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Analysis of pain prognosis, medication efficacy, treatment willingness and influencing factors in patients with burning mouth syndrome: a cross-sectional survey

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Abstract

Objective To explore the pain prognosis, medication efficacy and treatment willingness of patients with burning mouth syndrome (BMS) and to identify the factors influencing the pain prognosis, medication efficacy and treatment willingness of patients with BMS.

Methods Medical records of patients who were clinically diagnosed with BMS and who complained of oral mucosal pain at the Department of Stomatology, The First Affiliated Hospital of Zhengzhou University, were retrospectively collected from January 2019 to April 2022. Telephone follow-ups were conducted in August 2024 to investigate the patients' pain prognosis, medication efficacy, willingness for treatment and related treatment information.

Results Among the 192 patients, only 31.77% (61/192) reported complete elimination of pain; 37.50% (72/192) reported that the pain still existed but had improved, and 30.73% (59/192) reported no improvement at all. A total of 31.25% (60/192), 34.90% (67/192), and 32.81% (63/192) of the BMS patients evaluated medication efficacy as significantly effective, effective, or ineffective, respectively. Among the 131 patients who still had pain symptoms, 38.17% (50/131) intended to continue treatment. Logistic regression revealed that patients who were older ($P=0.023$), who had visited multiple hospitals for treatment ($P=0.001$), who were afraid of cancer ($P=0.011$) and who were prone to anxiety or depression ($P<0.001$) had poorer pain improvement. Patients who had visited multiple hospitals ($P<0.001$) and those who were prone to anxiety or depression ($P<0.001$) had significantly lower evaluations of medication efficacy. Males ($P=0.041$) and those who had visited multiple hospitals ($P<0.001$) were more willing to continue treatment.

Conclusion The prognosis for most BMS patients tends to be relatively poor. Age, anxiety or depression, and fear of cancer may affect the pain prognosis of patients with BMS, whereas psychological factors may also impact the efficacy of medication.

Keywords Burning mouth syndrome, Prognosis, Medication efficacy, Treatment willingness, Influencing factors, Survey

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Introduction

Burning mouth syndrome (BMS) is a group of symptoms primarily characterized by burning pain in the tongue area, often without significant clinical signs of damage or characteristic histopathological changes. The prevalence of BMS is estimated to be between 0.1% and 3.9% [1, 2], with an overall prevalence of 1.73% in the general population [3]. There are variations in prevalence across different regions, sexes, and age groups. Over 70% of patients are middle-aged and elderly women [2, 4–6], with a male-to-female ratio of approximately 1:7 [7]. The etiology of the disease remains unclear, but it is currently believed to be associated with neuropsychiatric factors [8], local factors [9–11], and systemic diseases [12–14]. Treatment primarily focuses on pharmacological interventions, and studies have shown that laser therapy and psychotherapy may also be effective [15–20]. Regrettably, it has been difficult to achieve satisfactory results with various treatment plans for BMS [21–24]. Patients are plagued by long-term pain, which not only affects their quality of life but also increases their mental burden, inducing or exacerbating anxiety and depression. Some patients even develop a fear of cancer, living in constant dread. Previous research has focused mainly on the etiological factors and treatment methods of BMS. However, given the suboptimal efficacy of existing medical treatments, studying the long-term prognosis characteristics and factors affecting the prognosis of patients with BMS is particularly important. Therefore, this study collected medical histories and conducted telephone follow-ups with 192 patients who complained of oral mucosal pain due to BMS between January 2019 and April 2022, with a primary discussion of the prognosis and factors influencing the prognosis of patients with BMS. The study also revealed that patients have different attitudes and intentions towards the disease, which piqued the author's interest and were included in the research.

Materials and methods

Study design

This retrospective study collected data from patients who visited the Department of Stomatology at The First Affiliated Hospital of Zhengzhou University from January 2019 to April 2022 and were ultimately diagnosed with BMS. Before February 2020, the diagnosis was based on the International Classification of Headache Disorders 3rd edition (ICHD-3) [25], and after February 2020, the newly released International Classification of Orofacial Pain 1st edition (ICOP) [26] was used as a reference. To unify the standards, the medical records of the collected cases were reviewed to ensure that all selected cases were consistent with the diagnostic criteria of BMS in the ICOP. These patients underwent a careful oral examination when they visited our hospital, and no abnormalities in the appearance of the oral mucosa were found, nor were significant local pathogenic factors found. Our hospital's doctors also inquired about the patient's medical history in detail, reviewed the medical records and examination reports provided by the patient, and provided corresponding examinations, including salivary flow tests and bloodwork, to patients who needed further investigation of other causes of pain. Medical records were retrieved, and telephone follow-ups were conducted individually in August 2024. The inclusion criteria were complete clinical data; diagnosed with BMS; clear oral mucosal pain at the time of visit; contact by telephone; and willingness to complete the follow-up survey. The exclusion criteria were patients with other oral mucosal diseases or oral mucosal pain caused by other reasons and patients who were unreachable or unwilling to cooperate with the follow-up survey.

