Seminars in Oncology Nursing 000 (2021) 151159

Contents lists available at ScienceDirect

Seminars in Oncology Nursing

journal homepage: https://www.journals.elsevier.com/seminars-in-oncology-nursing

Development and Validation of the Oral Mucositis Risk Assessment Scale in Hematology Patients

Özlem Fidan*, Sümeyye Arslan

Faculty of Health Sciences, Department of Nursing, Pamukkale University, Denizli, Turkey

ARTICLE INFO

Key Words:
hematology
Oral Mucositis
risk assessment
Scales
Methodological Study

ABSTRACT

Objectives: This study was conducted as a methodological study to develop a valid and reliable scale to evaluate the risk of developing oral mucositis in hematology patients.
Data Sources: The universe and sample were comprised of one hundred eighty-seven in-patients who were taken to receive chemotherapy in the hematology clinics over a six-month period. The data were collected through the Patient Diagnosis Form, the World Health Organization's Mucositis Evaluation Form and Oral Mucositis Risk Assessment Scale in Hematology Patients developed. Risk of “taking high-dose chemotherapy regimen”, “neutropenia”, “dry mouth”, “pain”, “leukopenia”, “parenteral feeding”, “previous history of oral mucositis” and “chemotherapy or radiotherapy in the past” were found as an oral mucositis risk factor. We have added “using high-risk chemotherapeutic agents”, “bone marrow transplant”, “ head-neck or mouth cancer” which we consider clinically important. The scale consists of 11 items. The sensitivity value is 0.941 and the selectivity value is 0.724.
Conclusion: We recommend that use the Oral Mucositis Risk Assessment Scale in Hematology Patients. Similar studies should be performed in oncology clinics and especially in patients receiving head and neck, oral radiotherapy. Implications for nursing practice: Oral mucositis is an important problem for hematology patients. nurses' risk assessment and early intervention to oral mucositis prevent the formation and complications of oral mucositis.

Introduction

Oral mucosa is an area that is easily affected by chemotherapy (CT) and radiotherapy (RT) due to the frequent renewal of its cells. Therefore, oral mucositis (OM) is one of the most common complications in the treatment of malignancy. OM is defined as a disturbance in oral mucosa, erythema, and ulcerative lesions. OM causes pain, inability of nutrition, and infection.[1]

The risk factors of OM development are divided into two depending on the treatment and the patient. Patient-associated risk factors are laboratory findings such as genetic factors, age, sex, inadequate oral hygiene, periodontal diseases, infections, comorbidity (such as diabetes, chronic renal failure), alcohol and tobacco use, xerostomy, low body mass index (BMI), neutropenia, thrombocytopenia, and leukopenia.[2] Treatment-related risk factors are chemotherapeutic medications (especially alkylating agents and antimetabolites) and high doses of these medications, RT application area, dose, chemoradiotherapy, and induction therapies used in leukemia.[2,3]

Although no standard method has been developed for the prevention and treatment of OM, early diagnosis and intervention of OM may prevent many problems.[4] It is important to evaluate oral cavity regularly at first hospitalization and before, during, and after the treatment in the prevention of OM. Nurses are required to evaluate and determine whether patients are at risk for developing OM resulting from CT or patient-derived reasons; early interventions will prevent the occurrence of OM in the patients with a high risk of OM development.[5-7]

Although there are scales evaluating OM toxicity and oral cavity in the literature, no scale was found concerning the risk of OM. These available scales do not make an assessment by addressing the risk factors of OM. The scales used in clinics are subjective or assessing toxicity of OM. Subjective scales, such as Oral Assessment Guide (OAG), Oral Mucosa Rating Scale (OMRS), and Oral Mucositis Index (OMI), focus on less common changes such as edema and atrophy besides mucosal tissue damage, including erythema and ulceration.[8] Scales assessing toxicity are generally used for reducing toxicity and in the conduction of clinical studies on cancer treatment. Toxicity scales in which the World Health Organization (WHO) and National Cancer Institute (NCI) combine objective and subjective findings of OM under a single parameter to assess OM severity are the common ones. Unfortunately, any scale that may help clinicians in prioritizing

* Address correspondence to: Özlem Fidan, Pamukkale University, Faculty of Health Sciences, Nursing Department, Denizli, Turkey.
E-mail address: osirik@pau.edu.tr (Ö. Fidan).

https://doi.org/10.1016/j.soncn.2021.151159
0749-2081/

the patients who may benefit from the interventions and works as a mucositis risk assessment scale is not yet available.[9] Developing a valid and reliable scale that assesses OM development risk in hematology patients will help provide risk assessment in these patients and will lead physicians to take necessary precautions before the development of OM and prevent many complications that may occur as a result.

Purpose

The study was conducted to develop a valid and reliable scale to evaluate the risk of developing OM in hematology patients.

Methods

Study Design

This was carried out as a methodological study.[10]

Place and Date of the Study

The study was conducted in adult hematology clinics of a university hospital between March 2019 and August 2019. The hospital had two adult hematology clinics.

Setting and Sample

The study sample was composed of the patients who were hospitalized for undergoing CT in the adult hematology clinics of a university between March 2019 and August 2019 (n = 187). The sample of the study included patients who were approved to participate and were older than 18 years old. Sample size was determined to be 10 times the number of items in the draft scale because the proposed sample size for methodological research should be 5-10 times more than the number of items in the scale.

