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Review

Patient-reported outcome measures (PROMs) in the management of lung cancer: A systematic review

Youssef Ben Bouazza[a,e], Ibrahim Chiairi[a], Ouiam El Kharbouchi[c], Lesley De Backer[b], Greetje Vanhoutte[b], Annelies Janssens[a,b,d], Jan P. Van Meerbeeck[a,b,d,*]

[a] Faculty of Medicine and Health Care, Antwerp University, Universiteitsplein 1, 2610 Antwerpen, Belgium
[b] Multidisciplinary Oncological Center Antwerp (MOCA), Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium
[c] Department of Medical Oncology, Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium
[d] Department of Pulmonology & Thoracic Oncology, Antwerp University Hospital, Wilrijkstraat 10, 2650 Edegem, Belgium
[e] Rietbeemd 36, 4907 ED Oosterhout, The Netherlands

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ABSTRACT

Lung cancer is often associated with a poor quality of life, as reflected by patient-reported outcome measures (PROMs). The aim of this paper is to describe and compare the PROMs that are available.

In this manuscript, we review the impact of PROMs on the management of lung cancer. Quality of the study and risk of bias were assessed using the appraisal tools recommended by the Dutch Cochrane Center. Out of 51 studies included in this review, ten instruments were identified and categorized as either generic, cancer- or lung cancer-specific. PROMs are primarily applied in scientific research to compare the therapy outcomes and in drug development to support labeling claims. The interest for the routine use of PROMs in daily practice is growing, which has positive effects on the communication with the patient, mutual decision making and the monitoring and managing of the patient. Besides that, PROMs have an independent prognostic value for survival in lung cancer and economic evaluations can be conducted using their results. Electronic platforms simplify the implementation of PROMs in the daily clinic.

The EORTC QLQ-C30 and its lung cancer-specific module QLQ-LC13 are the most frequently used instruments in lung cancer patients. PROMs have the potential to improve the quality of care with a proper implementation in the routine practice. PROMS are needed to value and understand the experience of the patient.

1. Introduction

Lung cancer is worldwide the most common form of cancer. In 2012 counted approximately 1.8 million new cases and 1.6 million deaths. This makes lung cancer responsible for almost 20% of cancer related deaths [1]. The incidence and mortality are highest in the developed countries of Europe, North-America and Australasia [2]. It has a poor survival with an average five-year survival rate of 15% [3].

Initially there is a symptom-free course after which nonspecific and bothersome symptoms arise like e.g. cough, pain, dyspnea and hemoptysis. Due to the symptom-free course, lung cancer is often diagnosed in an advanced stage and its symptoms impact on quality of life (QoL) [4]. Moreover the chemotherapy that improves survival frequently have adverse effects, which also influence quality of life [5].

Health-related quality of life (hrQoL) includes several domains, which consider the general perception of the patient on the impact of disease or treatment on physical as well as psychological and social aspects of life [6]. Given the prognosis and the impact of both disease and treatment on the morbidity and outcome of lung cancer patients, the preservation and evaluation of the hrQoL is very important [7,8]. The concept of QoL is used for a long time in the oncology, but the term patient-reported outcome measure (PROM) is new [9].

Patient-reported outcomes (PROs) are outcomes regarding the health of the patient and are directly reported by the patient [10]. They can range from simple symptomatic (fatigue, pain,…) to more complex concepts like hrQoL and its associated domains [6]. The instruments used for measuring PROs are called PROMs. The popularity of PROMs has grown and they are increasingly used (Fig. 1). They might contribute to the paradigm shift to patient-centered care and improve the objective outcomes of the patients.

Up to date, no review article has described the use of PROMs in lung cancer and no comparison between all lung cancer-specific instruments has been published. Therefore, the main objective of this review is to analyze the use of PROMs in the treatment of lung cancer with the aim of improving the quality of care. The secondary objective is to evaluate which instruments are currently being used in the care of lung cancer. Finally, the development, content and validation of lung cancer-specific

* Corresponding author at: Department of Pulmonology, Antwerp University Hospital, Wilrijkstraat 10, 2650 EDEGEM (Belgium).
E-mail addresses: youssef.benbouazza@student.uantwerpen.be (Y.B. Bouazza), jan.van.meerbeeck@uza.be (J.P. Van Meerbeeck).

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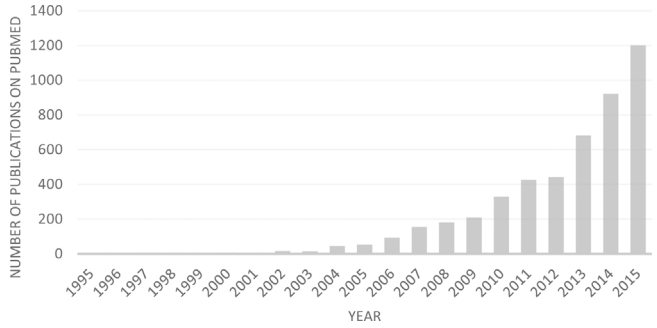

Fig. 1. The increase in the use of PROMs. The number of hits per year on Pubmed using the following search: "patient reported outcomes".

instruments are concisely summarized.

2. Methods

This review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [11]. The database search is conducted in PubMed, Web of Science and Google Scholar with a restriction from January 2010 to February 2016. The aim of the time restriction is to give an overview of the current situation. The last search was conducted on February 21, 2016. The included studies were assessed for their quality using appraisal tools recommended by the Cochrane Netherlands [12].