Data collection

The collected data comprised two parts: clinical medical records and survey questionnaire data. The medical records included sex, age at the time of visit, medical history, chief complaints, and medications used. The self-designed telephone follow-up questionnaire included the current degree of pain improvement (completely eliminated, relieved, no change), evaluation of medication efficacy (significantly effective, effective, ineffective), current willingness to continue treatment (yes, no), previously used medications, treatment experiences, whether they generally feel anxious/depressed, and whether there is a fear of cancer. The detailed questionnaire is shown in Appendix A. A total of 192 patients were included, with 30 males and 162 females, and the average age was 55 years.

Statistical analysis

The quantitative data are presented as medians and interquartile ranges [M(P25,P75)], whereas the qualitative data are presented as counts and percentages. The statistical tables show the characteristics of patients with BMS. The chi-square test, Fisher–Freeman–Halton exact test, and Mann–Whitney U test were used to compare the prognosis and willingness for retreatment with different characteristics of patients with BMS. Ordinal logistic regression was adopted to explore the factors influencing pain improvement and medication efficacy, and a proportional odds assumption test was conducted. Logistic regression was adopted to explore the relationships between multiple factors and the willingness to continue treatment. SPSS 19.0 software (IBM Corp.) was used for data analysis and processing. All tests were two-sided,

with a significance test level of 0.05 ($\alpha = 0.05$). $P < 0.05$ indicated that the difference was statistically significant.

Results

Sample characteristics

Among the respondents, 30 were male (15.63%), and 162 were female (84.38%). The median time from the onset of symptoms to follow-up (August 1, 2024) was 4.45 (3.82, 5.21) years, ranging from 2.69 to 17.55 years. The median age of the patients was 55 (49, 63) years. The pain site was mainly in the tongue (147 patients, 76.56%), 7 patients (3.65%) experienced pain at other single sites, such as lips, cheeks and palate, and 38 patients (19.79%) experienced widespread pain throughout the entire oral mucosa. There were differences in pain location between genders (χ^2=9.528, P=0.009). 38.54% of the BMS respondents (74/192) had a history of malignant tumors or systemic diseases. Approximately half (92/192, 47.92%) had changed multiple locations for treatment; that is, they had visited more than 3 different hospitals. 46.88% (90/192) of the respondents were prone to anxiety or depression, and 25.00% (48/192) of the respondents had a fear of cancer after they became ill (Table 1).

Table 1 Demographic characteristics of patients with BMS

Characteristics	Male (n=30)	Female (n=162)	Total (N=192)
Basic information and medical records			
Age, n(%)[a]			
< 55 years old	12(40.00)	83(51.23)	95(49.48)
≥ 55 years old	18(60.00)	79(48.77)	97(50.52)
Pain location, n(%)[a]			
Tongue	21(70.00)	126(77.78)	147(76.56)
Lips, cheeks, palate and other single parts	4(13.33)	3(1.85)	7(3.65)
Extensive pain of the whole mouth mucosa	5(16.67)	33(20.37)	38(19.79)
Combined with malignant tumor or systemic history, n(%)[a]			
Yes	14(46.67)	60(37.04)	74(38.54)
No	16(53.33)	102(62.96)	118(61.46)
Time from pain onset to follow-up, years, $M(P_{25},P_{75})$[a]			
	4.36(3.54,5.20)	4.45(3.92,5.21)	4.45(3.82,5.21)
Medical experience and psychological status			
Changed to multiple locations for medical treatment (visited more than 3 different hospitals), n(%)[b]			
Yes	15(50.00)	77(47.53)	92(47.92)
No	15(50.00)	85(52.47)	100(52.08)
Fear of cancer after being diagnosed, n(%)[b]			
Yes	4(13.33)	44(27.16)	48(25.00)
No	26(86.67)	118(72.84)	144(75.00)
Usually prone to anxiety or depression, n(%)[b]			
Yes	11(36.67)	79(48.77)	90(46.88)
No	19(63.33)	83(51.23)	102(53.13)

[a] The data were collected from medical records, with age based on the initial visit

[b] The data were collected from telephone follow-up during the August 2024

Pain prognosis, medication efficacy and treatment willingness of patients with BMS

Regarding the pain improvement, only 31.77% (61/192) of the BMS respondents had completely eliminated pain; 37.50% (72/192) of the patients indicated that their pain had persisted but was alleviated. Conversely, 30.73% (59/192) of patients said that there was no improvement or change at all. Among the 131 patients who still had pain symptoms, 38.17% (50/131) expressed a desire for subsequent treatment, whereas 61.83% (81/131) had no intention of pursuing further treatment. The reasons mentioned mainly included that the existing pain did not significantly impact their daily lives and that further treatment was not expected to eradicate the pain (Table 2).

