

Patient reported outcome measure applicability in clinical oncology

Aplicabilidade das medidas de resultados relatados pelo paciente na oncologia clínica

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ABSTRACT

Patient Reported Outcomes (PROs) are a report that comes from patients on a specific subject, describing how they feel about a condition or therapy. The term includes a range of constructions and methodology and can cover concepts such as symptoms to physical assessment, well-being and social involvement. The process can be described as a measure of patient reported outcome (Patient Reported Outcome Measure - PROM). In oncology, PROMs help healthcare professionals and systems to reduce the impact of treatment on patient's quality of life. In recent years, several studies have shown improvement in the evaluated outcomes. In our country, there is still little information on this subject, especially when it comes to cancer patients. Hence, we think that it is of utmost importance to review the particularities of this tool, in order to stimulate further discussion of the subject in our country.

Keywords: Patient reported outcome measures; Medical oncology; Quality of life.

RESUMO

Os resultados relatados pelo paciente (RRPs) são relatórios provenientes de pacientes sobre um assunto específico, descrevendo como eles se sentem a respeito de uma condição ou terapia. O termo inclui uma gama de construções e metodologia, e pode abranger conceitos como sintomas para avaliação física, bem-estar e envolvimento social. O processo pode ser descrito como uma medida de resultado relatado pelo paciente (Patient Reported Outcome Measure - PROMs). Em oncologia, os RRP ajudam os profissionais e sistemas de saúde a reduzir o impacto do tratamento na qualidade de vida do paciente. Nos últimos anos, diversos estudos demonstraram melhora nos resultados avaliados. Em nosso país, ainda são poucas as informações sobre o assunto, principalmente quando se trata de pacientes com câncer. Assim, pensamos ser da maior importância rever as particularidades desta ferramenta, a fim de estimular uma maior discussão sobre o assunto em nosso país.

Descritores: Medidas de resultados relatados pelo paciente; Oncologia médica; Qualidade de vida.

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INTRODUCTION

Advances in oncology have recently promoted higher cure rates in some cases as well as significantly improved the survival of patients with metastatic disease. However, many of the new treatments are accompanied by non-negligible toxicities. Patients receiving cancer treatment have a variety of associated side effects such as fatigue, nausea and vomiting, alopecia, and pain.^[1] In clinical practice, it is necessary to seek a balance between the benefits of prolonged survival or delayed progression with the possible negative effects of treatment on quality of life.^[2]

In cancer treatment trials, the standard source of adverse symptom data is clinician reporting by use of items from the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE),^[3] and these outcomes are analysed only under clinician's impressions.

Despite the existence of validated questionnaires using information reported by patients to assess quality of life, these are processed within a methodology to provide a metric as a way of scoring.^[4] Currently, there is a new emphasis on "survival" in which self-management and quality of life assessment have key roles to play.^[5]

In this context, Patient Reported Outcome (PROs) are reports that come directly from patients on a specific subject without interpretation, describing how they feel about a condition or therapy.^[6] The report includes a wide range of terms and methodology, covering concepts that can range from symptoms to physical assessment, well-being, and social involvement. The process can be described as a measure of patient reported outcome (Patient Reported Outcome - PROM).^[4]

PROMs are tools used to capture a patient's perspective of their own treatments and care.^[7] PROMs can be generic (measuring aspects of health status and quality of life common to most patients), disease-specific (e.g., cancer) or condition-specific (applicable to a service sector such as rehabilitation or mental health services or to a population segment such as the elderly).

In the specific case of oncology, PROMs can help doctors and health systems to reduce the impact of treatment on patients' quality of life thus contributing to better outcomes. In the last decade, several studies in different areas of oncology have included PROMs as part of the outcome's assessment.

In Brazil, there is still little information about PROMs, especially in the oncology area. The aim of this article is to review the usage history of this tool, its implications, benefits, and perspectives in cancer treatment. To demonstrate the importance of this approach and reinforce its use as an outcome in cancer treatment, we reviewed the literature and discussed the results and challenges for its use in an expanded way.

