

Original Research Article

A study to assess the quality of life among patients with high grade non-muscle invasive carcinoma urinary bladder receiving immunotherapy

Manish Kumar*, Gurpreet Singh Bhangu, Darpan Bansal

Department of Surgery, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India

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*Correspondence:

Dr. Manish Kumar,

E-mail: mk66979@gmail.com

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ABSTRACT

Background: Urinary bladder lesions are a great health concern as it lies among the top ten most common cancers in the world. These range from benign, harmless lesions that do not recur to life-threatening tumors. The present study was undertaken to assess the quality of life among patients with high-grade non-muscle invasive carcinoma of the urinary bladder receiving immunotherapy.

Methods: A hospital-based experimental study was conducted in the Department of General Surgery of Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar from April 2021 to July 2022. To examine the Quality of Life of 60 patients before and after immunotherapy, the WHOQOL-BREF tool was employed. The participants were followed for a total of six months, with two follow-ups carried out at intervals of three months each.

Results: The pre-test physical scores (20.70 ± 8.66) were substantially lower than the other domains. At three and six months, the psychological scores were 21.93 ± 8.51 and 49.37 ± 12.27 respectively, while social scores were 23.93 ± 12.16 and 49.15 ± 24.09 correspondingly. Environment scores ($p=0.45$) showed no significant difference between groups after BCG treatment.

Conclusions: It was vivid that the negative effects of NMIBC on QOL are most pronounced in the physical realm. Quality of life for those with high-grade NMIBC who had BCG treatment improved significantly across all dimensions except the environment. The quality of life of high-grade NMIBC patients was not affected by any of the socio-demographic characteristics except for education and occupational status.

Keywords: Quality of life, High-grade NMIBC patients, BCG, Immunotherapy

INTRODUCTION

Urinary bladder cancer accounts for 3.0% of all newly diagnosed cancer and 2.1% of all cancer deaths. It is the sixth most common cancer in men and the seventeenth most common cancer in women. Bladder cancer is ranked 10th in incidence in the world. In India, it is ranked 17th in incidence and 19th in mortality, with a varying incidence across the Indian population.¹

The prevalence and mortality of bladder cancer increase dramatically with age, and about two-thirds of cases occur in individuals 65 years of age and older. Many factors contribute to bladder cancer development and malignancy; however, a significant proportion of cases are due to exposure to toxic fumes in the environment or occupational chemicals. In particular, the greatest risk factor for bladder cancer is smoking tobacco, which accounts for approximately 50-65% of new cases each year and 40% of all bladder cancer deaths. Other etiologies have been shown to contribute to the development of

bladder cancer. These include genetic factors, hereditary predisposition, diet, and urinary tract disease.² The most common presenting sign of bladder cancer is painless hematuria. Patients with carcinoma urinary bladder can also present with irritative voiding symptoms like urinary frequency, urgency, nocturia, dysuria, and less commonly with obstructive symptoms such as diminished or irregular urine flow. Patients who present in the advanced stage may experience symptoms related to metastatic involvement. The most common form of bladder cancer is urothelial (transitional cell) carcinoma, accounting for around 90% of cases. These range from benign, harmless lesions that do not recur to fatal, dangerous tumors. Squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and mixed histology tumors are non-urothelial bladder cancers.³ Upon presentation, Bladder cancer is divided into two major categories based on the level of invasion of the muscularis propria in the bladder wall: non-muscle-invasive bladder cancer (NMIBC) (stage Ta/CIS –T1) and muscle-invasive bladder cancer (MIBC) (stage T2-T4a). Non-muscle-invasive bladder cancer (NMIBC) is primarily represented by stages Ta, which is confined to the mucosa, and stage T1, a superficially invasive tumour that has invaded the lamina propria layer of the bladder wall. All subsequent stages represent muscle-invasive disease which is much more aggressive and lethal. NMIBC is subdivided into three grades according to the World Health Organization (WHO) 2004/2016 grading classification: papillary urothelial neoplasm of low malignant potential (PUNLMP), low-grade, and high-grade.⁴ The current gold-standard treatment for patients with intermediate (multifocal low-grade Ta) to high grade (T1, CIS, or high-grade tumour) NMIBC is TURBT, followed by Intravesical BCG immunotherapy, which is the direct instillation of BCG into the bladder. The current course of treatment consists of an initial induction phase of six weekly treatments, followed by a one-year maintenance phase of at least three BCG maintenance courses of weekly instillations for three weeks at 3, 6, and 12 months after the start of induction BCG. High-risk patients commonly require a three-year maintenance phase. Several studies have shown that adjuvant BCG has been more effective in reducing tumour recurrence in patients, compared to TURBT alone, by 56%.⁵