Regarding the use of medications, 2 patients (1.04%) did not take any medications, while the remaining patients had used more than one type of medication. A total of 115 patients used vitamins (including mecobalamin), 63 patients were treated with lipoic acid, 18 patients used oryzanol, 115 patients used antibacterial mouthwashes, 6 patients used lidocaine ointment and other painkillers, 8 patients took oral antibiotics, and 73 patients used Chinese herbal medicines. For the overall evaluation of medication efficacy, only 31.25% of patients (60/192) said that medication was significantly effective in improving pain, 34.90% (67/192) indicated that the drugs were effective and could provide mild relief, and 32.81% (63/192) expressed that the drugs were ineffective (Table 2).

Factors influencing the pain prognosis of patients with BMS

The cure rates of different groups of people were analysed by taking the disappearance of pain as the criterion of recovery (Table 3). Compared with the recovery rate of 38.95% (37/95) in the group under 55 years of age, the recovery rate of the group over 55 years of age was lower, at 24.74% (24/97). The cure rate of the group that had visited multiple hospitals for treatment (18.48%, 17/92) was lower than that of the other group (44.00%, 44/100). The cure rate of patients with cancer fear (8.33%, 4/48) was lower than that of patients without fear of cancer (39.58%, 57/144). The cure rate of patients who were

Table 2 Pain prognosis, medication efficacy, and treatment willingness of patients with BMS

Characteristics	Male ($n=30$)	Female ($n=162$)	Total ($N=192$)
Pain prognosis, n(%)			
Completely eliminated	9(30.00)	52(32.10)	61(31.77)
Relieved	10(33.33)	62(38.27)	72(37.50)
No change	11(36.67)	48(29.63)	59(30.73)
Medication efficacy (Self-evaluation of the effect of medication on pain relief), n(%)			
Significantly effective	10(33.33)	50(30.86)	60(31.25)
Effective	11(36.67)	56(34.57)	67(34.90)
Ineffective	8(26.67)	55(33.95)	63(32.81)
None(no medication for treatment)	1(3.33)	1(0.62)	2(1.04)
Treatment willingness, n(%)			
Yes	11(36.67)	39(24.07)	50(26.04)
No	10(33.33)	71(43.83)	81(42.19)
None(pain completely eliminated)	9(30.00)	52(32.10)	61(31.77)

prone to anxiety or depression was 4.44% (4/90), which was lower than that of the comparison group, at 55.88% (57/102), and the above differences were all statistically significant (χ^2=4.468, P=0.035;χ^2=14.398, P<0.001;χ^2=16.218, P<0.001;χ^2=58.359, P<0.001). There was no statistical difference in the cure rate among patients of different sexes (χ^2=0.051, P=0.821), different pain sites (χ^2=1.379, P=0.495), different onset times of pain symptoms (Z=−0.462, P=0.644), or a combination of malignant tumors or systemic history (χ^2=0.026, P=0.871).

With pain improvement as the dependent variable (1=completely eliminated, 2=relieved, 3=no change), ordered logistic regression was further used for multivariate analysis, which satisfied the proportional odds assumption (χ^2=8.366, P=0.498). The results (Table 4) revealed that age, multiple hospital visits, fear of cancer after illness, and susceptibility to anxiety or depression had statistically significant effects on pain prognosis in patients with BMS (all P<0.05). Specifically, compared with patients<55 years old, patients≥55 years old had worse pain improvement (P=0.023, OR=2.028). Patients who had changed multiple hospitals for medical treatment had poor pain improvement (P=0.001, OR=2.697), and fear of cancer after illness (P=0.011, OR=2.764) and susceptibility to anxiety or depression (P<0.001, OR=9.214) negatively affected disease-related pain.

Factors influencing medication efficacy in patients with BMS

The drug is considered effective if it is significantly effective or has a certain ability to relieve pain. The medication efficacy of patients with different characteristics was compared. As shown in Table 3, the medication efficacy in patients with BMS who had visited multiple hospitals for treatment (51.65%, 47/91) was lower than that in the other groups (80.81%, 80/99, χ^2=18.191, P<0.001). The medication efficacy of patients with cancer fear (44.68%, 21/47) was lower than that of patients without cancer fear (74.13%, 106/143), and the difference was statistically significant (χ^2=13.838 P<0.001). Compared with patients without anxiety or depression (83.17%, 84/101), patients who were prone to anxiety or depression had a lower medication efficacy of 48.31% (43/89, χ^2=25.931, P<0.001). The median time from the onset of pain to follow-up in the drug-effective group was 4.38 years, which was lower than the 4.59 years in the drug-ineffective group (Z=−2.334, P=0.020).

