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REVIEW ARTICLE

Quality of life assessment using EORTC QLQ questionnaires in the prostate cancer population treated with radical prostatectomy: a systematic review

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ABSTRACT

Context: In recent years, quality of life has become an increasingly common outcome measure for assessing the effectiveness of treatment and surgical techniques.

Objective: The aim of our systematic review is to explore changes in health-related quality of life in patients suffering from prostate cancer and treated by means of radical prostatectomy.

Evidence acquisition: We focus on studies in which EORTC QLQ-C30 and EORTC QLQ-PR25 questionnaires are used because these instruments have shown high internal and external validity in many studies and include questions grouped in cancer-specific scales. Following the application of exclusion and inclusion criteria, we select eight studies for qualitative synthesis.

Conclusions: Our results indicate that most quality of life scales do not present a large decline. However, prospective studies with detailed descriptions of methodology, and in particular descriptions of participants, are still needed before general conclusions can be drawn. Moreover, scoring of results in accordance with questionnaire guidelines is essential for the performance of meta-analysis.

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Introduction

A diagnosis of prostate cancer is associated with physical, psychological, emotional, social, and economic burdens, and has an adverse effect on quality of life in the population of men suffering from prostate cancer [1–3]. Such changes in quality of life may significantly depend on factors directly associated with the tumor (e.g. stage and localization) and/or on treatment (e.g. type of treatment, surgical technique, hospitalization time) [4,5]. For these reasons, quality of life is an important issue in cancer care and research.

Nowadays, quality of life is increasingly being used in studies as a primary outcome measure of effectiveness of treatment and as an endpoint for different types of treatment comparison [6]. Moreover, the current multiplicity of treatment methods and surgical techniques, and the possibility of combined treatments, necessitates a greater focus on patients' sensations, expectations, and subjective perceptions of the effects of treatment. Consideration of patient-related outcomes is essential to the assessment of the physical and psychosocial burdens associated with treatments applied, and to the implemention of targeted interventions which may improve patients' prospects and wellbeing. Therefore, it seems desirable that validated multidimensional questionnaires with standardized methodologies which can enable researchers and clinicians to assess the impact of quality of life changes should come into general use [6,7].

The aim of the present systematic review is to explore changes in health-related quality of life in the prostate cancer population before and after radical prostatectomy. Moreover, we aim to determine which aspects of the lives of patients suffering from prostate cancer are most significantly affected by radical prostatectomy.

Materials and methods

Following the high methodological standards required for performance of a systematic review, we have used the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [8]. A search of the literature for purposes of the present study was conducted from March to April 2020.

Search strategy

Systematic literature searches were performed in nine databases: PubMed/MEDLINE, EMBASE, Cochrane Library, Science Direct, Web of Science, Scopus, Polish Medical Library, LiSSA, and Pascal et Francis. We searched for articles in the English, Polish and French languages. The search terms (Quality of Life, Health-Related Quality of Life, QoL or HRQoL), (EORTC QLQ-C30), (EORTC QLQ-PR25), (Prostate Cancer or Prostate Carcinoma), and (Radical Prostatectomy) were used, the search strategy being adjusted for each database, including changes in the language of the search terms. An example of a search strategy is given in Table 1. The resulting references to studies and other sources were then screened manually.

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Table 1. Example search strategy.

Database	Terms
PubMed/MEDLINE	(1) Quality of Life
	(2) Health-Related Quality of Life
	(3) QoL
	(4) HRQoL
	(5) (1) OR (2) OR (3) OR (4)
	(6) EORTC QLQ-C30
	(7) EORTC QLQ-PR25
	(8) Prostate Cancer
	(9) Prostate Carcinoma
	(10) (8) OR (9)
	(11) Radical Prostatectomy
	(12) (5) AND (6) AND (7) AND (10) AND (11)

Inclusion and exclusion criteria

Papers were screened based on the following inclusion criteria: population of men with prostate cancer who undergo radical prostatectomy; assessment of quality of life using EORTC QLQ-C30 and/or EORTC QLQ PR25 questionnaires; assessment of quality of life before and at least once after surgery. Articles meeting the following criteria were excluded: radical prostatectomy not a form of treatment; no assessment of quality of life before or after surgery. Disagreements between authors concerning inclusion of particular studies in the analysis were reconciled *via* consensus through discussion among the authors.

