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Review Article

CD147 and MMP-9 for the diagnosis and prognosis evaluation of laryngeal cancer

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Abstract: Objective: This study aimed to explore the value of extracellular matrix metalloproteinase inducer (EMMPRIN), also known as CD147, and matrix metalloproteinase 9 (MMP-9) in laryngeal cancer (LC). Methods: We measured the serum levels of CD147, MMP-9, C-reactive protein (CRP), and interleukin 6 (IL-6) in 51 LC patients (research group, RG) and 49 healthy participants (normal group, NG) using the enzyme-linked immunosorbent assay (ELISA) and detected the expression of CD147 and MMP-9 proteins in LC tissues to analyze their diagnostic and prognostic value in LC. Results: The serum levels of CD147, MMP-9, CRP, and IL-6 were markedly higher in RG than in NG. The positive expression rates of CD147, MMP-9, CRP, and IL-6 were markedly higher in LC tissues than those in adjacent tissues. The area under the curve (AUC) was 0.825 for CD147 and 0.886 for MMP-9 in diagnosing LC. The results of 3-year survival favored patients in the low expression groups over patients in the high expression groups and favored patients with negatively expressed CD147/MMP-9 over patients with positively expressed CD147/MMP-9. The receiver operating characteristic (ROC) curve suggested that CD147 and MMP-9 had a high predictive value for poor prognosis. Multivariate Cox regression analysis revealed that high CD147 and MMP-9 levels indicate a poor prognosis of LC. Conclusion: CD147 and MMP-9 levels were increased in the serum of patients with LC, so they can be used as potential serum biomarkers for the diagnosis and prognosis assessment in LC.

Keywords: CD147, MMP-9, laryngeal cancer, diagnosis, prognostic factors

Introduction

Laryngeal cancer (LC) is the most prevalent malignant tumor of the head and neck, whose main pathological type is squamous cell carcinoma. Patients with LC have severely impaired swallowing, breathing, and vocal function and lower life quality [1-3]. The increasing industrial pollution and living pressure result in a growingly high incidence of LC in recent years, posing a serious threat to the life and health of patients [4]. Due to the lack of obvious early symptoms, LC is often mistakenly regarded as cold or laryngitis, hard to be taken seriously by patients. But when obvious symptoms arise, the condition develops rapidly, so many patients found them at advanced cancer stage at the time of diagnosis [5-7]. The mortality of patients with stage III-IV LC is very high, and the main factors behind the 5-year death are the recurrence and metastasis of LC [8, 9]. The main existing diagnostic methods for LC are electronic laryngoscope and pathological biopsy, which provide very important information for the diagnosis, treatment, and preoperative preparation of LC [10, 11]. However, the deep infiltration of LC cannot be predicted early by electronic laryngoscope and pathological biopsy. Therefore, the search for a useful detection indicator for the accurate early diagnosis of LC is strongly beneficial to a timely and effective staging, a suitable treatment plan, and a reasonable prognostic analysis, which has become a focus of clinical research [12, 13].

Pathological biopsy has good clinical value for the diagnosis of tumors, but its efficiency in the assessment of tumor staging is limited [14]. Extracellular matrix metalloproteinase inducer (EMMPRIN), also known as CD147, which is an extracellular matrix metalloproteinase inducer, can stimulate the secretion of matrix metallo-

Table 1. General clinical data of participants [n (%)]

Group	RG (n = 51)	NG (n = 49)	X^2	P
Sex			0.127	0.722
Male	34 (66.67)	31 (63.27)		
Female	17 (33.33)	18 (36.73)		
Age (year)			1.032	0.310
≤ 65	12 (23.53)	16 (32.65)		
> 65	39 (76.47)	33 (67.35)		
Weight (kg)			1.449	0.229
≤ 60	14 (27.45)	19 (38.78)		
> 60	37 (72.55)	30 (61.22)		
Drinking			0.623	0.430
Yes	29 (56.86)	24 (48.98)		
No	22 (43.14)	25 (51.02)		
Eating habits			0.320	0.572
Light diet	35 (68.53)	31 (63.27)		
Heavy diet	16 (31.37)	18 (36.73)		
Smoking			1.101	0.294
Yes	41 (80.39)	35 (71.43)		
No	10 (19.61)	14 (28.57)		
Clinical stage			-	-
Stage I	5 (9.8)	-		
Stage II	14 (27.45)	-		
Stage III	25 (49.02)	-		
Stage IV	7 (13.73)	-		
T stage			-	-
T1	11 (21.57)	-		
T2	16 (31.37)	-		
T3	19 (37.26)	-		
T4	5 (9.8)	-		
N stage			-	-
N0	8 (15.69)	-		
N1	14 (27.45)	-		
N2	17 (33.33)	-		
N3	9 (17.65)	-		
N4	3 (5.88)	-		
TNM stage			-	-
M0	28 (54.90)	-		
M1	23 (45.10)	-		