Taking medication efficacy as the dependent variable (1=significantly effective, 2=effective, mildly relieved, 3=ineffective), multiclass ordered logistic regression was conducted with a test for the proportional odds assumption (χ^2=14.170, P=0.116). The results (Table 4) revealed that multiple visits to hospitals, proneness to anxiety or depression, and a history of malignant tumors or systemic diseases all had statistically significant effects on medication efficacy (all P<0.05). Specifically, patients who had visited multiple hospitals (P<0.001) and those who were prone to anxiety or depression (P<0.001) rated medication efficacy lower. However, patients with malignant tumors or systemic disease histories had greater evaluations of medication efficacy (P=0.002).

Factors influencing the willingness to retreat in patients with BMS

The results of the univariate analysis in Table 5 revealed that 52.00% of the patients who had visited multiple hospitals were willing to continue treatment, which was higher than that of the other group (19.64%, χ^2=14.223, P<0.001). Compared with 31.03% of patients who were not afraid of cancer and were willing to continue treatment, patients with a fear of cancer were more inclined to continue treatment, accounting for 52.27%, and the difference was statistically significant (χ^2=5.585, P=0.018). 52.38% of the males were willing to continue treatment, which was higher than 35.45% of the females. 43.10% of those aged<55 years were willing to continue treatment, whereas only 34.10% of those aged≥55 years were willing to continue treatment. 34.72% of patients with relieved pain were willing to continue treatment, while the proportion of patients with no improvement in pain was greater, reaching 42.37%. As the efficacy of the drug decreased, patients' willingness to treat increased, but the above factors had no statistically significant effect on treatment willingness (all P>0.05).

Table 3 Recovery and medication efficacy of BMS patients with different characteristics

Characteristics	Cure			Medication efficacy		
	Yes ($n=61$)	No ($n=131$)	χ^2/Z(*P*)	Significantly effective/ Effective ($n=127$)	Ineffective ($n=63$)	$\chi^2/t/Z$(*P*)
Age, n(%)						
< 55 years old	37(38.95)	58(61.05)	4.468(0.035)[a]	65(68.42)	30(31.58)	0.214(0.644)[a]
≥ 55 years old	24(24.74)	73(75.26)		62(65.26)	33(34.74)	
Sex						
Female	52(32.10)	110(67.90)	0.051(0.821)[a]	106(65.84)	55(34.16)	0.479(0.489)[a]
Male	9(30.00)	21(70.00)		21(72.41)	8(27.59)	
Pain location, n(%)						
Tongue	44(29.93)	103(70.07)	1.379(0.495)[b]	98(67.12)	48(32.88)	0.474(0.862)[b]
Lips, cheeks, palate and other single parts	2(28.57)	5(71.43)		4(57.14)	3(42.86)	
Extensive pain of the whole mouth mucosa	15(39.47)	23(60.53)		25(67.57)	12(32.43)	
Combined with malignant tumor or systemic history, n(%)						
Yes	23(31.08)	51(68.92)	0.026(0.871)[a]	54(73.97)	19(26.03)	2.720(0.099)[a]
No	38(32.20)	80(67.80)		73(62.39)	44(37.61)	
Time from pain onset to follow-up, years, $M(P_{25},P_{75})$						
	4.44(3.98,5.07)	4.46(3.80,5.29)	−0.462(0.644)[c]	4.38(3.77,4.96)	4.59(4.14,5.86)	−2.334(0.020)[c]
Changed to multiple locations for medical treatment (visited more than 3 different hospitals), n(%)						
Yes	17(18.48)	75(81.52)	14.398(< 0.001)[a]	47(51.65)	44(48.35)	18.191(< 0.001)[a]
No	44(44.00)	56(56.00)		80(80.81)	19(19.19)	
Fear of cancer after being diagnosed, n(%)						
Yes	4(8.33)	44(91.67)	16.218(< 0.001)[a]	21(44.68)	26(55.32)	13.838(< 0.001)[a]
No	57(39.58)	87(60.42)		106(74.13)	37(25.87)	
Usually prone to anxiety or depression, n(%)						
Yes	4(4.44)	86(95.56)	58.359(< 0.001)[a]	43(48.31)	46(51.69)	25.931(< 0.001)[a]
No	57(55.88)	45(44.12)		84(83.17)	17(16.83)	

[a] Chi-square test

[b] Fisher-Freeman-Halton exact test

[c] Mann-Whitney U test

Treatment willingness was used as the dependent variable (yes = 1, no = 0), and the indicators in Table 5 were included as independent variables in the binary logistic regression model (Table 6). The results revealed that sex and multiple hospital visits were independent influencing factors for the treatment willingness of patients with BMS. Specifically, the treatment willingness of men was 3.667 times greater than that of women (95% CI: 1.005 ~ 12.745, $P=0.041$). The willingness of patients who had visited multiple hospitals to continue treatment was 6.275 times greater than that of patients who had not visited multiple hospitals (95% CI: 2.351 ~ 16.749, $P<0.001$).

