Supportive Care in Cancer (2019) 27:4697–4704
https://doi.org/10.1007/s00520-019-04777-2

ORIGINAL ARTICLE

The role of patient-reported outcomes in outpatients receiving active anti-cancer treatment: impact on patients' quality of life

Chiara Baratelli[1,2,3] · Carmela Giovanna Cleopatra Turco[1,2] · Gaetano Lacidogna[1] · Elisa Sperti[1] · Francesca Vignani[1] · Donatella Marino[1,2] · Clizia Zichi[1,2] · Emmanuele De Luca[1,2] · Marco Audisio[1,2] · Daniela Ballaminut[1] · Annalisa Bellezza[1] · Paola Chiotto[1] · Giovanna Ciriolo[1] · Rossella Comite[1] · Fulvia Codegone[1] · Santina Florio[1] · Luisa Fusco[1] · Laura Polimeno[1] · Donatella Pozzi[1] · Eliana Zilio[1] · Sabrina Terzolo[1] · Massimo Di Maio[1,2]

Received: 28 August 2018 / Accepted: 25 March 2019 / Published online: 4 April 2019

Abstract

Introduction Patient-reported outcomes (PROs) are the gold standard to describe subjective symptoms. Nurses can be successfully involved in collecting symptom information, because of their direct relationship with the patient. In order to improve clinical management of outpatients receiving active anti-cancer treatment, we introduced in routine clinical practice an assessment of patient-reported symptoms and toxicities, starting from January 2018. Our hypothesis was that this could help to better control symptoms, improving patients' quality of life (QoL).

Methods Eligible patients were receiving an active anti-cancer treatment, as outpatients. Patients included in the control group (treated in 2017) underwent "usual" visits (group A), while patients treated in 2018, before each visit received a questionnaire by a dedicated nurse, in order to provide information about symptoms and toxicities (group B). Primary objective was the comparison of QoL changes, measured by EORTC QLQ-C30.

Results A total of 211 patients have been analyzed (119 group A; 92 group B). After 1 month, mean change from baseline of global QoL was − 1.68 in group A and + 2.54 in group B ($p = 0.004$, effect size 0.20). Group B showed significantly better mean changes for fatigue, pain, and appetite loss. Proportion of patients obtaining a clinically significant improvement in global QoL score was higher in group B (32.6%) compared to group A (19.3%, $p = 0.04$). Patients' satisfaction with questionnaire was high.

Conclusion Introduction of PROs in clinical practice, thanks to an active role of nurses, was feasible, produced high patients' satisfaction and a significant QoL improvement, compared to the traditional modality of visit.

Keywords Patient-reported outcomes · Quality of life · Side effects · Toxicity

Introduction

The proper management of cancer patients receiving antineoplastic treatments is based on many factors, including an adequate collection of the information about symptoms and side effects. Oncological therapies can significantly affect quality of life (QoL) of patients, and a proper description of subjective symptoms is crucial.

Several instruments can be used to describe an adverse event and its impact on patient's daily activities; they include the Common Toxicity Criteria for Adverse Events (CTCAE), which provide a list of potential side effects and a grading scale to quantify the entity of each toxicity [1] and the questionnaires on health-related quality of life (as the European Organization for Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ) (http://groups.eortc.be/

Equally contributing first authors Chiara Baratelli, Carmela Giovanna Cleopatra Turco

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00520-019-04777-2) contains supplementary material, which is available to authorized users.

✉ Massimo Di Maio
massimo.dimaio@unito.it

[1] Division of Medical Oncology, Ordine Mauriziano Hospital, Turin, Italy

[2] Department of Oncology, University of Turin, Via Magellano 1, 10128 Turin, Italy

[3] Present address: Division of Medical Oncology, San Luigi Gonzaga Hospital, Orbassano, TO, Italy

qol/eortc-qlq-c30) or the Functional Assessment of Cancer Therapy (FACT)) (http://www.facit.org/FACITOrg/Questionnaires) which, in addition to functional scales and questions about global quality of life and well-being, ask the patient about the presence and intensity of several symptoms.

As a matter of fact, data about anti-cancer drug toxicities and patient symptoms are mainly based on clinicians' reports [2]; nevertheless, an adequate collection of subjective symptoms requires a targeted discussion with the patient, in order to reduce the risk of under-reporting [3, 4], which may have clinical consequences.