EORTC QLQ-C30 and EORTC QLQ-PR25

The EORTC quality of life questionnaire (EORTC QLQ-C30) is a tool for assessing health-related quality of life in patients suffering from cancer diseases which does not take into consideration either the type of cancer or its character and localization. It was created by the European Organization for Research and Treatment of Cancer, based in Brussels. The EORTC QLQ-C30 (version 3.0) comprises 30 questions which assess quality of life on functional scales (physical, role, emotional, cognitive and social), symptom scales (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and also financial difficulties), and one scale pertaining to global health status.

Respondents reply to questions on a four-point scale (1 – not at all, 2 – a little, 3 – quite a bit, 4 – very much) for assessing the intensity of the parameter analyzed. The only exceptions are the two last questions, which concern global health status, and in which a seven-point scale is applied. For assessing quality of life in specific patient populations, supplementary modules which can provide more detailed information have been developed [9,10].

One such supplementary module is EORTC QLQ-PR25, which is used specifically for assessing quality of life in patients suffering from prostate cancer [11]. This questionnaire consists of 25 questions, respondents providing answers in the same way as for EORTC QLQ-C30. The questions are again grouped into symptom (urinary symptoms, incontinence aid, bowel symptoms and hormonal treatment-related symptoms) and functional scales (sexual activity and sexual functioning).

In order to assess changes in quality of life (e.g. before and after surgery or other methods of treatment) we can use the recommendations for interpreting results proposed by King and Osoba [12,13]. According to them, a points difference equal to 10 or more points (on scale from 0 to 100) is considered a clinically significant value indicating improvement or worsening of quality of life. A difference of 20 points is deemed to be particularly important, while a difference of 5 points is barely significant.

Results

Study selection

A total of 495 potentially relevant articles were retrieved. After review, it was determined that eight studies fulfilled the eligibility criteria and as such, they were selected for qualitative synthesis. Figure 1 presents a PRISMA Flow Chart diagram of the selection process.

Description of studies

The studies included in this review all used the EORTC QLQ questionnaires as a concept. Of these, six were from Europe and were conducted in four different countries, and the remaining two were from Asia. One of the studies had a clinical trial design, while the other seven had a cohort design, with a total of 1936 patients. The most frequent follow-up time for assessment of quality of life after radical prostatectomy was one year post-surgery or earlier [14–20], but study evaluated the cohort only once after surgery (i.e. at 6 months) [21]. The mean age of patients in the the majority of the studies was over the age of 60. The clinical stage of tumor in the patients, where such information was included, was similar: cT1-cT2 [15,16,20], cT1-cT3 [14,18], However, one of the studies evaluated a group of patients at the cT2-cT3 stage of tumor. The most commonly used surgical technique was radical retropubic prostatectomy (RRP), while laparoscopic radical prostatectomy (LRP) was the rarest technique used in this review. Characteristics and summaries of the studies included in the qualitative synthesis are shown in Table 2.