Discussion

BMS is a mucosal disease of the oral cavity that predominantly affects middle-aged and elderly individuals, with a particularly high incidence rate among women during menopause and perimenopause. The main symptom is burning pain in the tongue, and some patients also experience numbness and dry mouth. This condition has a long course and is difficult to cure, and there is a lack of effective treatment options in clinical practice, making it a significant challenge in the academic community. This study investigated the pain prognosis, medication efficacy, and treatment willingness of 192 patients with BMS and investigated the related influencing factors.

Table 4 Ordinal logistic regression results of factors affecting pain prognosis and medication efficacy

Variable	Pain prognosis			Medication efficacy		
	B	*P*	OR	B	*P*	OR
Threshold[ref = No change/Ineffective]						
Completely eliminated/Significantly effective	1.027	.030	2.793	0.546	.254	1.727
Relieved/Effective	3.502	.000	33.193	2.728	.000	15.302
Sex(ref = Female)						
Male	0.706	.107	2.026	0.020	.962	1.021
Age(ref = < 55 years old)						
≥ 55 years old	0.707	.023	2.028	0.079	.800	1.082
Pain location(ref = Tongue)						
Extensive pain of the whole mouth mucosa	−0.282	.467	.755	−0.125	.740	.882
Lips, cheeks, palate and other single parts	0.720	.400	2.055	0.665	.429	1.945
Fear of cancer after being diagnosed(ref = no)						
Yes	1.017	.011	2.764	0.412	.296	1.509
Usually prone to anxiety or depression(ref = no)						
Yes	2.221	.000	9.214	1.914	.000	6.780
Changed to multiple locations for medical treatment (visited more than 3 different hospitals, ref = no)						
Yes	0.992	.001	2.697	1.411	.000	4.098
Time from pain onset to follow-up(years)	0.025	.756	1.026	0.065	.452	1.067
Combined with malignant tumor or systemic history(ref = no)						
Yes	−0.309	.319	.734	−1.006	.002	.366

Pain prognosis of the disease and influencing factors

Among the 192 patients, only 31.77% (61/192) experienced complete disappearance of pain; 37.50% (72/192) reported some alleviation of pain, and 30.73% (59/192) reported no improvement. This means that 68.23% of the patients still experienced pain, indicating a poor long-term prognosis for patients with BMS. An early study reported 43 patients who were affected by BMS for nearly 6 years, and 13 reported complete healing during the telephone interview; that is, the healing rate was 30.23%, which is similar to that reported in this study [27]. A study reported the results in the BMS group using alpha-lipoic acid therapy, with complete resolution in 31% and some improvement in 81% after 2 months [28]. Another study reported that 50% of BMS patients experience complete or partial relief with or without any treatment, and 20% of patients achieve complete spontaneous remission within 6–7 years after onset [29]. However, two other studies reported that only 3% to 4% of patients achieved complete spontaneous remission within 5 to 6 years after the clinical manifestation of BMS, and fewer than 50% of patients experienced symptom improvement after treatment [30, 31]. The possible reasons for these differing results may be the differences in sample selection, social environments, treatment methods and variations in the follow-up period. Another factor that may lead to different prognostic results is the strictness of diagnosis and case screening. As the understanding of the pathophysiology and classification of BMS continues to evolve, the diagnostic and classification criteria have been changing constantly, and even now, they are not fully unified. Later studies used more stringent diagnostic criteria, which may lead to lower reported rates of complete symptom relief. The relatively higher cure rate in this study is considered to be that the overall sample of this study is relatively younger, with an average age of 55 years old. This study shows that increased age may worsen the prognosis, which may also be one of the reasons for the higher pain relief rate in this study. Second, it is due to the differences in treatment methods and follow-up periods. The recovery rate is closely related to the basic characteristics of patients and the treatment plans [32]. In addition, although this study adopted the latest standards, it is a retrospective study and cannot systematically observe the cases. Therefore, it has certain limitations in the strictness of case screening, which may also have a certain impact. This is discussed in more detail in the limitations section.