In the last decades, advances have been made for a better analysis of the quality of life of patients during health treatment. In this period, there is a greater

involvement of patients in decision-making, aiming at a better quality of life for them.^[11] PROMs are tools that give support to this analysis, and their study has grown in different areas of health. Nowadays, the countries with the most trials and the greatest implementation of PROMs in clinical practice are England, the Netherlands, Sweden, and the United States.^[7]

In 1975, prior to the studies related to PROMs, Sweden started using the "quality of life records", which were records with information about symptoms presented by patients noted by health professionals at the time. PROMs started to be introduced in England in the 2000s.^[7,11] In 2008, one of the first analyses took place with the evaluation of the satisfaction of patients undergoing mastectomy and breast reconstruction. In the following year, different studies investigated patients who underwent hip surgery, herniorrhaphy and varicose vein, showing benefits with the use of PROMs. After these studies, the use of this tool became mandatory in such elective surgeries in different centers in England.^[11] The evaluation of PROMs in the cardiology field started in 2013, and one of its first studies have analysed the quality of life after myocardial revascularization.^[11,12]

In recent years new studies have appeared in Oncology. In 2017, a review from the Memorial Sloan Kettering Cancer Center demonstrated benefits with the use of PROMs as regarding quality of life and overall survival in patients undergoing cancer treatment.^[14]

In 2019, the use of PROMs showed that women with breast cancer who underwent adjuvant radiotherapy had an impaired body image.^[15] On the other hand, despite its advances, studies in certain areas are still lacking. As an example, a systematic review of 2019 evaluated studies related to quality of life in patients with ovarian cancer, however none of them used PROMs as a tool.^[13]

METHODS

Research on scientific articles was carried out on the PubMed platform (*pubmed.ncbi.nlm.nih.gov*) with the following terms: PROMS - Patient Reported Outcome, cancer and quality of life, from March to April of 2020. All the 18 studies identified in the search were included and are listed in Table 1. The present work is a narrative of the reviewed studies, regardless of the methodology applied in each study.

Improved outcomes

The number of new drugs approved for cancer treatment has increased exponentially in recent years. However, in many cases these treatments have received approval from regulatory agencies based on substitute outcomes (such as tumour reduction and/or progression-free survival), postponing the assessment of overall survival and quality of life after drug use is released.^[16]

A data analysis study carried out between 2008 and 2012 showed that 67% of the drugs approved by the FDA (Food and Drug Administration) for cancer treatment did not demonstrate gains in overall survival

Table 1. Insert description.

ARTICLE	BODY LOCATION	PROM ASSESSMENT METHOD	CONCLUSION
Kundu et al. (2019) ²⁶	PROSTATE	PROMIS application for symptom assessment (anxiety, depression, pain, fatigue) during hormone therapy	The use of online tools may assist in reducing the adverse effects of hormone therapy in men with prostate cancer.
Lane et al. (2016) ²⁷	PROSTATE	Questionnaires already validated EPIC; ICIQ-UI; ICSmalaSF; HADS; EQ-5D-3L	PROMS of cancer patients were like that of patients without cancer.
Hoque et al. (2019) ²⁸	PROSTATE	The expanded prostate cancer index composite responded by email	Email is an interesting tool for collecting PROM information.
Cuypers et al. (2018) ²⁹	PROSTATE	Patients participated in online treatment decisions with forms and counselling	Patients who have not used online counselling need further guidance for decision making.
Yue et al. (2018) ³⁰	LUNG NON-SMALL CELLS	Questionnaire: MD Anderson symptom inventory lung cancer module	The use of PROMS allowed cancer patients to be identified with a greater risk of developing symptoms related to radiotherapy.
Lenderking et al. (2019) ³¹	LUNG NON-SMALL CELLS	Questionnaire: QLQ-C30 and GHS/QOL	The outcomes reported by patients were associated with the response to treatment with brigatinib.
Felip et al. (2018) ³²	SQUAMOUS LUNG	Questionnaire: QLQ-C30 and GHS/QOL	Afatinib showed better quality of life than erlotinib.
Lee et al. (2018) ³³	LUNG NON-SMALL CELLS	Questionnaire: EORTC QLQ-LC13; EORTC QLQ-C30	Patients who used osimertinib had better quality of life as described by PROMS.
Wu et al. (2018) ³⁴	EGFR MUTATED LUNG	Questionnaire: EORTC QLQ-LC13; EORTC QLQ-C30	Afatinib presented a better symptom profile as described by PROMS.
Sebastian et al. (2018) ³⁵	LUNG NON-SMALL CELLS	Questionnaire: PRO-CTCAE analyses	Reported symptoms were mild to moderate in the group using osimertinib.
Bordoni et al. (2018) ³⁶	LUNG NON-SMALL CELLS	Questionnaire: HRQoL	Afatinib presented a better symptom profile as described by PROMS.
Brow et al. (2018) ³⁷	COLON	Questionnaire: Short form 36QoL outcomes included the short form (SF)-36 GBFQ; FS	Aerobic exercise has improved many HRQoL.
Price and Bednarski et al. (2017) ³⁸	COLON	Trimodal combination: minimally invasive cx, ERP and Telerecovery	
Blaby et al. (2014) ³⁹	BLADDER	Questionnaire: Develop EORTC for bladder cancer	
Staehler et al. (2018) ⁴⁰	KIDNEY	Questionnaire: EORTC QLQ-C30)	Patients using sunitinib had greater symptoms and worsened quality of life but were not clinically significant.
Abernethy et al. (2009) ⁴¹	BREAST	Questionnaire: FACT-G; FACT-B; MDASI; FACIT-F; FACIT-Self-Efficacy Scale; PCM, an 86-item survey for common cancer- and treatment-related symptoms; Satisfaction and acceptability survey	33.3% of clinicians disclosed that their clinical decisions were influenced by symptom alerts; clinicians' email responses to symptom alerts were to maintain treatment course (46%), to assess the patient at the following clinic appointment (33%), or to prescribe a new symptom treatment (8%).
Anderson et al. (2015) ⁴²	BREAST	Questionnaire: IVR-related pain and symptom List; MDASI; BQ-II; PMI PROMs	16 of 50 (32%) of patients, at the first visit, felt encouraged to address symptoms with clinicians that they otherwise would not have discussed, which increased to 48% (16 of 33 patients) by the fourth visit.
Bock et al. (2012) ⁴³	BREAST	Questionnaire: Unspecified PROM (symptoms and health history)	More than half of symptoms mentioned by both patients and clinicians were addressed, regardless of number of symptoms.

