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Quality of Life Assessment across the Cancer Continuum: Understanding the Role of an Exercise Rehabilitation Programme

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***Abstract*—**The Quality of Life (QoL) paradigm is multidimensional, dynamic and modular and its definition differs across the cancer continuum. The challenge in the interpretation of QoL data in clinical research is that QoL is influenced by psychological phenomena such as adaptation to illness. This research aims to obtain a valid and sensitive assessment of QoL change over the continuum disease, and to evaluate a rehabilitation programme aimed at inverting the observed decrease in QoL when patients return to daily living activities. The sample comprised 66 men. Patients were first assessed to establish a baseline (P1-diagnosis). This was followed by a post-test (P2-discharge) and a then-test measurement (P3-retrospective evaluation) and after returning home patients were randomized in experimental and control groups. The experimental group attended a rehabilitation programme over 24 weeks (P4). Results show that from baseline to post-test, QoL decreased significantly. The recalibration then-test confirmed a low QoL in all periods evaluated. Significant differences between the experimental and control groups prove the positive effect of the Exercise Rehabilitation Programme (ERP) on QoL. Understanding the real dynamic of QoL over time would help to adapt rehabilitation programmes by improving sensitivity and efficacy and provide professionals with a more accurate perception of the impact of treatment and side effects on patients' QoL. Our results underline the importance of changing the approach adopted by health professionals towards one of watchful waiting on patients' QoL until their complete recovery in daily life.

***Keywords*—**Prostate cancer, quality of life, rehabilitation programme, response shift.

I. Introduction

THE concept of QoL is multidimensional, dynamic and modular in its paradigm and influenced by psychological mechanisms, affecting the individual's capacity to adjust to the disease [1], [2]. QoL measures are valuable for clinical studies for several reasons: a) for quantifying the impact of a condition and comparing the effects of the disease with the consequences of other morbidity problems; b) for evaluating changes resulting from therapeutic intervention or the course of the disease; c) as a central component of cost effectiveness analysis [3].

This research aims to obtain a valid and sensitive assessment of QoL change over the continuum disease which would bring beneficial effects to patients by providing professionals with a more accurate perception of the impact of treatment and side effects on patients' QoL [4].

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A cancer diagnosis has a major impact on an individual's QoL. Most research on QoL and cancer has focused on cancer patients in the early stages of the disease. Nowadays, survival rates for cancer have increased dramatically, for example, up to 85% in prostate cancer survival five years from diagnosis. Long-term survivors experience the burden of continuing symptoms due to persistent long-term effects, late effects of cancer and treatment or new symptoms from cancer recurrence or a second tumour. Moreover, research shows that long-term survivors have a poorer QoL [5].

Traditionally, research has shown that QoL plummets after treatment, measuring QoL by comparing a baseline point with post-treatment measures [6], [7]. However, Korfage [8] has argued that QoL evaluation has disregarded its dynamic and progressive character, that is, measurements have been taken place in concrete scores and not always at a relevant stage of the disease for the patient. Serdà [9] has shown how questioning relevant disease stages for patients can give us a more realistic, dynamic and progressive view of the QoL concept. Using the Then-test method, these authors show that patients have a poor QoL in all periods evaluated and identify an overvalued self-reported QoL during the treatment period. Patients are only able to perceive the real impact of symptoms and side effects on their QoL when they attempt to resume daily living activities. At this point, patients describe their QoL as going from bad to worse.

In summary, timing the measurement of QoL on the continuum of the disease is extremely important for long-term survivors, in order to identify the threshold for increasing the efficacy of rehabilitation programmes to improve their QoL.

The aims of this article are therefore to describe the QoL dynamic during the continuum of the disease and identify the said threshold for increasing the efficacy of rehabilitation programmes to improve QoL in long-term survivors, thereby reversing the naturally declining QoL curve.

II. Methods

A. Sample Selection

The study presented in this article was part of a larger randomized controlled clinical trial testing the efficacy of a complementary therapy programme to improve the QoL of prostate cancer patients [10]. Participants were selected by means of their medical record number using SPSS software (v.15). The sample size was calculated to detect at least a 5-point difference (standard deviation [SD] =9) between groups

in the FACT-P results [11]. Accepting an alpha risk of 0.05 and beta risk of less than 0.05 in a two-tailed test of paired averages, a total of 106 subjects were studied. A 20% loss to follow-up was estimated.

