Correlation between Survivin Expression and Laryngeal Carcinoma: A Meta-analysis

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Summary: In order to provide evidence for evidence-based medicine in the treatment and prognosis of laryngeal cancer in China, the meta-analysis electronically retrieved the case-control studies published in China about the Survivin expression and its association with clinical pathological features in the tissues of laryngeal carcinoma. The results showed that a total of 25 case-control studies were finally included with 1333 cases of laryngeal cancer and 528 cases of controls. The difference in the expression of Survivin between the two groups was statistically significant [OR=18.34, 95% CI (11.82, 28.47), *P*<0.00001]. The difference in the expression of Survivin between laryngeal carcinoma patients with lymph node metastasis or not was statistically significant [OR=0.25, 95% CI (0.17, 0.37), *P*<0.00001]. The expression of Survivin in clinical Ⅰ–Ⅱ stage group was significantly lower than in the clinical stage Ⅲ–Ⅳ group [OR=0.24, 95% CI (0.18, 0.32), *P*<0.00001]. The expression of Survivin in patients with low/medium differentiation was significantly lower than that in those with high differentiation [OR=0.33, 95% CI (0.26, 0.43), *P*<0.00001]. The difference in the expression of Survivin among different T stages of laryngeal carcinoma was statistically significant [OR=0.35, 95% CI (0.21, 0.58), *P*<0.00001]. In conclusion, Survivin may play an important role in the occurrence and development of laryngeal carcinoma, and its high expression is related to the poor prognosis of patients with laryngeal cancer.

Key words: Survivin; laryngeal carcinoma; prognosis; meta-analysis

Laryngeal cancer, also known as cancer of the larynx or laryngeal carcinoma, is mostly squamous cell carcinomas, reflecting their origin from the skin of the larynx[1]. Laryngeal carcinoma is one of the most common malignant tumors and threatens the human health seriously[2]. Laryngeal carcinoma is increasing year by year in recent years. In recent years, more and more research results have shown that the whole course of occurrence, advance and prognosis of malignant tumor may be associated with abnormal regulation of cell apoptosis and proliferation[3]. Survivin is a member of the inhibitor of apoptosis protein (IAP) family, which is the strongest inhibitor of apoptosis. Many studies have indicated that Survivin plays an important role in the occurrence and development of tumor. Survivin is highly expressed in most tumors, but is undetectable in most terminally differentiated cells, which provides a new target for the diagnosis and treatment of tumor. Recent studies have shown that over-expression of Survivin is closely related to laryngeal cancer, which may be a new target for the prevention and treatment of la-

ryngeal cancer[4, 5]. At present, the domestic research viewpoint on Survivin expression with the age, sex, smoking and the length of duration of the disease in patients with laryngeal cancer is basically consistent. However, the academic holds the different points about Survivin expression with T staging, the degree of differentiation, clinical stage, lymph node metastasis and tumor location in patients with laryngeal cancer. In order to provide evidence for evidence-based medicine in the treatment and prognosis of laryngeal cancer in China, we performed this systematic review of the literature with meta-analysis.

1 MATERIALS AND METHODS

1.1 Inclusion and Exclusion Criteria

To be eligible for inclusion, studies had to meet the following criteria: (1) Papers reported in domestic journals included a case-control study of the relationship between Survivin expression and clinicopathological features of laryngeal carcinoma. (2) All patients had complete clinical and pathological data, without radiotherapy or chemotherapy before sampling. (3) Control group was normal laryngeal mucosa tissue or vocal cord polyps. (4) Survivin testing methods, and assessment criteria are consistent.

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The exclusion criteria were as follows: (1) Survivin test method and the positive judgment standard were not consistent. (2) Repeated reports or similar information, poor quality and other documents could not be used. (3) Only abstract, no full text data, etc.

1.2 Literature Search

The case-control studies published about the Survivin expression and association with clinicoopathogenic features in the tissues of laryngeal carcinoma were electronically retrieved in CBM, CNKI and WanFang Data (1996 to October 2012). Search words included: Survivin, laryngeal carcinoma and laryngeal squamous cell carcinoma, prognosis, etc.

1.3 Literature Selection and Data Extraction

Two investigators extracted data from eligible studies independently, discussed discrepancies and reached consensus for all items. The following information was extracted from each article: number, title, author, year of publication, original literature source, sample size, laryngeal carcinoma and lymph node metastasis, clinical stage, and histological grading.

1.4 Quality Assessment

NOS was performed for quality assessment on all studies. NOS included research object selection (4 items, 4 points), group comparability (1 item, 2 points) and results measurement (3 items, 3 points), a total of 9 points. In case of disagreement, we can discuss or nego-

tiate according to the third party opinion to reach an agreement.

1.5 Statistical Analysis

Meta-analysis was performed using RevMan 5.1 software. OR and 95% CI were used to estimate the impact. Firstly, Q test was used to examine the heterogeneity of the included studies and test level $\alpha=0.1$, namely, P value ≤0.10 was considered statistically significant for heterogeneity. Quantitative analysis of heterogeneity was conducted by using I^2. 50%> I^2 ≥25% was considered a low heterogeneity, 75%> I^2 ≥50% a middle heterogeneity, and a value ≥75% a high heterogeneity. If there was no heterogeneity or low degree of heterogeneity among the research results, the fixed effect model was used for meta-analysis. If the results of the study had moderate or high heterogeneity and no clinical heterogeneity, the random effects model was used for meta-analysis. If the heterogeneity was too large to be carried out by meta-analysis, the descriptive analysis was used.