Quality assessment of the studies was performed using the Critical Appraisal Skills Programme (CASP). To assess the observational studies and clinical trials, the tools for cohort studies and randomized clinical trials, respectively, were used. Studies were appraised according to the CASP checklists and classified as having a risk of low quality when only 25% of criteria were met. Respectively studies were appraised and classified as having high quality when 100% of the criteria were met. The methodological drawbacks in clinical trial study included to analysis were concentrated around no blinding of participants, investigators and people assessing outcomes and no precision of the estimate of the intervention or treatment effects. In turn, the observational studies included to present systematic review show methodological disadvantages relating to no identification of important cofounding factors, and consequently no taking

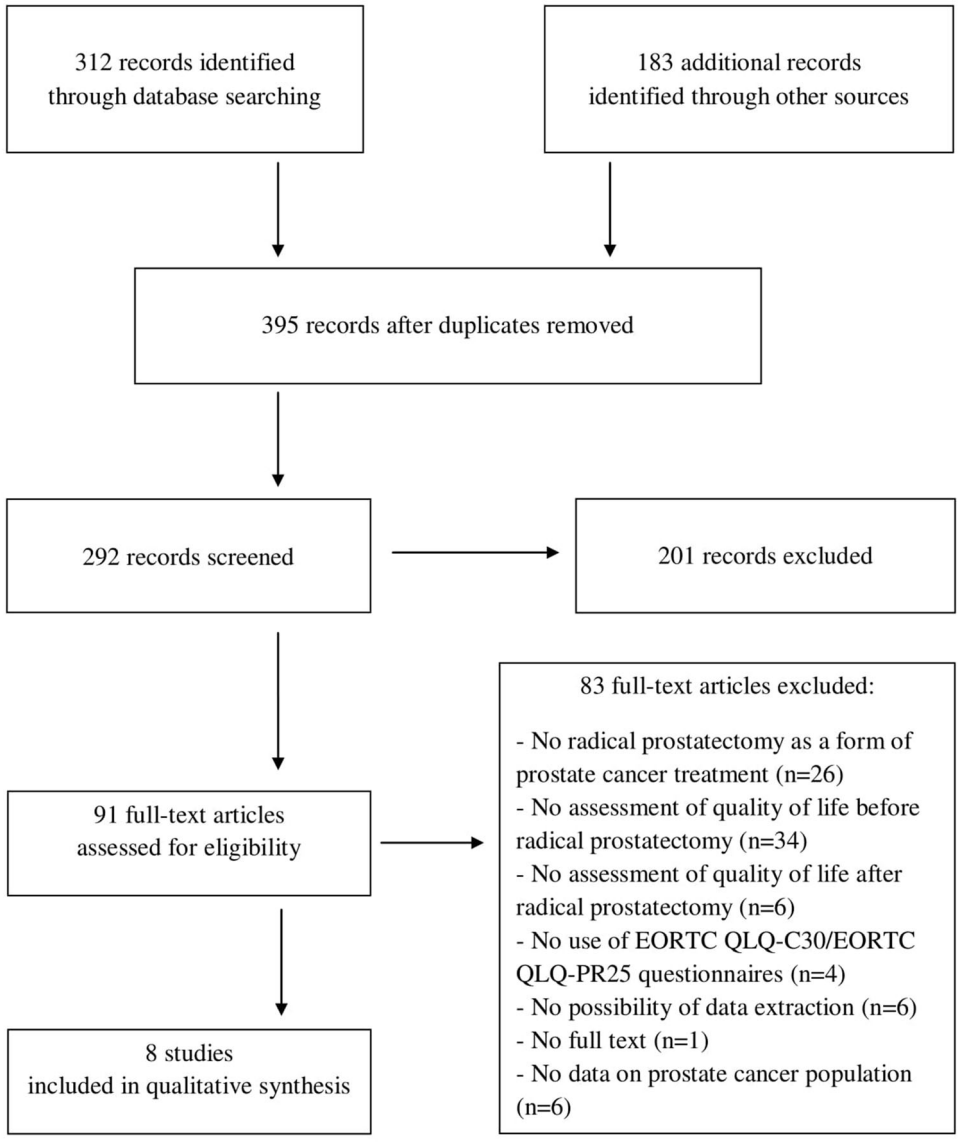

Figure 1. PRISMA flow chart.

account those factors in the design and analysis. Moreover, the follow up of subjects was not complete enough. The results of the quality assessment are shown in Table 2.

