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Original Article

Tongue features of patients with coronavirus disease 2019: a retrospective cross-sectional study

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ABSTRACT

Background: Traditional Chinese medicine (TCM) has been widely used in the treatment of coronavirus disease 2019 (COVID-19). Tongue features should be referred for diagnosis and treatment of diseases in TCM. Therefore, it is necessary to analyze the tongue features of the patients suffered from COVID-19.
Methods: COVID-19 Symptom Database (established by Evidence-based Medicine Center of Tianjin University of TCM) was searched for eligible tongue pictures. The tongue pictures were assessed by TCM experts to extract the data of tongue color, coating color, tongue body shape and coating proper feature. The relationship between tongue features and patient's condition was analyzed.
Results: Patients diagnosed as mild and moderate COVID-19 commonly had light red tongue and white coating. Severe patients had purple tongue and yellow coating. The proportion of critical patients with tender tongue increased to 75%. Greasy coating was a significant characteristic of patients with COVID-19. The proportions of greasy coating were 53.33%, 73.30%, 83.67 and 87.5% in disease category of mild, moderate, severe and critical. In addition, the thick coating proportion increased from mild (24.89%) to critical (50.00%).
Conclusions: Tongue features have certain relationship with the category of COVID-19. Tongue features can serve as potential indicators for the evaluation of patient's condition and prognosis. Further studies are needed to enhance the quantification of tongue features and develop standards.

1. Introduction

Coronavirus disease 2019 (COVID-19) has been rampaging all over the world.[1,2] Until July 13, 2020, more than 12 million people have been infected worldwide, and the mortality rate has reached 4.4%.[3] Now COVID-19 has been well controlled in China.[5] Totally, there were 83,605 confirmed cases with 4634 deaths.[4] Traditional Chinese medicine (TCM) has played an important role in controlling COVID-19.[6]

Treatment according to syndrome differentiation is the major feature of TCM. Tongue features are important bases of syndrome differentiation and treatment at TCM. Disease diagnosis at TCM should refer to tongue features.[8,9]

Several clinical trials investigated tongue features as the symptoms of COVID-19 and found statistically significant differences between COVID-19 patients and healthy people. Red or light red tongue, yellow coating and greasy coating were common in patients with COVID-19.[10–12] The tongue features varied significantly in the different types of COVID-19.[13–15] However, the results were not robust, due to the small sample sizes and heterogeneity of the prior studies. This study analyzed a large number of tongue pictures of confirmed cases and found out the valuable features of tongue for the diagnosis and treatment of COVID-19.

2. Methods

2.1. Study design

This study was a retrospective cross-sectional study. The relationships between tongue features and types of COVID-19, age, gender were analyzed.

2.2. Study registration

The protocol of this study was registered on Chinese Clinical Trail Registry (ChiCTR2000033780).

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2.3. Data sources

The Research Project, *Clinical Research on Integration of Traditional Chinese Medicine and Western Medicine for COVID-19*, was performed to evaluate the efficacy of TCM. Based on this project, a symptom database of COVID-19 was established by Evidence-based Medicine Center of Tianjin University of TCM, which included information about patient's condition, age, gender and tongue pictures of COVID-19.

2.4. Inclusion and exclusion criteria

2.4.1. Inclusion criteria

(1) The tongue pictures were identifiable. (2) The first tongue picture of each confirmed case was eligible. (3) The basic information of patients and disease categories was accessible.

2.4.2. Exclusion criteria

(1) Tongue was not fully exposed. (2) The tongue images had severe noise, such as the oxygen suction tubes and other devices covering part of the tongue; insufficient light made the surface of the tongue too dark to identify. (3) Lack of data on age, gender and clinical types.

2.5. ***Tongue features identification and data extraction***

Eligible tongue pictures were imported into the Tongue Features Objective Research System (TFORS) developed by the Evidence-Based Medicine Center at Tianjin University of TCM. A table for identifing tongue features was designed according to *Diagnostics of Chinese Medicine* and *Color Atlas of Chinese Medical Tongue Diagnosis*.[16,17] The table contents included tongue color, coating color, tongue body shape and coating proper (Supplement 1). Two TCM experts independently logged into TFORS to identify the tongue features based on tongue pictures. Disagreements were resolved after consensus or consultant with a third TCM expert.