Instruments

"Patient Identification Form," "WHO Mucositis Assessment Form," and "Oral Mucositis Risk Assessment Scale for Hematology Patients" were used and were generated by the researchers in accordance with the relevant literature used in the study.

Patient Identification Form

This form included demographic and clinical characteristics information about the patient (age, height, weight, body mass index [BMI], sex, marital status, and education level of the patient) and descriptive information about the disease (diagnosis of the patient, form of treatment, treatment protocol, the number of CT cycles, presence of any comorbid disease and laboratory findings, including white blood count, platelet count, creatinine, albumin, C-reactive protein).

WHO Mucositis Assessment Form

This is a diagnostic tool that is commonly used to identify toxicity caused by the cytostatic agents, especially in clinical studies. In this assessment, anatomical changes of oral mucosa and severity of mucositis are graded between 0 and 4. Although grade 0 means that there is no mucositis, grade 1 is mild, grade 2 is moderate, grade 3 is severe, and grade 4 indicates a life-threatening level.[11]

OM Risk Assessment Scale for Hematology Patients

During the development phase of OM Risk Assessment Scale for Hematology Patients, literature data that identify the factors affecting OM risk were first examined. Then, some interviews were done with the nurses working in hematology clinics about the characteristics of patients who developed OM. At the end of these studies, a scale item pool was generated. This scale item pool was composed of 29 items.

Implementation Process of the Study

The study was carried out in two phases. These were preparation and implementation (Figure 1).

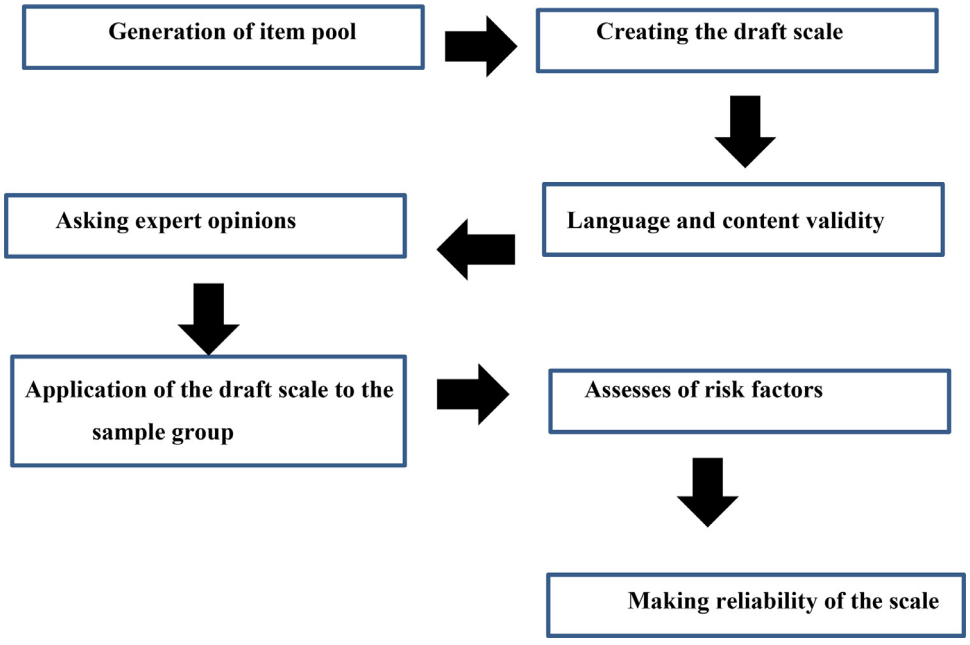

Fig. 1. Research implementation process flow chart.

Preparation Phase

1. Generation of item pool: During the development phase of OM Risk Assessment Scale for Hematology Patients, literature data that identified the factors affecting OM risk were first examined.[2,12-34] Some interviews were made with the nurses working in hematology clinics about the characteristics of patients who developed OM. The nurses stated reasons such as the number of CT cycles, xerostomia, lack of oral hygiene, etc. At the end of these studies, a scale item pool was generated (29 items). These items were taking a high-dose CT regimen, neutropenia, xerostomia, pain, leukopenia, parenteral nutrition, previous history of OM, history of previous CT or RT, using a high-risk chemotherapeutic agent, being transplant, having a diagnosis of head-neck or oral cancer, RT from the head and neck region, RT (except for the head and neck area), steroid therapy, thrombocytopenia, high creatinine level, low albumin level, high C-reactive protein level, not having a tooth brushing habit, dental prosthesis, impaired oral mucosal integrity, tooth decay, periodontal disease, female gender, being older than 65 years of age, having oxygen therapy, taking alcohol and smoking, low BMI, and comorbidity.

2. Language and content validity: Items, that were generated by the researchers were sent to 11 experts (one dentist, two hematologists, one oncologist, three registered nurses, and four nursing instructors with PhD) for language and content validity. Experts were asked to grade their opinions on the statements by using Davis technique as (a) "Relevant," (b) "Highly Relevant-Item should be slightly reviewed," (c) "Somewhat Relevant-Item should be seriously reviewed," and (d) "Not relevant."[35] Moreover, they were asked to assess each statement as 1 (unclear) and 4 (clear) and to write their opinions and suggestions for each statement clearly. Content validity index (CVI) was calculated by dividing the number of experts who marked "a" and "b" options for each statement by the number of experts who gave opinions for the item.[35] Items that had a content validity index below 0.80 were excluded from the scale (no item was excluded), and some revisions were made for the suggestions provided.