Need of the study

Many of these treatments do not differ much in outcome improvement but rather differ in the impact on the patients' well-being. This increased variety in treatment options and the emphasis on mental well-being in the WHO definition of health has made patient well-being an important factor in the decision-making process. Patient well-being has long been considered subjective and difficult to measure objectively. Over the decades, different terminology has been proposed to encompass this concept from 'happiness' to 'health'. Nowadays, quality of life is the most commonly used term. In recent years, quality-of-life instruments have been acknowledged as very important in the evaluation of

health care.⁶

Quality of Life refers to the objective measurement of an individual's perception of their health status concerning the four different domains, namely physical, psychological, social relationships, and environment, as measured by the WHOQOL BREF questionnaire. Usually, a differentiation is made between the general quality of life and health-related quality of life (HR-QoL), where the general quality of life encompasses a broader sense of the concept and health-related quality of life relates only to the quality-of-life aspects, which are affected either by illness or the treatment thereof.⁷ Assessing and objectively measuring health-related quality of life in patients is important to develop a better understanding of the impact of the disease. For instance, a comparison among bladder cancer patients would provide insight into the health-related quality of life of an individual patient compared with an average health-related quality of life in similar patients. Recently, the scientific and medical communities have become more aware of the potential impact of health-related quality of life on health outcomes and/or the effectiveness of treatments.

Research has shown that lower health-related quality of life is associated with higher mortality in the general adult population, in those with chronic diseases such as chronic liver disease, cancer in general, and bladder cancer specifically.⁸ It is, therefore, all the more important that clinicians are aware of patient health-related quality of life to select the most effective treatment that has the least negative impact on patient quality of life. Measuring the health-related quality of life would allow for specific (targeted) additional support. The reason for this study is to find out the quality of life of individuals living with urinary bladder cancer. We are keen on finding out how the treatment for bladder cancer affects an individual's quality of life. We intend to utilize the findings from this study to help doctors to provide better care and information for patients with urinary bladder cancer.

METHODS

Study design

This investigation was conducted on a single-centered basis and one group pretest-posttest experimental research design has opted to assess the quality of life among patients with high-grade non-muscle invasive carcinoma urinary bladder receiving immunotherapy.

$$O1 - - - X1 - - - O2 - - - X2 - - - O3$$

Where; O₁=Assessment of quality of life after NMIBC diagnosis but before BCG treatment. X₁=BCG therapy. O₂=Assessment of quality of life after 3 months. X₂=BCG therapy and O₃=Assessment of quality of life after 6 months.

Study setting, duration and sample

The current investigation was undertaken at the Department of General Surgery, Sri Guru Ram Das institute of medical sciences & research, Amritsar. In the outpatient department, subjects were recruited for the research. The research period began in April 2021 and all individuals diagnosed with high-grade NMIBC throughout the research period were included in the sample. A formal informed consent form must be signed by all subjects who meet all inclusion requirements after receiving clearance from the institution's ethical committee.

Sample size and sampling technique

Throughout this investigation, a total of sixty patients were chosen. Under the non-probability sampling method, a consecutive sampling technique was adopted to pick up all the available subjects who were meeting the preset inclusion and exclusion criteria.

Inclusion and exclusion criteria

Patients with high-grade non-muscle invasive bladder cancer were included. Patient who was diagnosed with muscle invasive carcinoma and Patients who were not mentally sound were excluded.

Follow-up

The participants were followed for a total of six months, with two follow-ups carried out at intervals of three months each.

Data management and statistical analysis

When it came to determining whether the aims of the study had been met, the researcher used descriptive and inferential statistics. The researcher chooses to use the term "frequency, percentage distribution, mean \pm standard deviation, and median (range)" where appropriate when describing variables. Using the SPSS statistical program version 23, the information was examined. Parametric data is examined using a t test and ANOVA analysis of variance. The null hypothesis will be rejected if the p value obtained from the analysis of variance is less than 0.05. The participants of the study were informed of the goal of the investigation and given a verbal agreement to participate in the research study, which was recorded. The participants were given the assurance that any information they provided would be kept secret and utilized only for study.

