Development and Validation of a Patient-Reported Oral Mucositis Symptom (PROMS) Scale

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ABSTRACT

Background and Objective: Oral mucositis, a painful condition with potentially life-threatening sequelae, often develops in association with allogeneic bone marrow transplantation. This condition has an adverse impact on the oral-health-related quality of life of patients undergoing marrow transplantation therapy. The purpose of this study was to create and validate a Patient-Reported Oral Mucositis Symptom (PROMS) scale. This scale allows evaluation of symptoms of oral mucositis that threaten quality of life.

Materials and Methods: The PROMS scale was compared with previously validated tools measuring quality of life (Functional Assessment of Cancer Therapy—Bone Marrow Transplant), symptoms of depression (Center for Epidemiologic Studies Depression Scale), psychological well-being (Affect Balance Scale) and stressful life events, as well as an objective, clinician-rated assessment of oral mucositis (Visual Analogue Scale—Oral Mucositis Assessment Scale). Thirty-four patients who were to undergo allogeneic bone marrow transplantation at Princess Margaret Hospital in Toronto, Ontario, were enrolled in this validation study.

Results: The PROMS scale had high internal reliability, as well as good convergent and discriminant validity relative to subjective measures of well-being. Longitudinal assessments showed that changes in PROMS scores were strongly correlated with changes in clinical assessment of oral mucositis over the first 2 weeks after transplantation, when the onset of oral mucositis typically occurs and the lesions are most severe.

Conclusions: Oral mucositis in patients who have undergone bone marrow transplantation can be quantified reliably with the easily administered PROMS scale. The PROMS scale provides a valid measure of the impact of oral mucositis on the oral-health-related quality of life of patients affected by this malady.

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Oral mucositis, which is characterized by painful erythematous, erosive and ulcerative lesions of the oral mucosa, is a common complication of many cancer treatments, including myeloablative forms of bone marrow transplant therapy. Between 30% and 69% of patients undergoing bone marrow transplantation experience oral mucositis,[1] and nearly all such patients experience some form of oral complications, including oral mucositis, dysfunction of the salivary glands, infection, dysgeusia, dentinal hypersensitivity

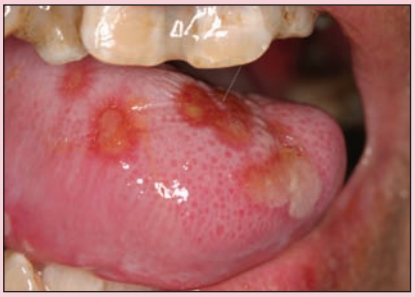

Figure 1: Oral mucositis on the dorsum of the tongue is characterized by patchy erythema with ulceration.

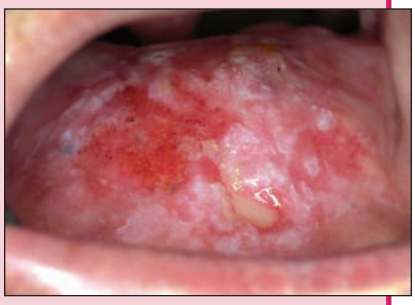

Figure 2: Oral mucositis of the tongue appears as multiple ulcers surrounded by erythema.

and soft-tissue pain.[2] Many patients consider mucositis the single most debilitating side effect of the transplant process.[3] In addition to the pain associated with these lesions, they can be a portal for microorganisms, and bacteremia or even lethal sepsis may result. Moreover, severe oral mucositis may necessitate treatment modifications that can adversely affect patient survival.[2] Overall, then, oral mucositis, in combination with the social isolation that is required for these severely immunocompromised patients, has an impact on quality of life. To date, there is no prevention or cure for oral mucositis.

Traditionally, successful cancer therapy has been defined in terms of disease-free years of survival, mortality and rate of relapse; morbidity associated with therapy has not usually been considered.[4] However, medically successful treatment may be associated with significant morbidity; therefore, it is necessary to examine treatment in relation to quality of life.