A patient-reported outcome (PRO) is the direct report of a patient's condition, not interpreted nor modified from a clinician [5]. Currently, PROs are considered the gold standard to describe subjective symptoms [6, 7]. Several studies have compared the description of a subjective toxicity using PROs versus the report by physicians; in most cases, a relevant difference has been described, with a suboptimal agreement and a relevant underestimation of the incidence and the entity of symptoms by clinicians [3, 4, 8–11].

Even when the report of side effects by patients and clinicians has been analyzed using data prospectively collected within randomized trials, a low level of agreement was demonstrated, with a significant underreporting by the physicians of the presence and the severity of each side effect [11]. As reported by Basch et al. [2], some models estimating overall survival according to the entity of the reported symptoms demonstrated more accuracy when based on both patient and clinician description of symptoms and toxicities than when including the clinician estimation alone. The same author presented at ASCO 2017 how an adequate collection of symptoms and toxicities directly from the patients is strictly related to the outcome; median overall survival in the arm using PROs was 5 months longer than the one of the standard arm (31.2 vs. 26.0 months, $p = 0.03$) [12].

Several trials, designed to analyze the usefulness of patients' self-reporting of symptoms and toxicities during oncologic treatments, have directly involved the nurses [13, 14]. However, their role mainly consisted in receiving e-mail alerts in case of a high-grade side effect or worsening symptoms; in particular, in the two mentioned trials, patients receiving chemotherapy for solid tumors were asked to directly report their symptoms through electronic devices, and in case of relevant disturbs, the dedicated nurses received a warning. More generally, nurses could be successfully involved in collecting toxicity information, because of their direct relationship with the patient. Agreement in the description of symptoms between patients and nurses can be stronger than the agreement between patients and physicians [10].

In order to optimize the involvement of nurses and to improve the clinical management of outpatients receiving active anti-cancer treatment, we decided to introduce a patient-based assessment of symptoms and toxicities in routine clinical practice, starting from January 2018. Before each medical visit, information was collected using dedicated questionnaires, administered by nurses and self-filled by patients. Nurses collected the questionnaires, making the written information available to physicians before the medical visit.

In this report, we describe the results of this clinical single-center experience. In detail, the study is designed as a comparison of two groups of patients: a first group, who had been visited in 2017 using the "usual" modality of toxicity and symptoms collection and management, and a second group, visited in 2018, after the introduction of patient-based assessment of symptoms and toxicities in routine clinical practice. Primary measure of outcome was the impact on global QoL: when this observational comparison was planned, our hypothesis was that the collection of patient-reported symptom toxicities could help to better control side effects, improving patients' QoL.

Materials and methods

Patients and procedures

To be eligible for the analysis, all the patients had to be treated with an active anti-cancer treatment, as outpatients, at the Day Hospital of the Division of Medical Oncology, Mauriziano Hospital in Turin, Italy. In addition, to be suitable for toxicity data collection, the patients must have received at least one administration of therapy at the time of the first evaluation. Patients included in the control group (who were treated in 2017) underwent only "usual" medical visits, while to patients treated in 2018, a dedicated nurse administered before each visit a specifically designed questionnaire, in order to estimate symptoms and toxicities. The role of the nurse was to explain the patient the correct way of filling the questionnaire; subsequently, the nurse collected the questionnaire and delivered it to the physician, who could consult it before the visit. When the questionnaire was introduced in clinical practice, all the physicians were instructed to pay attention to the information reported in the questionnaire. After the visit, the questionnaire was transcripted into the study database and then archived into the patient's medical records.

With the aim of describing QoL changes, all patients received two EORTC QLQ-C30 questionnaires [15]: the second was scheduled approximately 1 month after the first, although the interval between visits was imposed by clinical practice, determining some variability in timing of administration of questionnaires among patients. All patients signed a written consent before filling questionnaires.

Study objectives

Primary objective was the comparison between the two patients' groups in terms of QoL changes, in order to verify if the patient-based assessment of toxicities and symptoms by nurses could significantly improve patients' QoL.

Secondary objectives were the description of the evaluation of toxicities and symptoms in terms of feasibility, patients' compliance and patients' satisfaction.

Questionnaires

Using a dedicated paper questionnaire, a patient-reported collection of symptoms and toxicities was performed, starting in January 2018. Before its introduction in clinical practice, the questionnaire was specifically designed by physicians and nurses; this instrument has not been externally validated.