Implementation Phase

The scale was applied at first admission to the hospital, and the 1st, 7th, and 14th days of CT. OM begins to occur in patients undergoing CT especially at 2nd and 3rd days of CT, and it reaches to the highest level at days 7 and 14. It enters the recovery phase after day 14 in the absence of infection.[3,36] The scale was applied by a single observer (researcher).

Statistical Analysis

Data were analyzed by SPSS 25.0 package program. Continuous variables were expressed as mean plus or minus standard deviation, median (minimum-maximum values), and categorical variables were given as numbers and percentages. The compliance of data with normal distribution were examined by Kolmogorov-Smirnov and Shapiro Wilk tests. Mann Whitney U test was used to compare differences between independent groups. Risk factors were assessed by logistic regression analysis following the implementation phase. Based on this analysis, the items to be included in the scale and risk scores were determined. Cut-off points of the scale were identified by receiver operator characteristics (ROC) curve analysis. Cut-off point, sensitivity, specificity, and positive and negative predictive values were evaluated for construct validity. The scores of each risk factor were obtained from the regression coefficient values by using SPSS program. According to this scoring, risk factors got scores of 1, 3, and 5 points. Total scores varied between 0 and 33; and high scores indicated a higher risk for OM development Figure 2.

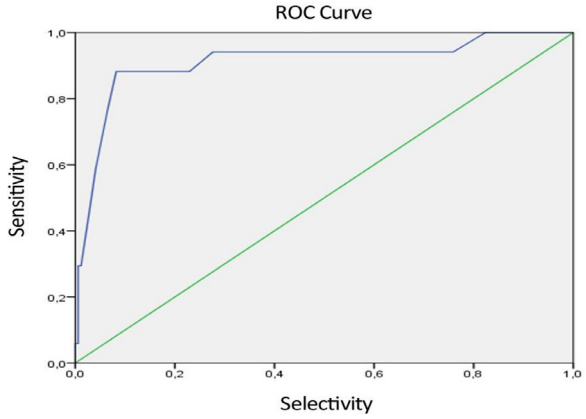

Fig. 2. Determination of sensitivity, selectivity and cut-off point according to ROC analysis.

Ethical Issues

Ethics approval was received from the relevant Ethics Committee (date: 01.09.2019; no: 60116787-020/1934) for the conduction of the study. Permission was obtained from the institution where the study was carried out. A verbal/written consent was taken from the patients who met the inclusion criteria and who approved to participate in the study. Patients who were included in the study were informed about the fact that they were free to decide whether to participate in the study and to withdraw from the study whenever they wanted; the principle of autonomy was respected. It was further ensured that the information taken from the patients would not be used for many other reasons except this study and would not be accessed by the others; principles of loyalty and confidentiality were adhered. The research was conducted in accordance with the Helsinki Declaration.

Results

The demographic and clinical characteristics of the patients in the study are provided in Table 1. More than half of the patients were males (57.2%) and elementary school graduates (65.8%), and most of them were married (82.4%). The most common diagnoses were found to be lymphoma (41.7%) and acute myeloblastic leukemia (AML; 33.7%), and they were followed by multiple myeloma (MM; 11.2%). More than half of the patients (65.2%) had taken their first cycle of CT, and nearly half of them have taken their first to fifth cycles. No comorbid disease was seen in more than half of the patients (78.1%) in addition to their hematological malignancies.

The distribution of the patients based on OM development is shown in Table 2. It was determined that OM developed in 9.1% of the patients since their hospitalization, at the onset of CT, and until day 14 (Table 2).

At the end of logistic regression analysis in Table 3 "taking a high dose CT regimen" (RF3), "neutropenia" (RF4), "xerostomia" (RF6), "pain" (RF7), "leukopenia" (RF13), "parenteral nutrition" (RF20), "previous history of OM" (RF21). and "history of previous CT or RT" (RF22) were found as risk factors. Odds ratio and confidence of interval values of the risk factors included in the scale at first hospitalization, CT onset, CT day 7, and CT day 14 were given in Table 3. Although a few numbers of patients were found to develop OM based on the cut-off points of risk factors, the factors such as "using a high-risk chemotherapeutic agent," "being transplanted," and "having a diagnosis of head-neck or oral cancer," which we considered as clinically important, were added to the scale items. The latest version of the scale was composed of 11 risk factors and a patient who had all risks got a score of 33.

Table 1
Demographic and Clinical Characteristics of participants (N = 187).