It is only in the past 2 decades that the effect of bone marrow transplantation on quality of life has been investigated.[5] Some studies have assessed patients who survived for more than 1 year after the transplant,[6–10] whereas others have examined effects on quality of life during the hospital stay.[11,12]

Clinical Course of Oral Mucositis and Rationale for Creation of Measurement Instrument

Low-dose methotrexate, which is used to prevent graft-versus-host disease, and the preparative regimens for transplantation are responsible for oral mucositis. The most symptomatic ulcerative phase begins 5 to 7 days after completion of the chemotherapy and peaks 7 to 10 days after transplantation (**Figs. 1** and **2**).[13,14] Unless complicated by infection, the oral lesions heal approximately 2 to 3 weeks after transplantation in 90% of patients. The ulcers may persist beyond this period if the patient acquires an oral infection.

Because oral mucositis is a significant side effect of bone marrow transplantation, several clinician-rated measures of this condition have been developed, but only 2 self-reported measures of quality of life related to oral mucositis exist, both of which are undergoing initial psychometric evaluation.[15,16] This is an unfortunate situation, given that a valid, reliable and simple patient-reported measure of the symptoms of oral mucositis could assist in the development of new therapeutic regimens. The purpose of this study was to create and validate a new scale, the Patient-Reported Oral Mucositis Symptom (PROMS) scale, which is based on the patient's perception of the impact of oral mucositis on oral-health-related well-being.

Methods

Patient Selection and Treatment

Volunteers for this study had a hematological malignancy requiring treatment by allogeneic bone marrow transplantation. Conditioning regimens for the transplant included chemotherapy alone or with total body irradiation. Participants were recruited during pretransplant dental assessment at Princess Margaret Hospital, Toronto, Ontario. The inclusion criteria were age 18 years or older, competency in written and spoken English, and ability to consent to participate in the study. Informed consent was obtained in accordance with the University Health Network Ethics Review Board.

A priori sample size calculation indicated that 22 patients would be required to ensure a power of 80% to detect a difference of at least 25 mm on a 100-mm visual analogue scale between PROMS scores at baseline and on day 7 after the transplant procedure using the paired-sample *t* test. A standard deviation of 40 mm was used for a moderate effect size of 0.625. The effect size was calculated as the difference between the 2 means divided by the common standard deviation. An effect size of 1, whereby the difference between the 2 means is equal to the common standard deviation, is considered a large effect size; effect sizes of this magnitude are typically derived from animal studies. An effect size of 0.25 is considered small and would be typical of epidemiologic studies. Statistical significance was set at $p < 0.05$. Although the actual number of patients required was determined to be 22, but 12 additional patients were included to account for an estimated attrition rate of 35% (e.g., because of severe illness or death).

Procedures

The subjects were given 5 questionnaires at the pretransplant dental appointment, which were to be com-

Table 1 Schedule for administration of questionnaires

Questionnaire[a]	Baseline	Day 7	Day 14	Day 21	Day 28	Discharge	Day 60
Demographic characteristics	√						
PROMS	√	√	√	√	√	√	√
FACT-BMT	√					√	√
CES-D	√	√	√	√	√	√	√
ABS	√	√	√	√	√	√	√
SLE	√					√	√

[a]*PROMS: Patient-Reported Oral Mucositis Symptom Scale; FACT-BMT: Functional Assessment of Cancer Therapy—Bone Marrow Transplant*[17]*; CES-D: Center for Epidemiologic Studies Depression Scale*[18]*; ABS: Affect Balance Scale*[19]*; SLE: Stressful Life Events checklist.*[20]

pleted before admission for the transplant procedure (see assessment regimen, **Table 1**). Patients who were well enough completed the questionnaires themselves; for those who were too weak to do so, a friend or relative was asked to assist by verbally presenting the questions to the patient and completing the forms according to the patient's responses. Each patient was then interviewed and asked to comment on the comprehensiveness and clarity of the items and the degree of difficulty encountered in answering the questionnaires.