Toxicity questionnaire

In detail, the questionnaire contains 13 questions, corresponding to 13 symptoms/toxicities (mouth problems, nausea, vomiting, constipation, diarrhea, dyspnea, skin problems, nail problems, itching, hand/foot problems, fatigue, pain, other issues). Patient was asked to refer to the period elapsed since previous therapy, and a final question interrogated about the persistence of problems at the moment of the visit. All the questions had the same five response categories: "Not at all", "A little", "Quite a bit", "Much", and "Very much". When patients reported any pain, they had to fill a 11-point visual analog scale to describe its intensity.

Satisfaction questionnaire

Patients filling the toxicity questionnaire received also a satisfaction questionnaire, consisting of three questions asking if the instrument was clear and easy to fill, if it was useful to better describe toxicity, and if it was efficacious in improving communication between patient and physician. In detail, the three questions were (1) Do you judge the questionnaire of evaluation of side effects clear and easy to understand? (2) Do you judge the questionnaire of evaluation of side effects useful for the reporting of symptoms and side effects? (3) Do you think that the use of the questionnaire of evaluation of side effects made easier your communication with the physician?

Quality of life questionnaires

In both groups, two EORTC QLQ-C30 questionnaires were administered. EORTC QLQ-C30 [15] is a 30-item questionnaire composed of five multi-item functional subscales (physical, role, emotional, social, and cognitive functioning), three multi-item symptom scales (fatigue, pain, and emesis), a global health status subscale, and six single items to assess financial impact, dyspnea, sleep disturbance, appetite, diarrhea, and constipation, during the previous week. Global QoL is measured by items 29 ("How would you rate your overall health during the past week?") and 30 ("How would you rate your overall quality of life during the past week?"). With the exception of items 29 and 30, which have seven response categories, all the remaining items have the same four response categories: "Not at all", "A little", "Quite a bit" and "Very Much".

According to EORTC QLQ-C30 scoring manual, scores for multi-item scales are calculated by deriving mean raw scores, calculated by the addition of item responses divided by the number of items [16]. Subsequently, a linear transformation is used to standardize both mean raw scores for multi-item scales and scores for single items, transforming them linearly into scales ranging from 0 to 100, based on this formula: Score = [(raw score-1) × 100] / range. Range is the difference between the maximum and minimum possible value of the raw score: all items are scored from 1 to 4, giving a range = 3, with the exception of items 29 and 30, which are scored from 1 to 7, giving a range = 6.

For functional subscales and global health status, higher values represent better function. For symptom scales, higher values represent greater severity of symptoms.

Statistical issues

Before starting the observation, change in global QoL of QLQ-C30 was used to estimate sample size. A 90% power to detect an effect size of 0.50 (i.e., a difference between mean scores of global health status equal to 50% of the standard deviation) was planned. Such an effect size has been correlated with 'moderate' or 'very much' positive changes in a subjective satisfaction questionnaire [17]. With two-sided significance level 0.05, 172 evaluable patients were needed.

For each domain or symptom, mean changes within groups from baseline to the follow-up assessment were reported. A positive value represents an improvement in functional scales and a worsening in symptom scales. Only patients with available values at baseline and at follow-up assessment were included in the analysis. Differences from baseline scores were compared between groups by a multivariable linear regression model, using baseline values as covariates.

QoL response from baseline was derived for global QoL scores as follows: a change of at least 10 points from baseline was defined as clinically relevant [17]; patients were considered improved if they reported a score of 10 or more points better than baseline and were considered worsened if they reported a score of 10 or more points worse than baseline. Patients whose scores changed less than 10 points were considered stable.

All statistical tests were two-tailed and p values less than 0.05 were considered statistically significant. Because of the exploratory nature of the QoL analysis, adjustment for multiple item comparisons was not performed. Analyses were performed with SPSS for Windows, version 25.0.

Results

Overall, 229 patients, receiving an active anti-cancer treatment between November 2017 and June 2018, were eligible for this analysis. Namely, 131 patients were visited, in 2017, according to the standard modality (only medical evaluation) (group A) and 98 patients were visited, in 2018, adding the patient-based assessment of toxicity to the visit with the oncologist (group B). Eighteen patients (12 in group A and 6 in group B) have been excluded because they had only baseline evaluation, without follow-up questionnaires. Therefore, 211 patients are included in this report (119 in group A and 92 in group B).

