Tongue Picture is considered as a novel and non-invasive earlier diagnosis than ever for esophagus cancer

Xinhui Li
Thoracic Surgery of the Affiliated Hospital of Medical College,Qingdao University. Address: 16 Jiangsu Road, Qingdao 266000, China
xiongwaililun@163.com;

Yuqin Gao
Chinese Internal Medicine of the Affiliated Hospital of Medical College,Qingdao University. Address: 16 Jiangsu Road, Qingdao 266000, China
lilun2011@foxmail.com;

Xiaomei Dai
Chinese Internal Medicine of the Affiliated Hospital of Medical College,Qingdao University. Address: 16 Jiangsu Road, Qingdao 266000, China
lunli2011@foxmail.com;

Tingting Xu
Chinese Internal Medicine of the Affiliated Hospital of Medical College,Qingdao University. Address: 16 Jiangsu Road, Qingdao 266000, China
lilunchest@163.com;

Guojie Hu
Chinese Internal Medicine of the Affiliated Hospital of Medical College,Qingdao University. Address: 16 Jiangsu Road, Qingdao 266000, China
lilun2837@163.com

Abstract

Objective: The invasive, unpleasant and inconvenient nature of current diagnostic about esophagus cancer limits their application in clinical practice. There is a great need of novel non-invasive method for early esophagus cancer diagnosis. In the present study, we intend to determine whether the tongue pictures are suitable for early detection of esophagus cancer.

Materials and methods: The study aimed to assess the probability of detecting early esophageal cancer using endoscopy in the training set consisted of tumor endoscopic stage and tongue picture. Ulteriorly，whether we may examine early esophagus cancer using tongue picture. Indirectly, the probability of distinguishing the infiltrative depth and the longitudinal diameter of esophagus cancer apply between tumor endoscopic stage and tongue picture.

Results: The tongue color usually present the white light in the early patients of esophagus cancer, the liguliform and the sublingual-threads are normal, the coated tongue take on the thick white fur. The significant difference exist between the classification of mucosal color in endoscopy and the tongue color, the liguliform, the sublingual-threads, and the relation of the tongue color is the significance. The significance differences have between the classification of the surrounding mucosal lesions and the coated tongue in endoscopy, but the relation of that is weak. between the moss-like lesions and the coated tongue is significant difference, the relation of that is general. The significant difference is between the endoscopic stages and the filtration depth of cancer tissues, the vertical by carcinoma.

Conclusion： The changes of tongue picture consider as a recent，invasive and clinical approach in detecting early esophagus cancer. The approach have greatly potential, and the esophagus cancer is found in the early stage of "T" and the infiltration depth of carcinoma as soon as possible by the changes of tongue pictures. What is said above may increase the chance of operation and the time and survival.

Key words: the tongue picture; esophagus cancer; endoscopy; the early diagnosis

Introduction

Esophagus cancer is a very common malignancy in digestive tumor, the symptomatic esophagus cancer what found is the advanced cancer patients, and difficultly examined in early stage [1,2]. The common view had been formed which increased the survival of the esophagus cancer using the early diagnosis [3]. These are not the same with the early diagnosis of esophagus cancer for the tumor marker, the oncogene and antioncogene of it or the more objective gastroscope[4]. What we saw the malignant tumor of the digestive system in clinic, its differentiation is the worse and the faster in advance, and the earlier in metastasis. The tongue picture is tightly linked together by the main and collateral channels and viscera[5]. The vital essence of the viscera presents in the tongue. So the lesion, situation of the malignant tumor of the digestive system certainly influence the change of the vital essence ups and downs, in the meanwhile, is formed in tongue[6,7]. The tongue picture can objectively response the lesions levels in the malignant of the digestive system, and applies to the changes of the esophagus cancer[8]. Because the diagnosis of the tongue picture do not militate the subject feeling under a cloud, so it is more likely make patients acceptable. The tongue pictures provide a necessary method in the earlier diagnosis of the esophagus cancer.

