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A methodological investigation to define a clinically relevant cut-off point in the ordinal scale of the EORTC QLQ-C30 questionnaire.

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BACKGROUND

Symptom assessment has become standard in cancer clinical trials. This can be done by the clinical staff or alternatively by the patients. Interest in patient reported outcomes as a more objective approach has increased over the years. Current studies investigate the agreement between clinician and patient reported outcomes. Patient reporting of symptoms could add to the current approach for symptom monitoring in cancer treatment trials. Two frequently used instruments in cancer clincial trials are the NCI-CTC (assessed by the clinician) and the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 (assessed by the patient). More details about these are reported in the box below.

EORTC QLQ-C30

The EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of cancer patients. The questionnaire is designed to measure cancer patients' physical, psychological and social functions. The questionnaire is composed of 5 multi item scales (physical, role, social, emotional and cognitive functioning) and 9 single items (pain, fatigue, financial impact, appetite loss, nausea/vomiting, diarrhea, constipation, sleep disturbance and quality of life).

Symptoms, assessed by the NCI-CTC, are assessed on an ordinal scale, but reported on a binary level because of ease of interpretation (favourable vs unfavourable, good vs poor, etc.). A clinical relevant cut-off point is mostly used to determine the split on the ordinal level into a binary variable.

OBJECTIVES

The objective of this analysis was to develop an analytic methodology to identify a clinically relevant cut-off point in the EORTC QLQ-C30 ordinal pain scale by comparing patient and clinician reporting for the same symptom. The ability to translate between clinician and patient reported symptoms will be useful in planned future analyses.

DATA

A total of 9 closed European Organisation for Research and Treatment of Cancer (EORTC) Randomized Controlled Trials (RCT), including 1,671 patients from 6 different cancer sites, were selected for this study.

The number (p) of patients for each cancer site was reported as follows; ovarian (p=73), breast (p=86), pancreas (p=92), lung (p=408), colorectal (p=455), prostate (p=557).

Pre-treatment pain and fatigue were scored at baseline by the clinician Common Toxicity Criteria (CTC) version 2.0 and the patient on a 4-point response scale using the EORTC QLQ-C30.

METHODS

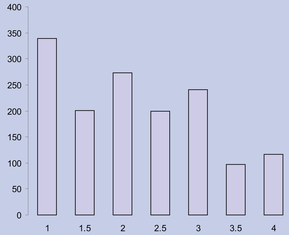
The CTC was dichotomized as <=2.0 vs >2.0; defined as a clinical relevant cut-off point for clinical practice. In cancer treatment trials, a decision is often made on whether to treat, reduce the dose or judge an adverse event as serious and hence reportable when a CTC grade is 3 or higher.

Percent agreement (for which clinicians and patients gave an identical grade) of the CTC dichotomized scale with various dichotomizations of the QLQ-C30 pain scale was calculated and McNemar's test applied.

The McNemar test is an alternative to the more popular and frequently used Kappa statistic. The McNemar test is a test on a 2x2 classification table when you want to test the difference between paired proportions. An advantage is that the McNemar test is more robust against low cell counts, mainly appearing in the tales of the CTC and QLQ-C30 scales. However, the McNemar test can only be applied on binary variables.

The dichotomization of the QLQ-C30 pain scale was explored on a data-driven approach by looking at the distribution of patient reported pain.

FIGURE 1 - Distribution of the QLQ-C30 pain scale



Finally, verification of the accuracy and the ability to generalise the findings was evaluated with a validation set and by applying the same cut-off point on another symptom, i.e. fatigue.

RESULTS

Both clinician and patient reported data were available for pain [number of trials (t)=8, number of patients (n)=1467] and fatigue [t=5, n=1671]. Model and validation set were obtained by splitting the dataset in half at random. Baseline characteristics of patients with completed pair data are reported in Table 1.

TABLE 1 - Patient characteristics reported at baseline

		Pain - Model	Pain - Validation	Fatigue
		Nr. Of Observations		
Performance status	WHO 0-1	616	597	1389
	WHO 2-3	118	136	282
Age	< 60 year	284	301	670
	> 60 year	450	432	1001
Distant Metastases	No	100	83	219
	Yes	592	622	1377
Gender	Male	502	516	1145
	Female	232	217	526

Percentage agreement and p values for McNemar tests, between patient and clinician dichotomized scores using different cut-off points for the QLQ-C30 pain scale are reported in Table 2. The three following methods were explored: median (<2.19 vs >2.19, 64%, p<.01), quartile (<=3.0 vs >3.0, 81%, p=0.55) and decile (<4.0 vs 4.0, 85%, p<.01). Results are displayed in Table 2.

TABLE 2 - Percentage agreement and p values for McNemar tests for the Model Set

		QLQ C-30					
		Quartile		Median		Decile	
		≤ 3.0	> 3.0	< 2.19	≥ 2.19	< 4.0	= 4.0
NCI CTC	≤ 2.0	562	71	393	240	602	31
	> 2.0	64	37	24	77	75	26
Agreement		81%		64%		85%	
P-value		0.55		< .01		< .01	

The quartile split reflects the best dichotomized CTC score as no significant differences were reported between patient and clinician. This was confirmed in the validation set (quartile cut-off point: 82%, p=0.86). However, when the quartile cut-off was applied to the QLQ-C30 fatigue scale, a significant difference (p<.01) between patient and clinician results was found.

CONCLUSION

Our results indicate that a quartile split of the QLQ-C30 pain score is the most optimal technique in defining a clinical relevant cut-off point in the pain score assessed by the patient using the QLQ-C30 questionnaire. However, a single cut-off point may not generalize to other QLQ-C30 symptoms; symptom specific cut-off points may be required. Future research should assess the effect of self reporting on clinical outcomes and efficiency.

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