Main characteristics of the two groups are detailed in Table 1. The majority of patients were males (59% and 58% in group A and group B, respectively, Chi-square test p = 0.86) and median age was 67 and 68 years, in group A and group B, respectively (Wilcoxon test $p = 0.55$). The two groups were similar in terms of type of tumor (the two most common tumors, in both groups, were colorectal and lung cancer, Chi-square test $p = 0.62$) and in terms of type of treatment (more than 90% of patients were treated with chemotherapy, being platinum-based treatment the most common therapy, Chi-square test $p = 0.60$) without statistically significant differences. The proportion of patients receiving a second- or next-line treatment was significantly higher in group A (Chi-square test $p = 0.045$). However, most patients were receiving a first-line treatment for advanced disease (58% and 67% in group A and group B, respectively), while a minority was receiving an adjuvant treatment (15% and 22%, respectively).

The two groups were comparable in terms of baseline QoL scores (Supplemental Table A1, online only). Mean baseline global QoL score was 57.14 (standard deviation 22.37) in group A and 61.14 (standard deviation 21.16) in group B (Wilcoxon test $p = 0.25$). Similarly, baseline scores for functional scales and symptoms were not significantly different between the two groups with the exception of cognitive functioning and social functioning, both worse in group A compared to group B. The time interval between the baseline and the second questionnaire was similar in the two groups: median number of days was 35 (interquartile range, 28–43) in group A and 35 (interquartile range 29–41) in group B (Wilcoxon test $p = 0.23$).

Mean changes from baseline of all QoL domains are displayed in Fig. 1, and results of the multivariable linear regression models for all QoL domains are reported in Supplemental Table A2. Global QoL was significantly improved in patients receiving the questionnaire about symptoms and toxicity compared to the control group. Namely, mean change from baseline of global QoL was − 1.68 (standard error 1.88) in group A and + 2.54 (standard error 2.32) in group B ($p = 0.004$, effect size 0.20). Difference in global QoL between the two groups remained statistically significant (p = 0.019) in an exploratory model including as covariates those items that were significantly different between groups (cognitive functioning and social functioning). There were no statistically significant differences in mean changes from baseline for all functioning scales between the two groups. As for symptoms, mean changes from baseline in the group of patients receiving the questionnaire about symptoms and toxicity compared to the control group were significantly better for fatigue, pain, and appetite loss. Namely, mean change from baseline was + 7.10 (standard error 1.88) in group A and + 2.54 (standard error 2.44) in group B for fatigue ($p = 0.029$, effect size 0.21); + 7.42 (standard error 1.92) in group A and 0.00 (standard error 3.17) in group B for pain ($p = 0.016$, effect size 0.28); + 5.88 (standard error 2.57) in group A and − 3.26 in group B (standard error 3.96) for appetite loss (p = 0.003, effect size 0.27). There were no significant differences between the two groups in terms of nausea and vomiting, sleeping disturbance, constipation, diarrhea, financial distress, and dyspnea.

The proportion of patients obtaining a clinically significant improvement in global QoL score was significantly higher in group B compared to group A ($p = 0.04$). As reported in Fig. 2, an improvement was observed in 23 patients in group A (19.3%, 95% confidence interval 13.2% - 27.3%) and in 30 patients in group B (32.6%, 95% confidence interval 23.9–42.7%).

All 98 patients of group B filled the satisfaction questionnaire about the administration of the toxicity questionnaire. Satisfaction was very high: 92% declared that the questionnaire was clear and easy to understand, 93% declared that it was useful to report symptoms and side effects, and 88% thought that the questionnaire was a valid instrument to improve communication with the physician.

Discussion

In our experience, the introduction in clinical practice of a patient-based evaluation of toxicity and symptoms was associated with a statistically significant improvement in health-related QoL, compared to the traditional modality of visit. Accordingly, we observed significantly better trends in several symptoms, namely in pain, in fatigue, and in appetite loss. Interestingly, the positive impact on global QoL and