1769 | P a g e
M a r c h 2 0 1 6
c o u n c i l f o r I n n o v a t i v e R e s e a r c h
w w w . c i r w o r l d . c o m

Materials and methods

1.1 patients with the inclusion criteria: (1) To fit the diagnosis standard of the esophagus cancer in gastroscope and to diagnose the esophagus cancer by the pathological examination. The pathological diagnosis standard refers to Clinical guidelines for the diagnosis and treatment-tumor **fascicule**. (2) To be able to tolerance the patients by the gastroscope examination. (3) To be newly diagnosed patients, all these are not the surgical contraindication and do not take medicine and food of the influencing tongue picture. (4) To not influence the tongue picture with the other system malignancy. (5) To not influence the tongue picture with the underlying diseases. (6) The gastroscope imagings do not influence the accurate of the esophagus cancer diagnosis. (7) All patients volunteer participant the research and have a good compliance.

1.2 general cases: The whole of specimens were obtained from patients who underwent competed surgical resection (R0) at Thoracic Surgery of the Affiliated Hospital of Medical College Qingdao University. All patients are 97, the men are 76, the women are 21, the ages rang 29 from 75, and the mean age is 59.1±9.3. The epidermoid carcinoma of esophagus is the most in all the pathologies of the esophagus cancer and ares 90 cases, that is 92.8%, adenocarcinoma is two cases, the undifferentiated carcinoma are three, adenosquamous carcinoma are two. Endoscopic classifications are base on programming the standard classification of Japan society of esophageal **disease (JSED)**. Written informed consent was obtained from all participants.

1.3 Tongue images: The diagnosis and obtaining pictures of tongue images certainly fix in natural light, quiet environment and preoperation, in the while, we must foreclose all the possible influencing factors in polluting coated tongue, for example, taking medicine, smoking and dietary structure. We observe the changes of tongue color, tongue shape, the shape and color of coating tongue and sublingual-threads on the diagnostic standard classification of the tongue diagnosis of Diagnostics of Chinese Medcine.

1.4 Gastroscopic observation: Reference on the Gastroscopic diagnostic standard of esophagus cancer. The study is focus on observing leisure location, mucosa color of surface morphology of the leisure, the surrounding mucosa morphology and the moss type of the nidus. All the observing what was completed by a special study department and people.

1.5 esophageal tumors: In the present study, we mostly observe the infiltration layers or lengths and tumor and affect the longitudinal diameter in esophageal patients.

1.6 Monitoring histopathology: All obtaining specimen were placed formalin-fixed in gastroscopic examination of preoperation or the histopathology of postoperation, and sent to pathology department of the Affiliated Hospital of Medical College Qingdao University, and programmed paraffin-embedded and HE-colored. The present study lays emphasis on observing infiltration lengths, the metastasis rate of the lymph gland and TNM stage of postoperation, and so on.

1.7 statistic analysis: the statistical software SPSS 17.0 ran all statistical analyses in the study. All of the tests were two-sided, and P <0.05 was considered statistically significant. The analysis mostly apply to the analysis methods of rank sum test and Pearson`s test.

RESULTS

2.1 Esophageal cancer on relation between gastroscopic stage and tongue picture

Tongue color mostly takes on light and white in I, II, III type of the early esophageal cancer, liguliform is normal. In the advanced esophageal cancer, tongue color mostly takes on red, liguliform is fat crescent in I, II type; III type is mostly crimson and fissured tongue; IV, V type mostly takes on purple and ecchymosis tongue. Coated tongue has white and thick in the early esophageal cancer. And in the advanced esophageal cancer, I, II type has thin and yellow, III, IV, V type has yellow and greasy. The significant difference exists between the classification of mucosal in endoscopy and the tongue color （ $\chi^2=33.221$ ， p<0.001 ） , the liguliform ($\chi^2=4.101$,p=0.043), coating tongue ($\chi^2=20.441$,p=0.001), the sublingual-threads ($\chi^2=12.85$,p<0.001), and the relationship of the liguliform (r=4.494), coating tongue (r=0.245), the sublingual-threads (r=0.179) are weak except the tongue color (r=0.570). (See table I).

1770 | P a g e
M a r c h   2 0 1 6
council for Innovative Research
www.cirworld.com

Table 1 The relationship between the classification of mucosal in endoscopy and the tongue color, the liguliform, coating tongue, the sublingual-threads.