Instruments

The PROMS scale consists of a 10-item visual analogue scale (VAS) covering the symptoms frequently reported by patients experiencing chemotherapy-induced oral mucositis. The maximum score is 100 (measured in millimetres) for each item and for the overall average. Respondents quantify the severity of symptoms experienced over the previous week using a 100-mm scale anchored at either end with various descriptors (**Appendix 1**). The items selected for the PROMS scale originated from previously published data that had been collected from in-depth personal interviews with a group of 38 patients who had recently undergone myeloablative therapy in advance of bone marrow transplantation.[3] Among the complications of this type of therapy, mouth sores were listed as the single most debilitating side effect (mentioned by 42% of those interviewed), making it difficult or impossible to eat (61%), swallow (55%), drink (45%) and talk (21%). The PROMS scale was administered at baseline, once a week during the hospital stay, at the time of discharge and on day 60 after the transplant procedure. Pilot testing with a few patients before the study indicated that the PROMS questionnaire could be completed in 5 to 7 minutes.

The Functional Assessment of Cancer Therapy—Bone Marrow Transplant (FACT-BMT) is a validated, cancer-specific quality-of-life instrument with a transplantation-specific subscale designed to identify areas of concern for transplant patients during the previous 7 days.[17] It consists of 4 core domains (physical, social/family, emotional and functional) from the general Functional Assessment of Cancer Therapy (known as FACT-G) and the transplantation-specific subscale (BMTS), which has 12 items. The subscale combined with the FACT-G (FACT-BMT) is a 39-item measure. The format of items for the subscale is the same as that for items in the FACT-G measure, consisting of 5 possible numeric responses, where 0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit and 4 = very much. The FACT-BMT is scored by summing the 5 subscales to yield a composite quality-of-life score for each person; higher scores indicate better quality of life. To avoid overburdening the patient, this detailed scale was administered only at baseline, at the time of discharge from hospital and on day 60.

The Center for Epidemiologic Studies Depression (CES-D) scale is a 20-item self-reported questionnaire designed to measure depressive symptoms in both the general[18] and medically ill[21] populations. Common depressive symptoms are elicited by asking respondents to rate (on a scale from 0 to 3) how often they experienced each of 20 symptoms during the preceding week. The overall sum (ranging from 0 to 60) is determined, with higher scores indicating more depressive symptoms. A cut-off point of 16 identifies respondents whose severity of distress is similar to that reported by psychiatric patients with depression.

The Affect Balance Scale (ABS) is used to measure psychological well-being.[19] It is a 10-item true-or-false self-reported measure, with 5 items measuring positive affect (sum = Positive Affect Score) and 5 items measuring negative affect (sum = Negative Affect Score) during the preceding week. The ABS is calculated by subtracting the Negative Affect Score from the Positive Affect Score and adding a constant of 5 to generate a single index that ranges from 0 (negative affect balance) to 10 (positive affect balance).

Stressful life events unrelated to the patient's cancer were documented with the Stressful Life Events (SLE) checklist, which was developed for medical purposes.[20] For this checklist, respondents identify which of 16 event-

Table 2 Patient demographic and clinical characteristics

Characteristic	No. (%) of patients[a]
Sex	
Male	20 (59)
Female	14 (41)
Mean age ± SD (range) (years)	44.2 ± 10.7 (23–61)
Race (self-reported)	
Caucasian	26 (76)
Asian	6 (18)
Black	1 (3)
Native Canadian	1 (3)
Marital status	
Single	4 (12)
Married or living with a partner	26 (76)
Separated or divorced	3 (9)
Data missing	1 (3)
Level of education	
Less than high school	3 (9)
High school	6 (18)
Technical or trade school	10 (29)
University or postgraduate	13 (38)
Data missing	2 (6)
Diagnosis	
Acute lymphocytic leukemia	8 (24)
Acute myelogenous leukemia	10 (29)
Chronic myelogenous leukemia	6 (18)
Myelodysplastic syndrome	3 (9)
Non-Hodgkin's lymphoma	2 (6)
Other hematological disorders	5 (15)
Donor marrow	
Sibling (not identical twin)	27 (79)
Other relative	3 (9)
Unrelated matched donor	4 (12)

SD: standard deviation.
[a]Except where indicated otherwise.

related and 6 chronic stressors have occurred during the preceding 2 to 3 months. In the present study, the scores represent the total number of reported stressors.

A self-reported questionnaire developed for this study documented sociodemographic and medical characteristics (**Table 2**).