Table 2. Expression levels of CD147, MMP-9, CRP, and IL-6 in RG and NG

Group	RG (n = 51)	NG (n = 49)	t	P
CD147 (pg/ml)	3.12 ± 0.56	2.64 ± 0.48	6.589	< 0.001
MMP-9 (ng/ml)	5.62 ± 1.18	3.94 ± 1.03	8.233	< 0.001
CRP (mg/L)	5.04 ± 0.17	4.91 ± 0.15	5.085	< 0.001
IL-6 (ng/L)	0.48 ± 0.06	0.43 ± 0.08	4.417	< 0.001

proteinases (MMPs) from fibroblasts and endothelial cells and affect the metastasis and proliferation of cancer cells [15, 16]. CD147 and matrix metalloproteinase 9 (MMP-9) have been studied in a variety of malignant tumors but are rarely discussed in LC [17, 18]. C-reactive protein (CRP) and interleukin-6 (IL-6) are two common inflammatory factors in the clinic and their expression levels are related to the progression of various diseases [19, 20]. So we compared these two factors with CD147 and MMP-9.

Here we measured the serum levels of CD147 and MMP-9 in LC patients to investigate the diagnostic and prognostic value of CD147 and MMP-9 in LC, aiming to provide effective molecular indicators for the diagnosis, treatment, and prognostic prediction of LC.

Materials and methods

Basic information of patients

We assigned 51 patients with LC admitted to the Affiliated Union Hospital of Fujian Medical University from January 2013 to August 2016 to the research group (RG) and collected 51 samples of cancer tissues and 51 samples of adjacent tissues. We also enrolled 49 healthy participants who received physical examinations during the same period in the normal group (NG). Inclusion criteria for RG: Patients diagnosed with LC by histopathology; patients with complete clinical data; patients with an expected survival of more than 3 months. Exclusion criteria for RG: Patients previously treated with chemoradiation before admission; patients with severe liver and kidney dysfunction or any other organic lesions; patients with cognitive impairment and communication disorders; patients lost to the follow-up. All subjects and their families signed the written informed consent and cooperated with the medical staff to complete the relevant diagnosis and treatment.

This experiment received the approval of the Medical Ethics Committee of the Affiliated Union Hospital of Fujian Medical

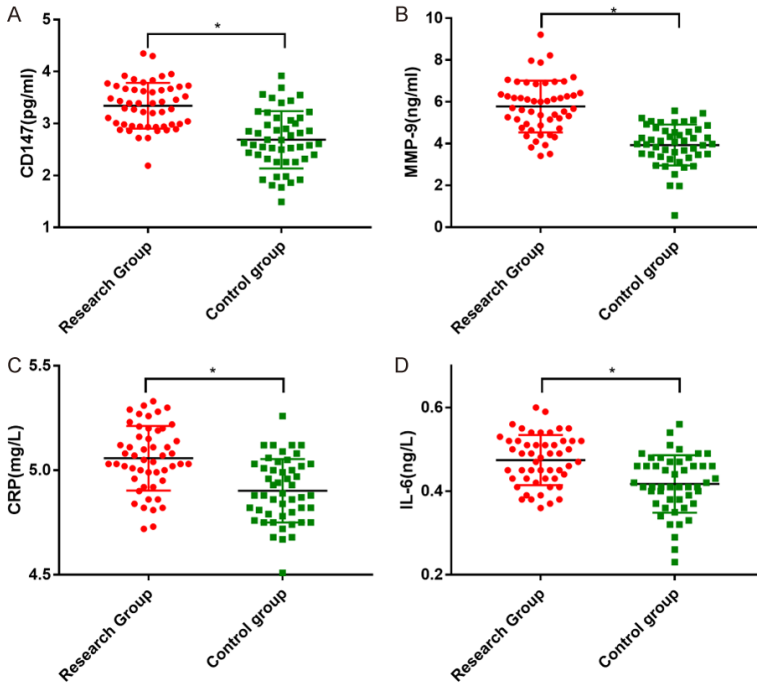

Figure 1. Serum expression levels of CD147, MMP-9, CRP, and IL-6 in RG and NG. A. Serum CD147 level in RG and NG. B. Serum MMP-9 level in RG and NG. C. Serum CRP level in RG and NG. D. Serum IL-6 level in RG and NG. Note: *P < 0.05.