This study further analysed the factors affecting the pain prognosis of patients with BMS. Both univariate group comparisons and logistic regression analysis indicated that older age, having sought treatment in multiple locations, and the presence of a fear of cancer and proneness to anxiety or depression significantly decreased the

Table 5 Willingness to continue treatment of BMS patients with different characteristics

Characteristics	Willingness to continue treatment		
	Yes (n = 50)	No (n = 81)	$\chi^2/t/Z(P)$
Age, n(%)			
< 55 years old	25(43.10)	33(56.90)	1.074(0.300)[a]
≥ 55 years old	25(34.25)	48(65.75)	
Sex			
Female	39(35.45)	71(64.55)	2.141(0.143)[a]
Male	11(52.38)	10(47.62)	
Pain location, n(%)			
Tongue	38(36.89)	65(63.11)	1.573(0.473)[b]
Lips, cheeks, palate and other single parts	1(20.00)	4(80.00)	
Extensive pain of the whole mouth mucosa	11(47.83)	12(52.17)	
Combined with malignant tumor or systemic history, n(%)			
Yes	19(37.25)	32(62.75)	0.029(0.864)[a]
No	31(38.75)	49(61.25)	
Time from pain onset to follow-up, years, $M(P_{25},P_{75})$			
	4.51(3.73,5.90)	4.43(3.83,5.25)	−0.024(0.981)[c]
Changed to multiple locations for medical treatment (visited more than 3 different hospitals), n(%)			
Yes	39(52.00)	36(48.00)	14.223(< 0.001)[a]
No	11(19.64)	45(80.36)	
Fear of cancer after being diagnosed, n(%)			
Yes	23(52.27)	21(47.73)	5.585(0.018)[a]
No	27(31.03)	60(68.97)	
Usually prone to anxiety or depression, n(%)			
Yes	37(43.02)	49(56.98)	2.501(0.114)[a]
No	13(28.89)	32(71.11)	
Pain prognosis, n(%)			
Relieved	25(34.72)	47(65.28)	0.804(0.370)[a]
No change	25(42.37)	34(57.63)	
Medication efficacy, n(%)			
Significantly effective	5(29.41)	12(70.59)	0.853(0.653)[a]
Effective	20(35.71)	36(64.29)	
Ineffective	23(41.07)	33(58.93)	

[a] Chi-square test

[b] Fisher-Freeman-Halton exact test

[c] Mann-Whitney U test

degree of pain improvement. A study on the pain behavior of patients with BMS has shown a strong correlation between pain intensity and emotions, with stress and fatigue being frequently cited as factors that exacerbate pain, whereas relaxation has been shown to alleviate pain [33]. Multiple studies have indicated a correlation between the onset of BMS and the presence of anxiety and depression [34–39]. Persistent oral burning pain can impose a significant psychological burden on patients [40], and some patients may also be afraid of cancer. In this study, some patients sought treatment in multiple locations, which may be due to severe conditions and poor treatment outcomes. This behavior reflects a state of anxiety and concern regarding their illness, and interestingly, this group tended to have a poorer pain prognosis. This study highlights the significant impact of psychological conditions on the prognosis of patients with BMS. Studies have shown that both cognitive–behavioral therapy and group psychotherapy can lead to significant improvements in reducing both pain intensity and anxiety levels in patients with BMS [18, 20]. This finding suggests that the patient's attitude towards the disease is crucial. "To cure sometimes, to relieve often, to comfort always" aptly summarizes and guides the treatment of

Table 6 Logistic regression analysis of factors influencing the willingness to continue treatment in patients with BMS

Variable	B	S.E	Wald χ^2	*P*	OR
Sex(ref = female)					
male	1.299	0.636	4.179	0.041	3.667
Age(ref = < 55 years old)					
≥ 55 years old)	−0.620	0.466	1.773	0.183	0.538
Pain location(ref = Tongue)					
Lips, cheeks, palate and other single parts	−1.746	1.374	1.615	0.204	0.174
Extensive pain of the whole mouth mucosa	0.896	0.558	2.579	0.108	2.450
Fear of cancer after being diagnosed(ref = no)					
Yes	0.888	0.514	2.978	0.084	2.430
Usually prone to anxiety or depression(ref = no)					
Yes	0.651	0.534	1.486	0.223	1.917
Changed to multiple locations for medical treatment (visited more than 3 different hospitals, ref = no)					
Yes	1.837	0.501	13.446	< 0.001	6.275
Time from pain onset to follow-up(years)	−0.152	0.114	1.777	0.182	0.859
Combined with malignant tumor or systemic history(ref = no)					
Yes	−0.606	0.472	1.647	0.199	0.546
Pain prognosis(ref = Relieved)					
No change	−1.317	0.829	2.526	0.112	0.268
Medication efficacy (ref = Significantly effective)					
Effective	−0.304	0.772	0.155	0.694	0.738
Ineffective	0.600	1.031	0.339	0.560	1.822

BMS. Physicians are advised to embrace an understanding and supportive stance towards their patients' experiences, acknowledging that the symptoms are real and not associated with any form of cancer. It is also important to accept realistic expectations regarding the outcomes of BMS treatment. This can help alleviate anxiety and fear of cancer, potentially leading to a significant reduction in patients' pain levels [41]. For patients with emotional and cognitive issues, physicians should actively provide emotional support, cognitive correction, and psychological treatment when necessary, which will be beneficial for improving patient prognosis.