Examination by Clinician

A clinician examined the patient's mouth for mucositis on days 3, 7, 10, 14, 17, 21, 24 and 28 after transplantation or at discharge. The grading system was based on the Oral Mucositis Assessment Scale (OMAS), which was designed by a panel of experts to provide an objective, simple and reproducible tool to be used in multicentre clinical trials.[22] The original assessment used ordinal grades of 0, 1 and 2 for the size of erythematous areas and 0, 1, 2 and 3 for the size of ulceration at each of 9 anatomic sites.[23] In the current study, a modification of the standard OMAS scale was used: a 100-mm VAS for erythema and ulceration at each of the 9 anatomic sites (VAS-OMAS). The modified scale also included a VAS for "total oral erythema" and a VAS for "total oral ulceration."

Data Analysis

Descriptive statistics were calculated for the demographic and clinical data. Scores for each scale were calculated at each time point, and floor and ceiling effects were reviewed using box plots and by examining univariate statistics. Because some item and scale distributions tended to be skewed, nonparametric tests were used. Significant changes over time were assessed by the nonparametric Friedman test for k related samples.

Validation of PROMS Scale

Internal consistency was reported as Cronbach's α at each time point. The acceptable level for the overall scale was set at 0.80. Test–retest reliability could not be evaluated because of rapid changes in the patients' health status occurring as a result of the bone marrow transplantation. This made it impossible to tease out whether a systematic shift in scores occurred over time. Convergent and discriminant validity were determined by correlation between clinical data derived from the clinician's assessment of oral mucositis (via the VAS-OMAS) and concurrent patient self-reporting on the validated instruments (FACT-BMT, CES-D, ABS and SLE), by Spearman correlation coefficients. The sensitivity of the quality-of-life instrument to changes in severity over time, as measured by VAS-OMAS, was also explored and tested with the Spearman correlation coefficient. The level of significance was set at $p < 0.05$ (2-tailed).

Results

Patient Characteristics

Thirty-four patients consented to participate in the study, 20 men and 14 women. Of the patients recruited, 28 (82%) were treated with chemotherapy and total body irradiation for marrow ablation; 6 (18%) were prepared with chemotherapy alone. The majority of bone marrow donors were siblings (27 or 79%) or other relatives (3 or 9%); the rest were matched unrelated donors (4 or 12%). Individual diagnoses and other patient characteristics are expressed in **Table 2**.

Missing Data

Response rates declined from 94% on day 7 to 65% on day 60 (**Table 3**). Data for day 28 were not available for all patients, as only 12 (35%) of the 34 patients remained in hospital at that point. Of the remaining 22 patients (65%), 15 (44%) had been discharged and 7 (21%) had died before day 28.

Table 3 Mean (± standard error) scores at baseline, on days 7, 14 and 21, at hospital discharge and on day 60

Scale (possible range)	No. of items (observed range)	Interpretation of scale	Baseline *n* = 34	Day 7 *n* = 32	Day 14 *n* = 28	Day 21 *n* = 24	Discharge *n* = 25	Day 60 *n* = 22	*p* value[a]
PROMS (range 0–100 per item and overall)	10 (0–91)	Higher scores = worse QoL	7.8 ± 2.3	44.7 ± 5.1	39.8 ± 5.3	28.7 ± 6.5	9.2 ± 1.9	7.3 ± 2.1	< 0.001
FACT-BMT (0–156)	39 (67–111)	Higher scores = better QoL	83.0 ± 1.6	—	—	—	90.7 ± 2.4	91.1 ± 1.8	0.002
CES-D (0–60)	20 (0–47)	Higher scores = more depressive symptoms[b]	13.4 ± 1.7	21.6 ± 1.5	20.7 ± 1.7	18.1 ± 2.5	17.8 ± 2.5	13.4 ± 2.0	0.004
ABS (0–10)	10 (0–9)	Higher scores = positive mood state	3.6 ± 0.4	4.8 ± 0.3	3.9 ± 0.2	4.4 ± 0.4	3.9 ± 0.5	3.7 ± 0.6	0.08
SLE (0–22)	22 (0–6)	Higher scores = more stressful life events	1.5 ± 0.2	—	—	—	1.5 ± 0.3	1.2 ± 0.3	0.12
Clinician-rated VAS-OMAS (0–100 per item and overall):[c]		Higher scores = more severe mucositis							
for erythema	9 (0–99)		0 (13.9 ± 3.6 at day 3)	48.1 ± 7.1	50.3 ± 7.7	24.7 ± 7.6	23.5 ± 7.8	—	0.001
for ulceration	9 (0–100)		0 (11.3 ± 4.3 at day 3)	42.1 ± 8.1	58.9 ± 7.8	33.2 ± 9.1	30.2 ± 10.1	—	0.003