Gastroscopic classification		tongue color					liguliform				sublingual-threads		coating tongue						
	n	A	B	C	D	E	F	G	H	I	J	K	L	M	S	O	P	Q	R
early I II III type	3	2	1	0	0	0	3	0	0	0	2	1	1	2	0	0	0	0	0
advanced I type	19	6	3	10	0	0	6	13	0	0	8	11	3	3	10	3	0	0	0
II type	12	2	2	7	1	0	3	6	2	1	6	6	2	1	7	1	1	0	0
III type	31	2	4	6	15	4	4	6	17	4	14	17	2	2	2	17	4	4	0
IV type	18	2	2	1	3	10	2	1	4	11	7	11	1	2	1	12	2	0	0
V type	14	1	1	2	3	7	1	1	4	8	6	8	1	2	4	7	0	0	0
total	97	15	13	26	22	21	19	27	27	24	43	54	10	12	24	40	7	4	0

A: light and white, B: light and red, C: red, D: crimson, E: purple, F: Normal, G: fat crescent, H: fissured tongue, I: ecchymosis tongue, J: normal, K: varix, L: white and thin, M: white and thick, S: thin and yellow, O: yellow and greasy, P: grey and black, Q: geographic tongue, R: mirror-like tongue.

2.2 The relation both the mucosal color and luster of esophageal gastroscopy and tongue picture.

It is significant difference both what we observe the mucosal color and luster of esophageal gastroscopy and the tongue color （$\chi2=49.224$，p<0.001）, the liguliform ($\chi2=4.152$,p=0.042), the sublingual-threads ($\chi2=4.654$,p=0.031) in statistics, but the relationship both the mucosal color and luster of esophageal gastroscopy and tongue picture are weak in the liguliform (r=4.326) , the sublingual-threads (r=0.186) except tongue color (r=0.735). (see table II)

Table 2 The relation both the mucosal color and luster of esophageal gastroscopy and the tongue color, the liguliform, the sublingual-threads.

v	N	tongue color					liguliform				sublingual-threads	
		A	B	C	D	F	F	G	H	I	J	K
Pale	9	6	2	1	0	0	6	1	2	0	7	2
Red and white to white-based	6	1	4	1	0	0	1	3	1	1	5	1
normal	7	0	5	1	1	0	7	0	0	0	7	0
Red and white to red-based	15	0	0	10	4	1	3	10	1	1	12	3
congestion	41	0	0	4	25	12	0	15	7	19	19	22
hemorrhage	19	0	1	1	4	13	0	8	0	11	9	10
total	97	7	12	18	26	34	17	37	11	31	59	38

A: light and white, B: light and red, C: red, D: crimson, E: purple, F: Normal, G: fat crescent, H: fissured tongue, I:

ecchymosis tongue, J: normal, K: varix, V: the mucosal color and luster of esophageal gastroscopy.

1771 | P a g e
M a r c h   2 0 1 6
council for Innovative Research
www.cirworld.com

2.3 The relation both the surrounding mucosal changes of the esophageal gastroscopic leisure and coating tongue.

It is significant difference both the surrounding mucosal changes of the esophageal gastroscopic leisure and coating tongue in statistics, but theirs´relationship are weak（$x2=8.057$，$p=0.005$，$r=0.317$）. (see table III)

Table 3 The relation both the surrounding mucosal changes of the esophageal gastroscopic leisure and coating tongue.

V	Coating tongue							
	N	L	M	S	O	P	Q	R
Normal	10	7	0	3	0	0	0	0
mucosal secreta	28	1	8	1	15	2	1	1
Bulky fold	16	1	1	1	5	2	1	5
tumidness	19	0	6	1	8	1	1	2
particle	11	0	3	4	1	1	1	1
nodule	13	0	0	0	6	2	4	1
total	97	9	17	10	35	8	8	10

L: white and thin, M: white and thick, S: thin and yellow, O: yellow and greasy, P: grey and black, Q: geographic tongue, R: mirror-like tongue, V: the surrounding mucosal changes of the esophageal gastroscopic leisure.

2.4 The relation both the moss type of the nidus changes of the esophageal gastroscopic leisure and coating tongue.

It is significant difference both what we observed the moss type of the nidus changes of the esophageal gastroscopic leisure and the classification of coating tongue in statistics, but theirs´ relationship are weak（$x2=13.666$，$p<0.001$,$r=0.446$）. (see table IV)

Table 4 The relation both the moss type of the nidus changes of the esophageal gastroscopic leisure and coating tongue.