Table 1 Main characteristics of patients eligible for the analysis

	Group A	Group B	*P* value	All patients
Number of patients	119	92		211
Gender			0.86	
Males	70 (58.8%)	53 (57.6%)		123 (58.3%)
Females	49 (41.2%)	39 (42.4%)		88 (41.7%)
Age			0.55	
Median (range)	67 (27–84)	68 (35–82)		67/ (27–84)
Type of tumor			0.62[b]	
Colorectal cancer	42 (35.3%)	27 (29.3%)		69 (32.7%)
Lung cancer	25 (21.0%)	17 (18.5%)		42 (19.9%)
Pancreatic cancer	14 (11.8%)	17 (18.5%)		31 (14.7%)
Genitourinary cancer	12 (10.1%)	8 (8.7%)		20 (9.5%)
Head and neck cancer	5 (4.2%)	9 (9.8%)		14 (6.6%)
Liver/biliary cancer	6 (5.0%)	5 (5.4%)		11 (5.2%)
Gastric cancer	6 (5.0%)	3 (3.3%)		9 (4.3%)
Mesothelioma	6 (5.0%)	2 (2.2%)		8 (3.8%)
Breast cancer	3 (2.5%)	2 (2.2%)		5 (2.4%)
Unknown primary	–	2 (2.2%)		2 (0.9%)
Type of treatment			0.60	
Cisplatin-based	27 (22.7%)	22 (23.9%)		49 (23.2%)
Oxaliplatin or irinotecan-based	43 (36.1%)	26 (28.3%)		69 (32.7%)
Carboplatin-based	5 (4.2%)	3 (3.3%)		8 (3.8%)
Other cytotoxic agents	33 (27.7%)	32 (34.8%)		65 (30.8%)
Immunotherapy	7 (5.9%)	8 (8.7%)		15 (7.1%)
Other agents	4 (3.4%)	1 (1.1%)		5 (2.4%)
Setting			0.045	
Adjuvant treatment	18 (15.1%)	20 (21.7%)		38 (18.0%)
First-line treatment[a]	70 (58.8%)	62 (67.4%)		132 (62.6%)
Second-line treatment	24 (20.2%)	8 (8.7%)		32 (15.2%)
Third- or fourth-line treatment	7 (5.9%)	2 (1.1%)		9 (3.8%)

[a] Including neo-adjuvant treatments

[b] For this test, tumors with less than 10 cases in both groups were grouped together

symptoms was relatively fast, being observed a few weeks after the start of observation.

Nurses had a fundamental role in the introduction of PROs in our clinical practice. In detail, a dedicated nurse administered the questionnaires, explained their objective and the proper way of filling, and finally delivered them to the physician before the visit. Given that, on average, patients spend more time with nurses than with physicians, this modality can be really useful to optimize the communication between patients and health personnel, particularly in terms of reporting of symptoms and toxicities.

In the traditional modality of visit, discussion of symptoms and toxicities was left to the unstructured interview performed by the physicians; this way of collection can imply substantial under-reporting of many symptoms, compared to the use of PROs [5]. However, under-reporting by physicians does not automatically imply under-treatment: in principle, even if not reporting one or more symptoms in patient's file, the physician could have adequately managed all clinically relevant problems.

Recently, important evidence has been produced supporting the role of PROs and proactive management of symptoms and toxicities in cancer outpatients [18–23]. In 2016, a randomized trial by Basch and colleagues was conducted in 766 outpatients receiving routine chemotherapy for advanced solid tumors [14]. Primary endpoint was QoL change after 6 months, measured by the EuroQoL EQ-5D Index. Patients assigned to control arm received usual care, while subjects assigned to the experimental arm were asked to electronically report their symptoms remotely from home (or during visits), using tablets or computer kiosks. Doctors received a report of symptoms referred by patients during visits, and in addition nurses received email alerts when patients reported severe or worsening symptoms. More patients in