PROMS: Patient-Reported Oral Mucositis Symptom scale; QoL: quality of life; FACT-BMT: Functional Assessment of Cancer Therapy—Bone Marrow Transplant[17]; CES-D: Center for Epidemiologic Studies Depression Scale[18]; ABS: Affect Balance Scale[19]; SLE: Stressful Life Events checklist[20]; VAS-OMAS: Visual Analogue Scale—Oral Mucositis Assessment Scale.[22,23]

[a] *Obtained with Friedman test.*

[b] *CES-D ≥ 16 indicates patients at risk for clinical depression.*

[c] *VAS-OMAS assessments were performed on days 3, 7, 10, 14, 17, 21, 24 and 28 after transplantation (if the patient was discharged before day 28, the assessment was performed at discharge).*

Validation of PROMS Scale

Descriptive statistics for all of the scales at baseline and at subsequent assessments are shown in **Table 4**. Analyses within each scale using the nonparametric Friedman test for repeated measures revealed that the scores changed significantly over the course of treatment for the PROMS, FACT-BMT, CES-D and VAS-OMAS (erythema and ulceration) scales, but not for the ABS scale or the SLE checklist.

The internal consistency of the PROMS scale was high (**Table 4**; Cronbach's α = 0.86–0.98) at all time points and did not seem to be affected, except at discharge, by the use of similar items related to difficulty and restriction of speech, eating and drinking. Specifically, at discharge, Cronbach's α was low (0.62) when 4 of the functional limitation items related to speaking, eating hard and soft foods, and drinking were removed. In addition, the "change in taste" item had low item-total correlations (0.1 to 0.6) at all assessment times (especially at discharge) relative to the other PROMS items (> 0.8). When this item was deleted, Cronbach's α was 0.95 at discharge.

During the first week after transplantation, patients experienced steep increases in PROMS item scores, corresponding to a decline in oral function, increased mouth pain and change in taste perception (**Fig. 3**). These increases were followed by a steady decline in PROMS until discharge from hospital; scores were similar at discharge and at day 60.

Convergent validity was assessed by examining the degree of correlation between the PROMS scores and subscales of the FACT-BMT, the clinician's assessment

Table 4 Internal consistency of Patient-Reported Oral Mucositis Symptom scale

Scale (no. of items)	Cronbach's α						
	Baseline	Day 7	Day 14	Day 21	Day 28	Discharge	Day 60
Overall scale (10 items)	0.93	0.96	0.96	0.98	0.95	0.86	0.93
Scale without data for difficulty speaking, eating hard or soft foods, and drinking (6 items)	0.88	0.92	0.89	0.95	0.89	0.62	0.85
Scale without data for restriction of speech, eating and drinking (7 items)	0.88	0.93	0.92	0.96	0.91	0.76	0.86
Scale without data for change in taste (9 items)	0.93	0.97	0.98	0.99	0.97	0.95	0.96

Table 5 Spearman correlation coefficients between Patient-Reported Oral Mucositis Symptom (PROMS) scores and other scores at 3 time points during transplantation treatment

Instrument	Spearman correlation coefficient[a]
FACT-G	
Baseline	
Physical well-being (7 items)	−0.41[b]
Social/family well-being (7 items)	0.28
Emotional well-being (6 items)	−0.37[b]
Functional well-being (7 items)	0.08
Discharge	
Physical well-being	−0.32
Social/family well-being	0.42[b]
Emotional well-being	−0.37
Functional well-being	0.40
Day 60	
Physical well-being	−0.53[b]
Social/family well-being	−0.13
Emotional well-being	−0.06
Functional well-being	0.34
BMTS (12 items)	
Baseline	0.02
Discharge	0.10
Day 60	0.27
FACT-BMT	
Baseline	−0.43[b]
Discharge	0.07
Day 60	0.12
SLE	
Baseline	0.35[b]
Discharge	0.26
Day 60	0.15