V	Coating tongue							
	N	L	M	S	O	P	Q	R
No tongue coating	16	6	1	3	1	1	3	1
White tongue coating	19	3	10	6	0	0	0	0
Yellow tongue coating	34	1	2	1	17	3	6	4
Filthy tongue coating	28	0	3	1	14	3	1	6
Total	97	10	16	11	32	7	10	11

L: white and thin, M: white and thick, S: thin and yellow, O: yellow and greasy, P: grey and black, Q: geographic tongue, R: mirror-like tongue, V: the moss type of the nidus changes of the esophageal gastroscopic leisure.

2.5 Esophageal cancer on relation between gastroscopic stage and what tumor infiltrates depth.

It is significant difference between gastroscopic stage and what tumor infiltrates depth in statistics, but theirs´ relationship are strong($x2=6.26$,$p=0.012$,$r=0.575$). (see table V).

1772 | P a g e
M a r c h 2 0 1 6
council for Innovative Research
www.cirworld.com

I S S N 2 3 4 7 - 6 8 9 3
V o l u m e 9 N u m b e r 1
J o u r n a l o f A d v a n c e s i n B i o l o g y

Table 5 Esophageal cancer on relation between gastroscopic stage and what tumor infiltrates depth.

V	A	B	C	D	E	total
0	2	1	0	0	0	3
Ⅰ	0	0	15	2	1	19
Ⅱ	0	0	9	2	1	12
Ⅲ	0	0	10	14	7	31
Ⅳ	0	0	2	7	9	18
Ⅴ	0	0	1	5	8	14
total	2	1	37	30	26	97

V: gastroscopic somatotype, A: carcinoma in situ, B: Intra-mucosa, C: muscular layer, D: Epineurium, E: Abjacent organs

2.6 Esophageal cancer on relation between gastroscopic stage and what the longitudinal diameter of esophageal tumor.

It is significant difference between gastroscopic stage and what the longitudinal diameter of esophageal tumor, that also has statistics meaning, but theirs´ relationship are strong($\chi 2$ =8.36,p=0.004,r=0.523). (see table VI).

Table 6   Esophageal cancer on relation between gastroscopic stage and what the longitudinal diameter of esophageal tumor.

V	the longitudinal diameter of esophageal tumor				
	≤3cm	3-5cm	5-7cm	≥7cm	total
0	2	1	0	0	3
Ⅰ	5	10	4	0	19
Ⅱ	3	7	1	1	12
Ⅲ	1	17	10	3	31
Ⅳ	1	7	9	1	18
Ⅴ	0	2	7	5	14
Total	12	44	31	10	97

V: gastroscopic somatotype.

Discussion

Though the tongue pictures of esophageal cancer were produced an effect on the different and objective factors, for example, age, gender, hormone secretion, living conditions for families, intercurrent diseases, and so on[9,10]. But by our present study we are able to diagnose the early esophageal cancer and infer gastroscopic stage, the mucosal color and luster of esophageal gastroscope, the surrounding mucosal changes of the esophageal gastroscopic leisure, the moss type of the nidus changes of the esophageal gastroscopic leisure through tongue pictures. And vice versa, using the gastroscopic stage of esophageal cancer may deduce the changes of the tongue pictures; using the mucosal color and luster of esophageal gastroscope may infer the changes of tongue color, liguliform, sublingual-threads; in the while, using the surrounding mucosal changes of the esophageal gastroscopic leisure and the moss type of the nidus changes of the esophageal gastroscopic leisure may deduce the changes of the tongue coating. On the top of the present experiment, we indirectly infer the "T" stages of the esophageal tumor by the tongue pictures, and gastroscope is considered as irrefutable evidence and approach. Hence, The changes of tongue picture consider as a recent，invasive and clinical approach in detecting early esophagus cancer and roughly assess the general prognosis of the esophageal cancer.