University and this study is in line with the Declaration of Helsinki.

Methods

We measured the serum levels of CD147, MMP-9, CRP, and IL-6 in all participants using the enzyme-linked immunosorbent assay (ELISA). We collected 4 ml of fasting peripheral venous blood from all participants in the morning and put those blood samples in a centrifuge (Beckman Coulter, Inc., USA) at 2000 r/min to separate the serum, then we stored the serum in a -20°C refrigerator (Thermo Fisher Scientific, Inc., USA). The serum levels of CD147, MMP-9, CRP, and IL-6 were measured using the human CD147 ELISA kit (Beijing Lvyuan Bode Biotechnology Co., Ltd.), human MMP-9 ELISA kit (Shanghai Zeye Biological Technology Co., Ltd.), human CRP ELISA kit (Shanghai Chuan Qiu Biotechnology Co., Ltd.), and human IL-6 ELISA kit (Shanghai Yubo Biological Technology Co., Ltd.). There were standard wells, blank wells, and sample wells. We added 50 μl of the standard to each standard well, 40 μl of the sample diluent and 10 μl of the sample to each sample well. After a gentle shaking, we sealed the plate and incubated it at 37°C. One hour later, we removed the sealing plate, discarded the liquid and dried the plate, filled each well with 100 μl of washing solution, sealed the plate for 30 seconds and discarded the solution. The washing was repeated 5 times. We added 100 μl of the enzyme-linked reagent to each standard well and sample well. After that, we added to each well color reagent A (60 μl) and reagent B (60 μl) and sealed the plate at 37°C in the dark for 30 minutes to perform the color development. Finally, we added 50 μl of stop solution to each well to stop the reaction of each well and immediately measured the optical density (OD) of each well at a wavelength of 450 nm using an enzyme-labeled analyzer (Bio-Tek Instruments, Inc., USA). Also, we calculated the serum concentrations of CD147, MMP-9, CRP, and IL-6.

Immunohistochemistry

The expressions of CD147 and MMP-9 proteins in LC tissues were determined by the immunohistochemistry. The tissue sections were dewaxed and hydrated. We blocked them in 10 ml of 3% hydrogen peroxide and immersed them in 8 ml of citric acid buffer for 5 minutes to repair the antigen. Then we blocked them with 10% sheep serum for 10 minutes and incubated them with the primary antibody at 4°C overnight. After that, we took the sections out and for rewarming for 30 minutes before mixing them with the secondary antibody to react for 30 minutes. Then we washed the sections, dehydrated and blocked them. Brownish yellow tumor cell membranes and cytoplasms indicated positive test result. We selected 4 fields of vision for each section under a high power microscope (×400) for cell counting.

Statistical analysis

Statistical analysis was performed using SPSS 21.0 software (Bizinsight Information Techno-

Table 3. Diagnostic value of CD147, MMP-9, CRP, and IL-6 in patients with LC

Factor	CD147	MMP-9	CRP	IL-6
AUC	0.825	0.886	0.757	0.726
95% CI	0.7425-0.9069	0.8230-0.9497	0.6635-0.8503	0.6276-0.8238
Std. Error	0.0419	0.0323	0.0476	0.0501
Cut-off value	3.005	4.660	5.005	0.495
Sensitivity (%)	73.47	75.51	71.43	75.51
Specificity (%)	68.63	80.39	66.67	54.90

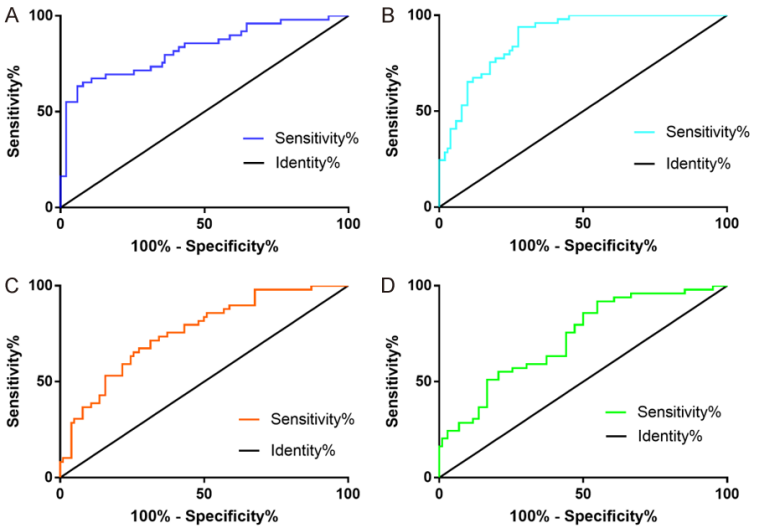

Figure 2. ROC curves demonstrating the diagnosis of LC by CD147, MMP-9, CRP, and IL-6. A. The ROC curve demonstrating the diagnosis of LC by CD147. B. The ROC curve demonstrating the diagnosis of LC by MMP-9. C. The ROC curve demonstrating the diagnosis of LC by CRP. D. The ROC curve demonstrating the diagnosis of LC by IL-6.