FACT-G: General Functional Assessment of Cancer Therapy[17]*; BMTS: Bone Marrow Transplant subscale*[17]*; FACT-BMT: Functional Assessment of Cancer Therapy—Bone Marrow Transplant*[17]*; SLE: Stressful Life Events checklist.*[20]

[a]*Relative to PROMS.*

[b]*Significant at the 0.05 probability level (2-tailed).*

of severity of oral mucositis and the SLE checklist; correlations between the PROMS scale and the ABS and CES-D scales were used to address discriminant validity (**Tables 5** and **6**). In support of convergent validity, the PROMS scores correlated most closely with the physical well-being subscale of FACT-G at baseline and day 60; the PROMS scores also correlated with the social/family well-being subscale at discharge (**Table 5**).

The PROMS scores were significantly correlated with symptoms of depression (CES-D scale), consistent with the new instrument's discriminant validity and with the premise that symptoms of oral mucositis are powerful stressors compromising quality of life. This correlation was most pronounced on days 7 and 14 (**Table 6**). The correlation between the PROMS and ABS scores was moderate (significant only on day 21). Supporting the convergent validity of the new scale, the PROMS scores correlated strongly with clinician-rated VAS-OMAS scores during the first 3 weeks after transplantation (**Table 5**). The PROMS and VAS-OMAS scores were not significantly correlated at the time of patient discharge, however, which suggests that once ulcerations have healed, patients still experience some discomfort.

To demonstrate sensitivity to detect change in oral-health-related quality of life during bone marrow transplantation treatment, the differences in PROMS scores between baseline and days 7, 14, 21 and 28 were plotted with changes in VAS-OMAS scores over the same time points (**Fig. 4; Table 7**). There were strong correlations in the extent of change during the first 2 weeks after the transplant procedure, when the onset of oral mucositis typically occurs and the lesions are at their most severe.

Discussion

The study reported here demonstrated high internal reliability, good construct validity (convergent and discriminant validity)[24] and sensitivity to clinically significant changes for the novel PROMS scale. In general, the PROMS scores correlated meaningfully and as expected

Table 6 Spearman correlation coefficients between Patient-Reported Oral Mucositis Symptom (PROMS) scores and other scores at 4 time points during transplantation treatment

Instrument	Spearman correlation coefficient[a]
CES-D	
Day 7	0.51[b]
Day 14	0.39[c]
Day 21	0.40
Discharge	0.28
ABS	
Day 7	0.32
Day 14	−0.12
Day 21	0.43[c]
Discharge	0.23
Clinician-rated VAS-OMAS for erythema	
Day 7	0.61[b]
Day 14	0.54[b]
Day 21	0.49[c]
Discharge/Day 28	0.19
Clinician-rated VAS-OMAS for ulceration	
Day 7	0.70[b]
Day 14	0.47[c]
Day 21	0.64[b]
Discharge/Day 28	−0.03

CES-D: Center for Epidemiologic Studies Depressions Scale[18]; ABS: Affect Balance Scale[19]; VAS-OMAS: Visual Analogue Scale—Oral Mucositis Assessment Scale.[22,23]
[a]*Relative to PROMS.*
[b]*Significant at the 0.01 probability level (2-tailed).*
[c]*Significant at the 0.05 probability level (2-tailed).*

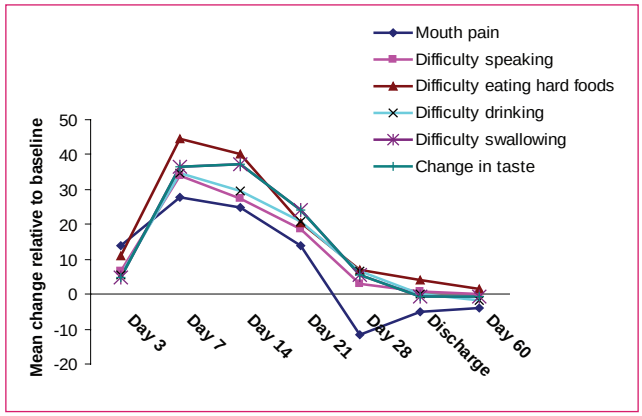

Figure 3: Mean changes in Patient-Reported Oral Mucositis Symptom (PROMS) scores relative to baseline for selected items of the scale.

