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Individual versus standard quality of life assessment in a phase II clinical trial in mesothelioma patients: Feasibility and responsiveness to clinical changes

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Summary
Background: In patients with malignant pleural mesothelioma undergoing a multimodality therapy, treatment toxicity may outweigh the benefit of progression-free survival. The subjective experience across different treatment phases is an important clinical outcome. This study compares a standard with an individual quality of life (QoL) measure used in a multi-center phase II trial.
Patients and methods: Sixty-one patients with stage I—III technically operable pleural mesothelioma were treated with preoperative chemotherapy, followed by pleuropneumonectomy and subsequent radiotherapy. QoL was assessed at baseline, at day 1 of cycle 3, and 1, 3 and 6 months post-surgery by using the Rotterdam Symptom Checklist (RSCL) and the Schedule for the Evaluation of Quality of Life-Direct Weighting (SEIQoL-DW), a measure that is based on five individually nominated and weighted QoL-domains.
Results: Completion rates were 98% (RSCL) and 92% (SEIQoL) at baseline and 98%/89% at cycle 3, respectively. Of the operated patients ($N = 45$) RSCL and SEIQoL were available from 86%/72%, 93%/74%, and 94%/76% at months 1, 3, and 6 post-surgery. Average assessment time for the

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SEIQoL was 24 min compared to 8 min needed for the RSCL. Median changes from baseline indicate that both RSCL QoL overall score and SEIQoL index remained stable during chemotherapy with a clinically significant deterioration (change $\geq$ 8 points) 1 month after surgery (median change of −66 and −14 for RSCL and SEIQoL, respectively). RSCL QoL overall scores improved thereafter, but remained beneath baseline level until 6 months after surgery. SEIQoL scores improved to baseline-level at month 3 after surgery, but worsened again at month 6. RSCL QoL overall score and SEIQoL index were moderately correlated at baseline ($r = .30$; $p \leq .05$) and at 6-month follow-up ($r = .42$; $p \leq .05$) but not at the other time points.

Conclusion: The SEIQoL assessment seems to be feasible within a phase II clinical trial, but may require more effort from staff. More distinctive QoL changes in accordance with clinical changes were measured with the RSCL. Our findings suggest that the two measures are not interchangeable: the RSCL is to favor when mainly information related to the course of disease- and treatment is of interest.

1. Introduction

Patients with malignant pleural mesothelioma are confronted with a potentially short survival time, with a median of 7—13 months after diagnosis [1,2]. The side effects of a treatment may outweigh the benefit of progression-free survival, in particular if patients have to undergo extensive multimodality therapy, including chemotherapy, surgery and radiotherapy. Given this situation the subjective experience of illness across the different phases of a treatment is an important outcome.

In clinical lung cancer trials quality of life (QoL) is usually assessed by using standardized, validated questionnaires (e.g. FACT-L [3], EORTC QLQ-LC13 [4], or the LCSS [5]), consisting of multi-item scales with predetermined questions, response formats and relative weights applied to the responses. Such standardized measures are easy and quick to complete and allow comparisons across studies. However, standardized assessments may not adequately reflect the perspective of the individual assessed [6]. In addition, standardized measures ignore individual variations of the relative importance of certain QL-domains, and in particular do not reflect changes in the relevance of QL-domains over time [7]. For example, patients with early colon cancer indicated an increasing importance of their functional performance some months after primary surgery [8]. These critical arguments led to the development of the Schedule for the Evaluation of Individual Quality of Life (SEIQoL; [9]) and its short form the SEIQoL-DW ('Direct Weighting' [7]). It is based on the definition that 'quality of life is what the individual determines it to be'. Respondents are allowed to nominate the five QoL domains most important to them, rate their level of functioning or satisfaction with each, and indicate the relative importance of each to their overall QoL. Based on this feature, the SEIQoL is expected to have a higher responsiveness to individually relevant disease and treatment sequelae. The information gained by this measure should enhance physicians 'insight into patients' view of a given situation.

The SEIQoL-DW has been validated in healthy individuals [10] as well as in non-healthy populations (i.e. cancer and non-cancer) [7,11—13]. Studies including phase I clinical trials reporting on the feasibility of the SEIQoL-DW in cancer patients or survivors have shown that this tool is quick to administer and easy to complete [14,15] and can provide helpful information for individual care [16—18].

However, in clinical trials the potentially higher patient burden as well as additional staff and time requirements needed to assess individual QoL have to be justified by useful information relevant for evaluating the outcome of treatments. To our knowledge, standard QOL instruments have never been compared to the SEIQoL-DW within a phase II clinical trial.

We prospectively evaluated the feasibility of using the SEIQoL-DW within a multi-center phase II clinical trial, and compared this measure with the Rotterdam Symptom Checklist (RSCL), a standard measure assessing psychological and physical distress in cancer patients [19], with respect to responsiveness to a multimodal treatment. Although the RSCL has not been validated particularly for patients with mesothelioma, two phase II trial investigating QoL in this patient group showed that the information gained with the RSCL adequately reflects the expected clinical changes [20,21].

The details and outcome of the clinical trial examining neoadjuvant chemotherapy followed by pleuropneumonectomy, and subsequent radiotherapy in patients with stage I—III pleural mesothelioma have been previously reported [21].

2. Material and methods

2.1. Patients

Sixty-one patients with histologically confirmed diagnosis of a stage I—III pleural mesothelioma, a WHO performance status of 0—2, and considered to be completely resectable were entered in the study between July 2000 and June 2003. Patients were to receive 3 cycles of preoperative chemotherapy (cisplatin 80 mg/m^2 at day 1 and gemcitabine 1000 mg/m^2 at days 1, 8, and 15, given every 28 days), followed by pleuropneumonectomy within 6 weeks. Radiotherapy to areas of incomplete resection and high-risk areas was planned to start 6—8 weeks after surgery. The protocol was developed by the Swiss Group for Clinical Cancer