2.6. Data classification

The tongue features of each patient were classified as follows: (1) Clinical type: patients were classified into mild, moderate, severe and critical, based on the criteria of Diagnosis and Treatment Protocol for COVID-19 Trial Version 7.[18] (2) Gender: female and male. (3) Age: there were five groups: 0 to17, 18 to 44, 45 to 59, 60 to 74, above 75. Distributions of tongue features in each category would be counted and compared to investigate the relationships between tongue features and clinical types, age, gender.

2.7. Statistical analysis

IBM SPSS statistic 19.0 was used for data analysis. Data on categorical variables (such as gender and clinical types) were presented as count and percentage, and continuous variables (age) were presented as mean ± standard deviation.

According to clinical type, gender and age, the samples were classified and presented as count and percentage. Since tongue color contains five types and coating color contains three types, chi-square for trend was used and the linear was obtained by linear association. For the tongue body shape and coating proper, Pearson chi-square was used. If the lattice theoretical frequency was more than 20% ($T < 5$) or there was 1 lattice theoretical frequency ($T < 1$), the p value was calculated by the Fisher's exact test, and p value < 0.05 was considered statistically significant difference.

3. Results

3.1. S***ample information***

A total of 1043 patients were included. There were 456 males (43.72%) and 587 females (56.28%). And the average age was 54.98 ± 14.59, ranging from 17 to 91 years old. There were 225 mild cases (21.57%), 663 moderate cases (63.57%), 147 severe cases (14.09%) and 8 critical cases (0.77%).

3.2. Typical pictures of different tongue features

The typical pictures of each COVID-19 tongue feature were shown in Supplement 2, including: (1) tongue color: pale tongue, light red tongue, red tongue, deep red tongue, purple tongue; (2) tongue coating color: white coating, yellow coating, grayish black coating; (3) tongue body shape feature: rough tongue, tender tongue, puffy tongue, thin tongue, spots and prickles tongue, fissured tongue, tooth-marked tongue; (4) tongue coating proper feature: thin coating, thick coating, moist coating, dry coating, greasy coating, curdy coating, peeled coating, partial coating.

3.3. Distribution of tongue features in different clinical types

The details of distribution of tongue features in different clinical types were shown in Table 1. As for tongue color, 50.22% of mild patients were light red. As the disease progressed, the proportion of patients with purple tongue increased from 17.78% to 75%. There was a significant difference between tongue color of the patients in different clinical types ($p < 0.001$) (Fig. 1A).

In terms of coating color, 63.56% mild patients had white tongue coating. With the progressing of the disease, the proportion of patients with yellow tongue coating increased to 62.50% in critical patients. There was a significant difference between tongue coating color of patients in different clinical types ($p < 0.001$) (Fig. 1B).

As for tongue body shape, no pathological change occurred in most of the mild patients. The proportion of critical patients with tender tongue was 75%. As for puffy and thin tongue, there was no statistically significant difference between different clinical types ($p = 0.143$). Besides, spots and prickles tongue also did not show statistically significant difference ($p = 0.06$). Fissured tongue and tooth-marked tongue showed statistically significant differences between different clinical types ($p = 0.009$ and $p = 0.017$). However, the proportion of patients with these features changed irregularly (Fig. 1C).

Only 24.89% of mild patients had thick coating. As the disease progressed, the proportion of patients with thick coating increased. In severe cases, it increased to 63.27%. The result showed that thick coating was correlated with disease progression. The proportion of greasy coating in mild patients was 53.33%, which increased to 87.5% in critical patients (Fig. 1D).