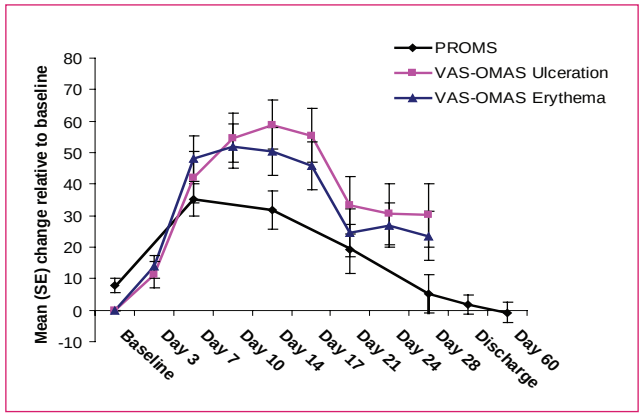

Figure 4: Mean changes in scores for Patient-Reported Oral Mucositis Symptom (PROMS) scale and clinician-rated Visual Analogue Scale—Oral Mucositis Assessment Scale (VAS-OMAS) for ulceration and erythema, relative to baseline, up to day 28.

Table 7 Spearman's ρ for the correlation between the change in mean scores of the PROMS and VAS-OMAS scales

	Spearman's ρ			
Mean change from baseline	**Day 7 – baseline**	**Day 14 – baseline**	**Day 21 – baseline**	**Day 28 – baseline**
PROMS and VAS-OMAS ulceration	0.72[a]	0.52[a]	0.31	−0.11
PROMS and VAS-OMAS erythema	0.72[a]	0.57[a]	0.27	0.42

PROMS: Patient-Reported Oral Mucositis Symptom Scale; VAS-OMAS: Visual Analogue Scale—Oral Mucositis Assessment Scale
[a]$p < 0.01$ *(2-tailed).*

with measures of health-related quality of life, symptoms of depression and psychological well-being at various points during the hospital stay and until 60 days after transplant. This study generated good longitudinal data, which showed that the PROMS scale could discriminate changes in oral mucositis over time, as measured by objective evaluation of oral mucosa (clinician-rated VAS-OMAS for ulceration and erythema). The most severe patient-reported effects of oral mucositis occurred between days 7 and 21, with the peak reported at day 7. In clinical terms, oral mucositis peaks between days 7 and 10.[23] Accordingly, clinician and patient scores were highly correlated on day 7.

The PROMS scale was designed to assess specific symptoms or groups of symptoms that would theoretically have a negative impact on quality of life, as well as other factors related to bone marrow transplantation and other cancer therapies. In this regard, symptoms can be so severe as to limit the treatment intervention, which might lead to treatment failure. Thus, it is critically important that oral mucositis is measured both from the clinician's perspective and, perhaps more important, from

the patient's perspective. A high ceiling effect (whereby more than 70% of scores had the highest possible value) was observed for the item "change in taste" at hospital discharge. Nonetheless, this item was retained because of its clinical relevance. In a study conducted in Hong Kong, dry mouth and distorted taste were the most common problems for patients with oral mucositis induced by therapy for head and neck cancer.[25] Altered taste could represent a form of chemotherapy-induced neuropathy or (more likely) an effect of treatment-induced xerostomia.