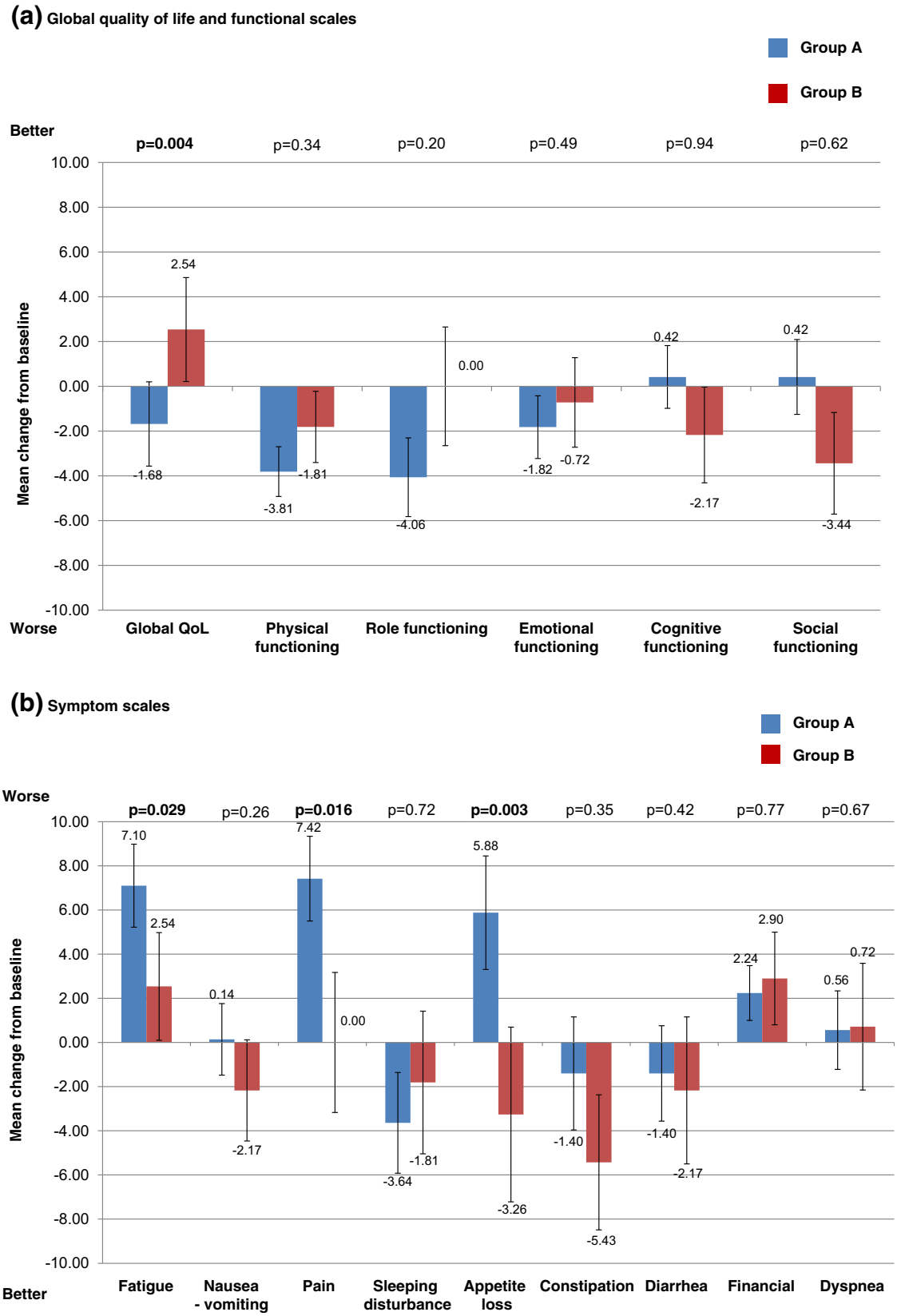

Fig. 1 Mean changes from baseline of all quality of life (QoL) domains. **a** Global QoL and functional scales (positive indicates improvement); **b** symptom scales (negative indicates improvement). Blue bars: group A ("usual" medical visit); red bars: group B (medical visit + patient-based assessment of symptoms and toxicities)

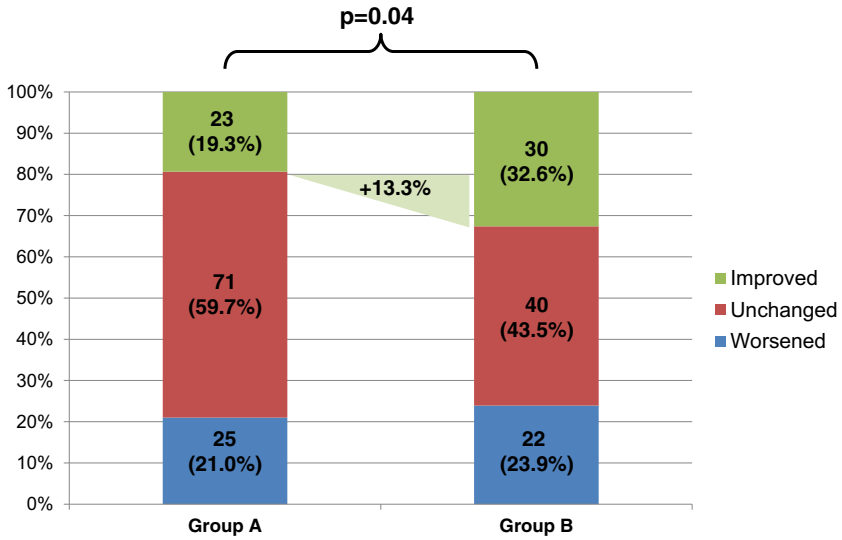

Fig. 2 Proportion of patients with health-related global quality-of-life (QoL) changes at second questionnaire compared with baseline. Patients were considered improved if they reported a score of 10 or more points better than baseline (green bars) and were considered worsened if they reported a score 10 or more points worse than baseline (blue bars). Patients whose scores changed less than 10 points were considered stable (red bars). *P* value was calculated using Chi-square test