or quality of life. Only 14% of the drugs approved demonstrated improvement in overall late survival when compared to previous treatments after an average of 4.4 years on the market.^[17]

In Europe, a study carried out between 2009 and 2013 of drug approvals by the EMA (European Medicines Agency) presented similar data, with 57% of approvals with no impact on overall survival or quality of life, only 15% of the drugs presented a significant result in overall survival after an average of 5.5 years of commercialization.^[18]

The clinical evaluation of the patient is crucial to start a new cancer therapy, with the performance scale (PS) of Karnofsky and the Eastern Cooperative Oncology Group (ECOG) being the most used. However, there is great variability between doctors, nurses, caregivers, and especially patients in this assessment. Health professionals tend to frequently overestimate the patient's PS when compared to their own perceptions of the PS.^[19] Therefore, data from previous studies have shown that up to 50% of terminal cancer patients receive some form of cancer treatment in their last 30 days of life.^[20,21]

In this scenario, PROMs can have an impact on behavior change since in treatments with marginal benefits the patient's perception can be decisive for the start of a new treatment. Reducing treatments that have a significant impact on quality of life without leading to a clinically significant outcome improvement.

Diseases assessed by PROMs

There are different impacts on quality of life among different types of cancer treatments. Symptoms and effects of treatment may vary according to the type of treatment such as surgery, radiotherapy, chemotherapy, immunotherapy, etc. Another determining factor is the location and type of cancer. Several studies have developed methods for PROM assessment according to the location of the tumour due to the different effects of treatments.

DISCUSSION

The rapid expansion in the number of available PROMs made it difficult to select the most appropriate instrument for a defined objective.^[8] This was exacerbated by the prolific development of digital tools and applications, many of which are well-intentioned, but lack rigorous development methods to assess item selection, validity, reliability, responsiveness, and interpretation.^[9]

The methods of evaluating the outcome measures reported by patients are generated after a rigorous testing and review process to be validated.^[22] Most of the scales developed are in the English language and were used in patients with mastery of that language.^[23] Most of the studies that evaluated outcomes reported by patients in Brazilian articles about cancer used international questionnaires without valid translation. It is of utmost importance that questionnaires are adapted to the culture and language of the country where they are applied to remain reliable.^[24,25]

The small volume of articles found in this period and the great variability in methodology limit the quality of a possible systematic review. In this sense, we choose to carry out a narrative review, showing all the literature found, in order to encourage a discussion about the need for standardization of these studies.

CONCLUSION

Cancer treatment involves different aspects, not only those related to objective outcomes such as free time for progression and overall survival, but also the possibility of providing a better quality of life for patients undergoing treatment. The use of PROMs meets this objective, and recent studies as mentioned in this review, have shown the benefits of using this tool in cancer patients. However, studies and standards are still lacking so that PROMs can have a wider coverage in different treatment centers. The approach of these aspects by the scientific community is extremely relevant so that we can standardize the evaluations and extract the best results from the application of PROMs.

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