2 RESULTS

2.1 Literature Selection

A total of 131 studies were retrieved after the initial search of databases. Additionally, 5 papers were obtained from other approaches. Through further screening, 25 case-control studies[6–30] were finally included (fig. 1).
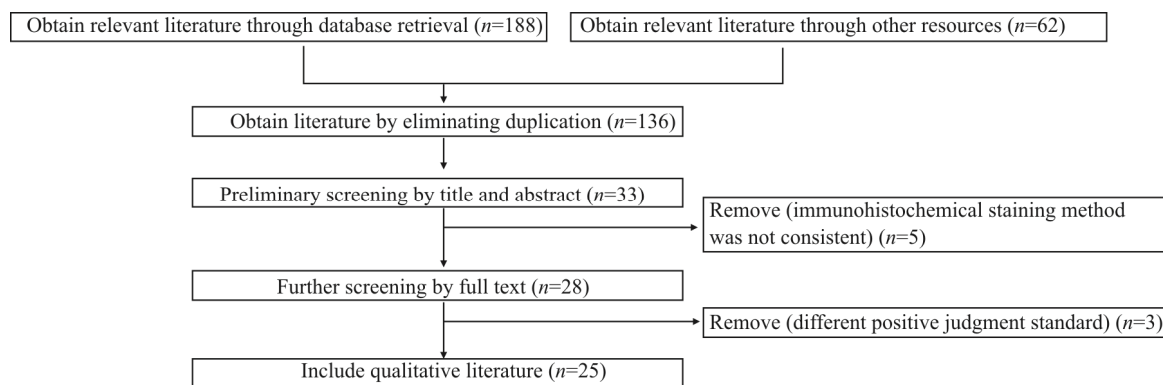
Fig. 1 Flow chart of studying inclusion

2.2 Characteristics and Quality Evaluation of the Included Studies

The results about characteristics and quality evaluation of the included studies are shown in tables 1 and 2. 1333 patients with laryngeal cancer were included in 25 studies in which the expression of Survivin in lymph node metastasis and clinical stage of laryngeal carcinoma were reported. Twenty-four of them reported

the expression of Survivin in different pathological grades of laryngeal carcinoma, and 13 studies reported the expression of Survivin in different parts and different ages. Nine studies reported the expression of Survivin in different genders of laryngeal carcinoma. Five studies reported the expression of Survivin in different T stages and 3 studies reported the relationship between smoking and Survivin in laryngeal cancer.

Table 1 The characteristics of the study

Studies	Source	Case group		Control group	
		n	Survivin (+)	n	Survivin (+)
Bai 2012[6]	Vocal cord polyp tissues	72	59	10	2
Chen 2004[7]	Vocal cord polyp tissues	81	41	81	0
Di 2005[8]	Vocal cord polyp tissues	40	23	8	0
Fu 2005[9]	Vocal cord polyp tissues	45	28	7	0
Guan 2004[10]	Vocal cord polyp tissues	71	36	12	0
Guo 2006[11]	Vocal cord polyp tissues	50	36	20	0
He 2005[12]	Vocal cord polyp tissues	57	29	22	0
Jiang 2005[13]	Vocal cord polyp tissues	45	36	10	2
Li 2004[14]	Vocal cord polyp tissues	54	38	10	0
Li2010[15]	Vocal cord polyp tissues	86	52	32	4
Li 2009[16]	Vocal cord polyp tissues	40	26	20	5
Li 2008[17]	Vocal cord polyp tissues	68	36	15	0
Liang 2009[18]	Vocal cord polyp tissues	65	46	34	5
Lin 2010[19]	Vocal cord polyp tissues	50	32	50	0
Liu 2010[20]	Vocal cord polyp tissues	42	28	12	0
Ren 2011[21]	Normal laryngeal mucosa	42	28	36	0
Sun 2006[22]	Normal laryngeal mucosa	33	21	21	6
Sun 2008[23]	Vocal cord polyp tissues	40	28	10	0
Wang 2005[24]	Normal laryngeal mucosa	64	43	28	1
Wen 2006[25]	Normal laryngeal mucosa	47	28	14	0
Wen 2004[26]	Normal laryngeal mucosa	42	28	10	0
Xue 2004[27]	Vocal cord polyp tissues	40	35	20	9
Zhang 2008[28]	Normal laryngeal mucosa	40	30	12	3
Zhu 2004[29]	Normal laryngeal mucosa	48	27	24	0
Zhu 2006[30]	Vocal cord polyp tissues	71	53	10	0