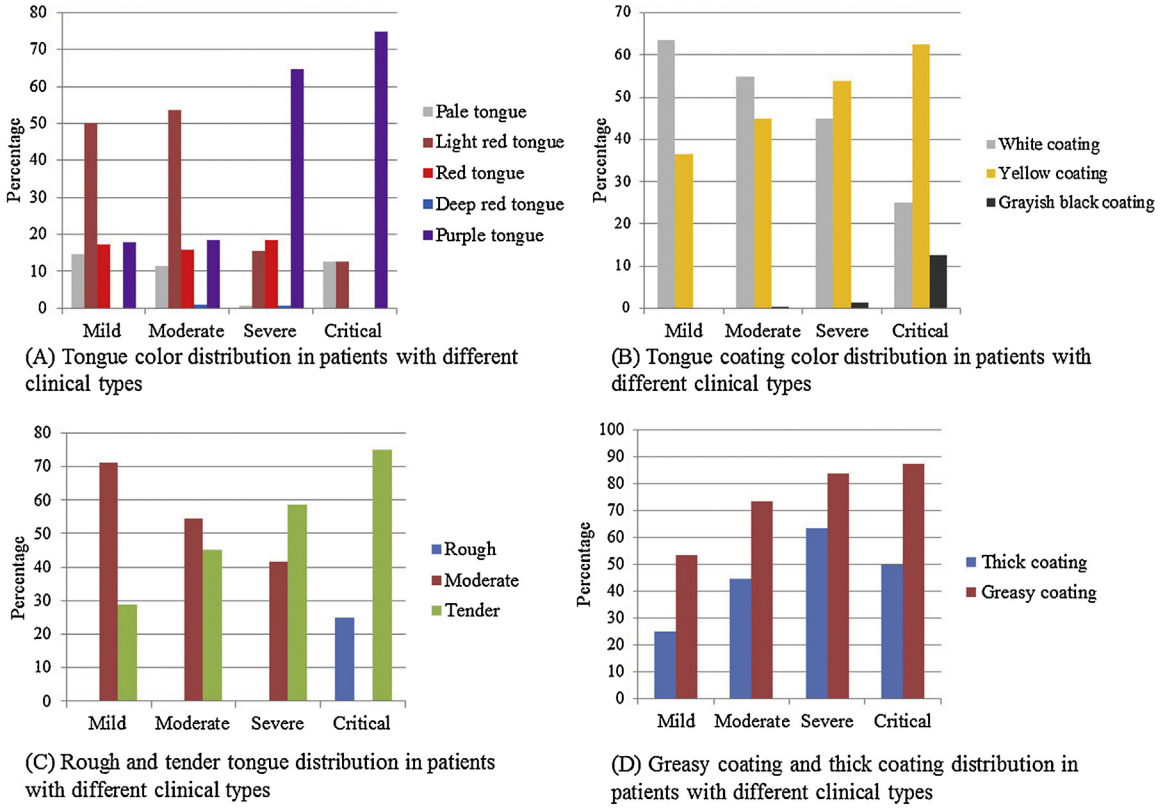
3.4. Distribution of tongue features according to gender and age

The details of distribution of tongue features according to gender were shown in Supplement 3. The distribution of tongue color and coating color was consistent between genders. There was no significant difference between patients in tongue color and coating color. The distribution of tongue body shape was similar between genders. There was no significant difference in tongue coating proper feature between genders. The results showed the gender was not an influential factor of tongue diagnosis in COVID-19.

The details of distribution of tongue features according to age were shown in Supplement 4. In terms of age, there were some differences in tongue color between patients. In patients aged below 45 years, the color of their tongues were mostly light red. With

