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Summary:
Lung cancer is the deadliest cancer worldwide. The majority of newly diagnosed lung cancer patients are diagnosed with non-small cell lung cancer (NSCLC). The preponderance of patients presents with (locally) advanced disease stages. Despite new diagnostic tools and treatments, the long-term survival of these patients remains limited. It is therefore important to take into account the impact of treatment on the overall wellbeing and functioning of NSCLC patients in treatment-decision making.

NSCLC patients may experience high symptom and treatment-related toxicity burden, possibly adversely affecting health-related quality of life (HRQoL). Treatment may also negatively affect patients’ neurocognitive functioning (NCF).

In the lung cancer population, evidence is mainly generated in traditional clinical trials with highly selected patient populations and treatments. To broaden this evidence with data obtained in daily clinical practice, data must be collected, analyzed and reported in a methodologically accurate manner. As such, real-world evidence could provide data on the heterogeneous group of lung cancer patients in daily clinical practice.

Hence, this thesis aimed to evaluate the impact of standard systemic treatment and/or loco-regional radiotherapy on HRQoL, toxicity and NCF in early-stage (ES-) and metastatic NSCLC patients enrolled in clinical trials as well as followed in real-life clinical practice.

This has led to three sub-objectives: 1. systematic reviews and methodological appraisals of HRQoL data retrieved from highly controlled clinical trials; analyses of HRQoL and toxicity and their associations in ES- and NSCLC patients undergoing different loco-regional radiotherapy techniques and treatment modalities enrolled in a prospective international real-world study; and 3. evaluation of individual changes in HRQoL, toxicity and NCF in LA- and metastatic NSCLC patients receiving standard treatment in a prospective single-institute real-world study.

To evaluate the first specific objective, two systemic literature reviews and methodological appraisal on recent prospective studies evaluating the impact of loco-regional radiotherapy and various systemic treatments on HRQoL in LA- and metastatic NSCLC patients were conducted. The data on HRQoL obtained in LA-NSCLC clinical trials (n=19) was scarce, particularly compared to metastatic disease trials (n=85). No conclusions could be drawn on the most optimal treatment in terms of HRQoL. Both reviews showed a large variability in the use of HRQoL instruments, analysing techniques, reporting of data, missing data and follow-up time. The methodological quality was generally poor but improved over time. Therefore, more awareness and encouragement to adequately collect, analyse and report HRQoL to inform policy and to aid clinical decision-making to maintain and improve HRQoL in this vulnerable population is needed.

The second specific objective aimed to evaluate HRQoL and toxicity in ES- and LA-NSCLC receiving loco-regional radiotherapy with(out) chemotherapy in the large international, prospective, real-world REQUITE study. In the entire population, HRQoL, nor its domains, did significantly change over time, except for a significant decrease in cognitive functioning. However, at an individual level, meaningful clinical deteriorations and improvements were seen, even if the majority of patients remained stable in terms of MCID in HRQoL and associated domains. The typical acute toxicities of radiation-dermatitis, dysphagia and esophagitis peaked at 3 months after start of radiotherapy and decreased thereafter. Radiotherapy also alleviated pre-existing symptoms, particularly dyspnea and cough. Individual radiation-induced toxicity, particularly dyspnea, chest wall pain and pericarditis subsequently affected HRQoL and its functional domains negatively. This stresses the importance of understanding individual toxicity and its impact on HRQoL to help maintain and improve HRQoL and general wellbeing in this heterogeneous patient population.

The last specific objective prospectively evaluated HRQoL, toxicity and NCF in LA- and metastatic NSCLC in a real-world institutional context. As was seen in the REQUITE study, standard systemic treatment with or without radiotherapy had a limited impact on overall HRQoL and its domains. At one year post-treatment, most improvement in overall HRQoL was seen. Furthermore, at that moment, meaningful improvements in pre-existing symptoms and occurrence of, mainly acute, treatment-induced toxicities were reported. Meaningful neurocognitive impairment following treatment was observed in only a small proportion of patients. This is contradictory with previously conducted studies in the same patient population, showing a higher impact. This may be explained by the differences in test battery and measurement moments, as our study only measured NCF at 2/3 months post-chemotherapy.

Systemic treatment and loco-regional radiotherapy may negatively impact HRQoL and NCF of all stages of lung cancer, but individual differences are substantial and meaningful improvements are equally observed. It is therefore necessary to understand treatment-induced toxicity and its impact on HRQoL and NCF on an individual patient level to support treatment decision-making in clinical practice, to optimize both the quality and the quantity of the remaining life.
CURRICULUM VITAE:

Professional positions

PhD fellow – Scientific employee | Ghent University Hospital, Belgium | 2015 - current

Intern | World Health Organisation Center for Health Development, Japan | 2014

Research intern | Medical Committee Netherlands-Vietnam (MCNV), Vietnam | 2013

EDUCATION

PhD program in Health Sciences | Ghent University, Belgium | 2015 – current

Master in International development studies | Université Grenoble Alpes, France | 2014

Master of science in Health Sciences | Free University of Amsterdam, the Netherlands | 2013

Bachelor of science in European Public Health | Maastricht University, the Netherlands | 2011

PUBLICATIONS

Van der Weijst L, et al. The impact of clinician-reported toxicity on patient-reported health-related quality of life in non-small cell lung cancer patients enrolled in the REQUITE study. [In preparation]


