Classification of painful bone metastases as mild, moderate, or severe using both EORTC QLQ-C15-PAL and EORTC QLQ-BM22

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Introduction

- The verbal descriptor scale (VDS) allows patients to describe their pain simply by using categories such as mild, moderate, and severe
- Categorizing pain on a VDS is useful because guidelines for pain management, such as the World Health Organization analgesic ladder and the Cancer Care Ontario cancer-related pain management guideline, incorporate these categories as indicators for treatment effects
- Visual analog scale (VAS) or numeric rating scale (NRS) are beneficial in that they may be more sensitive and used with patients of lower literacy they also allow for more in-depth statistical analyses compared to the simpler VDS
- Determining cut points (CPs) that accurately translate pain scores provided on an NRS to a corresponding VDS category is therefore worthwhile in both clinical and research settings, as doing so will capitalize on the most advantageous features of each scale

Objective

To determine the optimal CPs for mild, moderate, and severe pain in cancer patients with painful bone metastases by assessing impact on quality of life (QOL) using the QLQ-BM22 and QLQ-C15-PAL.

Methods

- This is a secondary analysis of the NCIC Clinical Trials Group Symptom Control Trial SC.23 (NCIC-CTG-SC.23)
- Patients reported worse pain score in past 3 days using BPI worse pain score to be eligible for the initial study, patients were required to have a worst pain score of $\geq$2 at the treated site
- Patients also self-reported QOL using the QLQ-BM22 and QLQ-C15-PAL at baseline
- Optimal CPs were determined to be those that yielded the largest *F* ratio for the between category effect on each subscale of the QLQ-BM22 and QLQ-C15-PAL using the multivariate analysis of variance (MANOVA)
- Overall survival distributions of the sets of three groups were estimated by the Kaplan-Meier curves and compared using log-rank test

Results

- A total of 298 patients were enrolled median age was 69 years (range 32-96) and slightly more (57%) were male
- Radiation therapy was most commonly prescribed to the pelvis, hips, or lower limbs and the mean worst pain score at the treated site was 6.3 (range 2-10)
- Wilk's λ, Pillai's Trace, and Hotelling's Trace were found to be the largest for CPs 5,6 (9.03, 8.69, and 9.39, respectively), and 5,7 (8.54, 8.12, and 8.97, respectively) for the QLQ-BM22
- CPs 5,6 and 5,7 were also found to have the largest *F* ratios (6.96, 6.81, 7.13, and 6.75, 6.58, 6.93, respectively) for the QLQ-C15-PAL
- Based on the combination of both the QLQ-BM22 and QLQ-C15-PAL, the optimal categories to differentiate pain severity were 1-5 for mild pain, 6 for moderate pain, and 7-10 for severe pain
- Global QOL was found to be negatively correlated with pain intensity the more severe the pain, the worse the global QOL scores (mean of 58.0, 47.2, and 41.9 for mild, moderate, and severe pain, respectively) however the difference in mean global QOL score was only significant when comparing mild vs moderate pain (P=.022) and mild vs severe pain (P<.0001)

Table 1. Mean and standard deviation (SD) of QOL scores of the QLQ-BM22 and QLQ-C15PAL

	Mild (n = 108)	Moderate (n = 32)	Severe (n = 158)	Mild vs moderate	Moderate vs severe	Mild vs severe
QLQ-BM22	Mean (SD)	Mean (SD)	Mean (SD)	*p* value	*p* value	*p* value
Painful sites	28.1 (16.1)	38.9 (18.0)	39.6 (17.5)	**0.002**	0.850	**< 0.0001**
Painful characteristics	34.0 (18.2)	50.0 (23.5)	52.9 (21.0)	**< 0.001**	0.496	**< 0.0001**
Functional interference	60.9 (20.4)	52.4 (20.3)	41.4 (21.4)	**0.045**	**0.011**	**< 0.0001**
Psychosocial aspects	56.8 (20.0)	50.9 (17.1)	45.6 (18.7)	0.151	0.152	**< 0.0001**
QLQ-C15-PAL						
Physical	82.5 (20.7)	71.1 (23.5)	67.4 (26.5)	**0.011**	0.478	**< 0.0001**
Emotional	74.1 (25.4)	76.1 (26.9)	64.1 (26.6)	0.707	**0.026**	**0.002**
Global QOL	58.0 (22.7)	47.2 (21.0)	41.9 (21.9)	**0.022**	0.227	**< 0.0001**