All articles that met the inclusion criteria underwent extraction for any kind of information on the use of PROMs and the impact on the quality of care. Furthermore, the identified instruments were evaluated based on the inclusion criteria and validity. Data pooling was not performed due to their high variability.

3. Results

The search yielded a total of 1438 hits along with nine additional articles after a manual search. After removing duplicates, 1118 articles remained for the screening process. After screening the titles and abstracts 1023 articles were excluded. The remaining 95 articles were evaluated for full text, which led to the exclusion of 55 more articles. The screening of reference lists yielded another 11 relevant articles. Therefore a total of 51 articles were included in this review (Fig. 2).

The assessment of the included articles is listed in the appendix.

To be accepted as a scientific measure, PROMs must have good psychometric properties. They must be valid, reliable and responsive [6,10]. Furthermore, the feasibility is important. Not only practical aspects such as costs and time play a part in this, but for example also the burden to the patient or staff. There are various PROMs available which differ from each other in the manner in which items were included during development. Patient input is essential for their development [6,13].

Sixteen instruments were identified that are used in the lung cancer population. Ten of these identified instruments met the criteria (Table 1). Six instruments which were not patient-reported, did not encompass relevant domains or were not validated, were excluded. The remaining ten instruments were categorized as either generic (n = 2), cancer-specific (n = 4) or lung cancer-specific (n = 4). The measures reviewed are briefly summarized below. The main focus is put on the lung cancer-specific instruments. In addition, the assessment of the validation, characteristics and evaluation of the domain categories of these lung cancer-specific instruments are presented in Table 2. The generic instruments are summarized in the appendix.

Cancer- and lung cancer-specific questionnaires

Five specific instruments have been developed and are in current use.

Firstly, the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Group has launched a major project in 1986 to develop an instrument that evaluates all aspects of the hrQoL [14]. The outcome is the EORTC Quality of Life Questionnaire–core module (EORTC QLQ-C30). This is a cancer-specific questionnaire which consists 30 items divided into four domains: functional scales (physical, role, emotional, social and cognitive; 15 items), symptom scales (fatigue, pain and nausea/vomiting; six items), single items (dyspnea, insomnia, appetite loss, diarrhea, constipation and financial difficulties; six items) and two items evaluating the overall QoL [14]. The core module is complemented by disease-specific modules like i.e. lung cancer (QLQ-LC13).

The EORTC QLQ-LC13 questionnaire (Table 2) was developed in 1994 [15]. Item generation was guided by three criteria:

1. Assess items that are specific to lung cancer and its standard treatment, which are insufficiently covered by the core questionnaire.
2. Have the same format and employ the same time frame as the core questionnaire.
3. Be reliable, valid and responsive to clinical status and change over time.

The project group selected 13 items through this framework. Extensive field testing was conducted for validity, reliability, responsiveness [15]. It was developed over 20 years ago when there were no guidelines for module development. So the development of an improved version of the QLQ-LC13, the QLQ-LC29, was initiated for a more optimal and relevant assessment of the QoL through the use of the *Module Development Manual* and by taking into account the new trends in treatment [16]. The QLQ-LC29 is currently being validated in an international phase four field study.

The QLQ-LC13 questionnaire consists of 13 items that evaluate lung cancer-specific symptoms: coughing (one item), hemoptysis (one item), dyspnea (three items), treatment side effects (sore mouth, dysphagia, alopecia, peripheral neuropathy; each one item), pain (three items) and pain medication (one item). It is impossible to use the EORTC QLQ-LC13 singly, since it is so designed that the content validity is based on the combination of the QLQ-C30 and QLQ-LC13 [15].

Extensive field studies have proven the validity of these instruments and the international use of them experienced an impressive increase [16]. In two international field studies, respectively, 883 and 735 lung cancer patients (from Europe, North America, Australia and Japan) completed the questionnaire pre- and on-treatment to assess the psychometric properties. The results demonstrated good reliability of the multi-item dyspnea scale (Table 2). Validity was evaluated with an analysis of variance by disease stage and by performance status [15]. Overall, the EORTC QLQ-LC13 has undergone extensive testing and demonstrated good psychometric properties.

The EORTC QLQ-C30, in combination with the lung cancer specific questionnaire, is the most frequently used instrument to assess the hrQoL in the lung cancer population [5,17]. The International Consortium for Health Outcomes Measurement (ICHOM) also recommends these instruments as PROMs for monitoring lung cancer [18].

Secondly, the Functional Assessment of Cancer Therapy–General (FACT-G) is also a core module which evaluates the global hrQoL in cancer patients. It is developed and mostly used in the United States. The FACT-G was published in 1993 and includes four domains with a total of 27 items: physical well-being (seven items), social/family well-being (seven items), emotional well-being (six items) and functional well-being (seven items) [19].

The FACT-G has additional disease-specific modules designed to complement the core module. The FACT–Lung (FACT-L) (Table 2) is the addition for patients with lung cancer [20]. Item generation was done by open-ended interviews and ranking by lung cancer patients. Highly rated items not included in the FACT-G were included in the Lung Cancer Subscale (LCS), which consists out of items that include the specific concerns of lung cancer and its treatment [20].

Currently, the fourth version is available that forms a compilation of 36 items. The FACT-L version 4 contains the core module with the additional LCS: dyspnea, ease of breathing, cough, tightness in chest,