Table 1
Distribution of Tongue features in Different Clinical Types

Part of the tongue	Tongue feature	Mild *n* (%)	Moderate *n* (%)	Severe *n* (%)	Critical *n* (%)	*p*-Value
Tongue color and coating color						
Tongue Color	Pale tongue	33(14.67)	76(11.46)	1(0.68)	1(12.50)	<0.001
	Light red tongue	113(50.22)	355(53.54)	23(15.65)	1(12.50)	
	Red tongue	39(17.33)	104(15.69)	27(18.36)	0(0)	
	Deep red tongue	0(0)	6(0.90)	1(0.68)	0(0)	
	Purple tongue	40(17.78)	122(18.40)	95(64.63)	6(75.00)	
Tongue Coating Color	White coating	143(63.56)	364(54.90)	66(44.90)	2(25.00)	<0.001
	Yellow coating	82(36.44)	297(44.80)	79(53.74)	5(62.50)	
	Grayish black coating	0(0)	2(0.30)	2(1.36)	1(12.50)	
Tongue body shape feature						
Rough and tender tongue	Rough	0(0)	1(0.15)	0(0)	2(25.00)	<0.001
	Moderate	160(71.11)	362(54.60)	61(41.50)	0(0)	
	Tender	65(28.89)	300(45.25)	86(58.50)	6(75.00)	
Puffy and thin tongue	Puffy	61(27.11)	199(30.01)	53(36.05)	5(62.50)	0.143
	Moderate	151(67.11)	421(63.50)	87(59.18)	2(25.00)	
	Thin	13(5.78)	43(6.49)	7(4.77)	1(12.50)	
Spots and prickles tongue	Yes	21(9.33)	37(5.58)	4(2.72)	0(0)	0.06
	No	204(90.67)	626(94.42)	143(97.28)	8(100)	
Fissured tongue	Yes	53(23.56)	232(34.99)	51(34.69)	4(50.00)	0.009
	No	172(76.44)	431(65.01)	96(65.31)	4(50.00)	
Tooth-marked tongue	Yes	134(59.56)	456(68.78)	109(74.15)	6(75.00)	0.017
	No	91(40.44)	207(31.22)	38(25.85)	2(25.00)	
Tongue coating proper feature						
Thin and thick coating	Thin	169(75.11)	367(55.35)	54(36.73)	4(50.00)	<0.001
	Thick	56(24.89)	296(44.65)	93(63.27)	4(50.00)	
Moist and dry coating	Moist	217(96.44)	656(98.94)	139(94.56)	7(87.50)	0.002
	Dry	8(3.56)	7(1.06)	8(5.44)	1(12.50)	
Greasy coating	Yes	120(53.33)	486(73.30)	123(83.67)	7(87.50)	<0.001
	No	105(46.67)	177(26.70)	24(16.33)	1(12.50)	
Curdy coating	Yes	6(2.67)	11(1.66)	8(5.44)	0(0)	0.065
	No	219(97.33)	652(98.34)	139(94.56)	8(100)	
Peeled coating	Yes	5(2.22)	14(2.11)	12(8.16)	3(37.50)	<0.001
	No	220(97.78)	649(97.89)	135(91.84)	5(62.50)	
Complete and partial coating	Partial	5(2.22)	22(3.32)	13(8.84)	2(25.00)	=0.001
	Complete	220(97.78)	641(96.68)	134(91.16)	6(75.00)	



(A) Tongue color distribution in patients with different clinical types

(B) Tongue coating color distribution in patients with different clinical types

(C) Rough and tender tongue distribution in patients with different clinical types

(D) Greasy coating and thick coating distribution in patients with different clinical types

Fig. 1. Distribution of tongue features with different type of COVID-19. (A) Tongue color distribution in patients with different clinical types. (B) Tongue coating color distribution in patients with different clinical types. (C) Rough and tender tongue distribution in patients with different clinical types. (D) Greasy coating and thick coating distribution in patients with different clinical types.

aging, the proportion of patients with purple tongue increased from 0 to 29.75%. The proportions of patients with pale, red and deep red tongue did not change significantly. As for tongue coating, most of the patients (>50%) in each age group had white coating. However, the proportion of patients with yellow coating increased with aging (from 33.33% to 48.16%). Therefore, age was an influential factor when evaluating the severity of COVID-19 by the color of tongue and coating.

The patients with rough and tender tongues did not show significant difference in terms of age, and similar results were observed in patients with puffy, thin, and tooth-marked tongue. More than 90% of the patients did not have spots and prickles in their tongues. With the age increasing, the proportion of patients with fissured tongue increased from 0% to 43.21%. There was no statistically significant difference in patients with thin and thick coating and greasy coating in terms of age.