Table 2 Quality evaluation of the included studies

Studies	(1)	(2)	(3)	(4)	(5)-A	(5)-B	(6)	(7)	(8)	NOS score
Bai 2012[6]	1	1	1	0	1	0	1	1	1	7
Chen 2004[7]	1	1	1	0	1	0	1	1	1	7
Di 2005[8]	1	1	1	0	0	1	1	1	1	7
Fu 2005[9]	1	1	1	0	1	0	1	1	1	7
Guan 2004[10]	1	1	1	0	0	0	1	1	1	6
Guo 2006[11]	1	1	1	1	1	0	1	1	1	8
He 2005[12]	1	1	1	0	1	0	1	1	1	7
Jiang 2005[13]	1	1	1	0	1	0	1	1	1	7
Li 2004[14]	1	1	1	0	1	0	1	1	1	7
Li2010[15]	1	1	1	1	0	0	1	1	1	6
Li 2009[16]	1	1	1	0	1	0	1	1	1	7
Li 2008[17]	1	1	1	1	1	0	1	1	1	8
Liang 2009[18]	1	1	1	0	1	0	1	1	1	7
Lin 2010[19]	1	1	1	0	1	0	1	1	1	7
Liu 2010[20]	1	1	1	0	1	0	1	1	1	7
Ren 2011[21]	1	1	1	0	0	1	1	1	1	7
Sun 2006[22]	1	1	1	0	1	1	1	1	1	8
Sun 2008[23]	1	1	1	0	0	0	1	1	1	6
Wang 2005[24]	1	1	1	0	1	0	1	1	1	7
Wen 2006[25]	1	1	1	0	1	0	1	1	1	7
Wen 2004[26]	1	1	1	0	1	0	1	1	1	7
Xue 2004[27]	1	1	1	1	0	0	1	1	1	7
Zhang 2008[28]	1	1	1	1	1	0	1	1	1	8
Zhu 2004[29]	1	1	1	0	1	0	1	1	1	7
Zhu 2006[30]	1	1	1	0	1	0	1	1	1	7

2.3 Detection of Survivin Expression

2.3.1 Expression of Survivin in Laryngeal Carcinoma and Normal Control Group The expression of Survivin in laryngeal carcinoma group and control group was detected in all 25 studies which included 1333 cases of laryngeal cancer and 528 cases of control individuals. The research results had low degree of heterogeneity (P=0.22, I^2=17%), then meta-analysis was

carried out using fixed effect model. The results showed that the difference of the expression of Survivin between the two groups was statistically significant [OR=18.34, 95% CI (11.82, 28.47), *P*<0.00001] (fig. 2).
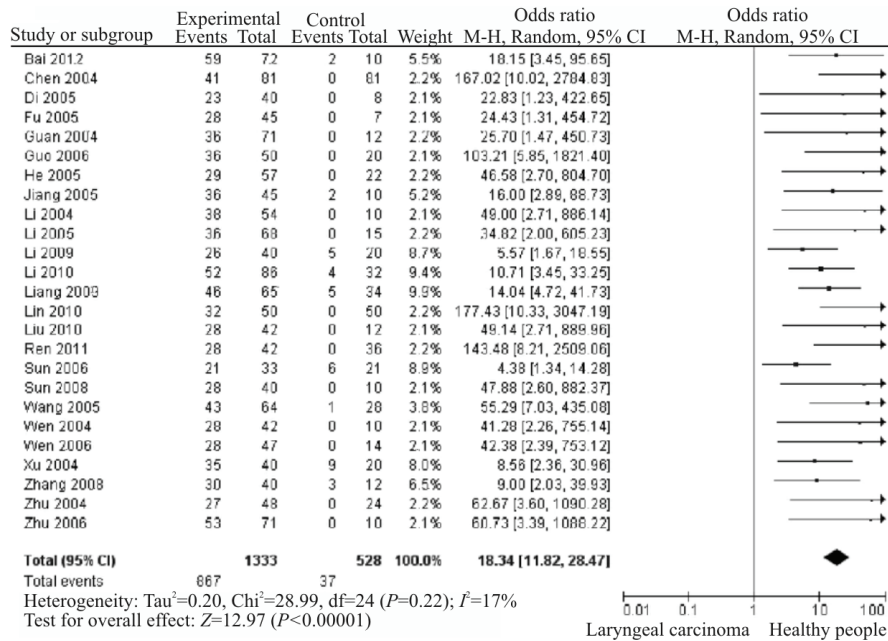

Fig. 2 Forest plots depicting the OR and 95% CI from studies examining the association between the expression of Survivin in laryngeal carcinoma and normal control group

2.3.2 Expression of Survivin in Laryngeal Carcinoma with or without Lymph Node Metastasis A total of 25 studies were included, of which 455 cases had lymph node metastasis and 878 cases had no lymph node metastasis. The research results had low degree of heterogeneity (*P*=0.13, *I*²=24%), then Meta-analysis was carried out using fixed effect model. The results showed that the difference in the expression of Survivin between the two groups was statistically significant [OR=0.25, 95% CI (0.17, 0.37), *P*<0.00001] (fig. 3).

Fig. 3 Forest plots depicting the OR and 95% CI from studies examining the association between the expression of Survivin in laryngeal carcinoma with lymph node metastasis or not

2.3.3 Expression of Survivin in Different Clinical Stages of Laryngeal Carcinoma A total of 25 studies were enrolled, including 628 cases of clinical stage Ⅰ–Ⅱ and 878 cases of clinical stage Ⅲ–Ⅳ. The research results showed low degree of heterogeneity (*P*=0.25, *I*²=15%), then meta-analysis was carried out using fixed effect model. The results showed that there was significant difference in the expression of Survivin between the two groups [OR=0.24, 95% CI (0.18, 0.32), *P*<0.000 01] (fig. 4).