Medication efficacy and influencing factors

The treatment of BMS relies primarily on medication. In China, commonly used drugs include B-vitamin drugs (such as mecobalamin and compound vitamin tablets), lipoic acid, and oryzanol [42–49]. The onset of BMS may also be related to candidiasis or bacterial infections; hence, in China, antibacterial mouthwashes, such as a 2% sodium bicarbonate solution, are sometimes used as adjunctive treatments for BMS [10]. Some BMS patients may also self-administer antibiotics or analgesics. A portion of patients seek treatment from traditional Chinese medicine (TCM). TCM practitioners use different herbal prescriptions on the basis of the patient's pulse diagnosis [50, 51]. Additionally, reports in the literature indicate that psychotropic drugs such as clonazepam can also be used to treat BMS [52]; however, in China, psychotropic drugs must be prescribed by psychiatrists, so they are rarely used in the oral treatment of BMS.

However, the therapeutic effect of medication on BMS has always been questioned [53–55]. Many researchers believe that improvements in BMS pain due to medication are very limited. Even if patients improve or recover, many patients may not recover from the medication. This study investigated feedback on the efficacy of medication in patients. Only 31.25% (60/192) reported that the medication was significantly effective in improving pain, 34.90% (67/192) reported that the drugs were effective and could provide mild relief, and 32.81% (63/192) considered the medication to be ineffective. These findings indicate that the prognosis for patients with BMS treated with medication is not ideal.

Further analysis of the impact of various factors on the efficacy of medication revealed that both univariate group comparisons and logistic regression analyses revealed that patients who had sought treatment in multiple locations and those prone to anxiety or depression had significantly lower evaluations of medication efficacy. These two groups also had poorer pain prognoses. Additionally, univariate group comparisons indicated that individuals with a fear of cancer and those with a longer duration from the onset of pain to follow-up reported

lower effectiveness of medication. Furthermore, the onset of BMS is often related to systemic diseases such as diabetes and thyroid diseases [12, 13]. Studies have shown that patients with BMS have poorer health status and more comorbidities [56]. Surprisingly, logistic regression analysis revealed that individuals with a history of tumors or systemic diseases had better feedback on the effectiveness of medication. Considering that such patients generally have a history of long-term medication use, this may reflect a higher level of acceptance of medication among this population and a more positive response to drug treatment.

Treatment experience and the willingness to continue treatment

The pain associated with BMS typically reduces the quality of life of patients [57]. Some patients also experience a decline in sleep quality [58]. A number of patients suffer significant psychological distress due to the pain associated with BMS. Studies have shown that 20% to 30% of patients with chronic pain have contemplated suicide [59, 60]. There have even been case reports of two BMS patients attempting suicide due to unbearable pain and despair about life [61, 62]. For chronic diseases that are difficult to cure, patients who undergo prolonged treatment with poor outcomes gradually lose faith in the therapeutic process. Owing to the poor treatment effects of BMS, many patients seek treatment at multiple hospitals, but with limited improvement, leading them to also gradually lose confidence in the treatment.

None of the 192 patients in this study are currently receiving treatment at our hospital, and none of them were taking medication or receiving clinical treatment during telephone follow-up. This study investigated their treatment experiences and found that the treatment was intermittent and unstable. 92 patients (47.92%) had sought medical advice from multiple locations, indicating that nearly half of the BMS patients might visit various hospitals for treatment. In fact, since BMS often has a long disease course and relatively poor treatment effects and is often unlikely to have a major impact on health, few BMS patients may persist in treatment at the same institution for several years. Among the 131 patients who still experienced pain during the follow-up, 38.17% (50/131) indicated a willingness to continue their treatment when asked. A total of 61.83% (81/131) of the patients responded negatively, and when asked about the reasons for not wanting to continue treatment, there were two main aspects: first, losing confidence in treatment and not wanting to try further; second, having adapted to the condition and believing that the symptoms did not affect their life; hence, no further treatment was needed. This result indicates that the vast majority of BMS patients, either actively or passively, choose to give up treatment and live with the disease. This result indicates that in the current context of a lack of effective treatment methods, physicians should encourage patients to come to terms with the existence of the disease, alleviate their anxiety, and minimize the impact of the disease on their daily lives as much as possible.