The sample for the present article comprised 66 patients recruited in Figueres Hospital and the Girona region (Catalonia, Spain) from October 2008 to October 2010. The study protocol was approved by the hospital's research ethics committee.

The participants included in this study had received a histological diagnosis of prostate cancer from a medical specialist following guidelines approved by the European Society for Medical Oncology (ESMO); information was available on the disease stage and treatment phase. All participants provided signed informed consent.

Participants were excluded if they had experienced side-effects prior to the diagnosis, if they did not return home after treatment, if they had contraindications to physical exercise, and if they presented cognitive deficit or a diagnosed psychotic disorder or did not understand and speak Spanish.

B. Study Design

QoL scores were collected during four periods in this experimental randomized trial:

P1. Baseline. Patients completed socio-demographic, QoL, and fatigue questionnaires during the diagnosis and treatment phase.

P2. Post-test. After discharge (2-3 weeks), when the patient was living independently at home, all P1 questionnaires except the socio-demographic questions were repeated.

P3. Then-test. The then-test method is a retrospective analysis of the pre-test design to minimize potential changes in the internal standard by which participants assign value to the questions; Kvam [12] recommends the Then-test be done two weeks after completing P2. Participants completed a retrospective evaluation of P1. The questionnaires completed in P2 were re-administered, but this time, questions referred to the time of diagnosis and treatment [13]. The difference between the baseline average and then-test scores provides an estimate of the direction and magnitude of response shift.

P4. Experimental condition. Three weeks after returning home, patients were randomized in experimental and control groups. The experimental group attended an ERP over 24 weeks. QoL was measured in both groups one week after the end of the experimental condition.

C. Measurements

QoL was evaluated using the Functional Assessment Cancer Therapy-Prostate (FACT-P) scale, v.4 (Range: 0-156). This questionnaire included five interrelated dimensions: general state of health, family and social environment, emotional state, personal functions, and additional concerns. A higher score indicates better QoL. The questionnaire has good psychometric reliability and validity in all of its dimensions and was given to participants for self-completion.

D. Statistical Analysis

Clinical and epidemiological characteristic of the subjects are summarized as mean standard deviations (SD) and range [minimum, maximum] for continuous variables and number (%) for categorical variables. The Wilcoxon test was used to detect differences in measurements across multiple test attempts (P1-P2, P1-P3, P2-P3). The Mann-Whitney U test was used to evaluate the differences between experimental and control groups in relation to P2 that is the P4-P2 score was created and assessed. The analysis was done using SPSS version 15. The significance level was set at 0.05.

III. Results

The average age of study participants was 71.78 years, with 90.90% married and 93.93% retired. Average body mass index was 28.67 kg/m^2 and 93.93% of patients were in Stage II or Stage III of the disease (Table I).

TABLE I
CLINICAL AND EPIDEMIOLOGIC CHARACTERISTICS OF PARTICIPANTS

Age (years) $\bar{x}$ (SD) [range]	71.78 (7.22) [55- 83]
Weight (Kg) $\bar{x}$ (SD) [range]	80.40 (11.60) [64.2 -111.5].
BMI (Kg/m^2) $\bar{x}$ (SD) [range]	28.67 (2.99) [24.16 - 33.97]
Tumour Classification, TNM Nº (%)	
Stage I	0 (0)
Stage II	26 (39.39)
Stage III	36 (54.54)
Stage IV	2 (3.03)
Unknown	2 (3.03)
Treatment Nº (%)	
Surgery (Prostatectomy)	30 (45.45)
Hormone therapy (ADT)	30 (45.45)
Combined	
Radiotherapy + ADT	2 (3.03)
Prostatectomy + ADT	4 (6.06)
Sociodemographic data	
Marital status	
Married	60 (90.91)
Widowed	5 (7.58)
Never married	1 (1.52)
Employment status	
Retired	62 (93.94)
Employed	4 (6.06)

Abbreviations: BMI, body mass index; ADT, androgen-deprivation therapy

The FACT-P questionnaire results decrease significantly from P1 (pre-test) 108.61 to P2 (post-test) 101.76 (≤0.001). Table II shows the significant decline in values for all five dimensions of the FACT-P.

The results of the baseline (P1) and Then-test (P3) are displayed in Table III for both overall QoL and each dimension. As can be observed, the QoL score decreases significantly between the Baseline (108.61) and the Then-test (100.41).