Discussion

This systematic review investigated changes in quality of life among the male population suffering from prostate cancer and undergoing radical prostatectomy, focusing on studies in which EORTC QLQ questionnaires were used. These questionnaires are well-known and have shown high internal and external validity in many studies. The EORTC QLQ-PR25 module has been applied to prostate cancer study results for almost fifteen years and is used as a specific complement to the EORTC QLQ-C30 questionnaire [11]. There are not other validated questionnaires assessing quality of life among prostate cancer population, and existing ones are focused on narrow aspect of life or treatment method. In this systematic review, changes in quality of life were compared with quality of life status before surgery. Therefore, one of our inclusion criteria was assessment of quality of life both before radical prostatectomy and at least once afterwards.

To our knowledge, this is the first systematic review focusing on changes in quality of life in prostate cancer patients before and after radical prostatectomy evaluated only by means of EORTC QLQ questionnaires.

According to our results, most of the functional and symptom scales of the EORTC QLQ-C30 and EORTC QLQ-PR25 questionnaires did not show significant differences in the male population suffering from prostate cancer. We observed that the role functioning and dyspnoea scales were the scales from the EORTC QLQ-C30 questionnaire which most commonly showed deterioration, whereas the most frequently improved scale was the emotional functioning scale. Turning to the EORTC QLQ-PR25 results, both functional scales (i.e. the sexual activity and sexual functioning scales) most commonly showed worsened results. In contrast, improved results were most frequently exhibited on the urinary symptoms and incontinence aid scales, although these improvements were not generally observed until at least six

Table 2. Summary of studies.

No	First Author, Year	Quality of study[a]	Characteristics of population undergoing radical prostatectomy					Quality of life assessment		Main results
			N	Age (SD)	Clinical stage	Pathological stage	Surgical technique	EORTC Questionnaire	Timing of assessment	
1	L□ppenberg, 2014 [14]	***	856	63.42 (6.6)	cT1-cT3	pT0-pT1	RRP	EORTC QLQ-C30	Before RP, 1 year after RP	Global health status results after surgery were statistically significantly better than before surgery but the increase was not clinically significant. Statistically and clinically significant increases were observed in a group of patients with high-grade perioperative complications. Statistically and clinically significant decreases were observed only on the role functioning scale while on the emotional functioning scale, an increase was noted. On the symptom scales, statistically and clinically significant changes were not observed.
2	Acar, 2014 [15]	***	65	59.5 (6.1)	cT1-cT2	NI	RALP	EORTC QLQ-C30 (only Global health status/ QoL), EORTC QLQ-PR25	Before RP, Min. 1 year after RP	Changes in global health status after surgery were not statistically or clinically significant. Results on scales from the EORTC QLQ-PR25 questionnaire were statistically and clinically significant only on the incontinence aid and sexual functioning scales. These results show a slight deterioration on the abovementioned scales.
3	Borchers, 2004 [16]	***	80[b]	[c]65.2(4.9) [d]59.2(4.6)	cT1-cT2	pT2-pT3	RPP	EORTC QLQ-C30	Before RP, 6 months and 1 year after RP	Only on the emotional functioning scale were statistically and clinically significant changes observed, indicating a marked improvement 1 year after surgery. Changes on other scales were not statistically or clinically significant.
4	Shin, 2019 [17]	***	209	66.6 (6.6)	cT2-cT3	pT2-pT3	RRP, LRP, RALP	EORTC QLQ-C30, EORTC QLQ-PR25	Before RP, 3 and 12 months after RP	Changes on the functional scales of the EORTC QLQ-C30 questionnaire were not observed as significant, whereas among the symptom scales statistically and clinically significant improvements were noted on the pain and financial difficulties scales 1 year after surgery. Even on the appetite loss scale, an increase in functioning was seen 1 year after radical prostatectomy (compared to results 3 months after surgery). Results among the symptom scales of the EORTC QLQ-PR25 questionnaire were statistically and clinically significant on the urinary

(*continued*)

Table 2. Continued.