Further analysis of the factors affecting the willingness to continue treatment revealed that both univariate group comparisons and logistic regression analysis indicated that individuals who had sought treatment from multiple locations had a significantly greater willingness to continue treatment. Univariate group comparisons also revealed that those with a fear of cancer after falling ill had a significantly greater willingness to continue treatment. Logistic regression analysis further revealed that males were significantly more willing to continue treatment than females were. Personalized management tailored to the circumstances of each patient can enhance their quality of life [63]. For those who are more willing to receive treatment, physicians should give them more confidence. Concurrently, physicians should also instruct them on how to reduce their anxiety about the disease and face it with a more peaceful attitude.

Strengths and limitations

Previous studies have focused primarily on the etiological factors and treatment methods for BMS. Unfortunately, current medical treatments are not effective for treating BMS. Therefore, this study adopts a new perspective, focusing on the prognosis and influencing factors of patients with BMS, as well as their attitudes towards disease treatment, and discusses what additional help physicians can provide for patients beyond medical means. Second, the methodology employed was multiclass ordered logistic regression, which allows the evaluation of the impact of different factors on changes in pain levels and efficacy levels and provides a more detailed analytical perspective than binary logistic regression to address ordered categorical outcome variables. However, this study also has certain limitations. First, the data obtained by telephone follow-up are limited, and the evaluation of pain prognosis and medication efficacy depends on the patient's subjective feelings. Second, although physicians conducted thorough examinations during the initial consultations, it is still not possible to completely rule out the possibility of secondary BMS when screening cases. For instance, 115 patients received antibacterial mouthwash, and 8 patients took oral antibiotics. If such treatments lead to symptom improvement, it suggests that the pain might be caused by oral infection rather than primary BMS. A study on patients with oral

burning symptoms but without obvious mucosal abnormalities suggested that even in the absence of mucosal abnormalities, patients who respond positively to antibiotics or antifungal agents should be considered potential cases of secondary BMS rather than primary BMS [64]. However, since this study is a retrospective survey, patients often used a combination of multiple medications. Those who received antibacterial mouthwash treatment often concurrently used other medications, such as alpha-lipoic acid and mecobalamin. Therefore, it is impossible to determine which specific medication contributed to the symptom relief. This makes it difficult to precisely re-screen and exclude cases that may be secondary BMS. This could potentially lead to some bias in the results. Additionally, because patients with BMS are relatively older, they are more likely to have various systemic diseases, and some patients may even have undetected systemic diseases. Therefore, it becomes difficult to determine whether oral mucosal pain in patients is due to BMS or merely a manifestation of systemic disease. One study investigated the comorbidities of patients with BMS and reported that only 9.5% of patients with BMS had no systemic disease and suggested that patients be diagnosed with BMS in the presence of symptoms without excluding comorbidities to reduce bias in BMS research [65]. This study incorporates systemic disease factors into the discussion of BMS prognosis precisely for such considerations, hoping to provide some new explorations. This study incorporates systemic disease factors into the discussion of BMS prognosis precisely for such considerations, hoping to provide some new explorations.

Conclusions

In summary, this study demonstrated that factors such as age, anxiety or depression, and fear of cancer may influence the pain prognosis of patients with BMS, and psychological factors may also impact the efficacy of medication. These findings can provide a reference for the early assessment of disease prognosis and the effectiveness of drugs. The experience of visiting multiple hospitals may affect the pain prognosis, medication efficacy and treatment willingness of patients with BMS. This study also revealed that the prognosis for the majority of BMS patients tends to be poor, indicating that guiding patients to adapt to the disease is an issue that clinical physicians need to consider.

Supplementary Information

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Supplementary Material 1. Appendix A. Translated Questionnaire.

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Authors' contributions
Q.Z. participated in data collection, study design, drafting of the manuscript and proofreading. Z.T. participated in the data interpretation, drafted the manuscript and proofread the manuscript. Q.M. participated in the statistical analysis, data interpretation and drafting of the manuscript..J.G. and Y.Y. participated in data collection. All the authors have read and approved the final manuscript.

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Data availability
The datasets generated during the current study are not publicly available because the data also form part of an ongoing study but are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study did not involve human experiments and did not use human tissue samples. The research protocol followed the principles of the Declaration of Helsinki, and the data collection and investigation process of complied with relevant ethical guidelines and regulations. Patients were informed in advance by telephone survey that their participation would be voluntary and anonymous. This study was approved by the Research and Clinical Trial Ethics Committee of the First Affiliated Hospital of Zhengzhou University (approval number: 2024-KY-0510–001). Since this study was retrospective and did not involve personal identifiable information, informed consent was waived by the ethics committee.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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