As can be seen in Table IV, the results also show that there is no significant difference in any QoL dimension between the Then-test (P3) and Post-test (P2), meaning there is no significant real change.

In P4, the results show a significant difference (≤0.001) between the experimental group (EG=109.30) and control group (CG=99.60).

TABLE II
QOL AND FATIGUE RESPONSE SHIFT, AVERAGE AND TYPICAL DEVIATION (TD)

Parametric Description			Pre-test (P1)		Post-test (P2)		
Dimensions**	Range	n	$\bar{x}$	tD	$\bar{x}$	tD	p^*
FACT-P***	[0-156]	66	108.61	18.75	101.76	19.65	<0.001
General state of physical health***	[0-28]	66	23.74	3.90	21.88	4.27	<0.001
Family and social environment***	[0-28]	66	17.95	5.41	17.33	5.58	0.001
Emotional state***	[0-24]	66	16.74	4.48	16.5	4.43	<0.001
Personal functions***	[0-28]	66	17.39	5.17	16.32	4.8	0.002
Additional concerns***	[0-48]	66	32.77	5.77	29.73	6.88	<0.001
FACIT fatigue scale***	[0-52]	66	32.64	5.66	29.05	6.85	<0.001

FACT-P: Functional Assessment Cancer Therapy Scale-Prostate; FACIT: Functional Assessment Chronic Illness Therapy Fatigue Scale. ***Wilcoxon test

TABLE III
PRE-TEST VS. THEN-TEST SCORES

Dimension***			Pre-test (p1)		Then-test (p3)		
Dimensions	Range	n	$\bar{X}$	tD	$\bar{X}$	tD	p
FACT-P***	[0-156]	66	108.61	18.75	100.41	17.17	<0.001
General state of physical health***	[0-28]	66	23.74	3.90	22.24	3.48	<0.001
Family and social environment***	[0-28]	66	17.95	5.41	17.08	5.28	<0.001
Emotional state***	[0-24]	66	16.74	4.48	16.47	4.38	0.002
Personal functions***	[0-28]	66	17.39	5.17	16.26	4.61	<0.001
Additional concerns ***	[0-48]	66	32.77	5.77	28.30	5.78	<0.001
FACIT fatigue Scale***	[0-52]	66	32.64	5.66	27.56	5.25	<0.001

FACT-P: Functional Assessment Cancer Therapy Scale-Prostate; FACIT: Functional Assessment Chronic Illness Therapy Fatigue Scale. ***Wilcoxon test

TABLE IV
PRE-TEST VS. THEN-TEST SCORES

Dimension***			Pre-test (p2)		Then-test (p3)		
Dimensions	Range	n	$\bar{X}$	tD	$\bar{X}$	tD	p
FACT-P***	[0-156]	66	101.76	19.65	100.41	17.17	0.602
General state of physical health***	[0-28]	66	21.88	4.27	22.24	3.48	0.177
Family and social environment***	[0-28]	66	17.33	5.58	17.08	5.28	0.931
Emotional state***	[0-24]	66	16.5	4.43	16.47	4.38	0.828
Personal functions***	[0-28]	66	16.32	4.80	16.26	4.61	0.663
Additional concerns ***	[0-48]	66	29.73	6.88	28.30	5.78	0.728
FACIT fatigue Scale***	[0-52]	66	29.05	6.85	27.56	5.25	0.663

FACT-P: Functional Assessment Cancer Therapy Scale-Prostate; FACIT: Functional Assessment Chronic Illness Therapy Fatigue Scale. ***Wilcoxon test

As Table V shows, when comparing the change in QoL between P2 and P4, QoL increased for the EG (P4-P2=7.48) while it decreased for the CG (P4-P2= -2.64).