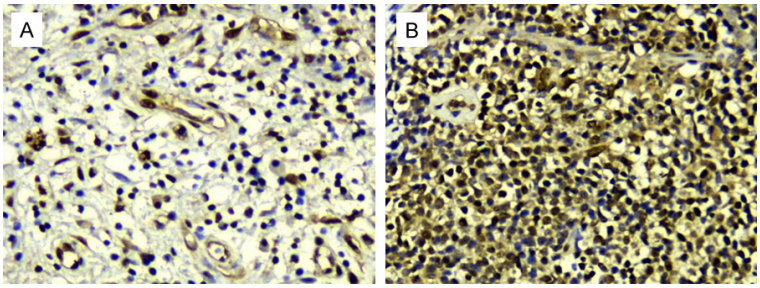

Figure 3. Expression of CD147 and MMP-9 in LC tissues. A. CD147 expression in LC tissues (×400). B. MMP-9 expression in LC tissues (×400).

logy Co., Ltd.). The count data were compared between the two groups by the X^2 test. The measurement data were denoted by the mean ± standard deviation (x ± sd) and compared between the two groups by the independent sample t-test. The receiver operating characteristic (ROC) curve was drawn to assess the value of serum CD147, MMP-9, CRP, and IL-6 for the diagnosis of LC. A Cox regression model was used to identify the risk factors of the poor prognosis of LC. A statistical difference was confirmed when $P < 0.05$.

Results

General clinical data

The comparison between RG and NG showed no obvious differences in sex ratio, age, weight, drinking, eating habits, and smoking ($P > 0.05$). More details are shown in **Table 1**.

Expression levels of CD147, MMP-9, CRP, and IL-6 in the two groups

CD147 level was markedly higher in RG than in NG (3.12 ± 0.56 pg/ml vs. 2.64 ± 0.48 pg/ml), and the difference was statistically significant ($t = 6.589$, $P < 0.001$). MMP-9 level was markedly higher in RG than in NG (5.62 ± 1.18 pg/ml vs. 3.94 ± 1.03 pg/ml), and the difference was statistically significant ($t = 8.233$, $P < 0.001$). CRP level was markedly higher in RG than in NG (5.04 ± 0.17 pg/ml vs. 4.91 ± 0.15 pg/ml), and the difference was statistically significant ($t = 5.085$, $P < 0.001$). IL-6 level was markedly higher in RG than in NG (0.48 ± 0.06 pg/ml vs. 0.43 ± 0.08 pg/ml), and the difference was statistically significant ($t = 4.417$, $P < 0.001$). More details are shown in **Table 2** and **Figure 1**.

Table 4. Expression of CD147 and MMP-9 in LC tissues [n (%)]

Tissue type	n	CD147		MMP-9	
		Positive	Negative	Positive	Negative
LC tissues	51	42 (82.35)	9 (17.65)	37 (72.55)	14 (27.45)
Adjacent tissues	51	8 (15.69)	43 (84.31)	3 (5.88)	48 (94.12)
X^2	-	45.350		47.550	
P	-	< 0.001		< 0.001	

Table 5. The comparison of the survival rate between the high expression groups and the low expression groups

	Number of 3-year death cases in the high expression group (3-year survival rate)	Number of 3-year death cases in the low expression group (3-year survival rate)	X^2	P
CD147	16 (38.46%)	8 (68.00%)	4.995	0.025
MMP-9	18 (30.77%)	6 (76.00%)	10.480	0.001
CRP	15 (42.31%)	9 (64.00%)	4.340	0.037
IL-6	13 (50.00%)	11 (56.00%)	0.453	0.501