A bold value indicates statistical significance (P<.05)

Discussion

- Our current study was the first to our knowledge to utilize only QOL assessment tools, and in particular QLQ-BM22 and QLQ-C15-PAL as outcome measures to determine CPs
- Previous studies suggested mild pain ranges from 1-4, however our results showed a greater range for mild pain, with the upper CP of 5 (mild pain categorized from 1-5) this may be due to a certain level of pain resulting in functional interference but not worsening QOL (i.e., pain score 5), and that once pain reaches 6/10, it may disrupt both functioning and QOL
- This suggests that the nonlinear relationship between pain and functional interference found previously is not the same as that between pain and QOL
- Our moderate category, and demonstrated in the sensitivity analysis, is similar to either the mild or severe category, depending on the QOL measure

Conclusion

- Optimal CPs vary depending on the outcome measures used, particularly whether or not the measure is designed to assess functional interference or QOL
- When using QOL tools as outcome measures, pain should be categorized as follows: 1-5 for mild pain, 6 for moderate pain, and 7-10 for severe pain
- The relationship between pain and functional interference is not the same as that between pain and disruption in QOL, therefore an improvement in functional interference does not necessarily correspond to an improvement in QOL of the same magnitude
- Consideration should be given to designing a novel scale that combines an NRS with QOL indicators basd on these CPs our study suggests mild pain categorized as 1-5 with little impact on QOL, moderate pain categorized as 6 with intermediate impact on QOL, and severe pain cat3egorized as 7-10 with significant impact on QOL

Select References:

1. World Health Organization (1990) Cancer pain relief and palliative care: report of the WHO expert committee on cancer pain relief and active supportive care. Technical Report Series 804, Geneva **2.** World Health Organization (1996) Cancer pain relief: with a guide to opioid availability. Geneva **3.** Cancer Care Ontario (2012) Cancer-related pain management. Program in evidence-based care evidence-based series no.: 16–2 [education and information 2011 Sep]. Cancer Care Ontario, Toronto (ON) **4.** Serlin RC, Mendoza TR, Nakamura Y, Edwards KR, Cleeland CS (1995) When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. Pain 61(2):277–284 **5.** Paul SM, Zelman DC, Smith M, Miaskowski C (2005) Categorizing the severity of cancer pain: further exploration of the establishment of cutpoints. Pain 113(1–2):37–44 **6.** Li KK, Harris K, Hadi S, Chow E (2007) What should be the optimal cut points for mild, moderate, and severe pain? J Palliat Med 10(6):1338–1346 **7.** Kalyadina SA, Ionova TI, Ivanova MO, Uspenskaya OS, Kishtovich AV, Mendoza TR, Guo H, Novik A, Cleeland CS, Wang XS (2008) Russian brief pain inventory: validation and application in cancer pain. J Pain Symptom Manag 35(1):95–102 **8.** Ferreira KA, Teixeira MJ, Mendonza TR, Cleeland CS (2011) Validation of brief pain inventory to Brazilian patients with pain. Support Care Cancer 19(4):505–511. doi:10.1007/s00520-010- 0844-7 **9.** Chow E, Ding K, Parulekar WR, Wong RK, van der Linden YM, Roos D, Hartsell WF, Hoskin P, Wu JS, Nabid A, Ong F, van Tienhoven G, Babington S, Demas WF, Wilson CF, Brundage M, Zhu L, Meyer RM (2015) Revisiting classification of pain from bone metastases as mild, moderate, or severe based on correlation with function and quality of life. Supp Care Cancer

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