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Does the generic cancer outcome measure EORTC QLQ-C30 work in Myelofibrosis?

Clara Mukuria, John Brazier, Rachid Rafia, ScHARR, University of Sheffield

INTRODUCTION

The EORTC Quality of Life Questionnaire-Core 30 (QLQ-C30) is a validated patient reported outcome measure for cancer patients which has been developed for application across different types of cancers to assess health related quality of life (HRQoL) [1]. Myelofibrosis (MF) is a rare but serious bone-marrow cancer in which proliferation of an abnormal type of bone marrow stem cell results in fibrosis, or the replacement of the marrow with collagenous connective tissue fibres. Spleen enlargement is a consequence of the resulting extra-medullary haematopoiesis and can cause symptoms (abdominal pain, early satiety and difficulty breathing) as well as complications such as portal hypertension, splenic infarction and vascular events. Patients also have symptoms such as fever, night sweats, weight loss and itching. There is limited evidence on the validity of the EORTC QLQ-C30 in this population therefore this study aimed to provide evidence of its validity.

METHODS

The EORTC QLQ-C30 was compared to the Myelofibrosis Symptom Assessment Form (MF-SAF 2.0) an MF specific measure and FACT-Lym which covers MF specific symptoms.

- The EORTC QLQ-C30 has 5 functioning dimensions (physical, role, cognitive, emotional and social functioning) and 9 symptoms (fatigue, pain and nausea/vomiting, dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties) as well as global quality of life scale each scored from 0 to 100.
- MF-SAF 2.0[2] has 7 symptoms (abdominal discomfort, pain under left ribs, early satiety, night sweats, itching, bone or muscle pain and inactivity) each scored from 0 (absent) to 10 (worst imaginable). A total symptom score (TSS) is generated for all symptoms excluding inactivity.
- FACT Lym subscale[3] is part of the Functional Assessment of Chronic Illness Therapy and includes questions on pain, fever, night sweats, itching, trouble sleeping, fatigue, weight and appetite loss and emotional impact of the condition scored from 0 (not at all) to 4 (very much). An overall FACT Lym subscale total score ranges from 0 to 60.

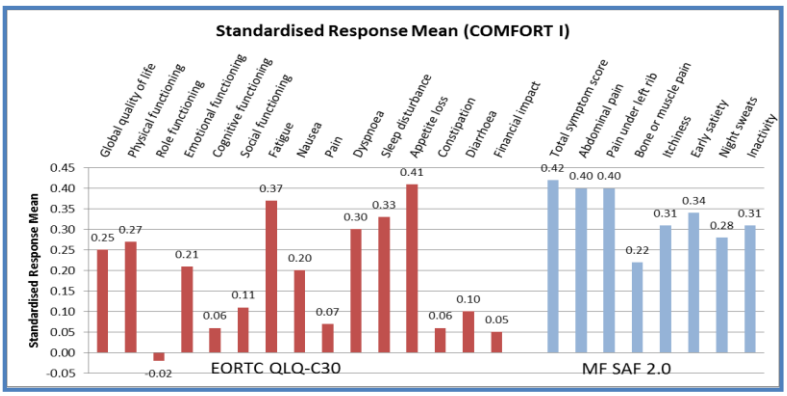
Analysis used data from two randomised trails of the oral JAK1/JAK2 inhibitor INCB018424 (ruxolitinib) in patients with primary myelofibrosis (MF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia myelofibrosis (PET-MF) (COMFORT I[4] (n=309) and COMFORT II [5](n=219)). MF-SAF 2.0 was used in COMFORT I and FACT Lym was used in COMFORT II. Analysis consisted of:

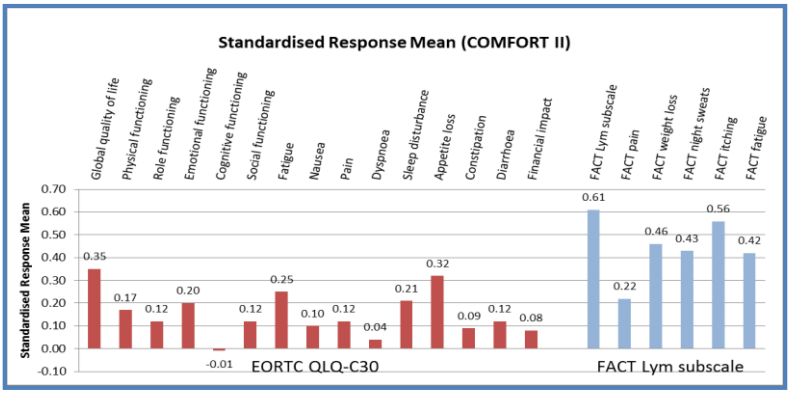
- Convergent validity based to assess the relationship between EORTC QLQ-C30 and the MF-SAF and FACT Lym dimensions using Pearson's and Spearman rank correlation assessed as strong (|≥0.5|), moderate (|≥0.3 and <0.5|) and weak (|<0.3|)[6]
- Known group analysis to assess the ability of the EORTC QLQ-C30 measure to discriminate between groups based on the MF-SAF 2.0 TSS and FACT Lym subscale score using Cohen's d effect size (ES) assessed as large (|≥0.5|), medium (|≥0.3 and <0.5|) and small (|<0.3|)[6]
- Responsiveness analysis to assess whether the EORTC QLQ-C30 reflected changes to the same degree as the other measures based on standardised response mean (SRM) assessed as large (≥0.8), medium (≥0.5 and <0.8) and small (<0.2)[6] . Floor (proportion with poorest score) and ceiling (proportion with best score) effects were also assessed

RESULTS

Convergent Validity

MF-SAF	FACT Lym
Strong correlations (|≥0.5|) between QLQ-C30 pain dimension and MF-SAF pain Strong correlations (|≥0.5|) between QLQ-C30 physical, role and social functioning, fatigue and MF-SAF inactivity	Strong correlations (|≥0.5|) between QLQ-C30 dimensions and FACT Lym dimensions/items of similar constructs (fatigue, pain, sleep trouble, appetite loss)
Moderate correlations (|≥0.3 and <0.5|) between QLQ-C30 dimensions and MF-SAF early satiety item	
Weak correlations (|<0.3|) between QLQ-C30 dimensions and MF-SAF itchiness and night sweats	Weak correlations (|<0.3|) between QLQ-C30 dimensions and FACT LymS itchiness, night sweats and losing weight
No correlations between EORTC dimensions of constipation and diarrhoea and most of the MF-SAF items	No correlations between QLQ-C30 dimensions of constipation and most of the FACT LymS items No correlation between QLQ-C30 dimensions and FACT LymS item of fevers





Known-group validity

Most QLQ-C30 dimensions were able to discriminate between MF-SAF (scores 0-10; 11-20; 21-30; 31-60) with better discrimination for the mild severity low score groups (0.2<ES<0.7) compared to high score groups (ES<0.2) who had higher severity and the FACT-Lym (scores 0-30; 31-40; 41-50; 51-60) groups.

Floor and ceiling effects

- A large proportion (n>50%) reported no problems (ceiling effects) in QLQ-C30 dimensions (nausea/vomiting, constipation/diarrhoea).
- There was some evidence of ceiling effects for weight loss, itching and night sweats (n>30%) in COMFORT II.
- There were no floor effects in the QLQ-C30 but itching (n=12%) and fatigue (n=16%) showed floor effects in COMFORT II.

CONCLUSIONS

- EORTC QLQ-C30 reflected functional and fatigue effects of MF but was less associated with MF specific symptoms such as itching and night sweats
- The EORTC QLQ-C30 pain dimension showed less responsiveness than the MF specific pain dimensions.
- EORTC QLQ-C30 dimensions related to constipation and diarrhoea were less relevant in this population than has been found in other cancer populations.
- EORTC QLQ-C30 does not reflect all the relevant symptoms in patients with MF

1 Aaronson et al. 1993 *J of the National Cancer Institute*, 85, (5) 365-376
2 Mesa et al. 2009 *Leukemia research*, 33, (9) 1199-1203
3 Hlubocky et al. 2013 *Lymphoma 2013*
4 Verstovsek et al. 2012 *NEJM*, 366, (9) 799-807
5 Harrison et al. 2013 *Br J Haematol*. 2013 162(2):229-39
6 Cohen 1992 *Psychological bulletin*, 112, (1) 155

Contact us:
c.mukuria@sheffield.ac.uk
www.scharrheds.blogspot.co.uk
www.facebook.com/scharrsheffield
www.sheffield.ac.uk/heds
@scharrheds