Study or subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds ratio M-H, Random, 95% CI	Odds ratio M-H, Random, 95% CI
Bai 2012	19	23	16	17	1.5%	0.30 [0.03, 2.93]	
Chen 2004	14	21	13	21	4.3%	1.23 [0.35, 4.36]	
Di 2005	11	21	18	36	5.6%	1.10 [0.37, 3.23]	
Fu 2005	8	19	10	14	3.3%	0.29 [0.07, 1.27]	
Guan 2004	5	11	23	29	3.3%	0.22 [0.05, 0.96]	
Guo 2005	7	15	21	27	3.8%	0.25 [0.06, 0.97]	
He 2005	6	12	30	33	2.7%	0.10 [0.02, 0.52]	
Jiang 2005	10	18	26	32	4.2%	0.29 [0.08, 1.04]	
Li 2004	5	13	23	29	3.5%	0.16 [0.04, 0.68]	
Li 2008	13	27	13	14	1.6%	0.07 [0.01, 0.63]	
Li 2009	18	34	14	16	2.8%	0.16 [0.03, 0.82]	
Li 2010	7	15	23	25	2.4%	0.08 [0.01, 0.44]	
Liang 2009	7	19	16	21	3.8%	0.18 [0.05, 0.72]	
Lin 2010	17	30	21	24	3.6%	0.19 [0.05, 0.76]	
Liu 2010	29	44	24	27	3.9%	0.24 [0.06, 0.93]	
Ren 2011	5	16	23	31	4.0%	0.16 [0.04, 0.60]	
Sun 2006	21	47	15	24	6.2%	0.48 [0.18, 1.33]	
Sun 2008	5	16	23	29	3.7%	0.12 [0.03, 0.47]	
Wang 2005	10	21	33	43	5.4%	0.28 [0.09, 0.84]	
Wen 2004	13	25	33	40	5.2%	0.23 [0.07, 0.71]	
Wen 2006	7	16	52	56	3.6%	0.06 [0.01, 0.25]	
Xu 2004	6	21	21	27	4.1%	0.11 [0.03, 0.42]	
Zhang 2008	33	63	19	23	4.8%	0.23 [0.07, 0.76]	
Zhu 2004	21	51	20	30	6.9%	0.35 [0.14, 0.90]	
Zhu 2006	9	30	27	38	5.9%	0.17 [0.06, 0.50]	
Total (95% CI)		**628**		**706**	**100.0%**	**0.24 [0.18, 0.32]**	
Total events	306		557				

Heterogeneity: Tau^2=0.00, Chi^2=20.20, df=24 (P=0.25); I^2=15%
Test for overall effect: Z=9.83 (P<0.00001)

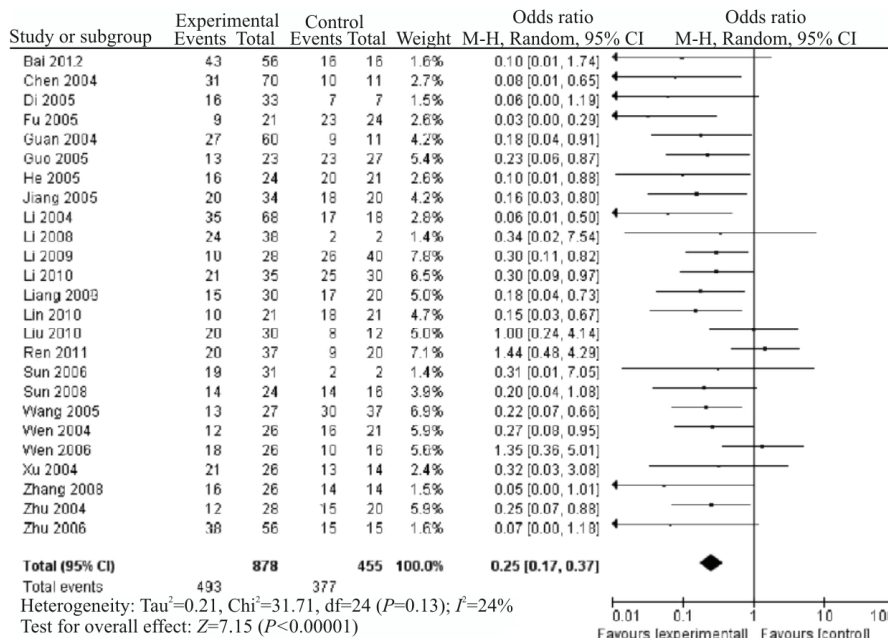0.01   0.1   1   10   100
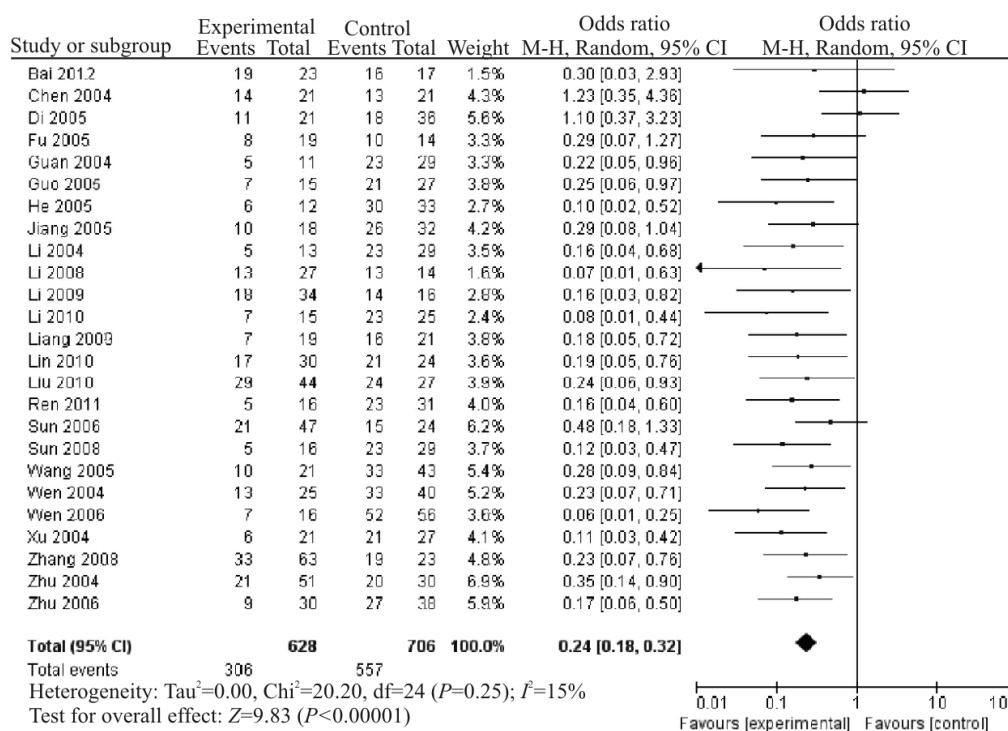Favours [experimental]   Favours [control]