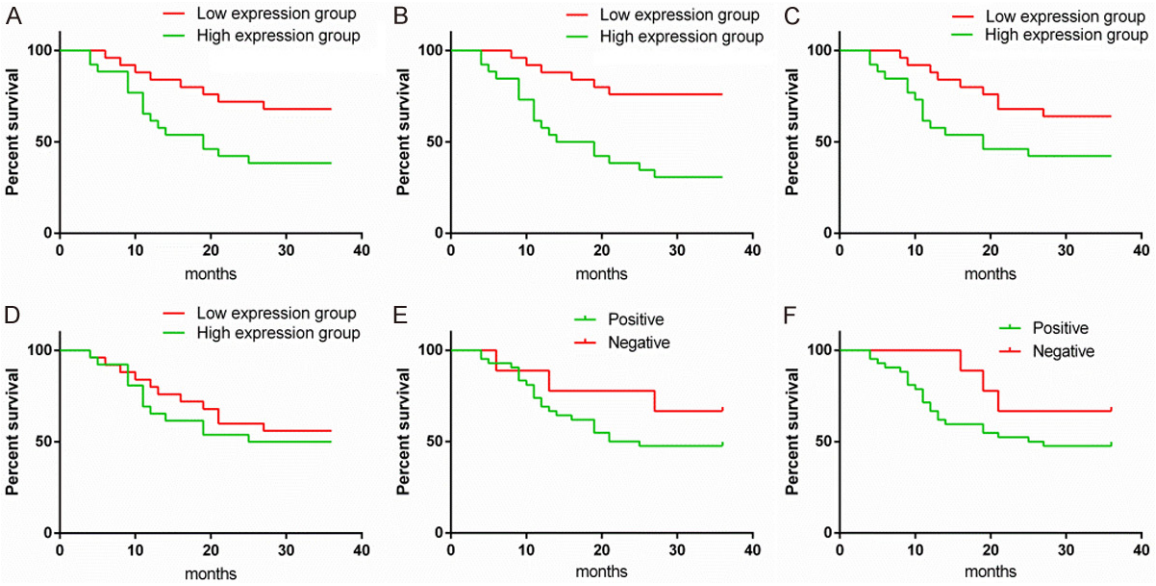

Figure 4. Effects of CD147, MMP-9, CRP, and IL-6 on the survival rate of LC. A. Effect of CD147 on the survival rate of LC and its predictive value for the prognosis. B. Effect of MMP-9 on the survival rate of LC and its predictive value for the prognosis. C. Effect of CRP on the survival rate of LC and its predictive value for the prognosis. D. Effect of IL-6 on the survival rate of LC and its predictive value for the prognosis. E. The survival rates of patients with positive or negative expression of CD147 in LC tissues. F. The survival rates of patients with positive or negative expression of MMP-9 in LC tissues.

Diagnostic value of CD147, MMP-9, CRP, and IL-6 in patients with LC

The sensitivity, specificity, area under the curve (AUC) for diagnosing LC were 73.47%, 68.63%, and 0.825 by CD147, 75.51%, 80.39%, and 0.886 by MMP-9, 71.43%, 66.67%, and 0.757 by CRP, and 75.51%, 54.90%, 0.726 by IL-6. More details are shown in **Table 3** and **Figure 2**.

Expression of CD147 and MMP-9 in LC tissues

In LC tissues, CD147 was mainly expressed in the cell membrane and cytoplasm of tumor cells and hardly expressed in stromal cells. MMP-9 was mainly expressed in tumor cells and slightly expressed in stromal cells. The positive expression rates of CD147 and MMP-9 were markedly higher in LC tissues than in adja-