The PROMS scores were also compared with a quality-of-life scale specific for patients who have undergone bone marrow transplantation (FACT-BMT), a depression scale (CES-D) and a psychological well-being scale (ABS). Patients were also screened for stressful life events. Although there were significant differences in quality of life from baseline to discharge and from baseline to day 60 after the transplant procedure, the information gathered in this study did not assess quality of life at the times when the most radical changes might be expected (e.g., during ulceration or at initial diagnosis).[26] Nevertheless, the study found significant correlations between the PROMS scores and the physical subscale of the FACT-G scale at baseline and on day 60, findings that support the convergent validity of the PROMS scale as a measure of oral mucositis symptomatology. Similar findings have been reported for patients undergoing cancer therapy in Hong Kong.[27]

The CES-D demonstrated minimal depressive symptoms at baseline. From day 7 until discharge, patients reported symptoms suggestive of heightened depression; these symptoms peaked at day 7 (as with PROMS, Spearman's $\rho = 0.51$) but had normalized by day 60. Hence, it appears that symptoms of depression paralleled PROMS scores, having an adverse impact on the affective state of patients undergoing transplantation, particularly while they were still in hospital. Generally, patients receiving chemotherapy who experience oral mucositis are more depressed than patients who do not experience this problem.

Psychological well-being, as measured by the ABS scale, did not vary substantially over the post-transplant period. Similarly, stressful life events were examined to identify any confounding situations that might have affected symptoms of oral mucositis. On average, no more than 1.2 events were reported per patient. The most common events were diagnosis of a chronic illness and employment or financial difficulties.

A potential confounding variable, which was not addressed in this investigation, was the use of analgesics and their possible effect on the ability of patients to report symptoms of oral mucositis. Nonetheless, the PROMS values obtained indicate that administration of analgesics might not have been a major factor for these patients.

Finally, it should be noted that the PROMS scores are based on VAS measurements and are therefore theoretically suitable for parametric testing. Parametric data sets can be analyzed with greater robustness than nonparametric data. However, most of the measures used in this study tended to be skewed, so nonparametric tests were used. Ongoing investigation and refinement of this evaluative instrument should allow evaluation of new treatments (preventive or palliative) for this potentially devastating oral condition.

Conclusions

The PROMS scale is a valid and reliable instrument that can be used to assess patient-reported symptoms of transplant-related oral mucositis. Scores obtained with this instrument were directly correlated with clinician-rated severity of oral mucositis and with other dimensions of health-related quality of life. The PROMS scores also changed in association with clinically meaningful milestones, which indicates the sensitivity of this scale to change, an important psychometric strength that is essential to meaningful outcomes for dynamic phenomena. Further research is required to validate this scale for other groups experiencing oral mucositis. For example, this patient-centred instrument could be useful in developing and evaluating new therapies for oral mucositis and for monitoring patient improvement.[28]

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Appendix 1 Questionnaire for Patient-Reported Oral Mucositis Symptom (PROMS) Scale

This questionnaire asks you to evaluate some situations you may have experienced in the past week. All of the situations refer to the condition of your mouth. You can indicate the severity of the situation by placing a vertical mark along the lines below.

First, we will use this type of line to rate temperature as an example.

On a hot day in the middle of the summer, if we asked you to rate how warm it was today, you would probably mark the line as follows:

not warm at all _____|_____ extremely warm

On a cool day in the fall, you might indicate:

not warm at all _____|_____ extremely warm

On a cold day in the winter, you might indicate:

not warm at all _____|_____ extremely warm

To practice: Please tell me how warm it is outside today by placing a mark on the line below.

not warm at all _____ extremely warm

Now that you know how to use this scale, please indicate to what degree these situations have affected you in the past week.

Mouth pain

no pain _____ worst possible pain

Difficulty speaking because of mouth sores

no trouble speaking _____ impossible to speak

Restriction of speech because of mouth sores

no restriction of speech _____ complete restriction of speech

Difficulty eating hard foods (hard bread, potato chips, etc.) because of mouth sores

no trouble eating hard foods _____ impossible to eat hard foods

Difficulty eating soft foods (Jello, pudding, etc.) because of mouth sores

no trouble eating soft foods _____ impossible to eat soft foods

Restriction of eating because of mouth sores

no restriction of eating _____ complete restriction of eating

Difficulty drinking because of mouth sores

no trouble drinking _____ impossible to drink

Restriction of drinking because of mouth sores

no restriction of drinking _____ complete restriction of drinking

Difficulty swallowing because of mouth sores

not difficult to swallow _____ impossible to swallow

Change in taste

no change in taste _____ complete change in taste