Fig. 4 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different clinical stages of laryngeal carcinoma

2.3.4 Expression of Survivin in Different Histological Grades of Laryngeal Carcinoma A total of 24 studies were enrolled, including 545 cases of high differentiation and 744 cases of low/medium differentiation. The research results showed medium degree of heterogeneity (P<0.0001, I^2=64%), then meta-analysis was carried out using random effect model. The results showed that there was significant difference in the expression of Survivin between the two groups [OR=0.33, 95% CI (0.26, 0.43), P<0.00001] (fig. 5).
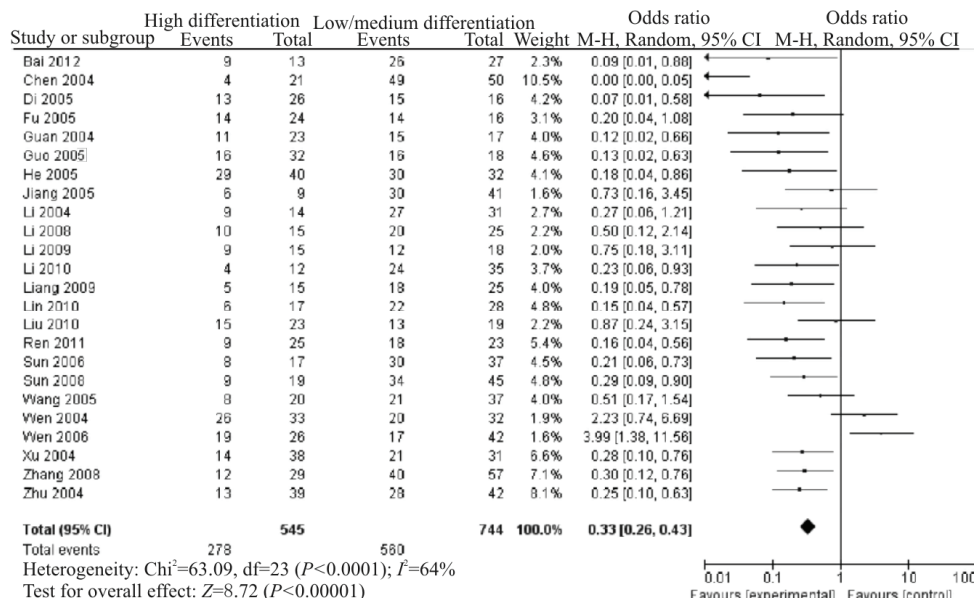
Study or subgroup	High differentiation Events	Total	Low/medium differentiation Events	Total	Weight	Odds ratio M-H, Random, 95% CI	Odds ratio M-H, Random, 95% CI
Bai 2012	9	13	26	27	2.3%	0.09 [0.01, 0.88]	
Chen 2004	4	21	49	50	10.5%	0.00 [0.00, 0.05]	
Di 2005	13	26	15	16	4.2%	0.07 [0.01, 0.58]	
Fu 2005	14	24	14	16	3.1%	0.20 [0.04, 1.08]	
Guan 2004	11	23	15	17	4.0%	0.12 [0.02, 0.66]	
Guo 2005	16	32	16	18	4.6%	0.13 [0.02, 0.63]	
He 2005	29	40	30	32	4.1%	0.18 [0.04, 0.86]	
Jiang 2005	6	9	30	41	1.6%	0.73 [0.16, 3.45]	
Li 2004	9	14	27	31	2.7%	0.27 [0.06, 1.21]	
Li 2008	10	15	20	25	2.2%	0.50 [0.12, 2.14]	
Li 2009	9	15	12	18	2.0%	0.75 [0.18, 3.11]	
Li 2010	4	12	24	35	3.7%	0.23 [0.06, 0.93]	
Liang 2009	5	15	18	25	4.0%	0.19 [0.05, 0.78]	
Lin 2010	6	17	22	28	4.8%	0.15 [0.04, 0.57]	
Liu 2010	15	23	13	19	2.2%	0.87 [0.24, 3.15]	
Ren 2011	9	25	18	23	5.4%	0.16 [0.04, 0.56]	
Sun 2006	8	17	30	37	4.5%	0.21 [0.06, 0.73]	
Sun 2008	9	19	34	45	4.8%	0.29 [0.09, 0.90]	
Wang 2005	8	20	21	37	4.0%	0.51 [0.17, 1.54]	
Wen 2004	26	33	20	32	1.9%	2.23 [0.74, 6.69]	
Wen 2006	19	26	17	42	1.6%	3.99 [1.38, 11.56]	
Xu 2004	14	38	21	31	6.6%	0.28 [0.10, 0.76]	
Zhang 2008	12	29	40	57	7.1%	0.30 [0.12, 0.76]	
Zhu 2004	13	39	28	42	8.1%	0.25 [0.10, 0.63]	
Total (95% CI)		**545**		**744**	**100.0%**	**0.33 [0.26, 0.43]**	
Total events	278		560				