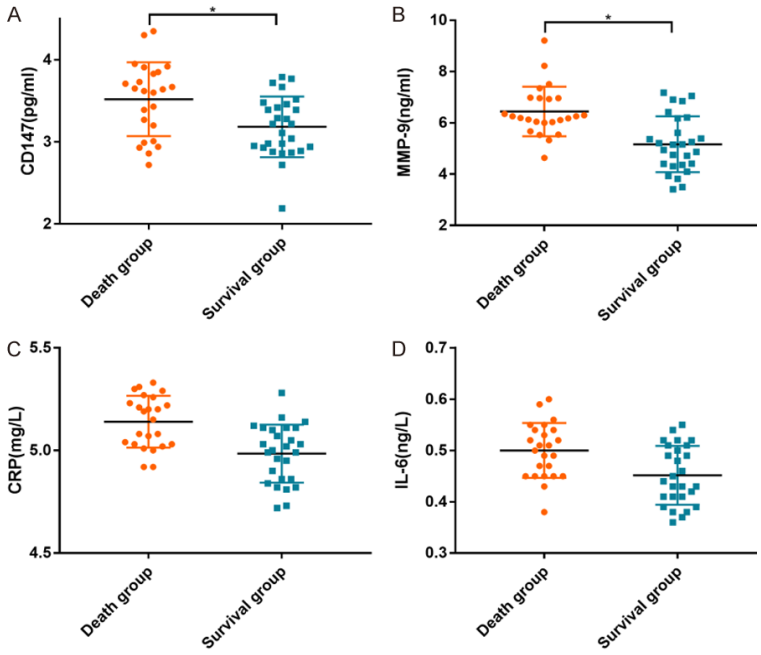

Figure 5. Serum expression levels of CD147, MMP-9, CRP, and IL-6 in the death group and the survival group. A. Serum CD147 level in the death group and the survival group. B. Serum MMP-9 level in the death group and the survival group. C. Serum CRP level in the death group and the survival group. D. Serum IL-6 level in the death group and the survival group. Note: *P < 0.05.

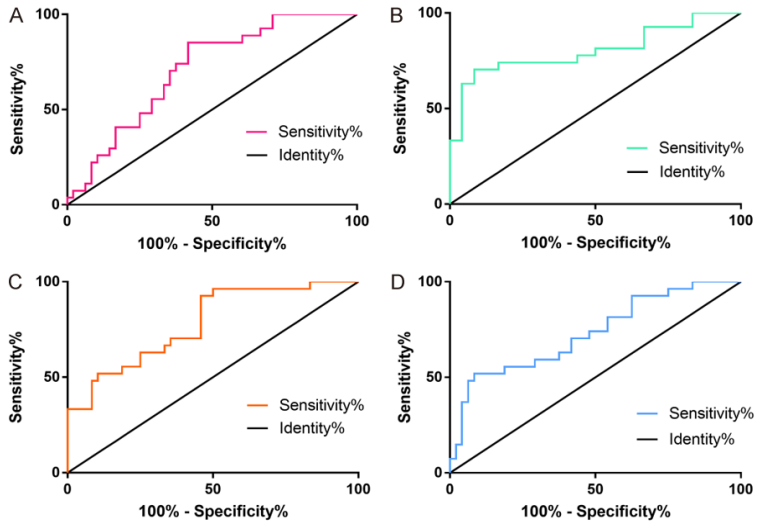

Figure 6. ROC curves demonstrating the predictive value of CD147, MMP-9, CRP, and IL-6 for the prognosis of LC. A. The ROC curve demonstrating the predictive value of CD147 for the prognosis of LC. B. The ROC curve demonstrating the predictive value of MMP-9 for the prognosis of LC. C. The ROC curve demonstrating the predictive value of CRP for the prognosis of LC. D. The ROC curve demonstrating the predictive value of IL-6 for the prognosis of LC.

cent tissues (P < 0.001). More details are shown in **Figure 3** and **Table 4**.

Effects of CD147, MMP-9, CRP, and IL-6 on the survival of LC

According to the median serum levels of CD147 (3.39), MMP-9 (5.70), CRP (5.04), and IL-6 (0.47), LC patients were divided into the high expression groups (26 cases) and the low expression groups (25 cases). The results of 3-year survival favored patients in the low expression groups over patients in the high expression groups (P < 0.05). According to the results of the immunohistochemistry, patients were divided into the positive CD147/MMP-9 group and the negative CD147/MMP-9 group. The results of 3-year survival favored patients with negative CD147/MMP-9 expression over patients with positive CD147/MMP-9 expression (P < 0.05). More details are shown in **Table 5** and **Figure 4**.

Predictive value of CD147, MMP-9, CRP, and IL-6 for the prognosis of LC

LC patients were divided into the death group (24 cases) and the survival group (27 cases) according to their prognosis. We compared the serum levels of CD147, MMP-9, CRP, and IL-6 between the two groups and discovered markedly higher serum CD147 and MMP-9 levels in the survival group (P < 0.05). More details are shown in **Figure 5**. According to the ROC curves, the AUC for predicting the poor prognosis was 0.709 for CD147 and 0.805 for MMP-9, which suggests high predictive value (P < 0.05). The death group and the survival group were not significantly different in serum levels of CRP and IL-6 (P > 0.05). More details are shown in **Figure 6**.