The normal person is different from the patients of the early esophageal cancer during the present experiment, the patient organism takes a compensatory conditions, for example, the metabolism and stomach qi and the secondary action of leisure of it[11-13]; but to the advanced stage, the pathogen erode into the inner, he metabolism and stomach qi and the secondary action of leisure of the patient organism takes so a decompensation conditions that the tongue color, liguliform and sublingual-threads are different from the normal person.

The tongue color of the esophageal cancer patients usually have light and white, the mucosa of the gastroscopic leisure mostly take on pale or Red and white to white-based[14]. It indicated that healthy atmosphere was able to compensate what stomach qi invaded. Chinese medicine thinks that the light and white tongue leads the deficiency of qi and blood and vital energy the role; if qi and blod owes empty, the blood will not take on the tongue; if the yang spirit owes so empty that it will not absolutely transport blood[15,16]. Finally, the tongue color will turn light and thin. Above those, all are the early

1773 | P a g e
M a r c h 2 0 1 6
council for Innovative Research
www.cirworld.com

manifestation of the esophageal cancer patients. In recent years, medical research that the color changes of the tongue nature is closed tied with the lingual blood circulation. When the body takes on anemia, the low metabolism, the peripheral vasoconstriction, the tongue will be color dodge. The behaviors make blood redistribute and concentrate on supplying to influence live, these help meet the important organs and tumor tissue an urgent need and hedge against pathogenic factor into inner. The purple is the most common tongue color in the patients of the esophageal cancer, followed by crimson and red. In addition, Ecchymosis tongue and Sublingual vein varicose are very familiar the tongue pictures, and the purple tongue appeared simultaneously. Poor blood circulations and hypostasis make crimson and red tongue further give into purple. Purple level react stagnation of qi and blood stasis and the extent of the panhandle pathogenic toxin in the body, and likewise manifest the resistivity of the metabolism and stomach qi of the patients at the same time. Ecchymosis tongue and Sublingual vein varicose show congestion. Medical research shows that tongue nature will turn red and crimson when tongue nature has hyperaemia , blood vessel show hyperplasia and basal metabolism increase. What is worse, the tongue pictures show purple, Ecchymosis and Sublingual vein varicose when reducing hemoglobin increases in congestion or anoxia. The mucosal color and luster of esophageal gastroscopy of patients mostly takes on congestion and haemorrhage when the tongue images show purple, Ecchymosis and Sublingual vein varicose [17]. That is why the patients is advanced and lose the operative chance when we examine the esophageal cancer.

Tumor infiltrating depth and the longitudinal diameter influence the survival times by oncogene and antioncogene, and we gain a good deal of enlightenment from the aforementioned[18]. By the gastroscopic bridge, we infer tumor infiltrating depth and the longitudinal diameter of the esophageal cancer. Tumor infiltrating depth and the longitudinal diameter of the esophageal cancer influence TNM-stage and the survival time of the patients of the esophageal cancer. So the content of our study can increase the positive predictive value with the other clinic parameter to detecting the early esophageal cancer.

Conclusion

The changes of tongue picture consider as a recent，invasive and clinical approach in detecting early esophagus cancer. The approach have greatly potential, and the esophagus cancer is found in the early stage of "T" and the infiltration depth of carcinoma as soon as possible by the changes of tongue pictures. What is said above may increase the chance of operation and the time and survival.

Acknowledgments

References:

1. Yu G, Gail MH, Shi J, Klepac-Ceraj V, Paster BJ, Dye BA et al. (2014) Association between upper digestive tract microbiota and cancer-predisposing states in the esophagus and stomach. Cancer Epidemiol Biomarkers Prev 23: 735-741. PubMed:24700175

2. Cook MB, Wild CP, Everett SM, Hardie LJ, Bani-Hani KE, Martin IG et al. (2007) Risk of mortality and cancer incidence in Barrett's esophagus. Cancer Epidemiol Biomarkers Prev 16: 2090-2096. PubMed:17890521

3. May A, Gossner L, Gunter E, Stolte M, Ell C (1999) Local treatment of early cancer in short Barrett's esophagus by means of argon plasma coagulation: initial experience. Endoscopy 31: 497-500. PubMed:10494693

4. Polkowski W, van Lanschot JJ, Offerhaus GJ (1999) Barrett esophagus and cancer: pathogenesis, carcinogenesis, and diagnostic dilemmas. Histol Histopathol 14: 927-944. PubMed:10425562