RESULTS

The primary focus of this chapter is to determine how well patients with high-grade NMIBC who are being treated with BCG immunotherapy fare in terms of quality of life. Study participants who met the eligibility criteria were identified and subsequently enrolled. 60 patients were

chosen utilizing a consecutive selection technique. The research began in April 2021 and continued through July 2022. WHOQOL-BREF scale was used to quantify the quality of life of the patients before a diagnosis of NMIBC and after immunotherapy was given. The use of descriptive and inferential statistics was undertaken to bring some structure to the vast quantity of data that had been collected.

The mean score of the physical domain was 20.70 ± 8.66 which was substantially lower than the scores for the other domains (Table 2). The mean score for the psychological, social, and environment domains was 21.93 ± 8.51 , 23.93 ± 12.16 , and 26.22 ± 7.46 respectively. Thus, it can be claimed that QOL in terms of the physical domain is impacted more than other domains. This occurred as a direct result of the considerable effect that high-grade NMIBC had in terms of pain and suffering. Furthermore, (Table 3) depict that the mean score for physical, psychological, and social domains improved considerably following immunotherapy. To initiate with the comparison of mean QOL domain score for a physical domain where the mean score before immunotherapy, at 3-months and the 6-month interval was 22.70 ± 8.66 , 45.73 ± 7.97 , and 78.8 ± 7.45 respectively. Furthermore, the psychological domain's mean score before immunotherapy, at 3 months and the 6-month interval was 21.93 ± 8.51 , 35.83 ± 11.53 , and 49.37 ± 12.27 correspondingly. Moreover, the mean social domain score before immunotherapy, at 3-month and 6-month intervals was 23.93 ± 12.16 , 24.75 ± 11.32 , and 49.15 ± 24.09 respectively. This substantial difference witnessed in the physical, psychological, and social domains was discovered statistically significant at the $p < 0.001$ level.

Now shifting the focus onto mean environment domain scores, with a p-value of 0.45, which shows that there was no significant difference between groups after BCG treatment was administered at intervals of three and six months. To conclude, it can be asserted that the use of BCG as a therapy regimen for high-grade NMIBC resulted in a considerable improvement in quality of life in terms of physical, psychological, and social domains. Thus, research hypothesis H_1 was accepted. Furthermore, the mean difference between all the domains concerning selected socio-demographic variables was statistically non-significant at $p < 0.05$ level. However, a contrary pattern was seen when it comes to the association of educational qualification with a physical domain. Patients who had completed their primary level of education reported having a greater quality of life after BCG treatment (84.27 ± 4.92), followed by patients who had completed their graduate level of education (80 ± 6.86). Non-literate, secondary education, and post-graduate or above patients had a quality of life that was 77.76 ± 6.69 , 75.54 ± 8.47 , and 69 ± 0 correspondingly when evaluating the physical domain. This difference in the mean was statistically significant at a $p < 0.05$ level. Therefore, the second hypothesis (H_2) of the investigation was also accepted.

Table 1: Frequency and percentage distribution of NMIBC patients according to socio-demographic variables (n=60).

Socio-demographic variables	NMIBC Patients	
	N	%
Age (years)		
20-40	07	11.67
41-60	20	33.33
61-80	30	50
81 or above	03	05
Gender		
Male	42	70
Female	18	30
Religion		
Hindu	13	21.67
Sikh	47	78.33
Christian	--	--
Muslim	--	--
Others	--	--
Habitat		
Rural	48	80
Urban	12	20
Marital status		
Single	01	1.67
Married	59	98.33
Educational Qualification		
Non-literate	25	41.67
Primary Education	15	25
Secondary Education	13	21.67
Graduate	05	8.33
Post Graduate or above	02	3.33
Occupational status		
Homemaker	19	31.67
Private Job	05	8.33
Government Job	00	00
Self-employed	36	60
Total monthly family income (Rupees)		
Below 10,000	01	1.67
10,001-20,000	28	46.67
20,001-30,000	20	33.33
30,001 or above	11	18.33
Dietary habit		
Vegetarian	32	53.33
Non- vegetarian	28	46.67
BMI (Weight (kg)/ Height (m)²)		
Underweight (below 18.5)	02	3.33
Healthy Weight (18.5-24.9)	39	65
Overweight (25-29.9)	11	18.33
Obese (30 or above)	08	13.34
Smoking		
Never Smoke	49	81.67
Former Smoker	02	3.33
Current Smoker	09	15
Ca Stage		
CIS	09	15
Ta	08	13.33
T1	43	71.67

Continued.

Socio-demographic variables	NMIBC Patients	
	N	%
Tumour size		
Below 2 cm	20	33.33
2-4 cm	34	56.67
Above 4 cm	06	10
No. of Tumour		
Single	52	86.67
Multiple	08	13.33

Table 2: Descriptive Summary for pre-immunotherapy QOL domains (n=60).