Heterogeneity: Chi^2=63.09, df=23 (P<0.0001); I^2=64%
Test for overall effect: Z=8.72 (P<0.00001)

0.01   0.1   1   10   100
Favours [experimental]   Favours [control]

Fig. 5 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different histological grades of laryngeal carcinoma

2.3.5 Expression of Survivin in Different T Stages of Laryngeal Carcinoma A total of 5 studies were enrolled, including 152 cases of T1/T2 stage and 143 cases of T3/T4 stage. The research results showed no heterogeneity (P=0.52, I^2=0%), then meta-analysis was carried out using fixed effect model. The results showed that there was significant difference in the expression of Survivin between the two groups [OR=0.35, 95% CI (0.21, 0.58), P<0.000 01] (fig. 6).
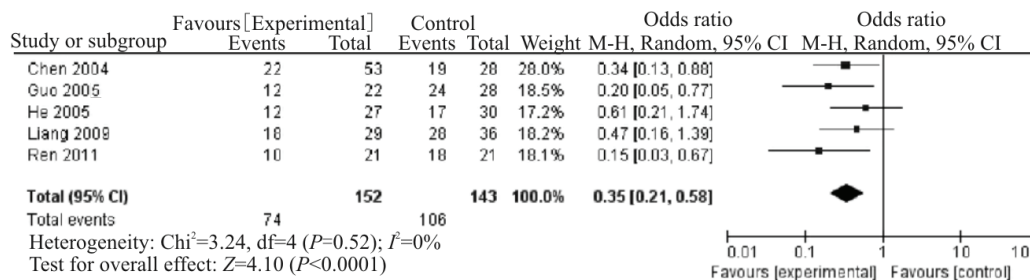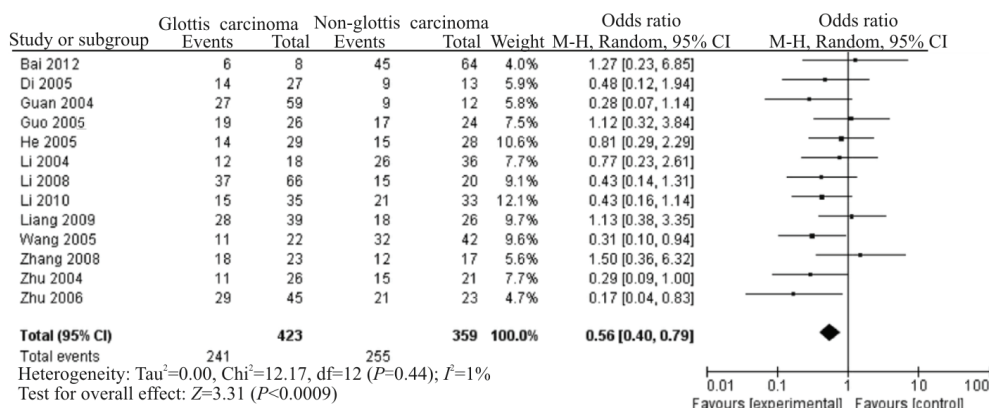
Fig. 6 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different T stages of laryngeal carcinoma

2.3.6 Expression of Survivin in Different Parts of Laryngeal Carcinoma   A total of 13 studies were enrolled, including 423 cases in the glottis, 305 cases in the supraglottis and 54 cases in the subglottis. The research results showed low degree of heterogeneity (P=0.44, I^2=1%), then meta-analysis was carried out using fixed effect model. The results showed that there was significant difference in the expression of Survivin between the two groups [OR=0.56, 95% CI (0.40, 0.79), P=0.0004] (fig. 7).

Fig. 7 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different parts of laryngeal carcinoma

2.3.7 Expression of Survivin in Different Ages of Laryngeal Carcinoma   A total of 13 studies were enrolled, including 366 cases of ≥60 years and 331 cases less than 60. The research results showed no heterogeneity (P=0.85, I^2=0%), then meta-analysis was carried out using fixed effect model. The results showed that there was no significant difference in the expression of Survivin between the two groups [OR=0.70, 95% CI (0.49, 1.00), P=0.05] (fig. 8).
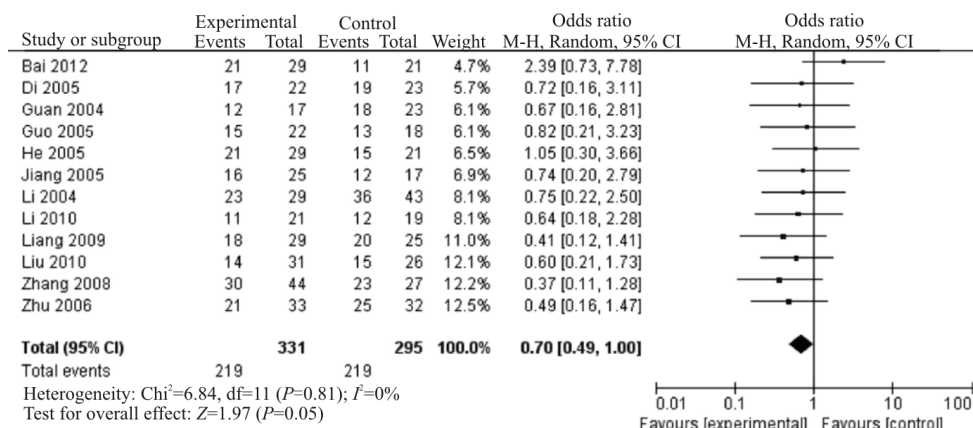