Characteristics	Number (%)	Number	%
Age (min-max) $\bar{X} \pm SD$	(19-88) 56.8 ± 15.5		
	18-32	18	9.6
	33-47	23	12.3
	48-63	76	40.7
	64-88	70	37.4
Height (cm) (min-max) $\bar{X} \pm SD$	(141-187) 164.4 ± 9.0		
Weight (kg) (min-max) $\bar{X} \pm SD$	(41-127) 72.1 ± 12.4		
BMI (min-max) $\bar{X} \pm ss$	(16.6-45) 26.8 ± 5.0		
	0-20	14	7.5
	20-25.9	76	40.6
	26-29.9	48	25.7
	30 and higher	49	26.2
Gender	Female	80	42.8
	Male	107	57.2
Marital status	Married	154	82.4
	Single	33	17.6
Education	Illiterate	23	12.3
	Elementary school	123	65.8
	High school	29	15.5
	University or higher	12	6.4
Diagnosis	ALL	13	7
	AML	63	33,.7
	Lymphoma	78	41.7
	MM	21	11.2
	MDS	5	2.7
	CLL	6	3.2
	CML	1	0.5
The number of cycle CT	First	122	65.2
	1st-5th	61	32.7
	5th-10th	4	2.1
Comorbidities	No	146	78.1
	DM	31	16.6
	CRF	9	4.8
	DM + CRF	1	0.5

ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; BMI, body mass index; CLL, chronic lymphoblastic leukemia; CML, chronic myeloblastic leukemia; CRF, chronic renal failure; CT, chemotherapy; DM, diabetes mellitus; MDS, myelodysplastic syndrome; MM, multiple myeloma; SD, standard deviation.

Table 2
Distribution of Patients According to OM Development Status (N = 187).

Oral Mucositis Development Status	n	%
Developing OM	17	9.1
Not developing OM	170	90.9
Total 187		100.0

OM, oral mucositis.

Based on ROC analysis, area under the curve was found as 0.911. It was also seen that the ability of risk scores to discriminate OM development was quite high (standard error: 0.046 and 95% confidence interval: 0.821-1, Figure 1). When 11.5 was accepted as the ideal cut-off point, sensitivity value was found to be 0.941, and specificity value was found as 0.724 (Figure 1, Table 4). However, using 12 as the cut-off point is suitable in clinical practice.

According to the determined cut-off point, it was observed that 17 patients who presented with the occurrence of OM had a score of 18.53 ± 5.11 and 170 patients who did not develop OM were found to have a score of 8.66 ± 4.67 (z = -5.608, $P = .0001$, Table 5).

Discussion

At the end of logistic regression analysis, "taking a high dose CT regimen," "neutropenia," "xerostomia," "pain," "leukopenia," "parenteral nutrition," "previous history of OM," and "history of previous CT or RT" were found as risk factors. The factors as "using a high-risk chemotherapeutic agent," "being transplanted," and "having a diagnosis of head-neck or oral cancer" were also included in the scale in line with the literature. OM may be affected by many risk factors that may change depending on the patient and treatment taken.[37] Identification of these risk factors helps make a proper clinical evaluation and treatment plan to minimize the incidence and severity of OM.[34,38,39]

One of the most important determinants of OM development is chemotherapy drugs.[40-43] Although the number of studies focusing on the comparison of incidence and severity of CT-associated OM is inadequate, it is generally accepted that antimetabolites and alkylating agents cause high OM rates.[16,44] OM may get more severe when chemotherapeutic drugs are given at high doses and frequently repeated programs, and these drugs may be more harmful when given in combination with other CT agents or ionizing radiation. Mucositis development risk is elevated in high-dose CT regimens because the doses of high-dose CT applications is several times more than standard treatment doses.[45]

Another risk factor in the study was "neutropenia." It has been considered that the decrease in neutrophile count may lead to an impairment in the protective ability against oral mucosal damage and affect the proliferation of oral epithelial cells.[46] Moreover, neutropenic patients are at high risk for microbial colonization. This situation causes an increase in the proinflammatory cytokines that make OM more severe.[47] Cheng et al[47] found in their study with children and adolescents that the most important factor in OM development

Table 3
Logistic Regression Analysis of Risk Factors Included in the Scale

No	Patient follow-up time/risk factors included in the scale	First hospitalization OR (CI)	CT onset [a] OR (CI)	CT day 7[b] OR (CI)	CT day 14[c] OR (CI)
RF3	Taking high-dose CT regimen	10.5 (0.6-176.9)	**5.9 (2.0-17.4)**	**6.0 (1.7-20.1)**	0.0 (0.0)
RF4	Neutropenia	**2.9 (1.0-8.0)**	2.6 (0.9-7.2)	**6.2 (1.7-22.3)**	2.6 (0.8-8.5)
RF6	Xerostomia	**5.4 (1.8-15.5)**	**8.5 (2.6-27.4)**	**8.5 (2.6-27.4)**	**8.2 (2.4-25.8)**
RF7	Pain	**11.2 (3.5-35.6)**	56.3 (−221.6)	193.2 (−)	52 (−202.9)
RF13	Leukopenia	1.2 (0.4-3.6)	1.3 (0.4-4.0)	**3.4 (1.0-10.8)**	**3.3 (1.0-10.6)**
RF20	Parenteral nutrition	10.5 (0.6-176.9)	10.5 (0,6-176.9)	10.5 (0.6-176.9)	**7.4 (1.1-47.9)**
RF21	Previous history of OM	**3.3 (1.2-9.2)**	**3.3 (1.2-9.2)**	**3.2 (1.1-8.9)**	**3.2 (1.1-8.9)**
RF22	History of previous CT or RT	**0.3 (0.1-1.0)**	**0.3 (0.1-1.0)**	**0.3 (0.1-1.0)**	**0.3 (0.1-0.9)**
RF2	Using high-risk chemotherapeutic agent	**0.0 (0.0−)**	**0.3 (0.1-1.1)**	**1.3 (0.4-3.9)**	**0.0 (0.0−)**
RF10	Being transplanted	**2.5 (0.2-24.6)**	**2.5 (0.2-24.6)**	**2.0 (0.2-18.7)**	**2.0 (0.2-18.7)**
RF 5	Having a diagnosis of head-neck or oral cancer	**10.5 (0.6-176.9)**	**10.562 (0.6-176.9)**	**10.5 (0.6-176.9)**	**5.2 (0.4-61.1)**