No	First Author, Year	Quality of study[a]	Characteristics of population undergoing radical prostatectomy					Quality of life assessment		Main results
			N	Age (SD)	Clinical stage	Pathological stage	Surgical technique	EORTC Questionnaire	Timing of assessment	
										symptoms and incontinence aid scales, indicating worsening 3 months after surgery, although significant improvement 1 year after surgery was also noted. Changes on all EORTC QLQ-PR25 functional scales show statistically and clinically significant worsening (compared to results before surgery).
5	Choe, 2005 [18]	***	34	64 (NI)	cT1-cT3	NI	RPP	EORTC QLQ-C30, EORTC QLQ-PR25	Before RP, Min. 1 year after RP	Changes among the functional scales of EORTC QLQ-C30 were noted on the global health status, physical functioning, role functioning, emotional functioning, and social functioning scales, indicating statistically significant decreases, albeit with only moderate clinically significance. Statistically and clinically significant results among the symptom scales of EORTC QLQ-C30 1 year after surgery were observed only on the fatigue and dyspnoea scales, showing a decrease in functioning. It is not possible to describe the results from the EORTC QLQ-PR25 questionnaire as the results were not presented by the authors in accordance with the recommendations and manual scoring of the EORTC.
6	Jakobsson, 2013 [19]	***	222[e]	62.7 (6.09)	NI	NI	RRP	EORTC QLQ-C30, EORTC QLQ-PR25	Before RP, 3 months, 1, 2, 3 and 5 years after RP	Results among the functional scales of the EORTC QLQ-C30 questionnaire were statistically and clinically significant only on the emotional functioning scale, indicating improvement either 3 months or 5 years after surgery. No statistically and clinically significant changes were noted among the symptom scales of the EORTC QLQ-C30 questionnaire. Changes among the functional scales of the EORTC QLQ-PR25 questionnaire demonstrated a significant worsening of function even 5 years after surgery. Among the symptom scales of EORTC QLQ-PR25, only on the incontinence aid scale were changes significant, indicating a decrease of function, although only over 3 months.

(*continued*)

Table 2. Continued.

No	First Author, Year	Quality of study[a]	Characteristics of population undergoing radical prostatectomy					Quality of life assessment		Main results
			N	Age (SD)	Clinical stage	Pathological stage	Surgical technique	EORTC Questionnaire	Timing of assessment	
7	Bach, 2011 [21]	**	370[f]	66.5 (NI)	NI	NI	RRP	EORTC QLQ-C30, EORTC QLQ-PR25	Before RP, Min. 6 months after RP	Results among the functional scales of the EORTC QLQ-C30 questionnaire were statistically and clinically significant only on the emotional functioning scale, indicating a marked improvement. Significant changes among the symptom scales of EORTC QLQ-C30 were noted only on two scales: dyspnoea and insomnia. Results from EORTC QLQ-PR25 presented no statistically or clinically significant changes.
8	Giberti, 2009 [20]	***	100	65.2(NI)	cT1-cT2	NI	RRP	EORTC QLQ-C30, EORTC QLQ-PR25	Before RP, 6 months, 1 and 5 years after RP	Results among the functional scales of EORTC QLQ-C30 were statistically and clinically significant only on the role functioning scale, indicating deterioration 6 months after surgery. Changes among the symptom scales of the EORTC QLQ-C30 questionnaire were not significant. From EORTC QLQ-PR25, only the urinary symptoms scale and hormonal treatment-related symptoms scale showed statistically and clinically significant changes, indicating a decrease in function 6 months after surgery.