Fig. 8 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different ages of laryngeal carcinoma

2.3.8 Expression of Survivin in Different Sexes of Laryngeal Carcinoma   A total of 9 studies were enrolled, including 416 males and 62 females. The research results showed no heterogeneity (P=0.46, I^2=0%), then meta-analysis was carried out using fixed effect model. The results showed that there was no significant difference in the expression of Survivin between the two groups [OR=1.30, 95% CI (0.68, 2.48), P=0.43] (fig. 9).
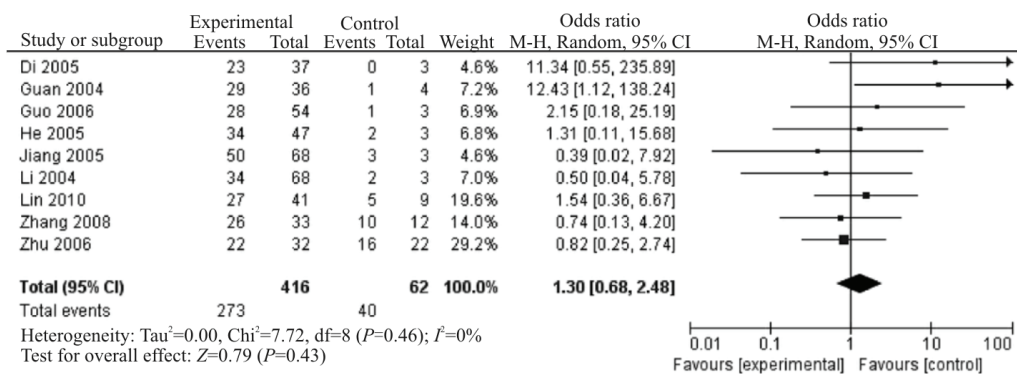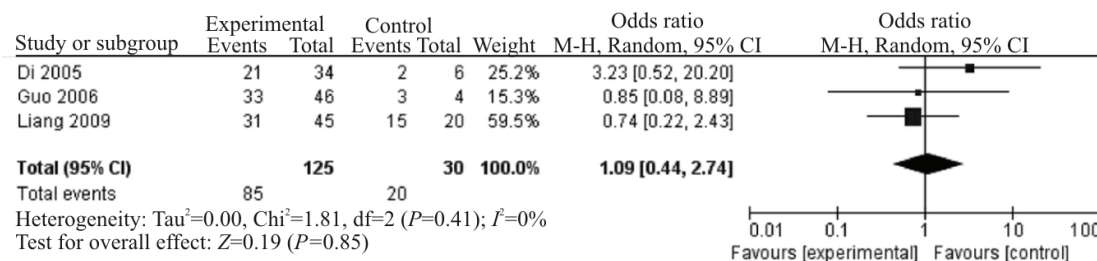
Study or subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds ratio M-H, Random, 95% CI	Odds ratio M-H, Random, 95% CI
Di 2005	23	37	0	3	4.6%	11.34 [0.55, 235.89]	
Guan 2004	29	36	1	4	7.2%	12.43 [1.12, 138.24]	
Guo 2006	28	54	1	3	6.9%	2.15 [0.18, 25.19]	
He 2005	34	47	2	3	6.8%	1.31 [0.11, 15.68]	
Jiang 2005	50	68	3	3	4.6%	0.39 [0.02, 7.92]	
Li 2004	34	68	2	3	7.0%	0.50 [0.04, 5.78]	
Lin 2010	27	41	5	9	19.6%	1.54 [0.36, 6.67]	
Zhang 2008	26	33	10	12	14.0%	0.74 [0.13, 4.20]	
Zhu 2006	22	32	16	22	29.2%	0.82 [0.25, 2.74]	
Total (95% CI)		416		62	100.0%	1.30 [0.68, 2.48]	
Total events	273		40				

Heterogeneity: Tau^2=0.00, Chi^2=7.72, df=8 (P=0.46); I^2=0%
Test for overall effect: Z=0.79 (P=0.43)

0.01 0.1 1 10 100
Favours [experimental] Favours [control]

Fig. 9 Forest plots depicting the OR and 95% CI from studies examining the association with the expression of Survivin in different sexes of laryngeal carcinoma

2.3.9 Expression of Survivin in Laryngeal Carcinoma with Smoking A total of 3 studies were enrolled, including 125 cases of smoking and 30 cases of non-smoking. The research results had no heterogeneity (P=0.41, I^2=0%), then meta-analysis was carried out using fixed effect model. The results showed that the difference in the expression of Survivin between the two groups was no statistically significant [OR=1.09, 95% CI (0.44, 2.74), P=0.85] (fig. 10).