TABLE V
EXPERIMENTAL GROUP VS. CONTROL GROUP

(P4-P2) Dimensions	Experimental N=33		Control N=33		
	$\bar{X}$	tD	$\bar{X}$	tD	p
FACT-P	7.48	5.77	-2.64	3.88	<0.001
General state of physical health*	0.87	1.74	-0.6	1.05	<0.001
Family and social environment*	1.81	1.79	-0.12	0.64	<0.001
Emotional state*	0.24	0.50	-0.3	0.63	<0.001
Personal functions*	2.72	2.64	-0.5	2.7	<0.001
Additional concerns*	1.81	2.29	-1.03	1.18	<0.001
FACIT fatigue Scale*	3.63	2.69	-1.63	2.80	<0.001

FACT-P: Functional Assessment Cancer Therapy Scale-Prostate; FACIT: Functional Assessment Chronic Illness Therapy Fatigue Scale. * Mann-Whitney U test

IV. DISCUSSION

Considering the classical evaluation of QoL (Pre-test – Post-test), we observe that QoL decreased. Failure in coping with the disease was evident in P2 (Post-test), additional concerns, fatigue and general state of health being the most affected dimensions, while the emotional dimension and family and social environment remained clinically stable, as reported in earlier studies [14], [15].

If we focus on the Then-test approach, we find that the QoL mean did not change. The then-test results showed no change in patients' perception of QoL between diagnosis (P3) and discharge (P2). They also indicated a multidimensional decrease in the QoL recorded in P3 compared with P1, meaning that QoL was continuously low from the beginning of disease onset (P1), particularly in the additional concerns dimension and on the fatigue scale [16]. These results are in accordance with other studies that have evaluated QoL in cancer patients [15].

The Then-test approach highlights that intervention on coping strategies should begin at the time of diagnosis and not be delayed until discharge, to ensure that patients recover their daily living activities using adaptive coping strategies [9]. This avoids the establishment of non-realistic expectations

regarding recovery, which leads to a significant decrease in QoL during P2 when the reality of daily living returns.

Our results show that after applying the ERP (P4), the EG experienced a significant increase in QoL, while that of the CG continued to decrease. These results support the hypothesis that the ERP has a positive effect on improving QoL and adaptive coping strategies when QoL is considered as a continuous and dynamic process. According to Schwartz [17] and Serdà [9], considering QoL as a dynamic and continuous process means attending to reprioritization, reconceptualisation and recalibration of QoL from disease onset. These processes are necessary for the patient to adapt to the new living situation. Within this framework, comprehensive ERP should focus on improving the multidimensional sequelae, attending patients' needs and preferences in the continuum of disease. A holistic, continuous, and dynamic approach to QoL that incorporates a rehabilitation-tailored programme reverses the classical QoL curve [18].

Monitoring the QoL continuum is a new concept in evaluation and allows health professionals to control parameters and act when necessary, anticipating the failure of QoL. Feedback is useful a) to identify the evolution of the clinical intervention, b) to ensure that the patient can continue his life with the desired quality, c) to identify the changes of the affected QoL dimensions, and d) to define rehabilitation procedures, determine their goals, and achieve them. In accordance with the findings of Barocas [5], our study supports watchful waiting intervention or active surveillance as the best treatment for maintaining QoL among low-risk prostate cancer patients. Our results on QoL highlight the importance of watchful waiting treatment described as a less intensive type of follow-up, which may entail fewer tests and relying more on changes in a man's symptoms to decide if/when/which treatment is needed to facilitate patient counselling regarding the expected harms and their possible impact on QoL [19], [20]. Furthermore, our study also confirms that watchful waiting is not sufficient to improve QoL. It is necessary to also implement a well-structured ERP tailored to the patient's needs. Our rehabilitation programme reduces the symptoms related to the prostate cancer and treatments, enriches coping strategies and enhances survivors QoL by reversing the severity of the symptoms, reducing the invasive medical treatments and minimizing toxicity and side effects.

V. Strengths and Limitations

Inevitably, the overall decrease in QoL detected retrospectively by Then-testing could be due to the bias resulting from relying on memory to assess a prior status. This could be considered a limitation of the methodology. Considering the implicit theory of response shift, patients would not recall their perception of QoL in P1 because their health during P2 would influence the final response shift of the internal value. This would suggest that it may be preferable to incorporate both Pre-test and Then-test in order to have more data to better describe the QoL continuum.

In addition, the small sample size (n=66) prevents us from generalizing our results to all prostate cancer patients.

VI. Conclusion

Our study illustrates the benefits of an ERP after discharge. Further research is needed to prevent the plummet collapse of the QoL continuum by exploring the potential benefits of a rehabilitation programme from cancer onset. The QoL approach encourages health professionals to become aware of the impact of cancer treatments on QoL and to be more proactive. Practitioners should play a pivotal role in exploring multidimensional QoL as a primary end point for cancer therapy, assessing baseline QoL in order to plan, evaluate and time suitable interventions.

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