CI, confidence interval; CT, chemotherapy; OM, oral mucositis; OR, odds ratio; RT, radiotherapy.
$P < .001$.
[a] Chemotherapy start.
[b] Seventh day of chemotherapy.
[c] Fourteen days of chemotherapy.

Table 4
Cut-Off Point of the Scale, Sensitivity, Selectivity, Positive, and Negative Expected Values and Area Under the Curve (AUC) Values

Cut-off Point	Sensitivity	Specificity	True positive rate	Negative expected value	Total accuracy rate	Kappa (ρ)
11.5	94.1	72.4	25.4	99.2	74.3	0.3 (0.0001*)

was neutropenia, and another study reported that neutropenia lasted longer in patients who developed OM.

At the end of logistic regression analysis performed in the study, xerostomia was found as the risk factor with the highest coefficient. Xerostomia may cause an accumulation of bacteria and other debris. The decrease in the amount of saliva increases OM risk.[38,48] McCarthy et al[13] indicated that mouth dryness was one of the two best determinants of mucositis development in patients who were treated with fluorouracil (5-FU).

Pain was found as the most important risk factor in the study. Pain is a significant subjective finding in the WHO scale, toxicity criteria by National Cancer Institute, and on many other scales. OM-associated pain is common and is the most common complaint in patients undergoing cancer) . Another study concluded that oral pain reported by the patient (subjective assessment) was significantly associated with OM and dysphagia scores.

The presence of leukopenia was found to be a risk factor for OM in the study. Because CT suppresses bone marrow, platelets, and leukocytes enter post-CT at least after 7-14 days, and this increases the risk for bleeding and infection among patients.[21] In a study with geriatric patients taking fluorouracil, a significant correlation was found between leukopenia and grade 3 or 4 mucositis, which supports these results.[48] Suresh et al[49] found a positive correlation between white blood cell count and occurrence of OM.

Other risk factors that we found in our study were previous history of OM and history of previous CT or RT. For instance, the probability of developing ulcerative OM for a patient who was treated with a traditional regimen for breast cancer is nearly 20% during the first cycle of CT and increases up to >60% at second cycle.[28] In the study by Goktuna,[39] it was found that development of mucositis during the previous CTs increased the risk for developing OM by 5.76-fold.

Nutritional deficiency and decrease in fluid intake affect cell renewal in a negative way and increases the risk for developing mucositis.[50] In the study, "parenteral nutrition" emerged as one of the risk factors. Both solid and fluid intake of patients are reduced due to OM pain. When this problem continues for a few days to a few weeks, dehydration occurs, and it brings along severe nutritional problems.[51]

OM is one of the common complications of hematopoietic stem cell transplantation (HSCT).[52] OM was observed at a rate of 85%-95% among the patients with HSCT who were taking a high-dose chemotherapy treatment.[53] In the performed studies, the risk and severity of mucositis were found to be higher in allogenic transplantations.[54,55] Although "being transplanted" was not found to be significant based on regression analysis due to less risk for OM development in the study, it was included in the scale because it was found to be effective in the literature.

The most significant risk factor for the common and severe cause of OM was seen to be RT, which was applied to the patients especially over head-neck region. Many studies have shown that OM occurs in almost all patients who undergo RT on the head neck region. This study was conducted on patients with hematological malignancy; but it should not be overlooked that there might be also patients who underwent head and neck RT. For this reason, it was included in the scale.

We aimed to develop a measurement tool that assesses OM risk in hematological patients by the end of this study. The developed measurement tool had 11 items. OM prevalence was used as a measure to prove the predictive validity of risk assessment scales.[56] OM prevalence was found to be 9.7% in this study; and sensitivity, specificity, and positive and negative predictive values of the scale were examined to test how accurately the risk assessment tool we developed could determine OM risk. It is ideal to have a risk assessment tool with a high sensitivity and specificity.[57] Area under the curve value was found as 0.911 in ROC analysis of Oral Mucositis Risk Assessment Scale for Hematology Patients. Based on these data, it is seen that discriminative power of the risk factors for OM development is high, and they can discriminate patients with and without OM risk significantly.

Table 5
Comparison of the Average Score of Patients with and Without OM Formation According to the Cut-Off Point Determined.

Occurence of OM	Mean Scores						
	Mean	Median	SD	min	max	z	p
Developing OM	18.53	19	5.11	5	27	-5.608	0.0001
Not developing OM	8.66	8	4.67	1	25		

OM, oral mucositis; SD, standard deviation.