QOL Domains	Mean±SD
Physical	20.70±8.66
Psychological	21.93±8.51
Social	23.93±12.16
Environment	26.22±7.46

Table 3: Comparison of pre-test and post-test mean scores of QOL domains (n=60).

QOL Domains	Before immunotherapy, Mean±SD	At 3 months interval, Mean±SD	At 6 months interval, Mean±SD	P value
Physical	20.70±8.66	45.73±7.97	78.8±7.45	F=788.27, df = 2, 177, p<0.001
Psychological	21.93±8.51	35.83±11.53	49.37±12.27	F=95.18, df=2,177, p<0.001
Social	23.93±12.16	24.75±11.32	49.15±24.09	F=43.15, df=2,177, p<0.001
Environment	26.22±7.46	27.93±6.92	26.93±8.01	F=0.79, df = 2,177, p=0.45

A similar trend was observed in occupational status with a social domain where homemakers had higher quality of life (79.11±8.40) than self-employed (79±7.76).

Quality of life in the social domain was 76.20±6.57 among patients with private-sector employment. This difference in the mean was statistically significant at a p<0.05 level. As a result of this, the second hypothesis (H₂) tested in the study was validated as well. Therefore, except for educational qualification and occupational status, it is possible to conclude that none of the socio-demographic variables had any significant influence whatsoever on the high-grade NMIBC patients' QOL.

DISCUSSION

Analysis of the first objective shows that the mean score of the physical domain was 20.70±8.66 which was substantially lower than the scores for the other domains.

Thus, it can be claimed that QOL in terms of the physical domain is impacted more than other domains. This occurred as a direct result of the considerable effect that high-grade NMIBC had in terms of pain and suffering. In a similar vein, Fung et al demonstrated that there was a substantial post-diagnosis drop in QOL in both the physical and psychological domains.⁹ Analysis of second

objective shows that BCG treatment did not have any effect on the environment domain of QOL. In addition to this, the mean score of a physical domain at three months was 45.73±7.97, and at six months was 78.8±7.45. A p value of less than 0.001 indicated that the two groups were statistically distinct. As a result, it was deduced that the quality of life of patients, measured in terms of the physical domain, dramatically improves throughout BCG therapy. Findings from this study corroborate those from previous studies by Bohle, which show that patients' quality of life significantly improved following BCG treatment.¹⁰ Analysis of third objective depicts that the mean score for physical, psychological, and social domains improved considerably following immunotherapy. Comparable declines in quality of life were seen by Siracusano following repeated BCG treatment sessions, with the declines being more pronounced in the areas of physical, emotional, and social functioning, as well as in pain, exhaustion, and sleeplessness.¹¹ Analysis of the fourth objective depicts that the mean difference between almost all the domains concerning selected socio-demographic variables was statistically non-significant at p<0.05 level. On the other side, there is a discrepancy between these results and what is reported in the relevant literature. According to Vaioulis, there is a considerable connection between age and smoking, both of which are associated with both physical and psychological domains of QoL.¹²

In a similar vein, Yu et al observed an improvement in the physical component in young, healthy, single males who had been diagnosed with an NMIBC and who did not smoke.¹³ In addition, gender, age, the stage of the tumor, and the presence or absence of comorbidities were all factors that influenced the preoperative psychological domain of QOL. Research conducted by Chung provides a piece of evidence that modifiable activities, such as exercise, nutrition, and smoking status, have a substantial impact on postoperative quality of life.¹⁴

Limitations

There are several caveats to this research. To begin, since there were only 60 participants in the sample, it is difficult to draw broad generalizations from the data. Ethical constraints also limited the sample collection to a single research setting. Lastly, there was no alternative treatment option included in the study to serve as a point of comparison with the BCG therapy.

CONCLUSION

To reiterate, it is vivid that the negative effects of NMIBC on QOL are most pronounced in the physical realm. As a result of this investigation, it was concluded that patients' physical quality of life drastically increases as BCG treatment progresses. In contrast, the quality-of-life dimension related to one's immediate surroundings was unaffected by BCG therapy. It is also conceivable to argue that having BCG treatment over a period of time improves not just one's mental health but also one's social and physical well-being. To sum up, it can be said that the quality of life for those with high-grade NMIBC who had BCG treatment improved significantly across all dimensions except environment. Finally, it can be concluded that the quality of life of high-grade NMIBC patients was not affected by any of the socio-demographic characteristics except for education and occupational status.

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