Table 6. Relationship between CD147 expression level and the clinical-pathological characteristics of LC patients

Group	RG (n = 51)	CD147 (pg/ml)	t/F	P
Sex			0.729	0.469
Male	34 (66.67)	3.19 ± 0.58		
Female	17 (33.33)	3.06 ± 0.64		
Age (year)			2.569	0.013
≤ 65	12 (23.53)	3.42 ± 0.67		
> 65	39 (76.47)	2.91 ± 0.58		
Weight (kg)			0.688	0.495
≤ 60	14 (27.45)	3.17 ± 0.55		
> 60	37 (72.55)	3.04 ± 0.62		
Eating habits			8.825	< 0.001
Light diet	35 (68.53)	2.72 ± 0.49		
Heavy diet	16 (31.37)	4.05 ± 0.52		
Smoking			8.695	< 0.001
Yes	41 (80.39)	4.13 ± 0.46		
No	10 (19.61)	2.69 ± 0.51		
Clinical stage			9.632	< 0.001
Stage I	5 (9.8)	2.75 ± 0.44		
Stage II	14 (27.45)	2.93 ± 0.51		
Stage III	25 (49.02)	3.15 ± 0.46		
Stage IV	7 (13.73)	4.03 ± 0.57		
T stage			10.310	< 0.001
T1	11 (21.57)	2.72 ± 0.48		
T2	16 (31.37)	3.01 ± 0.42		
T3	19 (37.26)	3.11 ± 0.56		
T4	5 (9.8)	4.19 ± 0.51		
N stage			15.13	< 0.001
N0	8 (15.69)	2.69 ± 0.46		
N1	14 (27.45)	2.77 ± 0.51		
N2	17 (33.33)	2.92 ± 0.48		
N3	9 (17.65)	4.05 ± 0.55		
N4	3 (5.88)	4.22 ± 0.57		
M stage			9.571	< 0.001
M0	28 (54.90)	2.81 ± 0.45		
M1	23 (45.10)	4.11 ± 0.52		

Relationship between CD147 expression level and the clinical-pathological characteristics of LC patients

CD147 level was not related to the sex and weight of LC patients ($P > 0.05$), but in relation to age, eating habits, smoking, clinical stage, T stage, N stage, and M stage ($P < 0.05$). See **Table 6** for more information.

Relationship between MMP-9 expression level and the clinical-pathological characteristics of LC patients

MMP-9 level was not related to the sex and weight of LC patients ($P > 0.05$), but in relation to age, eating habits, smoking, clinical stage, T stage, N stage, and M stage ($P < 0.05$). More details are shown in **Table 7**.

Predictive value of CD147 and MMP-9 for the prognosis of LC

Multivariate analysis of prognosis and related risk factors of LC: We set the clinical stage, T stage, N stage, M stage, CD147 level, and MMP-9 level as independent variables and assigned values. Meanwhile, we took death as the dependent variable and conducted the multivariate Cox regression analysis. The results revealed that the clinical stage, T stage, N stage, M stage, CD147 level, and MMP-9 level were independent risk factors for poor prognosis in patients with LC. More details are shown in **Tables 8** and **9**.

Discussion

LC, a malignant tumor occurring in the larynx, has a complex etiology that may be related to heredity, infection, and smoking [21]. LC is featured with early metastasis and high mortality and disability, and its biological behaviors are mostly highly malignant [22, 23]. The metastasis of LC is one of the main reasons for the treatment failure and even death of patients. The metastasis mechanism of malignant tumors is mainly that tumor cells detached from the lesion enter the blood or lymphatic system to participate in the internal circulation, and then gradually proliferate in other organs to form metastases, which is basically consistent with the metastasis of LC [25]. Previous studies [26, 27] found that CD147 and MMP-9 can affect the biological processes of cancers like cancer development, progression, and metastasis.

Here we tested the serum CD147 and MMP-9 levels of all participants using the ELISA and detected markedly higher serum CD147 and MMP-9 levels in RG than in NG. According to the immunohistochemistry results, the positive

Table 7. Relationship between MMP-9 expression level and the clinical-pathological characteristics of LC patients