Limitations

The limitation of the study was the inclusion of patients who were hospitalized in the hematology clinics of only a single university hospital. The other hospitals located in the same city did not have any hematology clinics.

Conclusion

OM Risk Assessment Scale for Hematology Patients is a valid and reliable scale that can be used by nurses and doctors to measure OM risk in hematology patients. At the end of this study, it was suggested to carry out studies for the identification of OM risk factors, to conduct these studies not only on hematology patients but also in all oncology clinics and especially on patients undergoing head-neck RT and to provide consistent and reliable data for the future similar studies. Also, it is recommended that nurses and doctors use Oral Mucositis Assessment Scale for Hematology Patients to determine OM risk in hematology patients undergoing chemotherapy.

Implications for nursing practice

Oral mucositis (OM) is an important problem for hematology patients. Risk assessment and early intervention by nurses may prevent the formation and complications of OM.

The incidence of OM can be reduced by sufficient knowledge and skills to evaluate oral health, correct practices of nursing interventions for oral care, and patient counseling and training.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

This study was supported by Pamukkale University Scientific Research Projects Coordination Unit through project numbers 2018SABE036.

References

1. Al-Ansari S, Zecha JAEM, Barasch A, Lange J, Rozema FR, Raber-Durlacher JE. Oral mucositis induced by anticancer therapies. Curr Oral Health Rep. 2015;2:202-211. doi: 10.1007%2Fs40496-015-0069-4.
2. Sonis ST. Oral mucositis in head and neck cancer: risk, biology, and management. *Am Soc Clin Oncol Educ Book*. 2013. https://doi.org/10.1200/EdBook_AM.2013.33.e236.
3. Can G. *Consensus from Evidence to Practice in Oncology Nursing*. Istanbul, Turkey: Nobel Medical Bookstores; 2015:314.
4. Erden Y. *Development of the Comfort Perception Scale in Oral Mucositis*. Erzurum, Turkey: Atatürk University Institute of Health Sciences; 2019:84.
5. Owlia F, Kazemeini S, Gholami N. Prevention and management of mucositis in patients with cancer: a review article. *Iran J Cancer Prev*. 2012;5(4):216–220.
6. Riley P, Glenny AM, Worthington HV, Littlewood A, Clarkson JE, McCabe MG. Interventions for preventing oral mucositis in patients with cancer receiving treatment: oral cryotherapy. *Cochrane Database Syst Rev*. 2015;12:1–96. https://doi.org/10.1002/14651858.cd011552.pub2.
7. Baysal E, Sarı D. Current approaches in oral mucositis prevention, care and treatment in hematopoietic stem cell transplantation: literature review. *J Hum Sci*. 2016;13(3):5721–5739. https://doi.org/10.46483/deuhfed.634402.
8. Eilers J, Epstein JB. Assessment and measurement of oral mucositis. *Semin Oncol Nurs*. 2004;20(1):22–29. https://doi.org/10.1053/j.soncn.2003.10.005.
9. Harris DJ, Eilers J, Harriman A, Cashavelly BJ, Maxwell C. Putting evidence into practice®: Evidence-based interventions for the management of oral mucositis. *Clin J Oncol Nurs*. 2008;12(1):141–152. https://doi.org/10.1188/08.cjon.141-152.
10. Polit DF, Beck CT. *Essentials of Nursing Research: Appraising Evidence for Nursing Practice*. 7th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010:284–304.
11. World Health Organization (WHO). *Handbook for Reporting Results for Cancer Treatment*. Geneva, Switzerland: WHO; 1979. Available at: https://apps.who.int/iris/bitstream/handle/10665/37200/WHO_OFFSET_48.pdf?sequenc. Accessed 12 March 2021.
12. Schubert MM, Williams BE, Lloid ME, Donaldson G, Chapk MK. Clinical assessment scale for the rating of oral mucosal changes associated with bone marrow transplantation development of an oral mucositis index. *Cancer*. 1992;69(10):2469–2477. https://doi.org/10.1002/1097-0142(19920515)69:10<2469::AID-CNCR2820691015>3.0.CO;2-W.
13. McCarthy GM, Awde JD, Ghandi H, Vincent M, Kocha WI. Risk factors associated with mucositis in cancer patients receiving 5-fluorouracil. *Oral Oncol*. 1998;34:484–490. https://doi.org/10.1016/s1368-8375(98)00068-2.
14. Epstein JB, Gorsky M, Guglietta A, Le N, Sonis ST. The correlation between epidermal growth factor levels in saliva and the severity of oral mucositis during oropharyngeal radiation therapy. *Cancer*. 2000;89(11):2258–2265. https://doi.org/10.1002/1097-0142(20001201)89:11<2258::AID-CNCR14>3.0.CO;2-Z.