the self-reporting arm experienced QoL benefit ($p = 0.001$). Of note, a secondary analysis of the same trial showed a significant prolongation in overall survival for patients assigned to the experimental arm, with a 5-month difference in median survival [12]. The authors themselves hypothesized that the integration of PROs into usual care, allowing early reaction to patient alerts, could prevent adverse downstream consequences, or could allow continuation of chemotherapy longer than usual care, with potential improvement in treatment efficacy.

Of note, we observed a better trend in pain control, which could reasonably play a relevant role in the better trend in global QoL. In principle, a written report of pain presence and severity could substantially help the communication, favoring a better management. On the other side, we described a better tendency in other symptoms that are not obviously managed with pharmacologic interventions. These could be false positive results (we did not correct for multiplicity), or a consequence of the improved pain control, or even a "placebo" effect of the questionnaire itself, giving the patients more satisfaction in reporting some symptoms that could be otherwise neglected.

We acknowledge that our observational analysis is methodologically weaker than a randomized trial. We originally planned to conduct a randomized study, assigning patients to usual modality of visit alone or with the addition of a dedicated evaluation of symptoms and toxicities. However, following the results of the trial by Basch [14], many oncologists and scientific societies encourage the adoption of patient-reported outcomes in clinical practice in order to improve patient-physician communication, especially in settings characterized by high amount of symptoms. Consequently, we convinced ourselves that randomization was no more acceptable, because adoption of PROs could not be considered experimental anymore. Consequently, we decided to simply describe the introduction of PROs in our clinical practice, in terms of feasibility, patients' compliance and satisfaction, and impact on QoL, using a previous cohort of patients as control group. The two groups were treated at a distance of a few months, by the same staff of physicians and nurses, and were quite similar in terms of age, type of tumor, type of treatment, and baseline QoL scores: consequently, the bias in the comparison between the two cohorts should be reasonably limited. Another relevant limitation of our experience is that the questionnaire adopted for the evaluation of symptoms and toxicities had not been previously validated, and this limits the validity of the results. However, the significant improvement we have observed in global QoL demonstrates that higher attention to the reporting of symptoms and toxicities can have a significant clinical impact. Following the discussion of results, the whole team of physicians and nurses agreed on continuing the administration of the questionnaire to all patients in clinical practice.

Of course, statistically significant differences are not necessarily clinically relevant. Difference in mean change from baseline in global QoL between the two groups was about 4 points, lower than the 10-point difference that has recently been defined as "clinically relevant" [17]. Coherently, the effect size (0.20) was quite small. However, there was a significant increase (+ 13.3%) in the proportion of patients obtaining a clinically significant improvement in global QoL, which considering the limited cost of our procedure (intended as a nurses and physicians time), can be considered cost-effective.

One reason for the limited magnitude of QoL benefit observed in our experience is that PROs were collected with a paper questionnaire at the time of visit, and there was no "real-time" report. In the future, we are planning to further improve the collection of PROs in our clinical practice, with the use of electronic instruments.

In conclusion, the introduction of PROs in clinical practice, thanks to an active role of nurses, was feasible, was associated with a high grade of patients' satisfaction, and was related to a significant QoL improvement, compared to the traditional modality of visit. These results encourage the wide application of PROs in clinical practice, as strongly suggested by a growing body of evidence in recent years.

Acknowledgments The authors wish to thank all the patients who were included in the analysis, and their caregivers.

Funding Massimo Di Maio is recipient of a research funding from the CRT Foundation (Turin, Italy) for this project on the impact on quality of life of the systematic evaluation of toxicity with patient-reported outcomes in patients with solid cancer (CRT grant number 46333, "Richieste ordinarie 2015"). This research funding allowed the attendance of Chiara Baratelli, Carmela Giovanna Cleopatra Turco and Donatella Marino at Ordine Mauriziano Hospital.

Compliance with ethical standards

Conflict of interest We state that there are no conflict of interest do declare. We have full control of all primary data and we agree to allow the journal to review our data if requested.

