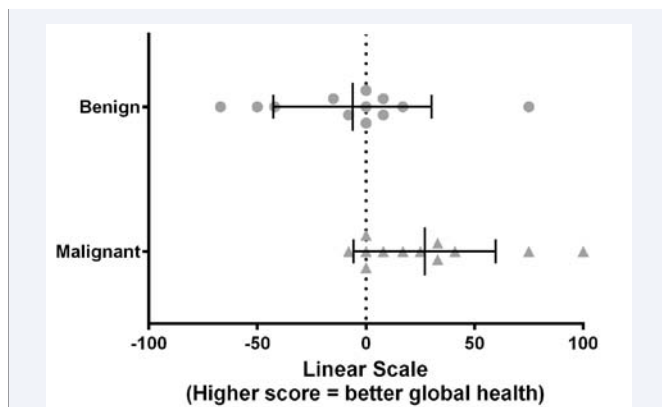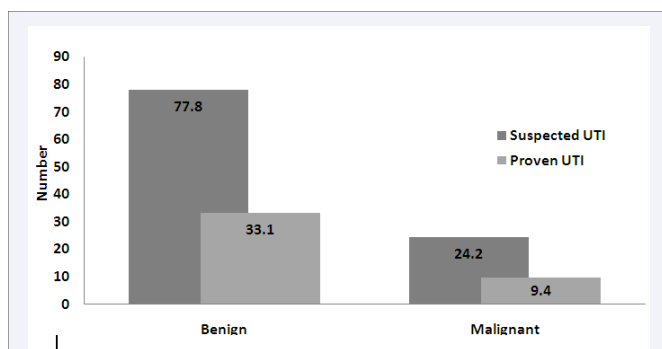om scales of the questionnaire. The retrospective nature of QoL assessment may be impacted by patient recollection or external factors. Additionally the small number of respondents limits statistical analysis.

We do however highlight that quality of life outcome in cystectomy for malignant conditions, which is well studied, does not directly translate to outcome in benign cystectomy. Further detailed study of these patient groups may be necessary to ensure satisfactory outcomes can be achieved in this group. Additionally even following cystectomy patients have frequent healthcare encounters and treatments. What is clear is that cystectomy for any indication is a significant life event and requires detailed preoperative counselling and informed consent to give a better understanding of outcomes and subsequently better life quality to patients.

CONCLUSION

Cystectomy patients have different expectations of cystectomy outcomes between those performed for benign versus malignant conditions, leading to significantly different QoL outcomes. Outcomes in the well-studied malignant group cannot be directly applied to those with benign indications for surgery. Further studies of QoL in benign cystectomy are needed.

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APPENDIX:

EORTC QLQ-C30 (version3)_____

	Not at All	A Little	Quite a Bit	Very Much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

During the past week:

	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you:

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor				Excellent		

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor				Excellent		

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