15. Bolwell BJ, Kalaycio M, Sobecks R, et al. A multivariable analysis of factors influencing mucositis after autologous progenitor cell transplantation. *Bone Marrow Transplant*. 2002;30(9):587–591. https://doi.org/10.1038/sj.bmt.1703694.
16. Barasch A, Peterson DE. Risk factors for ulcerative oral mucositis in cancer patients: unanswered questions. *Oral Oncol*. 2003;39(2):91–100. https://doi.org/10.1016/s1368-8375(02)00033-7.
17. Robien K, Schubert MM, Bruemmer B, Lloid ME, Potter JD, Ulrich CM. Predictors of oral mucositis in patients receiving hematopoietic cell transplants for chronic myelogenous leukemia. *J Clin Oncol*. 2004;22(7):1268–1275. https://doi.org/10.1200/JCO.2004.05.147.
18. Sonis ST, Elting LS, Keefe D. Perspectives on cancer therapy-induced mucosal injury. *Cancer*. 2004;100(S9):1995–2025. https://doi.org/10.1002/cncr.20162.
19. Redding SW. Cancer therapy-related oral mucositis. *J Dent Educ*.. 2005;69(8):919–929.
20. Grazziutti ML, Dong L, Miceli MH, et al. Oral mucositis in myeloma patients undergoing melphalan-based autologous stem cell transplantation: Incidence, risk factors and a severity predictive model. *Bone Marrow Transplant*. 2006;38(7):501–506. https://doi.org/10.1038/sj.bmt.1705471.
21. Jaroneski LA. The importance of assessment rating scales for chemotherapy-induced oral mucositis. *Oncol Nurs Forum*. 2006;33(6):1085–1090. https://doi.org/10.1188/06.onf.1085-1093.
22. Potting CMJ, Blijlevens NAM, Donnelly JP, Feuth T, Van Achterberg T. A scoring system for the assessment of oral mucositis in daily nursing practice. *Eur J Cancer Care*.. 2006;15(3):228–234. https://doi.org/10.1111/j.1365-2354.2005.00644.x.
23. Vera-Llonch M, Oster G, Hagiwara M, Sonis S. Oral mucositis in patients undergoing radiation treatment for head and neck carcinoma: risk factors and clinical consequences. *Cancer*. 2006;106(2):329–336. https://doi.org/10.1002/cncr.21622.
24. Elting LS, Cooksley CD, Chambers MS, Garden AS. Risk, outcomes, and costs of radiation-ınduced oral mucositis among patients with head-and-neck malignancies. *Int J Radiat Oncol Biol Phys*.. 2007;68(4):110–1120. https://doi.org/10.1016/j.ijrobp.2007.01.053.
25. Strobel ES, Bauchmüller K, Ihorst G, Engelhardt M. Frequency, severity and risk factors for oral mucositis after BEAM conditioning and autologous peripheral blood stem cell transplantation: A single center analysis and review of the literature. *Leuk Lymphoma*. 2007;48(11):2255–2260. https://doi.org/10.1080/10428190701636490.
26. Cheng KKF, Goggins WB, Lee VWS, Thompson DR. Risk factors for oral mucositis in children undergoing chemotherapy: A matched case-control study. *Oral Oncol*. 2008;44(11):1019–1025. https://doi.org/10.1016/j.oraloncology.2008.01.003.
27. Ciuraru NB, Braunstein R, Sulkes A, Stemmer SM. The influence of mucositis on oral thermometry: when fever may not reflect infection. *Clin. Infect. Dis*.. 2008;46(12):1859–1863. https://doi.org/10.1086/588290.
28. Sonis ST. Mucositis: the impact, biology and therapeutic opportunities of oral mucositis. *Oral Oncol*. 2009;45(12):1015–1020. https://doi.org/10.1016/j.oraloncology.2009.08.006.
29. Vokurka S, Steinerova K, Karas M, Koza V. Characteristics and risk factors of oral mucositis after allogeneic stem cell transplantation with FLU/MEL conditioning regimen in context with BU/CY2. *Bone Marrow Transplant*. 2009;44(9):601–605. https://doi.org/10.1038/bmt.2009.66.
30. Saito N, Imai Y, Muto T, Sairenchi T. Low body mass index as a risk factor of moderate to severe oral mucositis in oral cancer patients with radiotherapy. *Support Care Cancer*.. 2012;20(12):3373–3377. https://doi.org/10.1007/s00520-012-1620-7.
31. Krishna SG, Zhao W, Grazziutti ML, Sanathkumar N, Barlogie B, Anaissie EJ. Incidence and risk factors for lower alimentary tract mucositis after 1529 courses of chemotherapy in a homogenous population of oncology patients. *Cancer*.. 2011;117(3):648–655. https://doi.org/10.1002/cncr.25633.
32. Sarode SC, Sarode GS. Radiation-induced oral mucositis and periodontitis proposal for an inter-relationship. *Oral Dis*. 2014;20(6):631–632. https://doi.org/10.1111/odi.12245.
33. Al Ibraheemi AA, Shamoun S. Incidence and risk factors of oral mucositis in patients with breast cancer who receiving chemotherapy in Al-Bashir hospital. *Int J Hematol Oncol Stem Cell Res*. 2016;10(4):217.
34. Tao Z, Gao J, Qian L, et al. Factors associated with acute oral mucosal reaction induced by radiotherapy in head and neck squamous cell carcinoma A retrospective single-center experience. *Medicine*. 2017;96(50):1–5. https://doi.org/10.1097/md.0000000000008446.