RP: radical prostatectomy; RRP: radical retropubic prostatectomy; RPP: radical perineal prostatectomy; RALP: robot-assisted laparoscopic radical prostatectomy; LRP: laparoscopic radical prostatectomy; NI: no information.
[a]Critical assessment of the studies was graded according to different design specific CASP checklist (*25% of criteria met, **50% of criteria met, ***75% of criteria met, ****100% of criteria met).
[b]This number represents a group of patients with and without nerve sparing.
[c]This information relates to a group without nerve sparing.
[d]This information relate to a group with nerve sparing.
[e]The number of participants at baseline.
[f]This number comprises 2 groups of 185 patients whose results were processed using matched-pair analysis regarding age.

months after surgery. In accordance with the guidelines for interpreting score changes in EORTC QLQ questionnaire results, we observed that the changes in the functional and symptom scales were rarely statistically or clinically significant.

In summary, we note that patients do not present a large decline on quality of life scales after radical prostatectomy in relation to baseline quality of life assessed before surgery. This could indicate that radical prostatectomy, in conjunction with awareness of the risk of perioperative and postoperative complications (e.g. erectile dysfunction and urinary incontinence), does not result in a severe deterioration in perception of quality of life. Nevertheless, the clinical interpretation of these results remains difficult due to the fact that prospective randomized trials investigating quality of life before and after surgery are still lacking [12,21,22]. Many studies had to be excluded from the present study due to lack of assessment of quality of pre- or postoperative life. Moreover, results from retrospective studies cannot be regarded as a sufficient basis from which to draw general conclusions. As indicated by Bach *et al.*, in retrospective studies, patients with good post-surgical results and without peri- or postoperative complications more often take part in questionnaires. This could well have a 'positive' influence on results and falsify conclusions. More rigorous studies are needed in order to assess changes in quality of life after radical prostatectomy.

Care for patients suffering from prostate cancer is multidisciplinary in approach and involves various treatment methods including radical prostatectomy, for which surgical techniques have seen considerable evolution in recent years [23]. The selection of optimal treatment methods or surgical techniques is a complex process both for healthcare professionals and for patients themselves. It is for this reason that in recent years, research on quality of life has become an endpoint of clinical research conducted among patients suffering from prostate cancer [6]. This allows for better understanding of the possible after-effects (physical, psychological, emotional, and social) of different treatment methods and surgical techniques. Moreover, quality of life can also be an early indicator of progression of disease and therefore may assist healthcare professionals in daily clinical practice [4,24].

Limitations

A number of limitations in this systematic review are acknowledged. The language of publications studied was restricted to English, Polish and French because of limited translation resources. For this reason, we did not identify articles in Spanish or in any Asian language. Further systematic reviews without language limitations are needed.

A lack of research with detailed descriptions of participants was a major problem in the current systematic review. Moreover, methodological weaknesses in some studies, such as underspecified time of quality of life assessment (e.g. *minimum 1 year after surgery*) or scoring of results in a manner not in accordance with guidelines, precludes meta-analysis of the results of such studies, making it impossible to draw general conclusions.

Conclusions

Quality of life assessments should often be employed as tools for predicting and describing treatment results, and validated standardized tools should regularly be applied to assess quality of life among populations of men with prostate cancer treated by radical prostatectomy.

Radical prostatectomy as a treatment option does not lead to a decline of all quality of life aspects in patients suffering from prostate cancer. This systematic review indicates episodic changes in quality of life which demonstrate worsening and/or improvement equally.

This systematic review and the data from our analysis are essential to help patients in choosing between various therapeutic surgical options. Furthermore, the introduction of novel surgical options and approaches in recent years (e.g. robot-assisted laparoscopic radical prostatectomy or laparoscopic radical prostatectomy) implies the need for further research into changes in quality of life, as quality of life may be an important factor in comparing the various options available.

Implications for further studies

Further research including high-quality studies with detailed descriptions of participants (e.g. information about the clinical and pathological stage of the tumor) is recommended. Moreover, quality of life assessment should be performed repeatedly both before and after surgery. Furthermore, it is necessary to carry out the scoring and interpretation of questionnaire results in accordance with the guidelines of the questionnaire's authors and/or originating organizations.

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