References

1. The National Cancer Institute (2006) Common terminology criteria for adverse events, version 3.0. [online], http://ctep.cancer.gov/protocolDevelopment/17electronic_applications/docs/ctcaev3.pdf
2. Basch E, Bennett A, Pietanza MC (2011) Use of patient-reported outcomes to improve the predictive accuracy of clinician-reported adverse events. J Natl Cancer Inst 103:1808–1810
3. Petersen MA, Larsen H, Pedersen L, Sonne N, Groenvold M (2006) Assessing health-related quality of life in palliative care: comparing patient and physician assessments. Eur J Cancer 42:1159–1166
4. Fromme EK, Eilers KM, Mori M, Hsieh YC, Beer TM (2004) How accurate is clinician reporting of chemotherapy adverse effects? A comparison with patient-reported symptoms from the quality-of-life questionnaire C30. J Clin Oncol 22:3485–183490
5. Di Maio M, Basch E, Bryce J, Perrone F (2016) Patient-reported outcomes in the evaluation of toxicity of anticancer treatments. Nat Rev Clin Oncol 13(5):319–325
6. U.S. Food and Drug Administration (2015) Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. [online], http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf
7. European Medicines Agency (2005) Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQL) measures in the evaluation of medicinal products. [online], http://www.ema.europa.eu/docs/19en_GB/document_library/Scientific_guideline/2009/09/WC500003637.pdf
8. Basch E, Iasonos A, McDonough T, Barz A, Culkin A, Kris MG, Scher HI, Schrag D (2006) Patient versus clinician symptom reporting using the National Cancer Institute common terminology criteria for adverse events: results of a questionnaire based study. Lancet Oncol 7:903–909
9. Grossman SA, Sheidler VR, Swedeen K, Mucenski J, Piantadosi S (1991) Correlation of patient and caregiver ratings of cancer pain. J Pain Symptom Manag 6:53–57
10. Cirillo M, Venturini M, Ciccarelli L, Coati F, Bortolami O, Verlato G (2009) Clinician versus nurse symptom reporting using the National Cancer Institute-common terminology criteria for adverse events during chemotherapy: results of a comparison based on patient's self-reported questionnaire. Ann Oncol 20:1929–1935
11. Di Maio M, Gallo C, Leighl NB et al (2015) Symptomatic toxicities experienced during anticancer treatment: agreement between patient and physician reporting in three randomized trials. J Clin Oncol 33:910–915
12. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, Schrag D (2017) Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. JAMA 318(2):197–198
13. Judson TJ, Bennett AV, Rogak LJ, Sit L, Barz A, Kris MG, Hudis CA, Scher HI, Sabattini P, Schrag D, Basch E (2013) Feasibility of long-term patient self-reporting of toxicities from home via the internet during routine chemotherapy. J Clin Oncol 31(20):2580–2585
14. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett AV, Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA, Schrag D (2016) Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. J Clin Oncol 34(6):557–565
15. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, Haes JCJM, Kaasa S, Klee M, Osoba D, Razavi D, Rofe PB, Schraub S, Sneeuw K, Sullivan M, Takeda F (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85(5):365–376
16. Fayers P, Aaronson NK, Bjordal K et al (1999) on behalf of the EORTC Quality of Life Study Group EORTC QLQ-C30 Scoring Manual, 2nd edn. EORTC, Brussels (Belgium)
17. Osoba D, Rodrigues G, Myles J, Zee B, Pater J (1998) Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 16(1):139–144
18. Sperti E, Di Maio M (2017) Outcomes research: integrating PROs into the clinic - overall survival benefit or not, it's worth the trouble. Nat Rev Clin Oncol 14(9):529–530
19. Howell D, Molloy S, Wilkinson K, Green E, Orchard K, Wang K, Liberty J (2015) Patient-reported outcomes in routine cancer clinical practice: a scoping review of use, impact on health outcomes, and implementation factors. Ann Oncol 26:1846–1858
20. Valderas JM, Kotzeva A, Espallargues M, Guyatt G, Ferrans CE, Halyard MY, Revicki DA, Symonds T, Parada A, Alonso J (2008) The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Qual Life Res 17:179–193
21. Chen J, Ou L, Hollis SJ (2013) A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. BMC Health Serv Res 13(211)
22. Kotronoulas G, Kearney N, Maguire R, Harrow A, di Domenico D, Croy S, MacGillivray S (2014) What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 32:1480–1501
23. Stover AM, Basch EM (2016) Implementation of symptom questionnaires into oncology workflow. J Oncol Pract 12(10):859–862