35. Davis LL. Instrument review: getting the most from a panel of experts. *Appl Nurs Res*. 1992;5:194–197. https://doi.org/10.1016/S0897-1897(05)80008-4.
36. Cheng KKF. Oral mucositis, dysfunction, and distress in patients undergoing cancer therapy. *J Clin Nurs*. 2007;16:2114–2121. https://doi.org/10.1111/j.1365- 2702.2006.01618.x.
37. Cheng KKF, Yuen JKT. A pilot study of chlorhexidine and benzydamine oral rinses for the prevention and treatment of irradiation mucositis in patients with head and neck cancer. *Cancer Nurs*. 2006;29(5):423–430.
38. Yılmaz MÇ. Mucositis in cancer patients: clinical and economic consequences, associated risk factors. *EGEHFD*. 2008;24(2):166–176.
39. Göktuna G. *Investigation of oral mucositis incidence and Risk Factors in Patients Receiving Chemotherapy*. İzmir, Turkey: Dokuz Eylül Üniversitesi Sağlık Bilimleri Enstitüsü; 2017:84.
40. Barasch A, Peterson DE, Tanzer JM, et al. Helium-neon laser effects on conditioning-induced oral mucositis in bone marrow transplantation patients. *Cancer*. 1995;76(12):2550–2556. https://doi.org/10.1002/1097-0142(19951215)76:12%3C2550::aidcncr2820761222%3E3.0.co;2-x.
41. Grosvenor A, Bulcavage I, Chlebowski RT. Symptoms potentially influencing weight loss in a cancer population. *Cancer*. 1989;63:330–334. https://doi.org/10.1002/1097-0142(19890115) 63:2%3C330::AID-CNCR2820630221%3E3.0.CO;2-U.
42. Zerbe MB, Parkerson SG, Ortlieb ML, Spitzer T. Relationship between oral mucositis and treatment variables in bone marrow transplant patients. *Cancer Nurs*. 1992;15(3):196–205.
43. Wilkes JD. Prevention and treatment of oral mucositis following cancer chemotherapy. *Semin Oncol*. 1998;25:538–551.
44. Wuketich S, Heinz S, Marossi C. Prevalence of clinically relevant oral mucositis in outpatients receiving myelosuppressive chemotherapy for solid tumors. *Support Care Cancer*.. 2012;20:175–183. https://doi.org/10.1007/s00520-011-1107-y.
45. Avritscher EBC, Cooksley CD, Elting LS. Scope and epidemiology of cancer therapy-induced oral and gastrointestinal mucositis. *Semin Oncol Nurs*. 2004;20(1):3–10. https://doi.org/10.1053/j.soncn.2003.10.002.
46. Witko-Sarsat V, Rieu P, Descamps-Latscha B, Lesavre P, Halbwachs-Mecarelli L. Neutrophils: molecules, functions, and pathophysiological aspects. *Lab Invest*. 2000;80(5):617–653. https://doi.org/10.1038/labinvest.3780067.
47. Cheng KKF, Lee V, Li CH, et al. Incidence and risk factors of oral mucositis in paediatric and adolescent patients undergoing chemotherapy. *Oral Oncol*. 2011;47:153–162. https://doi.org/10.1016/j.oraloncology.2010.11.019.
48. Bensinger W, Schubert M, Ang KK, et al. NCCN Task Force Report. Prevention and management of mucositis in cancer care. *JNCCN*. 2008;6(1):1–21.
49. Suresh AV, Varma PP, Sinha S, et al. Risk-scoring system for predicting mucositis in patients of head and neck cancer receiving concurrent chemoradiotherapy. *J Cancer Res Ther*. 2010;6(4):448–451.
50. Sonis ST. The pathobiology oral mucositis. In: Sonis ST, ed. *Oral Mucositis*. London, UK: Springer Healthcare, Tarporley; 2012:7–13. https://doi.org/10.1007/978-1-907673-46-7_2.
51. Brown CG, Wingard J. Clinical consequences of oral mucositis. *Semin Oncol Nurs*. 2004;20(1):16–21. https://doi.org/10.1053/j.soncn.2003.10.004.
52. Shouval R, Kouniavski E, Fein J, et al. Risk factors and implications of oral mucositis in recipients of allogeneic hematopoietic stem cell transplantation. *Eur J Haematol*. 2019;103(4):402–409. https://doi.org/10.1111/ejh.13299.
53. Harman M. *Effect of Three Different Solutions Used in Patients with Hematological Malignity on Oral Mucositis*. Gaziantep, Turkey: Gaziantep University Institute of Health Sciences; 2016:73. MA thesis.
54. Rapoport AP, Miller Watelet LF, Linder T, et al. Analysis of factors that correlate with mucositis in recipients of autologous and allogeneic stem-cell transplants. *J Clin Oncol*. 1999;17(8):2446. https://doi.org/10.1200/jco.1999.17.8.2446. -2446.
55. Sonis ST, Oster G, Fuchs H, et al. Oral mucositis and the clinical and economic outcomes of hematopoietic stem-cell transplantation. *J Clin Oncol*. 2001;19(8):2201–2205. https://doi.org/10.1200/jco.2001.19.8.2201.
56. Hajian-Tilaki K. Receiver operating characteristic (ROC) curve analysis for medical diagnostic test evaluation. *Caspian J Intern Med*. 2013;4(2):627.
57. Efteli E. Development of a new risk assessment scale to compile the risk of developing pressure sores. PhD diss. İzmir, Turkey: University of Ege; 2017:112.