Study or subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds ratio M-H, Random, 95% CI	Odds ratio M-H, Random, 95% CI
Di 2005	21	34	2	6	25.2%	3.23 [0.52, 20.20]	
Guo 2006	33	46	3	4	15.3%	0.85 [0.08, 8.89]	
Liang 2009	31	45	15	20	59.5%	0.74 [0.22, 2.43]	
Total (95% CI)		125		30	100.0%	1.09 [0.44, 2.74]	
Total events	85		20				

Heterogeneity: Tau^2=0.00, Chi^2=1.81, df=2 (P=0.41); I^2=0%
Test for overall effect: Z=0.19 (P=0.85)

0.01 0.1 1 10 100
Favours [experimental] Favours [control]

Fig. 10 Forest plots depicting the OR and 95% CI from studies examining the association between the expression of Survivin in laryngeal carcinoma with smoking or not

3 DISCUSSION

Under normal conditions, Survivin is expressed only in embryos or immature tissues, but is undetectable in most terminally differentiated adult tissues. However, Survivin is highly expressed in most tumors, which provides a new target for the diagnosis and prognosis of tumor. Demir *et al* reported that Survivin, Bcl-2 and c-myc immunohistochemical positivity had prognostic value in synovial sarcoma[31]. Recent studies have shown that different expression of Survivin is closely related to occurrence and advance of laryngeal cancer, which may be a new target for the prevention and treatment of laryngeal cancer. Survivin, a kind of protein involved in angiogenesis, strongly promotes tumor survival by reducing apoptosis and favors endothelial cell migration. The VEGF-induced tumor angiogenesis via PI3K/Akt enhances beta-catenin/Tcf-Lef dependent transcription[32, 33]. It is important for preventing and controlling laryngeal carcinoma to clarify the relationship between Survivin and the occurrence, invasion, metastasis and other clinical characteristics of laryngeal carcinoma[34–36]. Rivadeneira *et al*[35] showed that the increased Survivin abundance correlates with metastasis and poor prognosis in human cancer. Pool of Survivin that is localized in the mitochondria of tumor cells enhances the stability of oxidative phosphorylation complex Ⅱ that promotes cellular respiration. Survivin also promotes the subcellular trafficking of mitochon-

dria to the cortical cytoskeleton of tumor cells, which is associated with increased membrane ruffling, increased focal adhesion complex turnover, increased tumor cell migration and invasion in cultured cells, and enhanced metastatic dissemination[34, 35]. Therefore, mitochondrial respiration enhanced by Survivin contributes to cancer metabolism, and relocalized mitochondria may provide a "regional" energy source to fuel tumor cell invasion and metastasis. This meta-analysis showed the that expression of Survivin in laryngeal carcinoma group was 22.97 times that of the normal control group [95% CI (16.00, 32.96)], indicating that the high expression of survivin may be related to the laryngeal carcinoma. In this study, the relationship between Survivin expression and lymph node metastasis was reported in 25 literatures. The results of meta-analysis indicated that the expression of Survivin was related to the invasion and prognosis of laryngeal carcinoma [OR=0.24, 95% CI (0.18, 0.33), P<0.00001]. In previous reports, Survivin expression is not unified in the different TNM clinical stages, different degrees of pathological differentiation and different T stages. This study suggested that the positive expression of Survivin in the high differentiation group was lower than that in the medium and low differentiation group [OR=0.30, 95% CI (0.19, 0.47), P<0.00001]. Some studies have reported that Survivin expression is closely related to T stage, and Survivin expression is significantly higher in T3/T4 than is T1/T2. However, others showed that the expression of Survivin is not

related to the T stage. This study showed that the positive expression of Survivin in laryngeal carcinoma was higher in T3/T4 than in T1/T2 [OR=0.35, 95% CI (0.21, 0.58), P<0.0001]. The positive expression of Survivin was higher in III–IV stages than is I–II [OR=0.24, 95% CI (0.19, 0.32), P<0.0001]. All these suggest that Survivin may play an important role in the occurrence and development of laryngeal carcinoma, and its high expression is related to the poor prognosis of patients with laryngeal cancer[37, 38]. Dziegielewska et al[37] reported that the high expression is related to the poor prognosis of ovarian cancer and the T-type Ca^{2+} channel may take important role in the anti-cancer effect of carboplatin through down-regulation of Survivin gene expression. Jafarlou et al[38] reported the high expression of Survivin is related to the poor prognosis of acute myeloid leukemia. In order to enhance the anti-cancer effect of etoposide in U-937 cells, the Survivin is silenced using the siRNA technique.

The site of the laryngeal carcinoma may be related to the the Survivin expression. This study showed that the positive expression of Survivin was higher in glottis carcinoma group than that in non-glottis carcinoma group with the difference being statistically significant [OR=0.55, 95% CI (0.40, 0.76), P=0.0004]. Furthermore, no significant difference was found in groups of age more than 60 years vs. no less than 60 years, male vs. female, and smokinging vs. non-smokinging (P>0.05). Of course, this study also has some limitations: (1) The inclusion was all the Chinese literature, and the quality was low; (2) Lack of gray literature may result in missing negative results and publication bias. In order to provide stronger evidence for evidence-based medicine in the treatment and prognosis of laryngeal cancer, more rigorous and meticulous high quality case-control studies should be carried out to further confirm the correlation between the expression of Survivin and the clinicopathological features of laryngeal carcinoma.

In summary, this study indicated that the Survivin expression in laryngeal carcinoma and normal tissue showed obvious difference, its expression was significantly related to the lymph node metastasis, TNM stage, histological grade, T stage, and tumor location and no significant difference was found in patients' age, sex, smoking. So, Survivin may be associated with the whole course of occurrence, advance and transfer of laryngeal carcinoma, and positively correlated to degree of tumor malignance, which may indicate poor prognosis.

Conflict of Interest Statement

We declare that there were no financial and personal relationships with any organization or individual that can inappropriately influence our work.

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