Group	RG (n = 51)	MMP-9 (ng/ml)	t/F	P
Sex			0.248	0.805
Male	34 (66.67)	5.65 ± 1.12		
Female	17 (33.33)	5.57 ± 1.01		
Age (year)			2.074	0.043
≤ 65	12 (23.53)	4.96 ± 1.34		
> 65	39 (76.47)	5.83 ± 1.25		
Weight (kg)			0.151	1.460
≤ 60	14 (27.45)	5.28 ± 1.23		
> 60	37 (72.55)	5.82 ± 1.19		
Eating habits			3.024	0.004
Light diet	35 (68.53)	4.48 ± 1.42		
Heavy diet	16 (31.37)	6.16 ± 2.55		
Smoking			2.323	0.024
Yes	41 (80.39)	5.79 ± 1.25		
No	10 (19.61)	4.83 ± 0.73		
Clinical stage			3.561	0.021
Stage I	5 (9.8)	4.05 ± 0.81		
Stage II	14 (27.45)	5.02 ± 1.27		
Stage III	25 (49.02)	5.74 ± 1.12		
Stage IV	7 (13.73)	5.81 ± 1.48		
T stage			5.880	0.002
T1	11 (21.57)	4.13 ± 0.94		
T2	16 (31.37)	5.22 ± 0.89		
T3	19 (37.26)	5.58 ± 1.07		
T4	5 (9.8)	5.91 ± 1.25		
N stage			3.733	0.010
N0	8 (15.69)	4.21 ± 1.09		
N1	14 (27.45)	5.17 ± 0.83		
N2	17 (33.33)	5.54 ± 1.14		
N3	9 (17.65)	5.81 ± 1.08		
N4	3 (5.88)	6.35 ± 1.21		
M stage			2.133	0.038
M0	28 (54.90)	5.41 ± 1.13		
M1	23 (45.10)	6.13 ± 1.28		

Table 8. Assignment of prognostic factors for LC

Related factors	Assignment
Clinical stage	Stage I-II = 0, stage III-IV = 1
T stage	T1-T2 = 0, T3-T4 = 1
N stage	N1-N2 = 0, N3-N4 = 1
M stage	M0 = 0, M1 = 1
CD147	≤ 3.39 = 0, > 3.39 = 1
MMP-9	≤ 5.70 = 0, > 5.70 = 1

expression rates of CD147 and MMP-9 were markedly higher in LC tissues than in adjacent tissues. CD147 can stimulate MMP-9 to degrade the extracellular matrix, promote the spread of cancer cells throughout the body, and facilitate tumors to invade surrounding tissues, lymph nodes, and blood vessels [28]. CD147 is highly expressed in salivary gland tumors [29]. In the present study, serum CD147 level was markedly higher in patients with stage III-IV tumors than in patients with stage I-II tumors, suggesting that CD147 may be involved in the metastasis and invasion of LC. Some scholars believe that CD147 can increase the expression level of vascular endothelial growth factor, boost the growth of tumor blood vessels, and promote tumor metastasis and invasion [30], which supports the results of this study. The role of MMP-9, an important factor in the human body, in the development and progression of malignant tumors has always been a hot topic [31]. A previous study revealed that MMP-9 can degrade laminin to produce soluble fragments that can participate in tumor cell proliferation, migration, and invasion [32]. This above study also confirms our findings here that serum MMP-9 level was markedly higher in LC patients than in normal participants, especially higher in patients with stage III-IV tumors compared with patients with stage I-II tumors. Currently, the prevalent diagnostic methods for LC are laryngoscope and pathological biopsy, so the sensitivity and specificity of CD147 and MMP-9 for LC diagnosis are rarely studied. Here we are the first to find that CD147 and MMP-9 have good sensitivity and specificity in the diagnosis of LC. The results of prognostic analysis here revealed that an increased CD147/MMP-9 level or positive expression of CD147/MMP-9 indicates poor prognosis. The results of Cox regression analysis revealed that the clinical stage, T stage, N stage, M stage, CD147 level, and MMP-9 level were independent risk factors for poor prognosis in patients with LC. In this study, CD147 and MMP-9 showed a certain value in diagnosing LC and predicting the prognosis of LC.

Here we confirmed the value of CD147 and MMP-9 expression levels in LC patients, but it is subject to some limitations. For example, we did not figure out the regulation effect of CD147 and MMP-9 on LC and their biological functions. Besides, we did not compare CD147 and

Table 9. Multivariate analysis of prognosis and related risk factors of LC

Factors	β	SE	Wald	P	Exp (β)	95% CI
Clinical stage	0.531	0.118	10.153	0.008	1.568	0.594-3.420
T stage	0.328	0.158	5.437	0.011	2.019	1.836-2.265
N stage	0.516	0.102	7.563	0.019	1.893	1.425-3.357
M stage	0.853	0.229	13.421	0.002	2.523	1.220-9.144
CD147	0.482	0.197	9.185	0.014	2.275	0.182-3.021
MMP-9	0.605	0.166	7.726	0.024	0.351	0.189-1.649

MMP-9 with other routine LC markers, making this study deficient. Therefore, we should make continuous efforts to address such problems and learn from the latest researches, aiming to perfect this study.

Conclusion

CD147 and MMP-9 levels are increased in the serum of patients with LC. They can be used as potential serum biomarkers for the diagnosis and disease assessment in LC.

Disclosure of conflict of interest

None.

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