4. Discussion

4.1. Summary of results

This study was a retrospective cross-sectional study of tongue features in 1043 patients with COVID-19. The results showed: (1) In terms of tongue color, patients with mild and moderate COVID-19 primarily had light red tongue while severe patients mainly had purple tongue. The tongue color of young patients were mainly light red. The proportion of middle-aged and elderly patients with red and purple tongue significantly increased. (2) As the disease progressed, the proportion of patients with white coating decreased while the proportion of patients with yellow coating increased. (3) The proportion of patients with tender tongue increased as the disease progressed. (4) There was significant difference in the proportion of patients with greasy coating in terms of clinical types. With the disease progressing, the proportion of patients with greasy coating increased. (5) There was no statistically significant difference in tongue features between different genders.

4.2. Mechanism analysis

The results of experimental study showed as follows: (1) The physiological color of the tongue body was light red, and microcirculation disorders, reduced arterial oxygen partial pressure, and increased platelet aggregation could cause the tongue color to change to purple.[19,20] With the progression of COVID-19, the blood oxygen saturation of patients decreased. Hence, microcirculation disorders caused the tongue color to change from light red to purple.[20] Therefore, the degree of purple color was significantly associated with the level of disease severity. (2) The physiological color of the tongue coating was white. Fever and infection may cause it to turn to yellow, and previous studies showed that the degree of yellow coating was positively correlated with the degree of lung infection.[21,22] Therefore, the degree of yellow coating was associated with the level of disease severity. (3) Tender tongue was correlated with organ failure, which could be caused by COVID-19.[23,24] Therefore, tender tongue was a potential indicator for critical cases of COVID-19. (4) Greasy coating was associated with oxygen free radical damage caused by enhanced peroxide reaction and decreased antioxidant capacity.[25,26] COVID-19 could cause oxidative stress and peroxide damage. Dysbiosis occurred in COVID-19 patients and changes in the gut microbial community were associated with disease severity.[27] Some COVID-19 patients showed microbial dysbiosis with decreased level of Lactobacillus and Bifidobacterium.[28] The degree of greasy coating was inversely correlated with the abundance of Bifidobacterium.[29] Therefore, the degree of greasy coating and the level of disease severity were positively correlated.

4.3. Applicability of the result

Color of tongue body and coating, degree of tender tongue and greasy coating, might be potential diagnostic indicators for the level of severity of COVID-19. In addition, the influential factors on tongue features such as age should be considered.

4.4. Limitations of this study

There were several limitations in this study: (1) Combined diseases and different medications in patients with COVID-19 would influence tongue features. (2) The sample size of critical patients was small, which reduced the robust of the result in critical types. (3) The duration from onset of disease to hospitalization of patients varied significantly, which might cause unbalanced baseline. (4) Tongue pictures taken under non-standard light sources might lead to errors in expert interpretation.

4.5. Implications of future research

In future research, multi-factor analysis of variance should be used to investigate the relationships between tongue features and types of COVID-19, age, underlying disease, dietary habit, treatments and duration from onset of disease to hospitalization. In order to objectively evaluate the severity of COVID-19 by tongue features, digital image technology should be used to analyze the tongue features quantitatively.

4.6. Conclusion

Tongue features are related to the level of severity of patients with COVID-19. The degree of greasy coating is the most sensitive factor. Further studies are needed to enhance the quantification of tongue features and develop standards.

Author contributions

Conceptualization: JZ. Methodology: JZ, DZ and WP. Investigation: WZ, DZ and HW. Formal Analysis: WP, NL, CL, FY and BP. Writing-Original Draft: DZ and WP. Writing-Review & Editing: JZ.

Conflicts of interest

The authors declare no conflicts of interest.

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Ethical statement

This study was approved by the Medical Ethics Committee of Tianjin University of Traditional Chinese Medicine (TJUTCM-EC20200004).

Data availability

The data used to support the findings of this study is not free of access. Requests for access to these data need formal application and authorization.

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Supplementary material

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.imr.2020.100493.

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