5. Iorio R, Luigetti M, Broccolini A, Pilato F, Profice P, Della Marca G et al. (2010) Neurological picture. Pseudoperipheral tongue weakness. J Neurol Neurosurg Psychiatry 81: 1024-1025. PubMed:20571042

6. Zou JP, Wang WD, Li GX (2003) [Study on relationship between quantitative data of tongue picture and state of illness in 224 patients with severe acute respiratory syndrome]. Zhongguo Zhong Xi Yi Jie He Za Zhi 23: 740-743. PubMed:14626185

7. Li CD, Lan QF, Zhang JJ (2003) [Study on relationship between tongue picture and cell apoptosis in patients with chronic gastritis]. Zhongguo Zhong Xi Yi Jie He Za Zhi 23: 433-435. PubMed:12872396

8. Qin JH, Jiang YC (1987) [Relation between the tongue picture and epithelial cells of the tongue in patients with gastric cancer]. Zhong Xi Yi Jie He Za Zhi 7: 30-32, 35. PubMed:3594710

9. Vallet AE, Verschueren A, Petiot P, Vandenberghe N, Nicolino M, Roman S et al. (2012) Neurological features in adult Triple-A (Allgrove) syndrome. J Neurol 259: 39-46. PubMed:21656342

10. Stanghellini V (2004) ReQuest-- the challenge of quantifying both esophageal and extra-esophageal manifestations of GERD. Best Pract Res Clin Gastroenterol 18 Suppl: 27-30. PubMed:15588792

11. Xiao Q, Freedman ND, Ren J, Hollenbeck AR, Abnet CC, Park Y (2014) Intakes of folate, methionine, vitamin B6, and vitamin B12 with risk of esophageal and gastric cancer in a large cohort study. Br J Cancer 110: 1328-1333. PubMed:24481406

12. Ye SM, Han M, Kan CY, Yang LL, Yang J, Ma QF et al. (2012) [Expression and clinical significance of Sema4C in

1774 | P a g e
M a r c h   2 0 1 6   c o u n c i l   f o r   I n n o v a t i v e   R e s e a r c h
w w w . c i r w o r l d . c o m

I S S N   2 3 4 7 - 6 8 9 3
V o l u m e   9   N u m b e r   1
J o u r n a l   o f   A d v a n c e s   i n   B i o l o g y

esophageal cancer, gastric cancer and rectal cancer]. Zhonghua Yi Xue Za Zhi 92: 1954-1958.   PubMed:22944267

13. Pellen MG, Sabri S, Razack A, Gilani SQ, Jain PK (2012) Safety and efficacy of self-expanding removable metal esophageal stents during neoadjuvant chemotherapy for resectable esophageal cancer. Dis Esophagus 25: 48-53. PubMed:21595778

14. Shroff HJ, Dashatwar DR, Deshpande RP, Waigmann HR (1993) AIDS-associated Kaposi's sarcoma in an Indian female. J Assoc Physicians India 41: 241-242.   PubMed:8270582

15. Zhang Y, Ma JP, Ma XL, Zeng L, Abudureyimu A, Li JR (2014) [Analysis of tongue figure features in 990 cases of sexually transmitted and intravenous drug use spread HIV infected population in Xinjiang]. Zhongguo Zhong Xi Yi Jie He Za Zhi 34: 816-818.   PubMed:25137847

16. Xu JT, Zhang ZF, Yan ZJ, Tu LP, Lu LM, Shi MY et al. (2009) [Analysis of tongue color under natural daylight based on chromatic aberration correction]. Zhong Xi Yi Jie He Xue Bao 7: 422-427.   PubMed:19435555

17. Yang ZJ, Zhang Y, Guo ZQ (1995) [Preliminary study on relationship between syndrome differentiation of esophageal cancer and changes of exfoliated cells of tongue coating]. Zhongguo Zhong Xi Yi Jie He Za Zhi 15: 277-280. PubMed:7640500

18. Linjawi A, Kontogiannea M, Halwani F, Edwardes M, Meterissian S (2004) Prognostic significance of p53, bcl-2, and Bax expression in early breast cancer. J Am Coll Surg 198: 83-90.   PubMed:14698315